DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2020

Food and Drug Administration

Justification of
Estimates for
Appropriations Committees

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LETTER FROM THE COMMISSIONER

I am pleased to present the FY 2020 Food and Drug Administration (FDA) Budget. FDA holds critical responsibility for ensuring the safety, effectiveness, and security of human and animal drugs, biological products, and medical devices; ensuring the safety of our nation's food supply, cosmetics, and radiation-emitting products; and regulating tobacco products.

Our mission impacts the life of every American, every day. Our FY 2019 accomplishments illustrate our dedication to protecting and promoting the health of the public we serve. Select, notable accomplishments include:

- Taking New Actions to Combat the Opioid Crisis – FDA began implementing the Opioid Policy Work Plan by accomplishing a broad array of scientific advances and regulatory actions. This work includes encouraging more appropriate prescribing to decrease exposure to opioids and prevent new addiction, as well as our initiatives to advance innovations in both novel pain therapies and better treatments to help those with opioid use disorder. For example, in 2018, FDA took steps to address concerns regarding intentionally misusing and abusing high doses of loperamide (Imodium), an anti-diarrhea medicine. FDA also took new steps to expand the use of safe and effective, FDA approved treatments for opioid use disorder, and the agency approved Lucemyra (lofexidine hydrochloride), the first non-opioid treatment for the mitigation of withdrawal symptoms associated with abrupt discontinuation of opioids. Our efforts to combat this public health emergency also extend to stopping the spread of illicit opioids and further securing all aspects of the supply chain for legitimate medications, including opioids. FDA focused new efforts on interdiction work to stop the flow of illegal controlled substances, including increased support of the Port of Entry (Imports) program, resulting in 91 arrests that led to 73 convictions. FDA also took new steps to expand its efforts to stop illegal opioid sales online, including efforts to limit the misuse and abuse of legally marketed opioid drugs by issuing warning letters to the marketers and distributers of 12 fraudulent opioid cessation products and to 17 online networks illegally marketing unapproved opioids. Additionally, FDA issued 21 abuse complaints to website registrars and registries for sites offering for sale opioids, as well as cancer and antiviral drugs. Furthermore, FDA solicited stakeholder and patient insights on approaches that address the crisis aggressively and protect patient needs.

- Fostering Drug Competition – FDA implemented the Drug Competition Action Plan to promote robust generic drug entry as a way to foster competition and lower drug prices. We focused new efforts on expanding competition to complex drugs that are no longer protected by patents or other exclusivities, and we approved the first generic version of the epinephrine auto-injector, which treats life-threatening allergic reactions. Our approval gives patients access to a lower-cost option and helps to protect against potential drug shortages. We approved seven biosimilars in 2018, a record for the number of biosimilar approvals in a single calendar year, and also released the Biosimilar Action Plan to continue to enhance competition for biologics and streamline the development of biosimilars.

- Advancing Food Safety and Nutrition – FDA launched its Nutrition Innovation Strategy to leverage nutrition as a tool to reduce the burden of chronic disease, and we took steps to empower consumers with nutrition information by supporting retail food establishments in meeting menu labeling

requirements. We also furthered implementation of the FDA Food Safety Modernization Act (FSMA) that builds proactive safety approaches into the production of human and animal foods.

- Developing a Comprehensive Plan for Tobacco and Nicotine Regulation – FDA took new action to reduce the morbidity and mortality associated with tobacco use, seeking input on potential public health benefits of limiting nicotine in cigarettes to minimally or non-addictive levels, and advancing new steps to warn youth about the risks of electronic cigarettes and limit the access and appeal of e-cigarette products to children. We also took the largest coordinated enforcement effort in FDA's history and issued more than 1,300 warning letters and fines to retailers who illegally sold e-cigarette products to minors during a nationwide, undercover blitz of brick-and-mortar and online stores.

The FY 2020 Budget will allow FDA to continue to deliver high-impact results that help Americans every day. FDA is requesting a total of $6.1 billion; an increase of $643.1 million compared to the FY 2019 Annualized Continuing Resolution (12 percent increase). FDA will invest in initiatives focused on the most urgent priorities, including efforts to:

- Reduce the Burdens of Addiction Crises that are Threatening American Families by reducing harms from opioids and reducing youth tobacco use;

- Foster Competition and Innovation by supporting production of quality compounded drugs, expanding FDA's capacity to review human food and animal feed ingredients, and continuing to implement the 21st Century Cures Act;

- Empower Consumers and Patients by continuing to support patient-focused medical product development, support medical innovation, provide consumers with information about healthy choices using the most up to date science, and modernize regulation and oversight of dietary supplements;

- Strengthen Science and Efficient Risk-Based Decision Making by advancing food safety, transforming medical device safety, ensuring the safety of the blood supply, and investing in FDA's capacity to facilitate the development and availability of medical countermeasures to respond to chemical, biological, radiological, and nuclear threats and emerging infectious diseases as well as FDA laboratory safety activities.

New scientific advances give us more opportunities to reduce the burden of disease and advance the public health. FDA's FY 2020 budget request enables the agency to ensure that we will be well positioned to leverage these scientific opportunities to secure the safety and well-being of Americans.

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

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EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2020 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. Here is a selection of recent accomplishments.

Reducing the Burden of Addiction Crises that are Threatening American Families

New Actions to Confront the Opioid Crisis

FDA is committed to finding new approaches to address emerging issues of the opioid crisis facing the Nation. We redoubled that commitment by taking steps to help those currently addicted to opioids, while taking steps to help prevent new cases of addiction, through FDA's four priority areas:

- 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 & Assessing Benefit-Risk.

In a public hearing held January 2018, FDA received stakeholder input on how FDA might, under its REMS authority, improve the safe use of opioid analgesics by curbing overprescribing to decrease the occurrence of new addictions and limit misuse and abuse of opioid analgesics.

Also, in January 2018, FDA took steps to address concerns regarding intentionally misusing and abusing high doses of loperamide (Imodium), an anti-diarrhea medicine. FDA issued a Drug Safety Communication and worked with sponsors to update drug labeling and packaging.

In 2018, FDA held two Patient Focused Drug Development (PFDD) public meetings on opioid use disorder and chronic pain. At the PFDD for Opioid Use Disorder held April 2018, FDA learned from patients' perspectives on OUD, including the effects on their health and well-being that have the greatest impact on daily life, their experience using prescription medical treatments and other treatments or therapies for OUD, and challenges or barriers to accessing or using medical treatments for OUD.

At the PFDD for Chronic Pain held July 2018, FDA heard patients' perspectives on chronic pain, views on treatment approaches, and challenges or barriers to accessing treatments for chronic pain. These meetings provided FDA with important insights on how to best take vigorous steps to confront addiction while also protecting the needs of these patients.

Furthermore, in June 2018, FDA convened internet stakeholders, government entities, academic researchers, and advocacy groups at a one-day Online Opioid Summit to discuss ways to

collaboratively take stronger action in combatting the opioid crisis by reducing the availability of illicit opioids online.

FDA approved the finalized Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS) to include immediate-release opioids, not already covered by another REMS program. The Opioid Analgesic REMS is one strategy among multiple national and state efforts to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics. The REMS requires companies to provide health care providers with continuing education on the fundamentals of acute and chronic pain management and provides a contextual framework for the safe prescribing of opioid analgesics.

FDA also approved Lucemyra (lofexidine hydrochloride), the first non-opioid treatment for the mitigation of withdrawal symptoms associated with abrupt discontinuation of opioids.

In addition, FDA issued the draft guidance for industry, "Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Medication-Assisted Treatment," which is intended to assist sponsors in developing drugs for medication-assisted treatment of opioid use disorder (OUD) and addresses the clinical endpoints acceptable to demonstrate effectiveness of such drugs. FDA also finalized the guidance, "Opioid Dependence: Developing Buprenorphine Depot Products for Treatment," which reflects the agency's current thinking regarding drug development and trial design issues relevant to the study of depot buprenorphine products (i.e. modified-release products for injection or implantation).

To help advance the development of evidence-based guidelines for appropriate opioid analgesic prescribing for acute pain resulting from specific conditions or procedures, FDA awarded a contract to the National Academies of Sciences, Engineering, and Medicine (NASEM) in August 2018. Currently, work is underway to understand what evidence is needed to ensure that all current and future clinical practice guidelines for opioid analgesic prescribing are sufficient, and what research is needed to generate that evidence in a practical and feasible manner.

In December 2018, FDA conducted an advisory committee meeting to discuss naloxone co-prescribing, where FDA asked for input and advice on strategies to increase the availability of naloxone products intended for use in the community. This meeting built upon past discussions regarding naloxone products and their availability in the community to reduce opioid overdose fatalities, which were held in 2012, 2015, and 2016. This year, FDA plans to announce the results of our Model Drug Facts Label (DFL) Comprehension Study for OTC Naloxone, including posting the model DFL and the supporting FDA review, to jumpstart the development of OTC naloxone products to promote wider access to this medicine. This is the first time FDA has proactively developed and tested a DFL for a drug to initiate the development of an OTC product.

Additionally, on May 30, 2018, the FDA announced the launch of the Devices to Prevent and Treat Opioid Use Disorder Challenge to spur the development of medical devices, including digital health and diagnostic devices, to help combat the opioid crisis and to help prevent and treat Opioid Use Disorder—a serious health condition which can be a devastating outcome of opioid drug use.

This challenge will provide those companies that are selected by the FDA under this new program with the opportunity to work closely with the agency to accelerate the development and review of their innovative products. The goal is to provide additional incentives for product

developers to invest in products that can address aspects of the addiction crisis and advance the development of promising technologies. FDA received more than 250 applications from medical device developers and based on these criteria, eight submissions were selected.

The engagement and participation from so many developers is indicative of the dire need we face for new ways to treat this disease, and that medical devices, including digital health technologies, like mobile medical apps, will play a critical role in the FDA's all hands on deck approach to confronting the opioid epidemic. In fact, in the past few years, FDA has cleared, granted, or approved more than 200 devices related to the treatment or management of pain, including 10 with new or novel technologies.

Tobacco Regulation

Tobacco product regulation represents one of FDA's greatest opportunities to save lives. FDA's comprehensive plan for tobacco and nicotine regulation serves as a multi-year roadmap to protect youth 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. Key features of the comprehensive plan include:

- regulatory policies on addiction, appeal and cessation
- Youth Tobacco Prevention Plan: announced April 24, 2018, to reduce access to - and use of - tobacco products, particularly e-cigarettes
- science-based review of tobacco products.

According to new findings from the 2018 National Youth Tobacco Survey (NYTS), there has been a dramatic increase in youth use of e-cigarettes and other electronic nicotine delivery systems (ENDS): From 2017 to 2018, there was a 78 percent increase in current e-cigarette use among high school students and a 48 percent increase among middle school students.

Therefore, on November 15, 2018, Commissioner Gottlieb outlined updates to FDA's policy framework to address the large increase in youth use of tobacco products. Our focus is on what appear to be the central issues—youth appeal and youth access to flavored tobacco products. FDA will be taking steps on the following product categories:

- flavored ENDS products (other than tobacco, mint, and menthol flavors or non-flavored products) that are not sold in an age-restricted, in-person location;
- flavored ENDS products (other than tobacco, mint, and menthol flavors or non-flavored products) that are sold online without heightened age verification processes;
- flavored cigars;
- ENDS products that are marketed to kids; and
- menthol in combustible tobacco products, including cigarettes and cigars.

This policy reflects FDA's aim of striking the right balance between closing the on ramp for kids to become addicted to nicotine while maintaining access to potentially less harmful forms of nicotine delivery for adult smokers seeking to transition away from combustible tobacco products.

In the largest coordinated enforcement effort in the FDA's history, the agency announced in September it had issued more than 1,300 warning letters and civil money penalty complaints (fines) to retailers who illegally sold e-cigarette products to minors during a nationwide, undercover blitz of brick-and-mortar and online stores.

Leveraging Innovation and Competition to Improve Health Care, Broaden Access, and Advance Public Health Goals

Advancing Drug and Medical Device Safety and Innovation

In the area of drug safety, on May 23, 2018, FDA announced that over-the-counter (OTC) oral health products containing the pain reliever benzocaine for the temporary relief of sore gums due to teething in infants or children should no longer be marketed and is asking companies to stop selling these products for such use. If companies do not comply, the FDA will initiate a regulatory action to remove these products from the market. Also, the agency is requesting that companies add new warnings to all other benzocaine oral health products to describe certain serious risks.

To support continued innovation in gene therapy products and provide clear recommendations to sponsors and researchers of novel therapies, FDA issued six human gene therapy guidances in July 2018. These guidances serve as the building blocks of a modern, comprehensive framework to help advance the field of human gene therapy while making sure new products meet the FDA's standards for safety and effectiveness. Three of these guidances are disease specific and three provide comprehensive updates to existing guidances that address manufacturing issues related to gene therapy.

The July 2018 approval of TPOXX (tecovirimat), the first drug with an indication for the treatment of smallpox, illustrates FDA procedures for facilitating medical countermeasure product development as part of FDA's public health mission. Smallpox as a naturally occurring disease was eradicated decades ago, however there are concerns that the virus could potentially be used as a biothreat agent. During tecovirimat development and review, FDA utilized expedited development and review pathways to enhance efficiency to advance the product's development and approval. The expedited pathways include Fast Track and Orphan Drug designations, Advisory Committee consultation regarding Animal Rule studies, Priority Review, and a Material Threat Medical Countermeasures Priority Review Voucher.

For medical devices, FDA advanced several meaningful initiatives and policy proposals to enhance medical device safety, including the safety of devices cleared through the FDA's 510(k) review process. In April 2018, FDA released its Medical Device Safety Action Plan, and, on November 20, 2018, FDA set an important and ambitious new goal: Ensuring that the FDA remains consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices.

FDA also continued to evolve beyond current, passive post-market surveillance system, working to build the National Evaluation System for health Technology (NEST), to effectuate active surveillance and help FDA fulfill its promise of ensuring safer devices for patients. The Agency also continued efforts to strengthen our Coordinated Registry Networks (CRN), as well as our focus on addressing clinical questions on device therapies that are unique to women.

FDA remains equally committed to advancing medical device innovation that can address unmet medical needs to reduce or prevent the adverse health effects from disease. Both objectives are

essential to meeting our public health mission, resulting in more lives saved and improved quality of life. Recent examples of this commitment to improving the safety and quality of life for patients include two novel device approvals from 2018 described below.

In June 2018, FDA expanded the approval of the MiniMed 670G hybrid closed loop system, expanding use of an artificial pancreas to include individuals aged 7 to 13 with Type 1 diabetes and approved a continuous glucose monitoring system with a fully implantable glucose sensor and compatible mobile app.

In March 2018, FDA expanded the approval of a heart valve to include a size small enough to be used in newborn pediatric patients to treat heart defects, making it the smallest mechanical heart valve approved in the world.

By continuing to enhance and implement the right tools and foster an environment that lets the FDA be innovative, while prioritizing patient safety, we'll continue to deliver on our public health mission.

Drug Competition

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

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]

FDA is currently assessing these comments as it continues to actively identify new initiatives that can enhance efforts to provide more safe, effective, and high-quality generic medicines to the public, and address "gaming," including abuses of the patent system, that exploits rules and loopholes in our system to delay generic approval and thereby extend a drug's monopoly beyond what Congress intended.

To further encourage generic drug development, FDA has:

- Prioritized complex generic drug development and application review
- Published a list of off-patient, off-exclusivity branded drugs
- Enhanced efficiency of submission process for generic drug applicants
- Issued guidance to enhance regulatory certainty for generic drug development and review.

In August 2018, FDA approved the first generic version of the epinephrine EpiPen and EpiPen Jr. auto-injector for the emergency treatment of allergic reactions, including those that are life-threatening – anaphylaxis. This approval advances access to safe and effective generic alternatives once patents and other exclusivities no longer prevent marketing entry. The availability of a generic version of EpiPen means that patients living with severe allergies who require constant access to life-saving epinephrine should have a lower-cost option, as well as another approved product to help protect against potential drug shortages.

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

The path to developing generic drug-device combination products like this one is challenging. FDA remains committed to providing scientific and regulatory clarity for sponsors seeking to develop complex generics, as well as prioritize the approval of medicines with little or no generic competition as part of FDA's effort to remove barriers to generic development and market entry of critically important medicines. Many of these steps were outlined in the Drug Competition Action Plan.

Also, FDA intends to implement policies and actions to enhance the efficiency of FDA's review of marketing applications for biosimilar and interchangeable products to:

- Increase regulatory certainty for biosimilar manufacturers and other stakeholders
- Educate patients, providers, and payors about biosimilar and interchangeable products
- Reduce the gaming of FDA regulations or other attempts to unfairly delay market competition.

In July 2018, FDA released the Biosimilars Action Plan[2] (BAP). Biologics are used to treat many serious and life-threatening diseases, such as cancer and autoimmune conditions. While less than two percent of Americans use biologics, they represent 40 percent of total spending on prescription drugs. Forging a path to competition for biologics from biosimilars is key to reducing costs and to facilitating more innovation. FDA is also focused on advancing policies that make the process for developing biosimilars more efficient. The Biosimilars Action Plan outlines the steps FDA is taking to achieve these goals. This plan is an important piece of the Administration's bold Blueprint to Lower Drug Prices and demonstrates the progress being made against its deliverables.

DQSA Implementation

Title I - Compounding

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. 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, FDA has completed the following actions:

- Conducted over 600 inspections of compounders, including over 160 inspections of compounders registered as outsourcing facilities
- Issued over 220 warning letters to compounders
- Issued over 200 recall notices regarding compounded drug products
- Issued 23 draft and revised draft guidance documents regarding compounding and related activities (16 of which have been finalized)
- Issued three proposed rules (two of which have been finalized)
- Issued a Federal Register Notice regarding the list of bulk drug substances that may be used in compounding under section 503B

[2] For additional information visit https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm613761.pdf

- Issued a draft and revised draft memorandum of understanding
- Convened eight Pharmacy Compounding Advisory Committee meetings
- Held seven intergovernmental working meetings with state regulatory partners and six listening sessions with more than 75 stakeholders.

Title II - Drug Supply Chain Security Act

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.

Since enactment of the DSCSA, FDA has issued ten draft guidance documents and six final guidances, including two final guidances to assist stakeholders in understanding when a product without a product identifier is grandfathered and when requirements will be enforced. In addition, FDA has held six public meetings as well as multiple stakeholder meetings on various strategies and issues related to enhanced drug distribution security provisions of the DSCSA. FDA continues to develop regulations, standards, policies, and programs to implement the law.[3]

Empowering Consumers and Patients

Protecting Consumers through Modern Regulatory Approaches

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

FDA supports efforts to increase patient safety and the efficiency for manufacturers of medical devices to sell their products globally – while still following high internationally-accepted quality systems – by proposing a new regulation to the existing Quality Systems regulations. And FDA promotes transformational approaches that will enable it to use real-world data in its regulatory decision making.

In support of maintaining FDA's gold standard for product review and consumer protection, FDA took the following actions in 2018 to alert the public and raise awareness regarding 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, and
- Alerted the public to the dangers of unproven and untested products.

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

Strengthening Science and Efficient Risk-Based Decision Making

Food Safety

In March 2018, the FDA Commissioner announced a comprehensive, multi-year Nutrition Innovation Strategy that focuses on reducing preventable death and disease related to poor nutrition. This new strategy gives consumers easier access to nutritious and affordable foods by providing them with information and by supporting industry innovation towards healthier foods.

Key elements of the strategy include modernizing health claims, modernizing ingredient labels and standards of identity, implementing the nutrition facts label and menu labeling requirements, and reducing sodium.

FDA is implementing menu labeling requirements and on May 7, 2018, finalized guidance to provide additional clarity and flexibility to covered establishments. Menu labeling regulations require the disclosure of certain nutritional information for standard menu items in chain restaurants and similar retail food establishments. The finalized guidance addresses concerns that were raised about challenges establishments faced in understanding how to meet their obligations under the new regulations. As of May 7, 2018, consumers now have consistent access to menu labeling information in covered eating establishments across the country.

FDA continues successful implementation of the FDA Food Safety Modernization Act (FSMA). FDA has published more than 20 draft and final guidances related to the FSMA rules including:

- Current Good Manufacturing Practices and Preventive Controls for Human Food;
- Current Good Manufacturing Practices and Preventive Controls for Animal Food;
- Produce Safety;
- Foreign Supplier Verification Program;
- Intentional Adulteration, Sanitary Transportation of Foods, and
- Registration of Food Facilities.

In 2018 FDA has strengthened oversight of imported foods by recognizing four accreditation bodies for the Third Party Accreditation Program and by launching FSMA's Voluntary Qualified Importer Program (VQIP). The Third Party Program and VQIP are two new FSMA tools FDA is using to help ensure that foods imported into the United States are produced in accordance with the same safety standards required of food produced domestically.

OVERVIEW OF THE BUDGET REQUEST

The FY 2020 Budget Request is $6.1 billion, an overall increase of 12 percent or $643.1 million compared to the FY 2019 Annualized Continuing Resolution (CR).[4] The request includes $3.3 billion for budget authority - or $361.9 million compared to the FY 2019 Annualized CR level - and $2.8 billion for user fees - or $281.1 million compared to the FY 2019 Annualized CR level.

All budget displays reflect the FY 2019 implementation of FDA's Working Capital Fund (WCF). As part of implementation, funds are realigned to shift service provider dollars and staff from FDA Headquarters to the Programs. This realignment results in a net reduction of $40.1 million ($18.8M BA / $21.3M UF) / 196 FTEs from FDA Headquarters and redistributes the funding to

[4] Includes a reduction to HHS OIG Transfer. See APT for details.

the Programs that will benefit from the services of the WCF. The APT and related tables have been comparably adjusted to reflect the realignment of: intergovernmental affairs (IGA) FTE to FDA HQ; operational support FTE from FDA HQ to the centers and offices as part of implementation of FDA's Working Capital Fund (WCF); and FDA HQ organizations as per the December 2018 Congressional Notification.

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.
- **Advancing Safe and Effective Medical Products** – ensures that safe and effective human and animal drugs, biological products, devices, and radiological products are available to improve the health and quality of life for the people in the U.S., including medical countermeasures - the drugs, vaccines, and diagnostic tests to diagnose, treat, and prevent the adverse health consequences associated with chemical, biological, radiological, nuclear (CBRN) agents, and emerging infectious disease threats, like pandemic influenza.
- **Tobacco Regulation** – protects Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products, and by educating the public about tobacco products and the dangers their use poses.
- **Infrastructure: Facilities and Rent Investments** – ensures FDA staff have optimally functioning offices and labs across the country to execute the agency's vital public health mission.

The Budget focuses on four strategic priorities:

- *Reduce the burdens of addiction crises* that are threatening American families
- *Leverage innovation and competition* to improve health care, broaden access, and advance public health goals
- *Empower consumers and patients* to make better and more informed decisions about their diets and health; and expand the opportunities to use nutrition to reduce morbidity and mortality from disease
- *Strengthen science and efficient risk-based decision making*

FDA's *Healthy Innovation, Safer Families: FDA's 2018 Strategic Policy Roadmap* provides an overview of some of the key priorities the Agency is pursuing to advance FDA's public health mission.[5]

FY 2020 Request

The FY 2020 budget will invest in new initiatives focused on the most urgent priorities as well as support needed for infrastructure. The BA Crosswalk provides full details of each level. New initiatives are summarized in the following sections by major activity with funding levels identified in parentheses.

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

FOOD SAFETY (BA $1.4B; UF $0.04B)

The FY 2020 Budget provides $1.4 billion for food safety, an increase of $67 million compared to the FY 2019 Annualized CR. The request includes $1.4 billion for budget authority – an increase of $38.4 million compared to the FY 2019 Annualized CR – and $44.4 million for user fees – an increase of $28.6 million compared to the FY 2019 Annualized CR. The Budget provides funding for FDA priorities for food safety across human and animal products. 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.

Strengthening Response Capabilities for Foodborne Outbreaks ($16.3M)

The FY 2020 budget includes $16.3 million to improve signal detection and response timelines for human and animal food contamination and outbreaks of foodborne illness so that contaminated food is detected and removed from the marketplace as quickly as possible, and implements recent OIG recommendations to strengthen FDA's food recall process.

Advancing FSMA ($16.5M)

The FY 2020 budget includes $16.5 million to support FSMA Cooperative Agreements with funding for animal and human foods preventive controls inspections and human foods produce safety inspections through the states cooperative agreement programs (CAPs).

Promoting Innovation and Emerging Technology While Maintaining Product Safety ($36.2M)

The FY 2020 budget includes $36.2 million to ensure that FDA keeps pace with how changes in the marketplace affect the human and animal food supply – including modernizing the regulatory framework for biotechnology products, assessing products in a risk-based manner, providing predictable pathways for commercialization, and enhancing the scientific review of human and animal food ingredients to foster innovative products getting to market and to improve nutrition. This funding level includes establishing new user fee program that would collect $28 million in its first year. FDA will invest $5.0 million in underfunded program areas in Center for Veterinary Medicine (CVM), including the premarket safety review of animal food ingredients to improve review times and eliminate unnecessary burdens to industry. FDA will make additional investments in CFSAN and FDA Headquarters (HQ) ($31.2M) to promote innovation and enhance FDA's ability to review plant and animal biotechnology products and other novel products.

ADVANCING SAFE AND EFFECTIVE MEDICAL PRODUCTS (BA $1.8B; UF $1.9B)

The FY 2020 Budget Request for medical product safety and availability is $3.8 billion, an increase of $428 million above the FY 2019 Annualized CR. The request includes $1.8 billion for budget authority – an increase of $316 million compared to the FY 2019 Annualized CR – and $1.9 billion for user fees – an increase of $112.1 million compared to the FY 2019 Annualized CR. The net BA increase is the result of $386 million in investments in new initiatives and -$70.3 million in adjustments.

The Budget provides funding for FDA priorities for medical product safety and availability. The request aligns to FDA's Strategic Policy Roadmap priorities to reduce the burden of the

addiction crises that are threatening American families and to leverage innovation and competition to improve healthcare, broaden access, and advance public health goals.

Integrated Pathogen Reduction of the Blood Supply ($20.0M)

The FY 2020 budget includes $20.0 million for a pilot program for pathogen inactivation technology which could help protect the blood supply from existing and emerging pathogens and potentially reduce or eliminate donor deferral and/or testing requirements.

Medical Countermeasures ($7.0M)

The FY 2020 budget includes $7.0 million for FDA review and regulatory science capacity to facilitate the development and availability of medical countermeasures to respond to chemical, biological, radiological, nuclear, and emerging infectious disease threats.

Modernize Generic Drug Reviews ($27.0M)

The FY 2020 budget includes $27.0 million to continue to modernize generic drug development by enhancing the efficiency of the review and approval of generic drug applications and by enabling more consistent regulatory decision making. This proposal would expand current efforts to streamline and automate the review of the drug quality section of the application to include other disciplines engaged in generic drug application assessments and would lead to faster generic drug approval.

Opioids ($55.0M)

The FY 2020 budget includes $55.0 million to support ongoing efforts to address the Opioids crisis, as well as support existing investments and additional lab needs for the International Mail Facilities initiative by increasing field and center operational capacity to review up to 100,000 packages annually.

Compounding ($13.5M)

The FY 2020 budget includes $13.5 million to catalyze development of policies and regulations for the outsourcing facilities, including advancement of the list of bulk drug substances that outsourcing facilities may use in compounding and current good manufacturing practice guidance and regulation specific to outsourcing facilities.

Promote Domestic Manufacturing: Advancing Modern Drug and Biological Product Manufacturing Technologies, Through the Development of Efficient Regulatory Pathways ($38.5M)

The FY 2020 budget includes $38.5M to promote domestic manufacturing. These technologies have great potential to accelerate new, more targeted therapies, enhance product quality, allow the vaccine supply to be more easily ramped up on short notice, and bolster stability in the U.S. drug supply to meet domestic and global needs. New manufacturing platforms contribute to development of personalized medicines and may help reduce the cost and uncertainty of adopting new manufacturing 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 ($12.0M)

The FY 2020 budget includes $12.0 million to create a "Center of Excellence on Compounding for Outsourcing Facilities" which 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.

Bring MedTech Manufacturing Home: Advance Medical Device Manufacturing and Quality ($12.0M)

The FY 2020 budget includes $12.0 million to establish a voluntary program for device manufacturers to receive certification for meeting objective manufacturing and product quality criteria. FDA will recognize third-party certifiers and offer regulatory incentives for those manufacturers who receive certification demonstrating their quality capability to increase manufacturing innovation, accelerate availability of high-quality devices to patients and foster a competitive marketplace.

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 ($60.0M)

The FY 2020 budget includes $60.0 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. This capability will allow FDA to conduct near-real-time evidence evaluation down to the level of individual electronic health records for at least 10 million individuals in U.S. healthcare settings.

Transform Medical Device Safety, Cybersecurity, Review, and Innovation ($55.0M)

The FY 2020 budget includes $55.0 million to build an integrated knowledge management system and portal for medical devices using modern, agile information technology systems with secure cloud-based data storage that will enable safety issues to be monitored along the total life cycle of the device from bench testing to premarket clinical trials to postmarket adverse events and real-world evidence. This capability to better leverage pre-existing and new data in near-real-time is essential for implementing FDA's new approaches for digital health technologies, breakthrough devices, use of real-world evidence, and cybersecurity. Overall, it will make device reviews, postmarket surveillance, and cybersecurity efforts significantly more efficient and informative, which could shorten review cycles, quickly identify and address safety signals and cyber vulnerabilities, and spur the development of innovative, safer, more effective devices.

Create a New Platform for How the Agency More Efficiently Develops and Validates Modern Science-Based Principles for New Drug Development ($50.0M)

The FY 2020 budget includes $50.0 million to build a knowledge management system and portal to apply cutting edge science to advance drug development and review as well as to support a new model for team-based product review and collaboration within the FDA Oncology Center of Excellence (OCE).

Stimulate Investment In, and Innovation of, Medical Products Targeted to Rare Diseases ($20.0M)

The FY 2020 budget includes $20.0 million[6] 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 and clinical outcomes of rare diseases.

Office of Laboratory Safety ($1.0M)

The FY 2020 budget includes $1.0 million for IT solutions, FDA-wide training programs, and maintaining the laboratory safety, biological safety, and industrial hygiene programs.

21st Century Cures - FDA Innovation Account (+$15.0M)

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.[7]

For FY 2020, the Cures Act authorized $75.0 million for the FDA Innovation Account. These resources will help FDA implement provisions to accelerate medical product innovation, reduce regulatory burden, increase efforts for critical scientific and methodological research, and increase the involvement of patients and their perspectives in research and the medical product development process.

INFRASTRUCTURE: FACILITIES AND RENT INVESTMENTS

The FY 2020 Budget provides a Budget Authority increase of $30.7 million over the FY 2019 Annualized CR 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 and increased facility costs related to real estate taxes, rental rates, expiring leases, maintenance, utilities, repairs, and improvements. This level also supports inflationary increases for White Oak campus logistics management, facilities operations, security infrastructure, utility infrastructure capacity and reliability improvements, and the campus safety program.

The FY 2020 Budget addresses planned lease costs for increasing facility needs in the National Capital Region and FDA field locations and 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, more demands will arise for repairs and non-standard maintenance requests.

[6] $10 million will support activities in CDER and $10 million will support policy related activities in FDA HQ.

[7] 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.

OVERVIEW OF PERFORMANCE

FDA accomplishes its core mission through activities that align to the priority areas in the FDA Strategic Policy Roadmap:

- Reduce the burdens of addiction crises that are threatening American families
- Leverage innovation and competition to improve health care, broaden access, and advance public health goals
- Empower consumers and patients to make better and more informed decisions about their diets and health; and expand the opportunities to use nutrition to reduce morbidity and mortality from disease
- Strengthen FDA's scientific workforce and its tools for efficient risk management.

FDA's FY 2020 Budget addresses these priority areas, 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. It demonstrates the value of FDA's contributions to public health, enables better leadership decision making with timely performance information, and provides a better mechanism for linking program activities with leadership priorities. 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 over 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, and
- 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.

ALL PURPOSE TABLE

(Dollars in Thousands)	FY 2018 Enacted		FY 2018 Actuals		FY 2019 Annualized CR		FY 2020 President's Budget		2020 President's Budget +/- FY 2019 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Foods	**3,861**	**1,070,187**	**3,861**	**1,059,291**	**3,905**	**1,070,187**	**4,008**	**1,122,047**	**103**	**51,860**
Budget Authority	***3,861***	***1,059,316***	***3,861***	***1,059,291***	***3,861***	***1,059,316***	***3,912***	***1,084,636***	***51***	***25,320***
User Fees	---	***10,871***	---	---	***44***	***10,871***	***96***	***37,411***	***52***	***26,540***
Center	1,147	327,044	1,147	326,210	1,150	327,044	1,230	361,678	80	34,634
Budget Authority	1,147	326,212	1,147	326,210	1,147	326,212	1,175	334,712	28	8,500
User Fees	---	832	---	---	3	832	55	26,966	52	26,134
Food and Feed Recall	---	243	---	---	1	243	1	253	---	10
Voluntary Qualified Importer Program	---	243	---	---	1	243	1	253	---	10
Third Party Auditor Program	---	346	---	---	1	346	1	360	---	14
Innovative Food Products (Proposed)	---	---	---	---	---	---	52	26,100	52	26,100
Field	2,714	743,143	2,714	733,081	2,755	743,143	2,778	760,369	23	17,226
Budget Authority	2,714	733,104	2,714	733,081	2,714	733,104	2,737	749,924	23	16,820
User Fees	---	10,039	---	---	41	10,039	41	10,445	---	406
Food and Feed Recall	---	1,000	---	---	4	1,000	4	1,040	---	40
Food Reinspection	---	4,575	---	---	19	4,575	19	4,760	---	185
Voluntary Qualified Importer Program	---	4,320	---	---	18	4,320	18	4,495	---	175
Third Party Auditor Program	---	144	---	---	---	144	---	150	---	6
Human Drugs	**6,335**	**1,633,743**	**6,335**	**1,755,609**	**6,560**	**1,713,629**	**6,715**	**1,980,030**	**155**	**266,401**
Budget Authority	***2,003***	***495,395***	***2,003***	***495,384***	***2,003***	***495,395***	***2,097***	***713,895***	***94***	***218,500***
User Fees	***4,332***	***1,138,348***	***4,332***	***1,260,225***	***4,557***	***1,218,234***	***4,618***	***1,266,135***	***61***	***47,901***
Center	5,261	1,432,054	5,261	1,554,711	5,502	1,510,169	5,624	1,749,191	122	239,022
Budget Authority	1,239	359,226	1,239	359,222	1,239	359,226	1,301	551,084	62	191,858
User Fees	4,022	1,072,828	4,022	1,195,489	4,263	1,150,943	4,323	1,198,107	60	47,164
Prescription Drug (PDUFA)	2,627	658,620	2,627	790,598	2,603	732,096	2,648	770,854	45	38,758
Generic Drug (GDUFA)	1,282	376,601	1,282	366,873	1,463	382,803	1,463	391,330	---	8,527
Biosimilars (BsUFA)	105	37,028	105	36,605	195	35,416	210	35,001	15	-415
Outsourcing Facility	8	579	8	1,413	2	628	2	922	---	294
Field	1,074	201,689	1,074	200,898	1,058	203,460	1,091	230,839	33	27,379
Budget Authority	764	136,169	764	136,162	764	136,169	796	162,811	32	26,642
User Fees	310	65,520	310	64,736	294	67,291	295	68,028	1	737
Prescription Drug (PDUFA)	54	8,101	54	7,753	38	9,003	38	8,801	---	-202
Generic Drug (GDUFA)	245	55,915	245	55,355	247	56,808	248	57,430	1	622
Biosimilars (BsUFA)	7	1,150	7	1,158	7	1,100	7	1,363	---	263
Outsourcing Facility	4	354	4	470	2	380	2	434	---	54
Biologics	**1,434**	**363,766**	**1,434**	**381,890**	**1,394**	**379,144**	**1,422**	**431,561**	**28**	**52,417**
Budget Authority	***806***	***217,138***	***806***	***217,135***	***806***	***217,138***	***826***	***262,138***	***20***	***45,000***
User Fees	***628***	***146,628***	***628***	***164,755***	***588***	***162,006***	***596***	***169,423***	***8***	***7,417***
Center	1,206	320,146	1,206	338,310	1,163	335,355	1,191	387,812	28	52,457
Budget Authority	583	175,132	583	175,131	583	175,132	603	220,132	20	45,000
User Fees	623	145,014	623	163,179	580	160,223	588	167,680	8	7,457
Prescription Drug (PDUFA)	553	130,171	553	151,195	520	144,529	527	151,782	7	7,253
Medical Device (MDUFA)	70	13,602	70	11,887	54	14,444	54	14,117	---	-327
Generic Drug (GDUFA)	---	1,055	---	78	4	1,072	4	1,085	---	13
Biosimilars (BsUFA)	---	186	---	19	2	178	3	696	1	518
Field	228	43,620	228	43,580	231	43,789	231	43,749	---	-40
Budget Authority	223	42,006	223	42,004	223	42,006	223	42,006	---	---
User Fees	5	1,614	5	1,576	8	1,783	8	1,743	---	-40
Prescription Drug (PDUFA)	4	1,410	4	1,370	7	1,566	7	1,532	---	-34
Medical Device (MDUFA)	1	204	1	206	1	217	1	211	---	-6
Animal Drugs and Feed	**944**	**200,465**	**944**	**210,732**	**956**	**220,030**	**983**	**239,515**	**27**	**19,485**
Budget Authority	***774***	***174,434***	***774***	***174,430***	***774***	***174,434***	***801***	***192,314***	***27***	***17,880***
User Fees	***170***	***26,031***	***170***	***36,302***	***182***	***45,596***	***182***	***47,201***	---	***1,605***
Center	627	133,595	627	145,181	632	152,942	659	166,904	27	13,962
Budget Authority	457	108,919	457	108,918	457	108,919	484	121,199	27	12,280
User Fees	170	24,676	170	36,263	175	44,023	175	45,705	---	1,682
Animal Drug (ADUFA)	117	16,095	117	24,865	115	27,267	115	27,706	---	439
Animal Generic Drug (AGDUFA)	53	8,469	53	11,375	60	16,644	60	17,882	---	1,238
Third Party Auditor Program	---	112	---	23	---	112	---	117	---	5
Field	317	66,870	317	65,551	324	67,088	324	72,611	---	5,523
Budget Authority	317	65,515	317	65,512	317	65,515	317	71,115	---	5,600
User Fees	---	1,355	---	39	7	1,573	7	1,496	---	-77
Animal Drug (ADUFA)	---	310	---	36	2	431	2	440	---	9
Animal Generic Drug (AGDUFA)	---	238	---	3	2	335	2	216	---	-119
Food Reinspection	---	807	---	---	3	807	3	840	---	33
Third Party Auditor Program	---	---	---	---	---	---	---	---	---	---

(Dollars in Thousands)	FY 2018 Enacted		FY 2018 Actuals		FY 2019 Annualized CR		FY 2020 President's Budget		2020 President's Budget +/- FY 2019 Annualized CR	
	FTE	$000	FTE	$000		$000	FTE	$000	FTE	$000
Devices and Radiological Health	**2,159**	**512,901**	**2,159**	**479,930**	**2,328**	**522,838**	**2,399**	**631,718**	**71**	**108,880**
Budget Authority	***1,539***	***332,893***	***1,539***	***332,885***	***1,539***	***332,893***	***1,565***	***423,893***	***26***	***91,000***
User Fees	***620***	***180,008***	***620***	***147,045***	***789***	***189,945***	***834***	***207,825***	***45***	***17,880***
Center	1,647	411,791	1,647	381,463	1,816	421,598	1,887	529,978	71	108,380
Budget Authority	1,045	247,888	1,045	247,884	1,045	247,888	1,071	338,888	26	91,000
User Fees	602	163,903	602	133,579	771	173,710	816	191,090	45	17,380
Prescription Drug (PDUFA)	5	1,320	5	987	10	1,460	15	4,272	5	2,812
Medical Device (MDUFA)	569	156,148	569	126,998	729	165,815	769	180,125	40	14,310
Mammography Quality Standards Act (MQSA)	28	6,435	28	5,594	32	6,435	32	6,693	---	258
Field	512	101,110	512	98,467	512	101,240	512	101,740	---	500
Budget Authority	494	85,005	494	85,001	494	85,005	494	85,005	---	---
User Fees	18	16,105	18	13,466	18	16,235	18	16,735	---	500
Medical Device (MDUFA)	11	2,110	11	2,086	10	2,240	10	2,179	---	-61
Mammography Quality Standards Act (MQSA)	7	13,995	7	11,380	8	13,995	8	14,556	---	561
National Center for Toxicological Research (BA Only)	**301**	**64,512**	**301**	**64,512**	**301**	**64,512**	**301**	**66,512**	**---**	**2,000**
Tobacco	**874**	**626,663**	**874**	**625,406**	**991**	**626,663**	**1,053**	**761,739**	**62**	**135,076**
Center	**821**	**611,979**	**821**	**614,794**	**932**	**611,979**	**992**	**747,055**	**60**	**135,076**
Family Smoking Prevention and Tobacco Control Act	**821**	**611,979**	821	614,794	932	611,979	992	647,055	60	35,076
Expand tobacco product (Proposed)	**---**	**---**	---	---	---	---	---	100,000	---	100,000
Field	**53**	**14,684**	**53**	**10,612**	**59**	**14,684**	**61**	**14,684**	**2**	**---**
Family Smoking Prevention and Tobacco Control Act	**53**	**14,684**	53	10,612	59	14,684	61	14,684	2	---
FDA Headquarters	**943**	**290,638**	**943**	**315,684**	**1,001**	**299,587**	**1,018**	**320,164**	**17**	**20,577**
Budget Authority	***591***	***171,195***	***591***	***171,001***	***591***	***171,195***	***620***	***180,195***	***29***	***9,000***
User Fees	***352***	***119,443***	***352***	***144,683***	***410***	***128,392***	***398***	***139,969***	***-12***	***11,577***
Prescription Drug (PDUFA)	176	50,082	176	60,244	186	56,391	187	59,194	1	2,803
Medical Device (MDUFA)	16	7,811	16	7,297	31	8,463	31	9,209	---	746
Generic Drug (GDUFA)	50	34,489	50	27,947	103	35,243	103	35,784	---	541
Biosimilars (BsUFA)	7	706	7	1,393	5	632	5	1,022	---	390
Animal Drug (ADUFA)	4	446	4	828	4	1,004	4	734	---	-270
Animal Generic Drug (AGDUFA)	1	63	1	73	1	785	1	26	---	-759
Family Smoking Prevention and Tobacco Control Act	97	24,491	97	46,921	74	24,491	61	30,867	-13	6,376
Mammography Quality Standards Act (MQSA)	1	92	1	-20	2	92	2	102	---	10
Food and Feed Recall	---	75	---	---	---	75	---	78	---	3
Food Reinspection	---	480	---	---	2	480	2	499	---	19
Voluntary Qualified Importer Program	---	277	---	---	1	277	1	288	---	11
Third Party Auditor Program	---	39	---	---	---	39	---	41	---	2
Outsourcing Facility	---	392	---	---	1	420	1	225	---	-195
Innovative Food Products (Proposed)	---	---	---	---	---	---	---	1,900	---	1,900
FDA White Oak Consolidation	**---**	**50,559**	**---**	**49,453**	**---**	**50,772**	**---**	**58,926**	**---**	**8,154**
Budget Authority	---	***43,044***	---	***43,044***	---	***43,044***	---	***50,927***	---	***7,883***
User Fees	---	***7,515***	---	***6,409***	---	***7,728***	---	***7,999***	---	***271***
Prescription Drug (PDUFA)	---	3,597	---	3,597	---	3,810	---	3,848	---	38
Medical Device (MDUFA)	---	---	---	---	---	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	---	3,918	---	2,812	---	3,918	---	4,151	---	233

(Dollars in Thousands)	FY 2018 Enacted		FY 2018 Actuals		FY 2019 Annualized CR		FY 2020 President's Budget		2020 President's Budget +/- FY 2019 Annualized CR	
	FTE	$000	FTE	$000		$000	FTE	$000	FTE	$000
Other Rent and Rent Related	**---**	**121,919**	**---**	**121,530**	**---**	**123,881**	**---**	**146,251**	**---**	**22,370**
Budget Authority	---	***71,943***	---	***71,943***	---	***71,943***	---	***93,444***	---	***21,501***
User Fees	---	***49,976***	---	***49,587***	---	***51,938***	---	***52,807***	---	***869***
Prescription Drug (PDUFA)	---	24,672	---	26,163	---	26,127	---	26,389	---	262
Medical Device (MDUFA)	---	5,187	---	8,672	---	5,239	---	5,291	---	52
Generic Drug (GDUFA)	---	12,946	---	9,426	---	13,075	---	13,206	---	131
Biosimilars (BsUFA)	---	805	---	766	---	1,070	---	1,081	---	11
Animal Drug (ADUFA)	---	720	---	720	---	790	---	797	---	7
Animal Generic Drug (AGDUFA)	---	273	---	261	---	264	---	266	---	2
Family Smoking Prevention and Tobacco Control Act	---	4,898	---	3,579	---	4,898	---	5,283	---	385
Food and Feed Recall	---	43	---	---	---	43	---	45	---	2
Food Reinspection	---	204	---	---	---	204	---	212	---	8
Voluntary Qualified Importer Program	---	170	---	---	---	170	---	177	---	7
Third Party Auditor Program	---	24	---	---	---	24	---	25	---	1
Outsourcing Facility	---	34	---	---	---	34	---	35	---	1
GSA Rental Payments	**---**	**238,487**	**---**	**219,283**	**---**	**241,024**	**---**	**240,928**	**---**	**-96**
Budget Authority	---	***170,208***	---	***170,208***	---	***170,208***	---	***171,570***	---	***1,362***
User Fees	---	***68,279***	---	***49,075***	---	***70,816***	---	***69,358***	---	***-1,458***
Prescription Drug (PDUFA)	---	33,373	---	20,205	---	35,341	---	35,695	---	354
Medical Device (MDUFA)	---	8,229	---	8,229	---	8,312	---	8,395	---	83
Generic Drug (GDUFA)	---	12,594	---	12,594	---	12,720	---	12,847	---	127
Biosimilars (BsUFA)	---	339	---	339	---	451	---	455	---	4
Animal Drug (ADUFA)	---	522	---	522	---	839	---	847	---	8
Animal Generic Drug (AGDUFA)	---	376	---	304	---	307	---	310	---	3
Family Smoking Prevention and Tobacco Control Act	---	12,030	---	6,882	---	12,030	---	9,960	---	-2,070
Food and Feed Recall	---	73	---	---	---	73	---	76	---	3
Food Reinspection	---	348	---	---	---	348	---	362	---	14
Voluntary Qualified Importer Program	---	290	---	---	---	290	---	302	---	12
Third Party Auditor Program	---	47	---	---	---	47	---	49	---	2
Outsourcing Facility	---	58	---	---	---	58	---	60	---	2
Color Certification	**36**	**10,125**	**36**	**10,006**	**37**	**10,062**	**37**	**10,534**	**---**	**472**
Export Certification	**22**	**4,696**	**22**	**4,166**	**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	**1**	**7,686**	**1**	**298**	**---**	**7,686**	**---**	**7,997**	**---**	**311**
Over the Counter Monograph (Proposed)	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**28,400**	**---**	**28,400**
Food and Drug Safety -- No Year (P.L. 113-6)	**---**	**---**	**---**	**766**	**---**	**---**	**---**	**---**	**---**	**---**
Food Safety	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**
Drug Safety	**---**	**---**	**---**	**766**	**---**	**---**	**---**	**---**	**---**	**---**
21st Century Cures (BA Only)	**100**	**60,000**	**100**	**41,458**	**100**	**60,000**	**100**	**75,000**	**28**	**15,000**
MCMi -- No Year	**---**	**---**	**5**	**3,554**	**---**	**---**	**---**	**---**	**---**	**---**
Opioids -- No Year	**8**	**94,000**	**8**	**12,749**	**8**	**94,000**	**---**	**---**	**-8**	**-94,000**
Subtotal, Salaries and Expenses	**17,018**	**5,350,347**	**17,023**	**5,356,317**	**17,607**	**5,488,711**	**18,062**	**6,130,298**	**483**	**641,587**
Buildings and Facilities (Budget Authority)	**---**	**11,788**		**14,618**	**---**	**11,788**	**---**	**11,788**	**---**	**---**
Total Program Level	**17,018**	**5,362,135**	**17,018**	**5,367,381**	**17,607**	**5,500,499**	**18,062**	**6,142,086**	**483**	**641,587**

(Dollars in Thousands)	FY 2018 Enacted		FY 2018 Actuals		FY 2019 Annualized CR		FY 2020 President's Budget		2020 President's Budget +/- FY 2019 Annualized CR	
	FTE	$000	FTE	$000		$000	FTE	$000	FTE	$000
Non-Field Activities	*12,012*	*3,614,266*	*12,012*	*3,755,335*	*12,560*	*3,745,630*	*12,965*	*4,385,201*	*405*	*639,571*
Field Activities	*4,898*	*1,171,116*	*4,898*	*1,152,189*	*4,939*	*1,173,404*	*4,997*	*1,223,992*	*58*	*50,588*
White Oak, Rent Activities, and B&F	---	*422,753*	---	*404,884*	---	*427,465*	---	*457,893*	---	30,428
Food and Drug Safety -- No Year	---	---	---	*766*	---	---	---	---	---	---
Opioids -- No Year	*8*	*94,000*	*8*	*12,749*	*8*	*94,000*	---	---	*-8*	*-94,000*
21st Century Cures	*100*	*60,000*	*100*	*41,458*	*100*	*60,000*	*100*	*75,000*	*28*	*15,000*
MCMi -- No Year	---	---	*5*	*3,554*	---	---	---	---	---	---
User Fees:										
Current Law										
Prescription Drug (PDUFA)	*3,419*	*911,346*	*3,419*	*1,062,112*	*3,364*	*1,010,323*	*3,422*	*1,062,367*	*58*	*52,044*
Medical Device (MDUFA)	*667*	*193,291*	*667*	*165,375*	*825*	*204,730*	*865*	*219,527*	*40*	*14,797*
Generic Drug (GDUFA)	*1,577*	*493,600*	*1,577*	*472,273*	*1,817*	*501,721*	*1,818*	*511,682*	*1*	*9,961*
Biosimilars (BsUFA)	*119*	*40,214*	*119*	*40,280*	*209*	*38,847*	*225*	*39,618*	*16*	*771*
Animal Drug (ADUFA)	*121*	*18,093*	*121*	*26,971*	*121*	*30,331*	*121*	*30,524*	---	*193*
Animal Generic Drug (AGDUFA)	*54*	*9,419*	*54*	*12,016*	*63*	*18,335*	*63*	*18,700*	---	*365*
Family Smoking Prevention and Tobacco Control Act	*971*	*672,000*	*971*	*685,600*	*1,065*	*672,000*	*1,114*	*712,000*	*49*	*40,000*
Subtotal, Current Law	**6,928**	**2,337,963**	**6,928**	**2,464,627**	**7,464**	**2,476,287**	**7,628**	**2,594,418**	**164**	**118,131**
Indefinite										
Mammography Quality Standards Act (MQSA)	*36*	*20,522*	*36*	*16,954*	*42*	*20,522*	*42*	*21,351*	---	*829*
Color Certification	*36*	*10,125*	*36*	*10,006*	*37*	*10,062*	*37*	*10,534*	---	*472*
Export Certification	*22*	*4,696*	*22*	*4,166*	*26*	*4,696*	*26*	*4,696*	---	---
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	---	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	*1*	*7,686*	*1*	*298*	---	*7,686*	---	*7,997*	---	*311*
Food and Feed Recall	---	*1,434*	---	---	*5*	*1,434*	*5*	*1,492*	---	*58*
Food Reinspection	---	*6,414*	---	---	*24*	*6,414*	*24*	*6,673*	---	*259*
Voluntary Qualified Importer Program	---	*5,300*	---	---	*20*	*5,300*	*20*	*5,515*	---	*215*
Third Party Auditor Program	---	*712*	---	*23*	*1*	*712*	*1*	*742*	---	*30*
Outsourcing Facility	*12*	*1,417*	*12*	*1,883*	*5*	*1,520*	*5*	*1,676*	---	*156*
Subtotal, Indefinite	**107**	**58,306**	**107**	**33,330**	**160**	**58,346**	**160**	**60,676**	**---**	**2,330**
Proposed										
Export Certification (Proposed)	---	---	---	---	---	---	---	*4,280*	---	*4,280*
Over the Counter Monograph (Proposed)	---	---	---	---	---	---	---	*28,400*	---	*28,400*
Innovative Food Products (Proposed)	---	---	---	---	---	---	*52*	*28,000*	*52*	*28,000*
Expand tobacco product (Proposed)	---	---	---	---	---	---	---	*100,000*	---	*100,000*
Subtotal, Proposed	---	---	---	---	---	---	*52*	*160,680*	*52*	*160,680*
Total User Fees	**7,035**	**2,396,269**	**7,035**	**2,497,957**	**7,624**	**2,534,633**	**7,840**	**2,815,774**	**216**	**281,141**
Total Budget Authority, Pre-Transfer	**9,983**	**2,965,866**	**9,988**	**2,872,978**	**9,983**	**2,965,866**	**10,222**	**3,326,312**	**239**	**360,446**
BA, S&E	*9,875*	*2,800,078*	*9,875*	*2,799,833*	*9,875*	*2,800,078*	*10,122*	*3,239,524*	*247*	*439,446*
BA, B&F	---	*11,788*	---	*14,618*	---	*11,788*	---	*11,788*	---	---
Opioids -- No Year	8	94,000	8	12,749	8	94,000	---	---	*-8*	*-94,000*
21st Century Cures	*100*	*60,000*	*100*	*41,458*	*100*	*60,000*	*100*	*75,000*	---	*15,000*
MCMi -- No Year	---	---	*5*	*3,554*	---	---	---	---	---	---
Total Program Level, Pre-Transfer	**17,018**	**5,362,135**	**17,023**	**5,370,935**	**17,607**	**5,500,499**	**18,062**	**6,142,086**	**455**	**641,587**
HHS OIG transfer (BA Only)	**---**	**-1,500**	**---**	**-1,500**	**---**	**-1,500**	**---**	**---**	---	*1,500*
Total Budget Authority, Post-Transfer	**9,983**	**2,964,366**	**9,988**	**2,871,478**	**9,983**	**2,964,366**	**10,222**	**3,326,312**	**239**	**361,946**
Total User Fees	***7,035***	***2,396,269***	***7,035***	***2,497,957***	***7,624***	***2,534,633***	***7,840***	***2,815,774***	***216***	***281,141***
Total Program Level, Post-Transfer	**17,018**	**5,360,635**	**17,023**	**5,369,435**	**17,607**	**5,498,999**	**18,062**	**6,142,086**	**455**	**643,087**
Hurricane Funding Transfer to S&E				**187**						

*For 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.

** FTE figures do not include an estimated 87 reimbursable, 2 CRADA, 2 FOIA, and 36 PEPFAR. The table also excludes Opioids – IMF FTE supported with one-time funding provided via the FY 2018 Omnibus. Table includes additional base funding as part of the Opioids IMF initiative to maintain these staffing levels.

***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.

*****In addition to the funding displayed in FY 2018 Enacted column, the Further Additional Supplemental Appropriations for Disaster Relief and Requirement Act, 2018 included $7.6 million in one-time, no-year funding for FDA.

******Does not reflect priority review voucher user fee for Medical Countermeasures as no companies have announced planned use of the voucher.

*******Funding and FTE levels for FYs 2018 - 2020 have been comparably adjusted to reflect the realignment of: intergovernmental affairs (IGA) FTE to FDA HQ; operational support FTE from FDA HQ to the centers and offices as part of implementation of FDA's Working Capital Fund (WCF); and FDA HQ organizations as per the December 2018 Congressional Notification.

********FY 2020 NEF budget allocations will be provided upon settlement of the FY 2019 NEF Congressional Notification.

*********FY 2019 Enacted reflects the amount specified in the August 2018 FR Notice for Outsourcing Facility Fees.

MAJOR ACTIVITIES TABLE

(Dollars in Thousands)	FY 2018 Omnibus						FY 2019 Annualized CR						FY 2020 President's Budget						FY 2020 President's Budget +/- FY 2019 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	**3,861**	**1,059,316**	**---**	**---**	**3,861**	**1,059,316**	**3,861**	**1,059,316**	**---**	**---**	**3,861**	**1,059,316**	**3,912**	**1,084,636**	**---**	**---**	**3,912**	**1,084,636**	**51**	**25,320**	**---**	**---**	**51**	**25,320**
Center	1,147	326,212	---	---	1,147	326,212	1,147	326,212	---	---	1,147	326,212	1,175	334,712	---	---	1,175	334,712	28	8,500	---	---	28	8,500
Field	2,714	733,104	---	---	2,714	733,104	2,714	733,104	---	---	2,714	733,104	2,737	749,924	---	---	2,737	749,924	23	16,820	---	---	23	16,820
Human Drugs	**---**	**---**	**2,003**	**495,395**	**2,003**	**495,395**	**---**	**---**	**2,003**	**495,395**	**2,003**	**495,395**	**---**	**---**	**2,097**	**713,895**	**2,097**	**713,895**	**---**	**---**	**94**	**218,500**	**94**	**218,500**
Center	---	---	1,239	359,226	1,239	359,226	---	---	1,239	359,226	1,239	359,226	---	---	1,301	551,084	1,301	551,084	---	---	62	191,858	62	191,858
Field	---	---	764	136,169	764	136,169	---	---	764	136,169	764	136,169	---	---	796	162,811	796	162,811	---	---	32	26,642	32	26,642
Biologics	**---**	**---**	**806**	**217,138**	**806**	**217,138**	**---**	**---**	**806**	**217,138**	**806**	**217,138**	**---**	**---**	**826**	**262,138**	**826**	**262,138**	**---**	**---**	**20**	**45,000**	**20**	**45,000**
Center	---	---	583	175,132	583	175,132	---	---	583	175,132	583	175,132	---	---	603	220,132	603	220,132	---	---	20	45,000	20	45,000
Field	---	---	223	42,006	223	42,006	---	---	223	42,006	223	42,006	---	---	223	42,006	223	42,006	---	---	---	---	---	---
Animal Drugs and Feeds	**584**	**127,181**	**190**	**47,253**	**774**	**174,434**	**584**	**127,181**	**190**	**47,253**	**774**	**174,434**	**607**	**141,061**	**194**	**51,253**	**801**	**192,314**	**23**	**13,880**	**4**	**4,000**	**27**	**17,880**
Center	281	64,579	176	44,340	457	108,919	281	64,579	176	44,340	457	108,919	304	72,859	180	48,340	484	121,199	23	8,280	4	4,000	27	12,280
Field	303	62,602	14	2,913	317	65,515	303	62,602	14	2,913	317	65,515	303	68,202	14	2,913	317	71,115	---	5,600	---	---	---	5,600
Devices and Radiological Health	**---**	**---**	**1,539**	**332,893**	**1,539**	**332,893**	**---**	**---**	**1,539**	**332,893**	**1,539**	**332,893**	**---**	**---**	**1,565**	**423,893**	**1,565**	**423,893**	**---**	**---**	**26**	**91,000**	**26**	**91,000**
Center	---	---	1,045	247,888	1,045	247,888	---	---	1,045	247,888	1,045	247,888	---	---	1,071	338,888	1,071	338,888	---	---	26	91,000	26	91,000
Field	---	---	494	85,005	494	85,005	---	---	494	85,005	494	85,005	---	---	494	85,005	494	85,005	---	---	---	---	---	---
National Center for Toxicological Research	**49**	**10,317**	**252**	**54,195**	**301**	**64,512**	**49**	**10,317**	**252**	**54,195**	**301**	**64,512**	**25**	**5,087**	**276**	**61,425**	**301**	**66,512**	**-24**	**-5,230**	**24**	**7,230**	**---**	**2,000**
FDA Headquarters	**200**	**54,239**	**391**	**97,956**	**591**	**171,195**	**200**	**54,239**	**391**	**97,956**	**591**	**171,195**	**200**	**54,239**	**420**	**108,456**	**620**	**180,195**	**---**	**---**	**29**	**10,500**	**29**	**9,000**
FDA White Oak Consolidation	**---**	**---**	**---**	**---**	**---**	**43,044**	**---**	**---**	**---**	**---**	**---**	**43,044**	**---**	**---**	**---**	**---**	**---**	**50,927**	**---**	**---**	**---**	**---**	**---**	**7,883**
Other Rent and Rent Related	**---**	**36,300**	**---**	**35,643**	**---**	**71,943**	**---**	**36,300**	**---**	**35,643**	**---**	**71,943**	**---**	**39,215**	**---**	**54,229**	**---**	**93,444**	**---**	**2,915**	**---**	**18,586**	**---**	**21,501**
GSA Rental Payments	**---**	**79,477**	**---**	**90,731**	**---**	**170,208**	**---**	**79,477**	**---**	**90,731**	**---**	**170,208**	**---**	**80,963**	**---**	**90,607**	**---**	**171,570**	**---**	**1,486**	**---**	**-124**	**---**	**1,362**
SUBTOTAL, BA Salaries and Expenses	**4,694**	**1,366,830**	**5,181**	**1,371,204**	**9,875**	**2,800,078**	**4,694**	**1,366,830**	**5,181**	**1,371,204**	**9,875**	**2,800,078**	**4,744**	**1,405,201**	**5,378**	**1,765,896**	**10,122**	**3,239,524**	**50**	**38,371**	**197**	**394,692**	**247**	**439,446**
Building and Facilities	**---**	**---**	**---**	**---**	**---**	**11,788**	**---**	**---**	**---**	**---**	**---**	**11,788**	**---**	**---**	**---**	**---**	**---**	**11,788**	**---**	**---**	**---**	**---**	**---**	**---**
Non-Field Activities	**1,677**	**455,347**	**3,686**	**978,737**	**5,363**	**1,453,084**	**1,677**	**455,347**	**3,686**	**978,737**	**5,363**	**1,453,084**	**1,704**	**466,897**	**3,851**	**1,328,325**	**5,555**	**1,812,722**	**27**	**11,550**	**165**	**349,588**	**192**	**359,638**
Field Activities	**3,017**	**795,706**	**1,495**	**266,093**	**4,512**	**1,061,799**	**3,017**	**795,706**	**1,495**	**266,093**	**4,512**	**1,061,799**	**3,040**	**818,126**	**1,527**	**292,735**	**4,567**	**1,110,861**	**23**	**22,420**	**32**	**26,642**	**55**	**49,062**
White Oak, Rent Activities, and B&F	**---**	**115,777**	**---**	**126,374**	**---**	**296,983**	**---**	**115,777**	**---**	**126,374**	**---**	**296,983**	**---**	**120,178**	**---**	**144,836**	**---**	**327,729**	**---**	**4,401**	**---**	**18,462**	**---**	**30,746**
Opioids -- No Year	**---**	**---**	**8**	**94,000**	**8**	**94,000**	**---**	**---**	**8**	**94,000**	**8**	**94,000**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**-8**	**-94,000**	**-8**	**-94,000**
21st Century Cures	**---**	**---**	**100**	**60,000**	**100**	**60,000**	**---**	**---**	**100**	**60,000**	**100**	**60,000**	**---**	**---**	**100**	**75,000**	**100**	**75,000**	**---**	**---**	**---**	**15,000**	**---**	**15,000**
Total BA	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,965,866**	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,965,866**	**4,744**	**1,405,201**	**5,478**	**1,840,896**	**10,222**	**3,326,312**	**50**	**38,371**	**189**	**315,692**	**239**	**360,446**
Total BA, Pre-Transfer	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,965,866**	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,965,866**	**4,744**	**1,405,201**	**5,478**	**1,840,896**	**10,222**	**3,326,312**	**50**	**38,371**	**189**	**315,692**	**239**	**360,446**

(Dollars in Thousands)	FY 2018 Omnibus						FY 2019 Annualized CR						FY 2020 President's Budget						FY 2020 President's Budget +/- FY 2019 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	
	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	---	**15,863**	**6,028**	**1,698,281**	**7,035**	**2,396,269**	**50**	**15,863**	**6,472**	**1,836,708**	**7,624**	**2,534,633**	**102**	**44,425**	**6,587**	**1,948,815**	**7,840**	**2,815,774**	**52**	**28,562**	**115**	**112,107**	**216**	**281,141**
Current Law																								
Prescription Drug (PDUFA)	---	---	3,419	911,346	3,419	911,346	---	---	3,364	1,010,323	3,364	1,010,323	---	---	3,422	1,062,367	3,422	1,062,367	---	---	58	52,044	58	52,044
Medical Device (MDUFA)	---	---	667	193,291	667	193,291	---	---	825	204,730	825	204,730	---	---	865	219,527	865	219,527	---	---	40	14,797	40	14,797
Generic Drug (GDUFA)	---	---	1,577	493,600	1,577	493,600	---	---	1,817	501,721	1,817	501,721	---	---	1,818	511,682	1,818	511,682	---	---	1	9,961	1	9,961
Biosimilars (BsUFA)	---	---	119	40,214	119	40,214	---	---	209	38,847	209	38,847	---	---	225	39,618	225	39,618	---	---	16	771	16	771
Animal Drug (ADUFA)	---	---	121	18,093	121	18,093	---	---	121	30,331	121	30,331	---	---	121	30,524	121	30,524	---	---	---	193	---	193
Animal Generic Drug (AGDUFA)	---	---	54	9,419	54	9,419	---	---	63	18,335	63	18,335	---	---	63	18,700	63	18,700	---	---	---	365	---	365
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	971	672,000	---	---	---	---	1,065	672,000	---	---	---	---	1,114	712,000	---	---	---	---	49	40,000
Mammography Quality Standards Act (MQSA)	---	---	36	20,522	36	20,522	---	---	42	20,522	42	20,522	---	---	42	21,351	42	21,351	---	---	---	829	---	829
Color Certification	---	---	---	---	36	10,125	---	---	---	---	37	10,062	---	---	---	---	37	10,534	---	---	---	---	---	472
Export Certification	---	2,003	22	2,693	22	4,696	---	2,003	26	2,693	26	4,696	---	2,003	26	2,693	26	4,696	---	---	---	---	---	---
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	---	1	7,686	1	7,686	---	---	---	7,686	---	7,686	---	---	---	7,997	---	7,997	---	---	---	311	---	311
Food and Feed Recall	---	1,434	---	---	---	1,434	5	1,434	---	---	5	1,434	5	1,492	---	---	5	1,492	---	58	---	---	---	58
Food Reinspection	---	6,414	---	---	---	6,414	24	6,414	---	---	24	6,414	24	6,673	---	---	24	6,673	---	259	---	---	---	259
Voluntary Qualified Importer Program	---	5,300	---	---	---	5,300	20	5,300	---	---	20	5,300	20	5,515	---	---	20	5,515	---	215	---	---	---	215
Third Party Auditor Program	---	712	---	---	---	712	1	712	---	---	1	712	1	742	---	---	1	742	---	30	---	---	---	30
Outsourcing Facility	---	---	12	1,417	12	1,417	---	---	5	1,520	5	1,520	---	---	5	1,676	5	1,676	---	---	---	156	---	156
Proposed																								
Export Certification (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	4,280	---	4,280	---	---	---	4,280	---	4,280
Over the Counter Monograph (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	28,400	---	28,400	---	---	---	28,400	---	28,400
Tobacco User fee for e-cigarettes and other (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	100,000	---	---	---	---	---	100,000
Food and Feed additive user fee (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	52	28,000	---	---	52	28,000	52	28,000	---	---	52	28,000
Total Program Level, Pre-Transfer	**4,694**	**1,382,693**	**11,317**	**3,223,485**	**17,018**	**5,362,135**	**4,744**	**1,382,693**	**11,761**	**3,361,912**	**17,607**	**5,500,499**	**4,846**	**1,449,626**	**12,065**	**3,789,711**	**18,062**	**6,142,086**	**102**	**66,933**	**304**	**427,799**	**455**	**641,587**
HHS OIG transfer	---	---	---	---	---	**-1,500**	---	---	---	---	---	**-1,500**	---	---	---	---	---	---	---	---	---	---	---	**1,500**
Total BA, Post-Transfer	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,964,366**	**4,694**	**1,366,830**	**5,289**	**1,525,204**	**9,983**	**2,964,366**	**4,744**	**1,405,201**	**5,478**	**1,840,896**	**10,222**	**3,326,312**	**50**	**38,371**	**189**	**315,692**	**239**	**361,946**
Total Program Level, Post-Transfer	**4,694**	**1,382,693**	**11,317**	**3,223,485**	**17,018**	**5,360,635**	**4,744**	**1,382,693**	**11,761**	**3,361,912**	**17,607**	**5,498,999**	**4,846**	**1,449,626**	**12,065**	**3,789,711**	**18,062**	**6,142,086**	**102**	**66,933**	**304**	**427,799**	**455**	**643,087**

* Total Budget Authority includes $10 million for the China Initiative for FY 2018, and $7.5 million for 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 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.

***In addition to the funding displayed in FY 2018 Omnibus column, the Further Additional Supplemental Appropriations for Disaster Relief and Requirement Act, 2018 included $7.6 million in one-time, no-year funding for FDA.

****Does not reflect priority review voucher user fee for Medical Countermeasures as no companies have announced planned use of the voucher.

*****Funding and FTE levels for FYs 2018 - 2020 have been comparably adjusted to reflect the realignment of: intergovernmental affairs (IGA) FTE to FDA HQ; operational support FTE from FDA HQ to the centers and offices as part of implementation of FDA's Working Capital Fund (WCF); and FDA HQ organizations as per the December 2018 Congressional Notification.

******NCTR Food Safety project ending in FY 2019 and reallocated to Medical Product Safety in FY 2020.

BUDGET AUTHORITY CROSSWALK

(Dollars in Thousands)	FY 2019 Annualized CR		HHS OIG transfer	Infrastructure	Food Safety								Total Food Safety	
					Food Safety Adjustments		Advancing FSMA		Strengthening Response Capabilities for Foodborne Outbreaks		Promoting Innovation and Emerging Technology While Maintaining Product Safety			
	FTE	$000	$000	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:														
Foods	**3,861**	**1,059,316**	---	---	---	**-1,800**	**1**	**10,600**	**40**	**13,300**	**10**	**3,220**	**51**	**25,320**
Center	1,147	326,212	---	---	---	-1,800	1	280	17	6,800	10	3,220	28	8,500
Field	2,714	733,104	---	---	---	---	---	10,320	23	6,500	---	---	23	16,820
Human Drugs	**2,003**	**495,395**	---	---	---	---	---	---	---	---	---	---	---	---
Center	1,239	359,226	---	---	---	---	---	---	---	---	---	---	---	---
Field	764	136,169	---	---	---	---	---	---	---	---	---	---	---	---
Biologics	**806**	**217,138**	---	---	---	---	---	---	---	---	---	---	---	---
Center	583	175,132	---	---	---	---	---	---	---	---	---	---	---	---
Field	223	42,006	---	---	---	---	---	---	---	---	---	---	---	---
Animal Drugs and Feeds	**774**	**174,434**	---	---	---	---	**1**	**5,880**	**10**	**3,000**	**12**	**5,000**	**23**	**13,880**
Center	457	108,919	---	---	---	---	1	280	10	3,000	12	5,000	23	8,280
Field	317	65,515	---	---	---	---	---	5,600	---	---	---	---	---	5,600
Devices and Radiological Health	**1,539**	**332,893**	---	---	---	---	---	---	---	---	---	---	---	---
Center	1,045	247,888	---	---	---	---	---	---	---	---	---	---	---	---
Field	494	85,005	---	---	---	---	---	---	---	---	---	---	---	---
National Center for Toxicological Research	**301**	**64,512**	---	---	---	---	---	---	---	---	---	---	---	---
FDA Headquarters	**591**	**171,195**	**-1,500**	---	---	---	---	---	---	---	---	---	---	---
FDA White Oak Consolidation	**---**	**43,044**	**---**	**7,883**	---	---	---	---	---	---	---	---	---	---
Other Rent and Rent Related	**---**	**71,943**	**---**	**21,501**	---	---	---	---	---	---	---	---	---	---
GSA Rental Payments	**---**	**170,208**	**---**	**1,362**	---	---	---	---	---	---	---	---	---	---
Subtotal, Salaries and Expenses Account	**9,875**	**2,800,078**	**-1,500**	**30,746**	---	**-1,800**	**2**	**16,480**	**50**	**16,300**	**22**	**8,220**	**74**	**39,200**
Buildings and Facilities Account	**---**	**11,788**	**---**	**---**			---	---	---	---	---	---	---	---
Total Budget Authority, Pre-Transfer	**9,875**	**2,811,866**	**-1,500**	**30,746**	---	**-1,800**	**2**	**16,480**	**50**	**16,300**	**22**	**8,220**	**74**	**39,200**
Non-Field Activities	**5,363**	**1,453,084**	**-1,500**	**---**	---	**-1,800**	**2**	**560**	**27**	**9,800**	**22**	**8,220**	**51**	**16,780**
Field Activities	**4,512**	**1,061,799**	**---**	**---**	---	---	---	**15,920**	**23**	**6,500**	**---**	**---**	**23**	**22,420**
Rent Activities, B&F, and White Oak	**---**	**296,983**	**---**	**30,746**	---	---	---	---	---	---	---	---	---	---
Opioids (No Year)	**8**	**94,000**	**---**	**---**	---	---	---	---	---	---	---	---	---	---
21st Century Cures	**100**	**60,000**	**---**	**---**	---	---	---	---	---	---	---	---	---	---
MCMi	**---**	**---**	**---**	**---**	---	---	---	---	---	---	---	---	---	---
Total Budget Authority with 21st Century Cures	**9,983**	**2,965,866**	**-1,500**	**30,746**	---	**-1,800**	**2**	**16,480**	**50**	**16,300**	**22**	**8,220**	**74**	**39,200**
HHS OIG transfer	**---**	**-1,500**	**1,500**	**---**	---	---	---	---	---	---	---	---	---	---
Total Budget Authority, Post-Transfer	**9,983**	**2,964,366**	**---**	**30,746**	---	**-1,800**	**2**	**16,480**	**50**	**16,300**	**22**	**8,220**	**74**	**39,200**

*CDER BA total includes $2.5 million for compounding (Bulks List) that explanatory statement calls out as "one-time."
**Biotech funding is in CFSAN BA total, but bill language identifies it in FDA HQ; will need to identify as correction in Operating Plan.
***In addition to the funding displayed in FY 2019 Annualized CR column, the Further Additional Supplemental Appropriations for Disaster Relief and Requirement Act, 2018 included $7.6 million in one-time, no-year funding for FDA.
****Funding and FTE levels for FYs 2018 - 2020 have been comparably adjusted to reflect the realignment of: intergovernmental affairs (IGA) FTE to FDA HQ; operational support FTE from FDA HQ to the centers and offices as part of implementation of FDA's Working Capital Fund (WCF); and FDA HQ organizations as per the December 2018 Congressional Notification.
*****Pay Inflation assumes a 2.6% increase in pay for Commissioned Corps and 0% for Civil Service personnel in FY 2020.

Medical Product Safety																													
Promote Domestic Manufacturing		New Domestic Drug Industry		MedTech Manufacturing		New Medical Data Enterprise		Transform Medical Device Safety, Cybersecurity, Review, and Innovation		New Platform for Drug Development		Modernizing Generic Drug Development and Review		Investment and Innovation for Rare Diseases		Opioids		Medical Countermeasures Initiatives		Integrated Pathogen Reduction of the Blood Supply		Office of Laboratory Safety		Compounding		Total Medical Product Safety		Total Changes		FY 2020 President's Budget	
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	FTE	$000	FTE	$000
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**51**	**25,320**	**3,912**	**1,084,636**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	28	8,500	1,175	334,712
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	23	16,820	2,737	749,924
2	**25,000**	**27**	**12,000**	—	—	**2**	**20,000**	—	—	**5**	**45,000**	**5**	**27,000**	**5**	**20,000**	**14**	**55,000**	**4**	**1,000**	—	—	—	—	**30**	**13,500**	**94**	**218,500**	**94**	**218,500**	**2,097**	**713,895**
2	25,000	17	10,000	—	—	2	20,000	—	—	5	45,000	5	27,000	5	20,000	2	33,158	4	1,000	—	—	—	—	20	10,700	62	191,858	62	191,858	1,301	551,084
—	—	10	2,000	—	—	—	—	—	—	—	—	—	—	—	—	12	21,842	—	—	—	—	—	—	10	2,800	32	26,642	32	26,642	796	162,811
4	**10,000**	—	—	—	—	**4**	**13,000**	—	—	—	—	—	—	—	—	—	—	**8**	**2,000**	**4**	**20,000**	—	—	—	—	**20**	**45,000**	**20**	**45,000**	**826**	**262,138**
4	10,000	—	—	—	—	4	13,000	—	—	—	—	—	—	—	—	—	—	8	2,000	4	20,000	—	—	—	—	20	45,000	20	45,000	603	220,132
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	223	42,006
—	—	—	—	—	—	**4**	**4,000**	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**4**	**4,000**	**27**	**17,880**	**801**	**192,314**
—	—	—	—	—	—	4	4,000	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	4,000	27	12,280	484	121,199
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5,600	317	71,115
—	—	—	—	**4**	**12,000**	**5**	**23,000**	**13**	**55,000**	—	—	—	—	—	—	—	—	**4**	**1,000**	—	—	—	—	—	—	**26**	**91,000**	**26**	**91,000**	**1,565**	**423,893**
—	—	—	—	4	12,000	5	23,000	13	55,000	—	—	—	—	—	—	—	—	4	1,000	—	—	—	—	—	—	26	91,000	26	91,000	1,071	338,888
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	494	85,005
—	**2,000**	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**2,000**	—	**2,000**	**301**	**66,512**
4	**1,500**	—	—	—	—	—	—	—	—	**25**	**5,000**	—	—	—	—	—	—	—	**3,000**	—	—	—	**1,000**	—	—	**29**	**10,500**	**29**	**9,000**	**620**	**180,195**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**7,883**	—	**50,927**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**21,501**	—	**93,444**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**1,362**	—	**171,570**
10	**38,500**	**27**	**12,000**	**4**	**12,000**	**15**	**60,000**	**13**	**55,000**	**30**	**50,000**	**5**	**27,000**	**5**	**20,000**	**14**	**55,000**	**16**	**7,000**	**4**	**20,000**	—	**1,000**	**30**	**13,500**	**173**	**371,000**	**247**	**439,446**	**10,122**	**3,239,524**
																										—	—	—	—	—	**11,788**
10	**38,500**	**27**	**12,000**	**4**	**12,000**	**15**	**60,000**	**13**	**55,000**	**30**	**50,000**	**5**	**27,000**	**5**	**20,000**	**14**	**55,000**	**16**	**7,000**	**4**	**20,000**	—	**1,000**	**30**	**13,500**	**173**	**371,000**	**247**	**439,446**	**10,122**	**3,251,312**
10	**38,500**	**17**	**10,000**	**4**	**12,000**	**15**	**60,000**	**13**	**55,000**	**30**	**50,000**	**5**	**27,000**	**5**	**20,000**	**2**	**33,158**	**16**	**7,000**	**4**	**20,000**	—	**1,000**	**20**	**10,700**	**141**	**344,358**	**192**	**359,638**	**5,555**	**1,812,722**
—	—	**10**	**2,000**	—	—	—	—	—	—	—	—	—	—	—	—	**12**	**21,842**	—	—	—	—	—	—	**10**	**2,800**	**32**	**26,642**	**55**	**49,062**	**4,567**	**1,110,861**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**30,746**	—	**327,729**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**-8**	**-94,000**	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**15,000**	—	**15,000**	**100**	**75,000**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10	**38,500**	**27**	**12,000**	**4**	**12,000**	**15**	**60,000**	**13**	**55,000**	**30**	**50,000**	**5**	**27,000**	**5**	**20,000**	**14**	**55,000**	**16**	**7,000**	**4**	**20,000**	—	**1,000**	**30**	**13,500**	**173**	**386,000**	**239**	**360,446**	**10,222**	**3,326,312**
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**1,500**	—	—
10	**38,500**	**27**	**12,000**	**4**	**12,000**	**15**	**60,000**	**13**	**55,000**	**30**	**50,000**	**5**	**27,000**	**5**	**20,000**	**14**	**55,000**	**16**	**7,000**	**4**	**20,000**	—	**1,000**	**30**	**13,500**	**173**	**386,000**	**239**	**361,946**	**10,222**	**3,326,312**

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 2020 Budget, since the location of programs may have changed in prior years or be proposed for change in FY 2020. This approach allows increases and decreases in this book to reflect true funding changes.

FY 2020 REALLOCATIONS

(Dollars in Thousands)	WCF Realignment		IGA Staff		HQ Reorganization		Total	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:								
Foods	**44**	**11,024**	**-1**	**-359**	**30**	**7,036**	**73**	**17,701**
Center	16	3,375	-1	-219	27	6,450	42	9,606
Field	28	7,649	---	-140	3	586	31	8,095
Human Drugs	**---**	**---**	**-3**	**-596**	**2**	**388**	**-1**	**-208**
Center	---	---	-3	-558	2	388	-1	-170
Field	---	---	---	-38	---	---	---	-38
Biologics	**8**	**1,821**	**---**	**-126**	**---**	**---**	**8**	**1,695**
Center	6	1,195	---	-115	---	---	6	1,080
Field	2	626	---	-11	---	---	2	615
Animal Drugs and Feeds	**8**	**1,969**	**---**	**-87**	**---**	**---**	**8**	**1,882**
Center	5	1,084	---	-70	---	---	5	1,014
Field	3	885	---	-17	---	---	3	868
Devices and Radiological Health	**12**	**2,762**	**---**	**-83**	**1**	**150**	**13**	**2,829**
Center	7	1,477	---	-58	1	150	8	1,569
Field	5	1,285	---	-25	---	---	5	1,260
National Center for Toxicological Research	**6**	**1,181**	**---**	**---**	**---**	**---**	**6**	**1,181**
FDA Headquarters	**-78**	**-18,757**	**4**	**1,251**	**-33**	**-7,574**	**-107**	**-25,080**
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	**-38**	**-10,445**	**---**	**231**	**-3**	**-586**	**-41**	**-10,800**
Field Activities	**38**	**10,445**	**---**	**-231**	**3**	**586**	**41**	**10,800**
Rent Activities, B&F, and White Oak	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**

*Reflects reallocated funding across the programs for FDA WCF OO realigment as well as to better align the funding structure to services related to intergovernmental affairs.

**This realignment results in a net reduction of $40.1 million ($18.8M BA / $21.3M UF) / 196 FTEs from FDA Headquarters and redistributes the funding to the Programs that will benefit from the services of the WCF. The APT and related tables have been comparably adjusted to reflect the realignment of: intergovernmental affairs (IGA) FTE to FDA HQ; operational support FTE from FDA HQ to the centers and offices as part of implementation of FDA's Working Capital Fund (WCF); and FDA HQ organizations as per the December 2018 Congressional Notification.

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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; $5,833,942,000: Provided, That of the amount provided under this heading, $1,062,367,000 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; $219,527,000 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; $511,682,000 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; $39,618,000 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; $30,524,000 shall be derived from animal drug user fees authorized by 21 U.S.C. 379j-12, and shall be credited to this account and remain available until expended; $18,700,000 shall be derived from generic new animal drug user fees authorized by 21 U.S.C. 379j-21, 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, biosimilar biological product user fees, animal drug user fees, and generic animal drug user fees that exceed the respective fiscal year 2020 limitations are appropriated and shall be credited to this account and remain available until expended: Provided further, That fees derived from prescription drug, medical device, human generic drug, biosimilar biological product, animal drug, and generic animal drug assessments for fiscal year 2020, including any such fees collected prior to fiscal year 2020 but credited for fiscal year 2020, shall be subject to the fiscal year 2020 limitations: Provided further, That the Secretary may accept payment during fiscal year 2020 of user fees specified under this heading and authorized for fiscal year 2021, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2021 for which the Secretary accepts payment in fiscal year 2020 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 innovative food products activities and over-the-counter monograph drug activities: Provided, That fees of $28,000,000 for innovative food products, shall be credited to this account and remain available until expended; $28,400,000 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 innovative food products and over-the-counter monograph drug user fees that exceed the respective fiscal year 2020 limitations are appropriated and shall be credited to this account and remain available until expended: Provided further, That fees derived from innovative food products, and over-the-counter monograph drug reviews for fiscal year 2020 received during fiscal year 2020, including any such fees assessed prior to fiscal year 2020 but credited for fiscal year 2020, shall be subject to the fiscal year 2020 limitations: Provided further, That the Secretary may accept payment during fiscal year 2020 of user fees specified in this paragraph and authorized for fiscal year 2021, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2021 for which the Secretary accepts payment in fiscal year 2020 shall not be included in amounts in this paragraph.
In addition, contingent upon the enactment of authorizing legislation establishing fees under 21 U.S.C. 387s with respect to products deemed under 21 U.S.C. 387a(b) but not specified in 21 U.S.C. 387s(b)(2)(B), the Secretary shall assess and collect such fees: Provided, That $100,000,000 shall be derived from such fees, which shall be credited to this account and remain available until expended, in addition to amounts otherwise derived from fees authorized under 21 U.S.C. 387s.

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", $75,000,000, 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.

Note.—A full-year 2019 appropriation for this account was not enacted at the time the budget was prepared; therefore, the budget assumes this account is operating under the Continuing Appropriations Act, 2019 (Division C of P.L. 115–245, as amended). The amounts included for 2019 reflect the annualized level provided by the continuing resolution.

FY 2020 PROPOSED GENERAL PROVISIONS

Sec. 723. 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 2020; 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
Innovative Food Products User Fee	The Administration will propose legislation to allow FDA to collect fees for Innovative Food Products. The additional resources are estimated at $28,000,000. This will modernizing FDA's regulatory oversight of innovative biotechnology products and emerging food production technologies
Tobacco Control Act Fee Increase	The Administration proposes legislation to increase the fees collected under the Tobacco Control Act by $100,000,000. This will allow FDA to include all deemed products in the tobacco user fee assessments
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.
Over the Counter Monograph	The Administration supports legislation to allow FDA to collect fees for over the counter monograph. The additional resources are estimated at $28,400,000. 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 2018 Final	FY 2019 Annualized CR	FY 2020 President's Budget
General Fund Discretionary Appropriation:			
Appropriation	2,964,366	2,964,366	3,326,312
Total Discretionary Appropriation	**2,964,366**	**2,964,366**	**3,326,312**
Mandatory Appropriation:			
CRADA	2,000	2,000	2,000
Total Mandatory Appropriation	**2,000**	**2,000**	**2,000**
Offsetting Collections:			
Non-Federal Sources:	2,396,269	2,534,633	2,815,774
Total Offsetting Collections	**2,396,269**	**2,534,633**	**2,815,774**
Total Obligations	**5,362,635**	**5,500,999**	**6,144,086**

*For FY 2018 an FY 2019 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 2020, FDA proposes to discontinue the transfer.

SUMMARY OF CHANGES

(dollars in thousands)	Budget Authority	User Fees	Program Level	*FTE
FY 2019 Annualized CR	**2,964,366**	**2,534,633**	**5,498,999**	**17,607**
FY 2020 Program Changes				
Budget Authority Changes				
Infrastructure and B&F	30,746	---	30,746	---
Seafood Decomposition Study; Biotech Education; Botanical Supplement Research	-1,800	---	-1,800	---
Advancing FSMA	16,480	---	16,480	2
Strengthening Response Capabilities for Foodborne Outbreaks	16,300	---	16,300	50
Promoting Innovation and Emerging Technology While Maintaining Product Safety	8,220	---	8,220	22
Promote Domestic Manufacturing	38,500	---	38,500	10
New Domestic Drug Industry	12,000	---	12,000	27
MedTech Manufacturing	12,000	---	12,000	4
New Medical Data Enterprise	60,000	---	60,000	15
Transform Medical Device Safety, Cybersecurity, Review, and Innovation	55,000	---	55,000	13
New Platform for Drug Development	50,000	---	50,000	30
Modernizing Generic Drug Development and Review	27,000	---	27,000	5
Investment and Innovation for Rare Diseases	20,000	---	20,000	5
Opiods-International Mail Facilities (IMF)	55,000	---	55,000	14
Medical Countermeasures Initiatives	7,000	---	7,000	16
Integrated Pathogen Reduction of the Blood Supply	20,000	---	20,000	4
Office of Laboratory Science and Safety	1,000	---	1,000	---
Compounding	13,500	---	13,500	30
Opioids (No Year)	-94,000	---	-94,000	-8
21st Century Cures	15,000	---	15,000	---
Total Budget Authority Changes	**361,946**	**---**	**361,946**	**239**
User Fee Changes				
Current Law				
Prescription Drug (PDUFA)	---	52,044	52,044	58
Medical Device (MDUFA)	---	14,797	14,797	40
Generic Drug (GDUFA)	---	9,961	9,961	1
Biosimilars (BsUFA)	---	771	771	16
Animal Drug (ADUFA)	---	193	193	---
Animal Generic Drug (AGDUFA)	---	365	365	---
Family Smoking Prevention and Tobacco Control Act	---	40,000	40,000	49
Indefinite				
Mammography Quality Standards Act (MQSA)	---	829	829	---
Color Certification	---	472	472	---
Export Certification	---	---	---	---
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	311	311	---
Food and Feed Recall	---	58	58	---
Food Reinspection	---	259	259	---
Voluntary Qualified Importer Program	---	215	215	---
Third Party Auditor Program	---	30	30	---
Outsourcing Facility	---	156	156	---
Export Certification (Proposed)	---	4,280	4,280	---
Over the Counter Monograph (Proposed)	---	28,400	28,400	---
Innovative Food Products (Proposed)	---	28,000	28,000	52
Expand Tobacco Product (Proposed)	---	100,000	100,000	---
Subtotal, Current Law	**---**	**281,141**	**281,141**	**216**
Net Program Changes	**361,946**	**281,141**	**643,087**	**455**
Total FDA Request for FY 2020	**3,326,312**	**2,815,774**	**6,142,086**	**18,062**

* FTE figures do not include an estimated 87 reimbursable, 2 CRADA, 2 FOIA, and 36 PEPFAR.

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2018 Final	FY 2019 Annualized CR	FY 2020 President's Budget
Salaries and Expenses Account:			
Foods	**1,059,316**	**1,059,316**	**1,084,636**
Center	326,212	326,212	334,712
Field	733,104	733,104	749,924
Human Drugs	**495,395**	**495,395**	**713,895**
Center	359,226	359,226	551,084
Field	136,169	136,169	162,811
Biologics	**217,138**	**217,138**	**262,138**
Center	175,132	175,132	220,132
Field	42,006	42,006	42,006
Animal Drugs and Feeds	**174,434**	**174,434**	**192,314**
Center	108,919	108,919	121,199
Field	65,515	65,515	71,115
Devices and Radiological Health	**332,893**	**332,893**	**423,893**
Center	247,888	247,888	338,888
Field	85,005	85,005	85,005
National Center for Toxicological Research	**64,512**	**64,512**	**66,512**
FDA Headquarters	**171,195**	**171,195**	**180,195**
FDA White Oak Consolidation	**43,044**	**43,044**	**50,927**
Other Rent and Rent Related	**71,943**	**71,943**	**93,444**
GSA Rental Payments	**170,208**	**170,208**	**171,570**
Subtotal, Salaries and Expenses Account	**2,800,078**	**2,800,078**	**3,239,524**
21st Century Cures	**60,000**	**60,000**	**75,000**
Opioids - No Year	**94,000**	**94,000**	**---**
Buildings and Facilities Account	**11,788**	**11,788**	**11,788**
Total Budget Authority	**2,965,866**	**2,965,866**	**3,326,312**
HHS OIG transfer	**-1,500**	**-1,500**	**---**
Total Budget Authority, Post-Transfer	**2,964,366**	**2,964,366**	**3,326,312**
FTE	**9,988**	**9,983**	**10,222**

*For FY 2018 and FY 2019 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 2020, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 83 reimbursable, 44 PEPFAR, and 5 Emerging Health Threats.

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	4,651,392,000
FY 2017 2/	4,953,946,000	4,649,566,000	4,655,869,000	4,655,089,000
FY 2018	5,044,110,000	5,095,301,000	5,098,341,000	5,138,041,000
FY 2019	5,632,141,000	5,624,076,000	5,475,365,000	
FY 2020	5,990,342,000			

* 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 excludes $10 million in no-year funding to address Emerging Public Health Threats.

Totals do not include funds for 21st Century Cures which are $20 million for FY 2018, $60 million for FY 2018, $70 million for FY 2019 and $75 million for FY 2020.

Buildings and Facilities

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation:				
FY 2008	4,950,000	4,950,000	4,950,000	2,433,000
FY 2009	2,433,000		12,433,000	12,433,000
FY 2010	12,433,000	12,433,000	12,433,000	12,433,000
FY 2011	12,433,000		9,980,000	9,980,000
FY 2012	13,055,000	8,788,000	8,788,000	8,788,000
FY 2013				
Base	5,320,000	---	5,320,000	5,176,000
Sequestration	---	---	---	-256,000
Subtotal	5,320,000	---	5,320,000	4,920,000
FY 2014	8,788,000	---	11,000,000	8,788,000
FY 2015	8,788,000	8,788,000	8,788,000	8,788,000
FY 2016	8,788,000	8,788,000	8,788,000	8,788,000
FY 2017	11,788,000	11,788,000	11,788,000	11,788,000
FY 2018	8,771,000	8,771,000	11,788,000	11,788,000
FY 2019	11,788,000	11,788,000	11,788,000	
FY 2020	11,788,000			

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OVERVIEW OF LEGISLATIVE PROPOSALS

The FY 2020 Budget Request includes legislative proposals to address drug pricing, medical product shortages, and other priority areas.

DRUG PRICING PROPOSALS

Amend the 180-day Exclusivity Forfeiture Provision Addressing Failure to Obtain Tentative Approval

Currently, a first applicant for a generic drug forfeits 180-day exclusivity if they fail to obtain tentative approval (TA) for their application within a specific timeframe. A first applicant can avoid forfeiture under this provision if the failure to obtain TA is caused by a change in or a review of the requirements for approval imposed after the application filing date. Currently, first applicants with deficient applications benefit from this provision by avoiding forfeiture even though they have deficiencies in their application unrelated to any change in or review of the requirements for approval. The proposal would clarify that the exception to forfeiture will only apply if the change in or review of the requirements for approval was the only cause of the applicant's failure to obtain TA within the specified timeframe. Depending on the factual circumstances, this change can result in increased generic competition and choice for consumers by allowing final approval of competing generic drugs that otherwise would generally have had to wait until the first applicant with the deficient application has been approved and the 180-day exclusivity period has run before being approved by FDA.

Provide FDA Enhanced Authority to Address Abuse of the Petition Process

Section 505(q) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) was intended, in part, to help prevent submission of sham citizen petitions intended to delay the approval of abbreviated new drug applications (ANDAs) and to avoid FDA delaying approval of ANDAs because of such citizen petitions. This proposal would amend section 505(q) to provide FDA with greater flexibility to summarily deny petitions that impede competition and eliminate the mandatory 150-day response timeframe, as it is no longer needed to prevent delay of approval of ANDAs given passage of the Food and Drug Administration Reauthorization Act of 2017, which reauthorized the Generic Drug User Fee Amendments, providing goal dates for FDA to take action on all ANDAs.

Generics Condition on Exclusivity to Spur Access and Competition

Under current law, a first applicant of an ANDA that does not have patent/exclusivity barriers to approval, but is not approvable due to substantive deficiencies that have not been resolved in a timely manner, can block subsequent ANDA approvals under the 180-day exclusivity provisions of the FD&C Act. Similarly, a first applicant whose ANDA is otherwise approvable could intentionally delay seeking final approval, "parking" their 180-day exclusivity and blocking subsequent ANDA approvals. Current law is often insufficient to address these circumstances and, as a result, consumers may be denied access to generic products. This proposal would make 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 to start the first applicant's 180-day exclusivity. The change will enhance competition and facilitate more timely access to generic drugs.

Revision of USP Compendial Compliance Requirements for Biological Products

FD&C Act provisions that relate to U.S. Pharmacopeial (USP) compendial standards, which were originally drafted to apply to drugs approved under section 505 of the FD&C Act, currently apply to biological products licensed under section 351 of the Public Health Service (PHS) Act. Current law could result in delays, related to compliance with USP standards, in the licensure of biosimilar and interchangeable products that meet FDA's robust scientific standards. This proposal would amend section 351(j) of the PHS Act to exclude all biological products licensed under the PHS Act from FD&C Act provisions that relate to USP standards for drugs. FDA seeks this change to facilitate biological product innovation and the timely licensure of biosimilar and interchangeable products.

Codify Our Active Moiety Approach for New Chemical Entity (NCE) Determinations

The Agency's regulation implementing the statutory provisions on 5-year New Chemical Entity (NCE) exclusivity focuses on evaluating a drug's active moiety. Under this regulation, eligibility for NCE exclusivity is available only for a drug containing no active moiety that has been previously approved by FDA. This approach ensures that only the most innovative drugs qualify for NCE exclusivity, while allowing for earlier generic competition for drugs that do not qualify. A recent district court decision (*Amarin Pharmaceuticals Ireland Ltd. v. FDA)* invalidated an FDA NCE exclusivity decision that applied FDA's active moiety regulation based on the court's interpretation of the statute's "plain meaning." This decision has resulted in uncertainty about FDA's ability to continue to apply its regulation. This proposal would codify FDA's long-standing "active moiety" approach, and would provide clarity about Congress' intent that only the most innovative new drugs qualify for NCE exclusivity.

PROPOSALS TO ADDRESS MEDICAL PRODUCT SHORTAGES

Lengthen Expiration Dates to Mitigate Critical Drug Shortages

Shortages of drugs that are life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, can be exacerbated when drugs must be discarded because they exceed a labeled shelf-life due to unnecessarily short expiration dates. This proposal would expand FDA's authority to require, when likely to help prevent or mitigate a shortage, that an applicant evaluate, submit studies to FDA, and label a product with the longest possible expiration date that FDA agrees is scientifically justified.

Improving Critical Infrastructure by Requiring Risk Management Plans

This proposal would expand FDA's authority to require application holders of certain drugs to conduct periodic risk assessments to identify the vulnerabilities in their manufacturing supply chain (inclusive of contract manufacturing facilities) and develop plans to mitigate the risks associated with the identified vulnerabilities. Currently, many applicants lack plans to assess and

address vulnerabilities in their manufacturing supply chain putting them at risk for drug supply disruptions following disasters (e.g., hurricanes) or in other circumstances.

Improving Critical Infrastructure Through Improved Data Sharing: Requiring More Accurate Supply Chain Information

This proposal would clarify FDA's authority to require information that would improve FDA's ability to assess critical infrastructure as well as manufacturing quality and capacity. For example, FDA is seeking to require detailed drug listings for finished drug product or in-process material, regardless of whether they were directly or indirectly imported into the U.S.

Device Shortages

No law requires medical device manufacturers to notify FDA when they become aware of a circumstance that could lead to a device shortage. Such circumstances may include, for example: discontinuation of a device; interruption of the manufacture of the device, e.g., due to scarcity of a raw material or unavailability of a component part; or loss of or damage to a manufacturing facility. This proposal would ensure FDA has timely and accurate information about likely or confirmed national shortages of essential devices to enable FDA to take steps to promote the continued availability of devices of public health importance. Specifically, FDA is seeking authority to: require firms to notify FDA of an anticipated significant interruption in the supply of an essential device; require all manufacturers of devices determined to be essential to periodically provide FDA with information about the manufacturing capacity of the essential device(s) they manufacture; and authorize the temporary importation of devices whose risks presented when patients and healthcare providers lack access to critically important medical devices outweigh compliance with U.S. regulatory standards.

OTHER FDA PROPOSALS

Updating the Labeling of Generic Drugs After the New Drug Application or New Animal Drug Application Reference Listed Drug is Withdrawn

FDA is aware that generic drug labeling sometimes becomes outdated after approval of the reference listed drug (RLD) is withdrawn at the request of its sponsor. This proposal would give FDA explicit authority to update the labeling of generic drugs with withdrawn new drug application (NDA) or new animal drug application (NADA) RLDs when the generic labeling becomes outdated, including to update the uses to reflect the current state of the science. This would ensure that labeling of generic drugs continues to provide healthcare professionals and consumers with the most up-to-date information about the use of the drugs even after the NDA or NADA RLD is no longer on the market.

Exemptions from "Wholesale Distribution" for Dispenser-to-Dispenser Transactions and for Entities That Distribute Drugs under Federally-Administered Programs

This proposal would allow certain dispenser-to-dispenser sales of drug products to be exempted

from the definition of wholesale distribution and authorize FDA to exempt entities that distribute drugs under Federally-administered programs from the wholesale distributor licensing requirements of the Drug Supply Chain Security Act (DSCSA). The proposed changes to the statutory definition of "wholesale distribution" would decrease regulatory burdens under the DSCSA for certain entities and help ensure patients who rely on Federally-administered programs have access to needed drug products.

Increase the Statutory Maximum and Add an Inflation Factor for FDA's Export Certificate Fee

Export certificates are required by some countries for a company to export a product from the U.S. into the requesting country. Multiple FDA centers provide export certificates in exchange for export certificate fees. Current law, originally enacted in 1996, limits the maximum export certification fee to $175, which is less than the current cost per certification to run this program. This proposal would increase the statutory maximum for the export certification fee to $600 per certification and include a provision to adjust this cap for inflation.

Advisory Committees/Public Discussions

Data and information relating to an issue that is appropriate for public consideration may be provided to FDA through varied medical product submission pathways like annual reports, periodic safety update reports, general correspondence, and in withdrawn submissions. These pathways can be outside the scope of regulations authorizing disclosure of summary safety and effectiveness information pursuant to a Commissioner's Finding, and FDA therefore typically cannot disclose these data and information at an FDA advisory committee or other appropriate public meeting without the sponsor's permission. This limitation hinders FDA's ability to have full and complete public discussions about important scientific and regulatory issues and this proposal would provide clear authority for FDA to publicly disclose a summary of any safety and/or effectiveness data and information pursuant to a determination that it is appropriate for public consideration of a specific issue; for example, for consideration at an open session of an FDA advisory committee; an FDA public hearing; or a public congressional hearing.

Post-Approval Quality Updates

FDA has commonly requested that applicants agree (or commit) to provide certain information or studies in post-approval supplements or reports to address residual quality risks that are identified pre-approval but are not found to be significant enough to delay approval. Unlike post-marketing requirement studies, reports on quality-related post-approval agreements are not legally enforceable requirements. FDA, therefore, has limited ability to take enforcement action if an applicant does not submit the agreed-upon information, short of proposing to withdraw approval of the application. This proposal would grant FDA authority to require NDA, biologics license application (BLA), or abbreviated new drug application (ANDA) applicants to submit a post-approval quality update to provide information or implement changes needed to ensure ongoing quality and, therefore, safety and efficacy of the product once approved and marketed.

Medical Device Cybersecurity

Currently, there is no statutory requirement (pre- or post-market) that expressly compels medical device manufacturers to address cybersecurity. This proposal would advance medical device safety by ensuring FDA and the public have information about the cybersecurity of devices. Specifically, FDA seeks to require: that devices have the capability to be updated and patched in a timely manner; that premarket submissions to FDA include evidence demonstrating the capability from a design and architecture perspective for device updating and patching; a phased-in approach to a Cybersecurity Bill of Materials (CBOM), a list that includes but is not limited to commercial, open source, and off-the-shelf software and hardware components that are or could become susceptible to vulnerabilities; and that device firms publicly disclose when they learn of a cybersecurity vulnerability so users know when a device they use may be vulnerable and to provide direction to customers to reduce their risk. The proposal also seeks to improve proactive responses to cybersecurity vulnerabilities.

Performance Criteria for Premarket Notification Determinations

Under this proposal, FDA would establish a voluntary alternative to the premarket notification (510(k)) pathway that would allow manufacturers of certain well-understood device types to rely on objective safety and performance criteria to demonstrate substantial equivalence, enabling FDA to help improve safety and performance and ensure new products can more easily reflect beneficial new advances. Current law requires sponsors of 510(k)s for medical devices to demonstrate substantial equivalence by comparing the intended use and technological characteristics of their device to a predicate device. The proposal would permit the marketing of certain Class II and Class I medical devices requiring premarket notification if such devices demonstrate conformance with pre-specified safety and performance criteria established by FDA based on the performance of modern predicates as well as FDA-recognized performance standards, or other FDA-recognized national and international standards, if applicable and appropriate, and as explained in Level 2 guidance. This voluntary alternative would provide more direct evidence of the safety and performance of a device and better information for patients and providers to make well-informed health care decisions while fostering a competitive marketplace for safer, more effective devices.

Progressive Approval for Devices

This proposal would permit FDA expedited access to devices that would otherwise be reviewed under the premarket approval or de novo classifications pathways if they are intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition and address an unmet medical need using a two-step approval. These devices would be eligible for provisional approval based on a demonstration of safety and performance plus additional risk mitigations and could remain on the market after an established time period only after a demonstration of reasonable assurance of safety and effectiveness. Companies would be required to gather postmarket data from established data sources to assure timely evidence generation. Permitting an initial, provisional approval of a device based on a standard of safety and performance would encourage manufacturers to seek introduction of their devices in the U.S. earlier, thereby allowing patients with few to no options for treatment earlier access to important medical

technology. Moreover, if a company did not demonstrate reasonable assurance of safety and effectiveness within a reasonable amount of time after initial approval is granted, the initial approval would automatically sunset and the device could no longer be legally marketed. This proposal would help improve patient access to technologies for some of the most challenging health circumstances, and would provide accountability to ensure that devices fully demonstrate safety and effectiveness to remain on the market.

Special Controls Via Order

Under this proposal, FDA would modernize the process to impose, add, revise, or eliminate special controls for class II devices by using an administrative order rather than regulation. This would ensure FDA is equipped to provide a nimbler process to mitigate risk and address safety signals in the postmarket setting, and allow timely patient access to innovative technologies. Currently, FDA can require companies to implement mitigations (e.g., labeling, user training, device features) through the imposition of additional special controls. However, because the establishment of special controls requires rulemaking, which can entail extensive resources and time, it can be challenging for FDA to mitigate risk and address safety issues quickly, and it can also delay marketing of useful devices that could benefit patients with appropriate risk mitigation measures. This proposal would increase transparency about FDA expectations and requirements for ensuring a device's safety and effectiveness and allow FDA to act more quickly in the interest of patients.

Enable FDA to Phase Out Publication of Animal Drug Approval Information in the Code of Federal Regulations

Under current law, when a new animal drug application is approved or conditionally approved, the Secretary must publish a Federal Register (FR) document that provides notice of the approval and creates a regulation for inclusion in the Code of Federal Regulations. This proposal would enable FDA to phase out publication of new animal drug approvals in the FR and make this information publicly available online only.

Enhance Availability of Generic Animal Drugs

This proposal would allow FDA to clarify labeling requirements for generic animal drugs by explicitly including an exception from the requirement that a generic animal drug's labeling be the same as the labeling of a reference-listed new animal drug (RLNAD) where the RLNAD is approved in more than one species. The exception would allow a generic animal drug manufacturer to seek approval for fewer species than on a RLNAD's labeling, particularly in situations where obtaining bioequivalence information for all species is impractical or scientifically challenging.

Enable Certain Products to be Excluded from Definition of "New Animal Drug" to Allow Their Regulation as Pesticide

This proposal would revise the definition of "new animal drug" to provide the ability to exclude certain products or categories of products that FDA and EPA agree are more appropriately regulated as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act. Revising the definition would increase transparency and decrease regulatory uncertainty, which currently contributes to inefficiencies and increased costs for sponsors.

Strengthen FDA's Implementation and Enforcement of DSHEA

In the 25 years since the Dietary Supplement Health and Education Act of 1994 (DSHEA) was enacted, the dietary supplement market in the U.S. has grown from approximately 4,000 products to somewhere between 50,000 and 80,000 products. Under current law, FDA is not clearly authorized to require listing of individual dietary supplement products on the market, and the Agency has no convenient mechanism for compiling basic information about those products. This proposal would require all products marketed as "dietary supplements" to be listed with FDA and give FDA authority to act against non-compliant products and the manufacturers and/or distributors of such products. This would allow FDA to know when new products are introduced, quickly identify and act against dangerous or otherwise illegal products, and improve transparency and promote risk-based regulation.

Amend FDA Authorities to Strengthen FDA's Training Programs

Due to gaps in current law, FDA has been unable to establish a comprehensive, in-house training program that meets its needs. FDA has relied heavily instead on participation in a contract program, known as the Oak Ridge Science Institute for Science and Education (ORISE) program, under an interagency agreement with the Department of Energy, to meet the agency's training needs. This proposal would enable FDA to establish its own comprehensive training. Because trainees will be subject by law to the same legal and ethical requirements as FDA employees, trainees will be subject to the same non-disclosure prohibitions as FDA employees and will be provided access to confidential information only on an as-needed basis.

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NARRATIVE BY ACTIVITY

FOODS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
Foods	**1,070,187**	**1,059,291**	**1,070,187**	**1,122,047**	**51,860**
Budget Authority	***1,059,316***	***1,059,291***	***1,059,316***	***1,084,636***	***25,320***
User Fees	***10,871***	---	***10,871***	***37,411***	***26,540***
Center	327,044	326,210	327,044	361,678	34,634
Budget Authority	326,212	326,210	326,212	334,712	8,500
User Fees	832	---	832	26,966	26,134
Food and Feed Recall	243	---	243	253	10
Voluntary Qualified Importer Program	243	---	243	253	10
Third Party Auditor Program	346	---	346	360	14
Innovative Food Products (Proposed)	---	---	---	26,100	26,100
Field	743,143	733,081	743,143	760,369	17,226
Budget Authority	733,104	733,081	733,104	749,924	16,820
User Fees	10,039	---	10,039	10,445	406
Food and Feed Recall	1,000	---	1,000	1,040	40
Food Reinspection	4,575	---	4,575	4,760	185
Voluntary Qualified Importer Program	4,320	---	4,320	4,495	175
Third Party Auditor Program	144	---	144	150	6
FTE	**3,861**	**3,861**	**3,905**	**4,008**	**103**

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.

In collaboration with the Office of Regulatory Affairs (ORA), the Center for Food Safety and Applied Nutrition (CFSAN) administers the Foods Programs. 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 Office of Food Policy and Response (OFPR) provides executive leadership, management, and strategic direction for FDA's foods initiatives. OFPR also directs efforts to integrate the programs, policies, and budgets of CFSAN, the Center for Veterinary Medicine (CVM), and ORA and thereby ensure the optimal use of all available FDA resources.

The following accomplishments demonstrate the Foods Program's delivery of its regulatory and public health responsibilities and progress towards reaching the goals outlined in the FDA Commissioner's FY 2019 Priorities.

Strengthen Science and Efficient Risk-Based Decision Making

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 Foods Program prioritizes the prevention of foodborne and feed-borne illness of both known and unknown origins through the implementation of the FDA Food Safety Modernization Act (FSMA) and other legislative authorities. 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.

Nutrition-related priorities are another focus area 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 2018,

[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

90 percent of the nation's health care expenditures were for people with one or more chronic medical conditions.[12]

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 listed above, the Foods Program conducts other important activities related to food safety, nutrition, and cosmetics. These activities 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

The FDA Food Safety Modernization Act (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.

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.[13] 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 heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. To date, FDA has awarded 46 states and 1 territory a total of $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. FDA also issued a cooperative agreement with the National Association of State Departments of Agriculture (NASDA) to develop a national consortium of state and federal regulators to further states' implementation of their produce safety programs. FDA also worked with NASDA in 2018 to finalize resource materials and to

[12] 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.

[13] https://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm

train states to implement the On-Farm Readiness Review (OFRR) program, which allows farms to request a review by regulators of the readiness of their operations for produce safety rule (PSR) implementation.

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

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.
Jan 2017	FDA 2011-N-0146	FSMA Final Rule: Amendments to Accreditation of Third-Party Certification Bodies to Conduct Food Safety Audits	Amends regulations on accreditation of third-party certification bodies to conduct food safety audits and to issue certifications to provide for a reimbursement (user fee) program to assess fees for the work FDA performs to establish and administer the third-party certification program under the FSMA.

Sanitary Transport of Food and Feed

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.

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 software tool for food facility owners and operators to use to create facility-specific food safety plans. 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.

Updated Guidance for Foreign Supplier Verification Programs (FSVP) Rule

FSVP is another one of the seven foundational FSMA rules. A central tenet of FSVP 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.

Selected Guidances Issued in 2018

Below are selected non-FSMA guidances issued by the Foods Program this calendar year. These guidances help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances**.** [14]

Date	#	Title	Description
Jun 2018	FDA 2018-D-1323	Guidance for Industry: Declaration of Certain Isolated or Synthetic Non-Digestible Carbohydrates as Dietary Fiber on Nutrition and Supplement Facts Labels	Permits manufacturers to move forward in updating labels regarding dietary fiber and implement the new Nutrition Facts and Supplement Facts label. The updated labels will better equip consumers with nutritional information on dietary fiber.
May 2018	FDA-2012-N-1210	Guidance for Industry: Revision of the Nutrition and Supplement Facts Labels and Serving Sizes	Provides questions and answers on topics related primarily to two final rules: (1) "Food Labeling: Serving Sizes of Foods and (2) "Food Labeling: Revision of the Nutrition and Supplement Facts Labels."
May 2018	FDA 2011-F-0172	Guidance for Industry: Menu Labeling Supplemental Guidance	Addresses stakeholder's' concerns about the implementation of nutrition labeling required for foods sold in covered

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

Date	#	Title	Description
			establishments. It also clarifies the additional options for complying with the labeling requirements and explains where FDA intends to be more flexible.
Apr 2018	FDA 2018-D-1189	Guidance for Industry: Highly Concentrated Caffeine in Dietary Supplements	Provides guidance to firms that manufacture, market, or distribute dietary supplement products that contain pure or highly concentrated caffeine, or are considering doing so.
Feb 2018	FDA 2006-P-0207	Guidance for Industry: Proper Labeling of Honey and Honey Products	Advise the regulated industry on the proper labeling of honey and honey products in accordance with sections 402 and 403 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 342 and 343) and its implementing regulations.

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 *E. coli* outbreak associated Romaine lettuce
- 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 20176, a total of 293 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 sixth year and has collected more than 280,000 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 better protect public health by:

- investigating outbreaks faster and more efficiently
- adding 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 2018, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions. To date, WGS has supported more than 370 cases of product adulteration and contaminated 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. Using WGS, likely prevented additional consumers from failing ill and conserved resources by limiting the scope of the FDA investigation to the specific facility producing the 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. Using WGS permitted source tracking back to specific overseas agricultural regions and allowed for the rapid identification of different serological variants of Salmonella as they emerged from contaminated papaya samples.[15]

FDA Finalizes Guidance on Mandatory Recall Authority

In November 2018, FDA released a final guidance regarding the agency's mandatory recall authority under FSMA.[16] The 2011 food safety law gave FDA mandatory recall authority for foods if there is a reasonable probability that the food is adulterated or misbranded under certain FDA authorities, and that the food could cause serious illnesses or death. FDA must give the responsible party an opportunity to conduct a voluntary recall before ordering a mandatory recall. Prior to the enactment of FSMA, FDA could only rely on manufacturers to voluntarily recall certain potentially harmful food products.

This final guidance follows a draft which was made available for public comment in 2015, and provides additional clarity including some modifications based on comments received. The guidance provides questions and answers on FDA's mandatory recall process, explains what FDA considers when moving forward with a mandatory recall, and more.

FDA has issued a mandatory recall order of a food product only once. In April 2018, FDA issued a mandatory recall order for all food products containing powdered kratom manufactured, processed, packed, or held by Triangle Pharmanaturals LLC, after several products were found to contain Salmonella. In two other instances, FDA started down the path of using its mandatory recall authority under FSMA until the companies ultimately chose to voluntarily recall their product.

While FDA's mandatory recall authority plays an important role in ensuring that potentially dangerous food products are removed from the marketplace, the agency remains committed to working with firms to facilitate the orderly and prompt voluntary removal of potentially

[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] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm445428.htm

dangerous products from the food supply. FDA Recall Coordinators are available to assist firms during the recall process.

Provided Resources for Food Producers in Flooded Areas Due To Hurricane Michael

FDA has provided several resources to aid farmers whose crops may have been impacted by the flooding and severe weather associated with Hurricane Michael. The FDA's Guidance for Industry: "Evaluating the Safety of Flood-affected Food Crops for Human Consumption," provides information that producers can use while assessing potential damage to their food crops.[17] This guidance is an important tool used in assuring the safety of flood-affected food crops for human consumption.

FDA reminds harvesters that generally, if the edible portion of a crop is exposed to contaminated flood waters, it is considered "adulterated" under the Federal, Food, Drug and Cosmetic Act and should not enter the human food supply. This applies to all food crops including underground crops such as peanuts and potatoes. For crops such as pecans that were in or near flooded areas but where flood waters did NOT contact the edible portions of the crops, the growers should evaluate the safety of the crops for human consumption on a case-by-case basis for possible food safety concerns.

Issued New Export Certificates for Certain Foods

In August 2018, FDA announced its new export certification program for certain FDA-regulated food products and the fees it will assess for issuing new export certifications to U.S.-based exporters of these products. The new export certification and fees were authorized by FSMA amendments to the FD&C Act and allow allowing the agency to collect up to $175 for the first export certification for food, which covers up to 25 products.

FDA issues different types of export certification for different food products. The "Certificate to a Foreign Government" and "Certificate of Exportability" are now available for food for human consumption, except for dietary supplements, medical foods, and foods for special dietary use.

The "Certificate to a Foreign Government" is available for conventional foods, food additives, food contact substances, and infant formula that meet the applicable requirements of the FD&C Act. This certificate certifies that a product (or products) may be marketed in and legally exported from the United States.

The "Certificate of Exportability" is available for export-only conventional foods, food additives, food contact substances, and infant formula. This certificate certifies that a product (or products) meet(s) the requirements of section 801(e)(1) of the FD&C Act and may be legally exported.

FDA anticipates that the new certificates will help facilitate exports by assisting industry in fulfilling importing country requirements for certification by FDA of FDA-regulated food products. Additionally, the electronic form for the new certificates responds to numerous industry requests for additional flexibility on regarding the information that is printed on export certificates.

FDA Recognizes New Accreditation Bodies under Accredited Third-Party Certification Program; Launches Voluntary Qualified Importer Program

[17] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm287808.htm

FDA has recognized four accreditation bodies under the voluntary Accredited Third-Party Certification Program, this voluntary program was developed as per Section 307 of the FDA Food Safety Modernization (FSMA).[18] The four entities recognized so far are: ANSI-ASQ National Accreditation Board (ANAB); American National Standards Institute (ANSI);

National Bureau of Agricultural Commodity and Food Standards (ACFS); and International Accreditation Services, Inc. (IAS). FDA has recognized all four entities for a five- year term of recognition.

Accreditation bodies recognized by FDA have the authority to accredit third-party certification bodies, also known as third-party auditors. These certification bodies, once accredited, can conduct food safety audits and issue certifications of foreign food facilities (including farms) and the foods – both human and animal – that they produce. As of November 13, 2018, one of the recognized accreditation bodies (ANSI) has accredited one certification body: Perry Johnson Registrars Food Safety, Inc. This certification body has been accredited for a two-year period. The FDA maintains public registries with information on recognized accreditation bodies and accredited certification bodies under the voluntary program: Recognized Accreditation Bodies Public Registry; Accredited Certification Bodies Public Registry.

FDA has also launched the Voluntary Qualified Importer Program (VQIP), a voluntary fee-based program which offers expedited review and entry of human and animal food into the United States. Importers interested in participating in VQIP will be required to meet a number of eligibility requirements, which include ensuring the facilities of their foreign supplier are certified under the Accredited Third-Party Certification Program.

In addition to being used to establish VQIP eligibility, FDA can also require, in certain circumstances, that imported products, or the facilities that produce them, be certified by an accredited certification body under the FDA's Accredited Third-Party Certification Program or by a foreign government agency before they enter the United States. While FDA does not generally require certification as a condition of entry into the United States, this is new tool granted by Section 303 of FSMA that will allow FDA to ensure that serious, ongoing food safety problems are corrected at their source.

These programs are additional tools FDA is using to help ensure that foods imported into the United States are produced in accordance with the same safety standards required of food produced domestically.

Issued Draft Guidance to Help Produce Farmers and Fresh-Cut Produce Processors

In October 2018, FDA issued two draft guidance documents to help farmers and fresh-cut produce processors comply with FSMA requirements.

The first draft guidance is a compliance and implementation guide to assist growers in meeting requirements of the Produce Safety Rule under FSMA.[19] The rule requires domestic and foreign farms to put preventative measures in place during growing, harvesting, packing and holding of their fruits and vegetables to protect against contamination. Flexibility was built into this rule to

[18] https://www.fda.gov/downloads/Food/GuidanceRegulation/ImportsExports/Importing/UCM564000.pdf

[19] https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM623178.pdf

accommodate regional and commodity-specific growing practices—which is reflected in this guidance through examples to demonstrate how farmers can implement the rule's requirements.

The second draft guidance, "Guide to Minimize Food Safety Hazards of Fresh-cut Produce," explains the FDA's current thinking on how fresh-cut produce processors may comply with the requirements found in the Preventative Controls for Human Food Rule under FSMA.[20] This rule requires food processors have a food safety plan that includes an analysis of hazards and preventive controls to minimize the likelihood that those hazards will contaminate the food.

Both guidance documents were opened for public comment for the 180-day period following their release and serve as an important supplemental educational tool in increasing consistent FSMA compliance.

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 in an effort to learn more about potential contamination in sprouts and how to protect consumers from disease-causing bacteria. Sprouts are especially vulnerable to pathogens given the plants' warm, moist and nutrient-rich growing conditions. This study was completed 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.

FDA's testing program was designed to estimate the prevalence of Salmonella, Listeria monocytogenes, and 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 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 learn more about 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 large scale surveillance sampling assignments, one focusing on fresh herbs and the other on processed avocados/guacamole. The assignments will be carried out were completed over the next 18 plus months to accomplish the following: The objectives of these assignments are to:

- determine the prevalence of select pathogens in the respective commodities
- identify common factors associated with positive findings (such as origin or variety)
- take regulatory action as warranted to protect consumers.

In May 2018, FDA published an update on traceback efforts related to recent E. coli outbreaks from Romaine lettuce – the largest outbreak in the U.S. in more than ten years. Tracebacks confirmed there is not a simple or obvious explanation for how this outbreak occurred within the

[20] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm623716.htm

supply chain. This particular outbreak illustrates the importance of moving forward with FSMA's Produce Safety Rule.

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. These herbs 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 before consumption. Both fresh herbs and processed avocados/guacamole have been associated with recalls and outbreaks of foodborne illness in recent years.

This 2018 sampling of fresh herbs also revealed two samples with the Cyclospora cayetanensis parasite from cilantro growers in Mexico and one sample in the United States. Though no known illness has been reported in relation to these products, the finding of the parasite through sampling highlights the importance of FDA surveillance activities to better define risks. These findings also highlight the importance of implementing the provisions of FSMA's Produce Safety Rule at home and abroad to reduce risk and prevent illnesses from occurring.

The Produce Safety Rule is designed to put science-based measures in place to prevent microbial contamination from occurring. State and foreign partners have an important role in working with FDA to implement the rule. These partnerships and others enhance FDA's ability to act swiftly to detain and remove any contaminated product from commerce to protect U.S. consumers, as happened after these findings in domestic and imported produce.

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 contaminated vegetables grown on the Delaware/Maryland/Virginia (Delmarva) peninsula.[21]The 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 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, detects the factors involved in survival differences among pathogens living in identical environments. Pilot studies with the technology have begun to

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

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.

Other Foods Program accomplishments included:

- 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 developing portable and rapid lab-in-a-backpack tools that integrate rapid sampling and diagnostic technologies such as 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. FDA's continued development aims to make existing tools more portable for FDA scientists using nanopore-based whole genome sequencing and smart-phone mediated qPCR devices.

FDA Expanded Outreach of Recall Information Through Social Media

FDA uses social media to successfully communicate important public health information out to a wide range of consumers. In June 2018, FDA used Twitter to announce a multi-state Salmonella outbreak associated with Kellogg's Honey Smacks cereal. FDA also announced via Twitter that Kellogg's had decided to recalled the Honey Smacks due to which had the potential of Salmonella presence. FDA's initial tweet received 109,713 impressions, which is the highest engagement and retweets of anything FDA has ever posted on Twitter. Facebook engagement on this recall was also was higher than previous high-profile recalls., indicating that social media is proving to be an increasingly effective and beneficial way to get important information out to a wider range of consumers.

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.

The module explains federal identity labeling requirements for seafood and helps to ensure proper labeling of seafood products by:

- listing the laws, regulations, guidance documents, and other materials relevant to the proper labeling of seafood
- helping stakeholders understand FDA's role in ensuring the proper labeling of seafood.
- providing tips for identifying mislabeled seafood in the wholesale distribution chain or at the point of retail.

FDA uses DNA barcoding to identify seafood, instead of protein profiles. Barcoding provides a DNA sequence that allows analysts to identify different seafood products. These sequences are accessible online in a curated FDA library. This online access helps FDA field staff to 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.

Exercised Science-Based Compliance Actions

FDA protects the public from impure, adulterated, and misbranded food and acts as an industry-wide deterrent for regulated entities and criminal enterprises through its authority to initiate criminal cases. In FY 2018, FDA issued eight injunctions and two seizures related to adulterated or misbranded food. 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.

This is especially true in cases where food, dietary supplement or cosmetic products have been linked with outbreaks. The Agency works with Federal, state and local partners to identify the products causing problems and take efficient and effective compliance actions. In one such case, the FDA pursued a permanent injunction against a raw milk cheese company after it was responsible for a Listeria monocytogenes (Lm) outbreak that sickened eight people and caused 2 deaths. This action required the firm to get expert assistance to eliminate unsanitary conditions and develop a program to control the Lm before resuming operations.

FDA also issues import controls when non-compliant food products are discovered or when food companies manufacture or ship non-compliant products. In FY 2018, FDA issued 946 import alert notices (of which 306 were reviewed by CFSAN). Additionally, CFSAN worked with the FDA field offices to assist in 623 cases where the district needed CFSAN's technical expertise to determine import admissibility.

FDA monitors the recalls of human food, cosmetic, and dietary supplement products and ensures the removal of violative products from commerce. In FY 2018, FDA classified 197 Class I (most serious), 332 Class II, and 60 Class III recall events for human food, cosmetic, and dietary supplement products. This included the Agency's first issuance of a final order using mandatory recall authority to require the removal of certain salmonella-contaminated Kratom products from the market.

FDA also 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 high lead levels in additional spices and spice products potentially rendering them injurious to health. Infants, small children, pregnant women, and people with underlying kidney disorders are particularly vulnerable to lead poisoning.

Published Timely Food Additive, Color Additive, Generally Recognized as Safe (GRAS), and Food Contact Substance Reviews

The Foods Program has statutory responsibility for the following premarket review activities that help to foster competition and innovation

- 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.

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 obtain regulatory approval, either by petition for a food additive or a color additive, or through notification programs for food contact substances and GRAS food ingredients. The petition and notification processes are unique to FDA's regulatory mission. In FY 2018, FDA ensured safe access to the food supply by reviewing10 Food Additive or Color Additive Petitions, 73 GRAS notifications, and 94 premarket notifications for Food Contact Substances.

Launched New Inventory of Substances Added to Food

In June 2018, FDA launched the new Substances Added to Food inventory, an upgraded version of the original Everything Added to Food in the U. S. (EAFUS) inventory.[22] The searchable inventory contains approximately 4,000 substances, and includes information on food additives, color additives, Generally Recognized As Safe (GRAS) and prior-sanctioned substances. Additional features include:

[22] FDA's New Substances Added to Food Inventory; http://FDA.gov/Food/Ingredients

- a new search function that allows users to search multiple related food ingredient and packaging inventories;
- direct links to any applicable regulations for a substance
- additional information such as other known names, common uses, and information by other entities when available.

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 and food contact substances
- ingredients 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.

Empower Consumers and Patients

The Foods Program is responsible for ensuring that foods sold in the United States are safe, wholesome, and properly labeled so that consumers and patients are empowered to make well-informed food choices. 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. FDA, 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.

Encouraged the Safe Production of Dietary Supplements

In FY 2018, 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:

- 75 warning letters
- 3 untitled letters
- 180 detentions
- 4 injunctions (filed).

Additionally, FDA initiated several regulatory actions aimed at protecting consumers from fraudulent and/or products that were marketed as dietary supplements. These include products marketed as dietary supplements that made unlawful claims about treating opioid use disorder

and other products that made unproven claims about protecting consumers from the harms that come from sun exposure without meeting the FDA's standards for safety and effectiveness.

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 2018, FDA responded to 38 NDI notifications. Of the notifications submitted, 10 were deemed incomplete or determined to not pertain to an ingredient intended to be used in a dietary supplement. Of the remaining 28 notifications, FDA acknowledged 17 with no objection and raised safety or identity concerns with 11.

In FY 2017, FDA received more than 2,700 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.

FDA Steps Up Efforts to Stop Illegal Sale of Highly Concentrated Caffeine

Products consisting of or containing pure or highly concentrated caffeine have been linked to at least two deaths in the United States in the last few years and continue to present a significant public health threat. Many products that consist of primarily or highly concentrated caffeine are sold as dietary supplements.

In April 2018, FDA issued guidance to industry on highly concentrated caffeine in dietary supplements. This document is intended to provide guidance to firms that manufacture, market, or distribute dietary supplement products that contain pure or highly concentrated caffeine, or are considering doing so.

In June 2018, FDA issued warning letters to parties illegally selling certain highly concentrated caffeine products. These letters build on our efforts to stop illegal sale of highly concentrated forms of life-threatening dose.

Provide Outreach and Education on FDA Regulated Products

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 launch this work, FDA hosted public meetings in Charlotte, NC, and San Francisco, CA as part of its Agricultural Biotechnology Education and Outreach Initiative. These meetings provided the public with an opportunity to share information, experiences, and suggestions to inform the development of this education and outreach initiative. An additional $1.5 million was invested in this effort in FY 2018 to further the education and outreach capacity.

Developed Seafood Product Labeling Online Learning Module

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

The module explains federal identity labeling requirements for seafood and helps to ensure proper labeling of seafood products by:

- listing the laws, regulations, guidance documents, and other materials relevant to the proper labeling of seafood
- helping stakeholders understand FDA's role in ensuring the proper labeling of seafood.
- providing tips for identifying mislabeled seafood in the wholesale distribution chain or at the point of retail.

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

FDA Released Final Guidance on Menu Labeling Compliance

In May 2018, FDA released final menu labeling guidance that provides flexibility on how covered establishments can provide calorie information in ways that meet various business models. For the first time, these new standards create a national and uniform method for the disclosure of calorie information on menus at chain restaurants.

The guidance includes many graphical depictions that convey FDA's thinking on various topics. For example, the guidance covers:

- calorie disclosure signage for self-service food
- various methods for providing calorie disclosure information
- criteria for distinguishing between menus and marketing material
- compliance, and enforcement, and; reasonable basis
- criteria for covered establishments; and standard menu items.

Completing work on menu labeling is an important part of a comprehensive, multi-year Nutrition Innovation Strategy announced in March of 2018 by FDA Commissioner Scott Gottlieb aimed at providing consumers with easier access to nutritious, affordable foods by empowering them with information and facilitating industry innovation toward healthier foods that consumers want.[23]

The menu labeling rule applies to restaurants and similar retail food establishments if they are part of a chain of 20 or more locations, doing business under the same name, and offering for sale substantially the same menu items. Covered establishments have to disclose the number of calories contained in standard items on menus and menu boards, or for self-service foods and foods on display, in a manner in close proximity and clearly associated with the standard menu item. Businesses must also provide, upon request, nutrition information, such as total fat, saturated fat, trans fat, cholesterol, and sodium.

[23] https://www.fda.gov/Food/LabelingNutrition/ucm602651.htm

Many establishments are already displaying menu labeling information. By May 7, 2018, covered establishments nationwide are were expected to comply with the rule. During the first year of implementation, the FDA will work cooperatively with covered establishments to achieve high levels of compliance with the menu labeling requirements.

FDA Extended Compliance Dates for Nutrition Facts Label Final Rules

In May 2018, FDA issued a final rule 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. The agency published a proposed rule to extend the compliance date in September 2017, and this rule finalizes that extension.[24]

After considering a range of stakeholder comments, the FDA recognizes the need for manufacturers to have additional time to make required changes. The approximately 18-month extension accomplishes this goal and will provide sufficient time to transition to the new version of the Nutrition Facts label.

FDA also is committed to ensuring that all manufacturers have guidance to help implement the required label changes by the upcoming compliance dates. A full list of Nutrition Facts-related guidance documents is available on the FDA website.[25]

FDA Published Final Guidance on Dietary Fiber

In June 2018, FDA published final guidance on dietary fiber. This guidance permits manufacturers to update their labels regarding dietary fiber and to implement the new Nutrition Facts and Supplement Facts label. The updated labels will better equip consumers with nutritional information about dietary fiber.

Fiber-containing fruits, vegetables and grain products, particularly soluble fiber, may reduce the risk of coronary heart disease and can help lower cholesterol levels. Certain dietary fibers also can increase calcium absorption in the intestinal tract, improve laxation, or reduce calorie intake.

After manufacturers update their labels, consumers will be able to trust that if a food label states that a product contains dietary fiber, the source of that fiber is scientifically shown to have a beneficial health effect.

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."

[24] 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

[25] FDA Nutrition Facts-related guidance,https://www. fda. gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/default. htm

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 FDA 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 FDA has ever received within the category of cosmetic hair cleansing products. The FDA 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[26]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$998,230,000	$998,230,000	$0
FY 2017 Actual	$1,025,503,000	$1,025,503,000	$0
FY 2018 Actual	$1,059,291,000	$1,059,291,000	$0
FY 2019 Annualized CR	$1,070,187,000	$1,059,316,000	$10,871,000
FY 2020 President's Budget	$1,122,047,000	$1,084,636,000	$37,411,000

[26] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

BUDGET REQUEST

The FY 2020 Budget Request for the Foods Program is $1,122,047,000 of which $1,084,636,000 is budget authority and $37,411,000 is user fees. Budget authority increases by $25,320,000 compared to the FY 2019 Annualized Continuing Resolution level and user fees increase by $26,540,000.[27] The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is $361,678,000. The Office of Regulatory Affairs amount is $760,369,000.

In FY 2020, 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 food system. 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.

Food Safety (+$51.8 million / 103 FTE)

Strengthening Response Capabilities for Foodborne Outbreaks (+$13.3 million / 40 FTE)

Center: +$6.8 million / 17 FTE

Additional resources are urgently required to ensure that contaminated food is detected and removed from the marketplace as quickly as possible. The increased number of detected outbreaks and subsequent investigations resulting from the success of Whole Genome Sequencing (WGS) has greatly increased FDA's workload to identify and mitigate potential food safety concerns. WGS has made it possible to more easily determine the source of contaminated food associated with human illness, and to better identify foodborne outbreaks that previously would have gone undetected. By reassigning staff to address the surge in detection and response needs, recall classification time has decreased from 79 days to less than 14 days, on average, while the number of outbreak responses has increased 44 percent from 18 in 2015 to 26 in 2018. However, CFSAN has reached maximum capacity to reassign staff to address these surge needs.

Just as WGS has greatly altered our ability to identify food products contaminated with bacteria and viruses, newly developed methods are now changing the landscape of food products contaminated with parasitic organisms. Outbreaks of human illness associated with contamination of produce with the parasite Cyclospora cayetanensis have been on the rise since first reported in the mid-1990's. The CFSAN parasitology team developed and subsequently validated a novel method to recover, detect (using PCR or Polymerase Chain Reaction), and characterize C. cayetanensis oocysts in produce. This method is being implemented in regional ORA laboratories for use in outbreak investigations and has now been used successfully to identify C. cayetanensis in a 2018 outbreak investigation involving McDonald's salads. The new method is currently being used to assess the contamination of a number of other implicated foods. This technological achievement advances FDA's ability to protect consumers against

[27] The net increase to the Foods program is $25.3m. The overall increase to the Foods Program funding reflects -$1.8m of base funding based on the proposals laid out in the House report for FY 2019. This includes increasing FDA's biotechnology education and outreach efforts by $1.5m from FY 2018's levels and decreasing spending on fish decomposition research and dietary supplement research by $2.8m and $500k from the FY 2018 levels, respectively.

foodborne parasitic infections, and it will add to the workload involved in identifying and responding to C. cayetanensis in produce.

In 2017, despite limited staffing resources, CFSAN responded to 794 recall events and oversaw the recall of 3,609 products, more than any other FDA Center. Other parts of FDA that oversaw comparable numbers of recalls did so with more than double the staffing resources. This initiative's additional FTE will facilitate more effective and efficient oversight of recall initiations and make faster determinations of recall final classification(s). The initiative will also lead to more thoroughly collecting recalled product information, distributing it to the retail level, and posting information for consumers. Additional FTE will facilitate the deployment of personnel to work on outbreaks involving imported food products and to hold foreign firms to the same standards as domestic producers.

Additional resources also will increase FDA's ability to leverage new technologies that make it easier to track and trace products throughout the product lifecycle, from the time that they are grown or manufactured, until they are used by a consumer. Efficiently tracking and tracing FDA-regulated products will enable FDA to work with stakeholders, including industry producers, to quickly remove harmful products or ingredients from the supply chain. Examples of "track and trace" technologies include blockchain technology, which uses a decentralized, secure, ledger shared by all parties in the supply chain to provide transparency on a product's origins. Increasing FDA's ability to track and trace will also lessen costs imposed on industry by minimizing the number of products implicated in outbreaks of foodbourne illness and other product problems. These costs can be considerable where the lack of transparency in supply chains delays the identification of contamination sources and the root causes of product problems.

Field: +$6.5 million / 23 FTE

In recent years FDA has refined its traceback methods to increase speed and efficiency during outbreaks and recalls. Additional resources are required to ensure that, as soon as possible, contaminated food is detected and removed from the marketplace and that consumers are alerted.

FDA is requesting additional resources to hire FTE and support new procedures for collecting, reviewing, and posting retail consignees for certain Class I and Class II recalls. To ensure we have complete information in these recall situations, FDA will expend significant resources collecting consignee lists throughout the distribution chain (recalling firm, distributors, etc.) and then reviewing them to identify retailers that may have sold the recalled product. The list of retailers will be consolidated into one master list and posted onto FDA's website. This will better protect public health by allowing consumers to recognize whether they have purchased recalled products.

Advancing FSMA (+$10.6 million / 1 FTE)

Center: +$0.280 million / 1 FTE

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct more than half of the domestic food and feed facility inspections required by FSMA. The increases proposed in the FY 2020 Budget will enhance compliance with the preventive control rules by funding cooperative agreements with state food regulatory programs. In addition, CFSAN will hire an additional FTE to provide technical support to the administration of the cooperative agreements.

Field Foods: +$10.3 million

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct domestic food and feed facility inspections required by FSMA. With the increases proposed in the FY 2020 Budget, ORA will enhance its oversight of industry's compliance with the human food preventive control rules by expanding funding of cooperative agreements with state food regulatory programs.

To ensure effectiveness and efficiency, FDA expects states to continue or increase their number of inspections as FDA transitions to prevention-oriented inspections and determines industry compliance with the new FSMA standards and rules. NASDA and AFDO also have requested funds for FDA to provide to states to conduct Preventive Control (PC) inspections.

Promoting Innovation and Emerging Technology While Maintaining Product Safety (Budget Authority: $3.2 million / 10 FTE; Proposed User Fee Program: Innovative Food Products User Fee: $26.1 million / 52 FTE)

Center: $3.2 million / 10 FTE

FDA carries out its public health protection mission by assisting industry to meet its statutory responsibilities as it develops and implements new technologies in food, including cosmetics and biotechnology products. This includes modernizing our regulatory oversight of innovative biotechnology products to reflect advances in scientific understanding and technology, by improving transparency, coordination, and predictability of the system, consistent with the administration's Agriculture and Rural Prosperity Task Force Report.

This initiative also will support public confidence in new and emerging food production technologies, such as food from cultured animal cells or production of macro- and micro-ingredients through innovative plant-based and microbial-based technologies. This initiative will enable FDA to assess product safety in a timely, predictable, science-based process centered on safety and risk reduction. Consumer confidence in the safety of innovative technologies is a key component of consumer's acceptance and the commercial success of these technologies and their application in food production.

In the past five years, FDA's food ingredient safety program has reviewed a steady number of industry submissions for new ingredients (Food Additive and Color Additive Petitions ca. 8/year, GRAS notices ca. 60/year) and food contact substances (ca.121). Due to advances in food technology and innovation, FDA anticipates that the number of industry submissions will increase as new innovative products seek FDA's safety evaluation prior to market entry to meet consumer expectations. A newly proposed user fee program will provide the additional resources needed to increase expertise and scientific review capacity and grow with the need to support novel emerging products. Examples include new proteins, new ingredients, and synthetic foods, all of which can help foster new products and ingredients coming to the market in a timely manner.

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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
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 2018: 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 2018: 838 enrolled Target: 827 enrolled (Target Exceeded)	853	868	+15
212404: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: Campylobacter species. *(Outcome)*	CY 2017: 19.1 cases/100,000 Target: 10.2 cases/100,000 (Target Not Met)	9.2 cases/ 100,000	8.6 cases/ 100,000	-0.6
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[28]: 0.95 cases/100,000 Target: 0.95 cases/100,000 (Target Met)	0.68 cases/ 100,000	0.60 cases/ 100,000	-0.08
212407: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: *Salmonella species*. *(Outcome)*	CY 2017: 16.0 cases/100,000 Target: 12.8 cases/100,000 (Target Not Met)	11.9 cases/ 100,000	11.4 cases/ 100,000	-0.5
214306: The average number of working days to serotype priority pathogens in food (Screening Only) *(Output)*	FY 2018: 3 working days Target: 3 working days (Target Met)	3 working days	3 working days	Maintain

[28] For STEC, all serogroups were combined and individual CY 2017 data is not available for this measure in the CDC Morbidity and Mortality Weekly Report (MMWR) https://www.cdc.gov/mmwr/volumes/67/wr/mm6711a3.htm?s_cid=mm6711a3_w#T2_down

Measure	Year and Most Recent Result /Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
214221: Percentage of Human and Animal[29] Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 90% (New Measure)	80%	80%	Maintain
214222: Percentage of Human and Animal[30] Food follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 78% (New Measure)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2018: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
214305: Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). *(Outcome)*	FY 2018: 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 2018 target of 80% by reviewing and completing 100% of the petitions received within 360 days of receipt, a result consistent with the FY 2017 performance of 100% completed within the same timeframe.

[29] Due to Program Realignment, ORA's Workplan now combines Human and Animal food inspection activities together, so this combination performance goal is repeated in both the Foods and Animal Drugs and Feed program narratives.

[30] Due to Program Realignment, ORA's Workplan now combines Human and Animal food inspection activities together, so this combination performance goal is repeated in both the Foods and Animal Drugs and Feed program narratives.

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 2018 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 2019 and FY 2020 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 2018, 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 2019 and FY 2020 are three days, maintaining the critically important progress in analytical return times achieved in FY 2018.

New ORA Field Performance Measures

ORA is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome-based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention, and allows for a more robust analysis.

FSMA High Risk Domestic Inspection Coverage

PROGRAM ACTIVITY DATA

Foods Program Activity Data (PAD)

Foods Program Activity Data			
CFSAN Workload and Outputs	**FY 2018 Estimate**	**FY 2019 Estimate**	**FY 2020 Estimate**
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	98	98	98
Notifications Reviewed [3]	98	98	98
Infant Formula Notifications			
Notifications Received [4]	28	28	28
Notifications Reviewed [5]	16	16	16
FDA Review Time	90 days	90 days	90 days
New Dietary Ingredient Notifications			
Notifications Received [6]	50	50	50
Notifications Reviewed [7]	50	50	50
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 Activity Data (PAD)			
Field Foods Program Workload and Outputs	**FY18 Actuals**	**FY2019 Estimate**	**FY2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***8,629***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	5,876	**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	162		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	234		
Domestic Fish & Fishery Products (HACCP) Inspections	809		
Import (Seafood Program Including HACCP) Inspections	191		
Juice HACCP Inspection Program (HACCP)	149		
Interstate Travel Sanitation (ITS) Inspections	1,046		
Domestic Field Exams/Tests	3,059	2,500	2,500
Domestic Laboratory Samples Analyzed	15,470	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,638***	***1,400***	***1,400***
All Foreign Inspections	1,638	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***10,267***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	185,761	168,200	168,200
Import Laboratory Samples Analyzed	20,895	35,300	35,300
Import Physical Exam Subtotal	**206,656**	**203,500**	**203,500**
Import Line Decisions	16,859,790	17,702,780	18,587,918
Percent of Import Lines Physically Examined	1.23%	1.15%	1.09%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	84,113	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***8,073***	***9,062***	***9,062***
State Contract Food Safety (Non HACCP) Inspections	7,210	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	788	1,000	1,000
State Contract Juice HACCP	57	100	100
State Contract LACF	117	100	100
State Contract Foods Funding	$13,620,000	$13,756,200	$13,893,762
Number of FERN State Laboratories	33	33	33
Annual FERN State Cooperative Agreements/Operations Funding	$15,865,891	$15,865,891	$15,865,891
Total State & Annual FERN Funding	**$29,485,891**	**$29,622,091**	**$29,759,653**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***18,340***	***18,462***	***18,462***

[1] The FY 2018 actual unique count of foreign inspections includes 171 OIP inspections (120 for China, 38 for India, & 13 for Latin America).

[2] ORA is currently evaluating the calculations for future estimates.

3 State partnership inspections have been removed from the PAD as they have been phased out. All state inspections are now accounted for under the "state contract" inspection category.

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Activity Data (PAD)			
Field Cosmetics Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***71***	***100***	***100***
Domestic Inspections	71	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***6***	***0***	***0***
Foreign Inspections	6	0	0
IMPORTS			
Import Field Exams/Tests	6,195	1,600	1,600
Import Laboratory Samples Analyzed	335	400	400
Import Physical Exam Subtotal	**6,530**	**2,000**	**2,000**
Import Line Decisions	2,729,584	2,866,063	3,009,366
Percent of Import Lines Physically Examined	0.24%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***77***	***100***	***100***

1 ORA is currently evaluating the calculations for future estimates.

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HUMAN DRUGS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020	
				President's Budget	+/- FY 2019 Annualized CR
Human Drugs	**1,633,743**	**1,755,609**	**1,713,629**	**1,980,030**	**266,401**
Budget Authority	***495,395***	***495,384***	***495,395***	***713,895***	***218,500***
User Fees	***1,138,348***	***1,260,225***	***1,218,234***	***1,266,135***	***47,901***
Center	1,432,054	1,554,711	1,510,169	1,749,191	239,022
Budget Authority	359,226	359,222	359,226	551,084	191,858
User Fees	1,072,828	1,195,489	1,150,943	1,198,107	47,164
Prescription Drug (PDUFA)	658,620	790,598	732,096	770,854	38,758
Generic Drug (GDUFA)	376,601	366,873	382,803	391,330	8,527
Biosimilars (BsUFA)	37,028	36,605	35,416	35,001	-415
Outsourcing Facility	579	1,413	628	922	294
Field	201,689	200,898	203,460	230,839	27,379
Budget Authority	136,169	136,162	136,169	162,811	26,642
User Fees	65,520	64,736	67,291	68,028	737
Prescription Drug (PDUFA)	8,101	7,753	9,003	8,801	-202
Generic Drug (GDUFA)	55,915	55,355	56,808	57,430	622
Biosimilars (BsUFA)	1,150	1,158	1,100	1,363	263
Outsourcing Facility	354	470	380	434	54
FTE	**6,335**	**6,335**	**6,560**	**6,715**	**155**

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; Biologics Price Competition and Innovation Act (BCPI) of 2009; 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); Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (SUPPORT) (2018).

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

FDA's Human Drugs Program is responsible for:

- Ensuring the safety and efficacy of new and generic prescription and over-the-counter (OTC) drug products
- Monitoring the safety of marketed drugs
- Overseeing drug quality to prevent and detect substandard or counterfeit drugs in the U.S. market.

FDA's Human Drugs Program consists of the Center for Drug Evaluation and Research (CDER) and Office of Regulatory Affairs (ORA) field drugs program. The Program operates with funding from budget authority and user fees.

The Program's mission is to promote and protect public health by ensuring 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 FDA's 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 2 Medicine for a Patient

REDUCE THE BURDEN OF ADDICTION CRISES THAT ARE THREATENING AMERICAN FAMILIES

Opioids

Opioids are effective medications that can help manage pain when properly prescribed for the right condition and used properly. Addressing the opioid crisis is one of FDA's highest priorities. FDA's regulates the drugs and devices used in the treatment of pain, as well as opioid addiction and overdose, to assure that the actions taken are in the best interest of public health.

FDA is taking immediate steps to reduce the scope of the opioid addiction epidemic. We continuously examine our role and policies in the regulation of opioids, drugs and devices used in pain treatment, and in opioid addiction and overdose to assure we act in the best interest of public health. In addition, FDA continues to accomplish goals laid out under the HHS Opioid Strategy, launched in April 2017. This plan 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.

As part of the HHS Opioid Strategy, FDA is committed to examining all facets of the epidemic: opioid abuse, misuse, addiction, overdose, and death, in the US. FDA has identified four priority areas in confronting the opioid epidemic:

- 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 Benefit-Risk.

FDA is working to improve the transparency of our benefit-risk paradigm for opioids, ensuring that we continue to consider appropriately the wider public health effects of prescription opioids. We are engaged in many ongoing activities aimed at furthering the overarching strategy, including:

- Working more closely with its advisory committees before making critical product and labeling decisions
- Enhancing safety labeling; requiring new data on long-term opioid analgesic use
- Seeking to improve treatment of both addiction and pain.

On October 24, 2018, the President signed into law the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act. The bipartisan legislation grants FDA additional authorities that will meaningfully advance our efforts to combat the opioid crisis. Through the SUPPORT Act, CDER is advancing efforts to:

- Address the challenges and barriers of developing non-addictive medical products intended to treat pain or addiction
- Promote the development of evidence-based opioid prescribing guidelines to treat acute pain resulting from specific conditions or procedures
- Implement our new authority to issue a mandatory recall for any controlled substance if there is a probability that it would cause serious adverse health consequences or death
- Implement our new authority to require certain packaging and disposal for opioids and other drugs, to mitigate the risk of abuse and misuse
- Implement our new authority to require post-market studies of the long-term efficacy of opioid analgesics to help FDA advance our understanding of opioid pain medicines.

FDA recognizes both the risks of opioid use and the benefits of these drugs for patients who need them, including those with debilitating chronic pain conditions. Opioid misuse and abuse remains one of our highest priorities, and we believe it is going to take carefully developed, sustained, and coordinated action by everyone involved to reduce the tide of opioid addiction and death afflicting our communities; while maintaining appropriate prescribing for patients in medical need.

FOSTER COMPETITION AND INNOVATION

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 FDA's high standards for safety and efficacy.

Novel drugs are often innovative products that serve previously unmet medical needs or otherwise advance patient treatment and public health. In calendar year 2018, CDER approved 59 novel drugs. From 2009 through 2017, CDER has averaged about 33 novel drug approvals per calendar year. More than 75% of novel drugs approved by CDER were approved in the U.S. before other countries, providing Americans first access to treatment.

The Human Drugs Program employs multiple 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 also helped expedite products to market.

FDA is working to increase speed and efficiency in several areas of the clinical trial phase of drug development including:

- Assisting with establishing flexible clinical development designs and accepting such designs when they support the 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
- Helping create clinical trial networks and "master protocols," to streamline clinical trials, reduce the cost of conducting, and reduce the time needed to carry them out.

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. The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) granted authorities that enabled FDA to coordinate with manufacturers to help prevent or mitigate drug shortages. These authorities included requiring manufacturers to provide early notification of permanent discontinuances or interruptions in manufacturing of covered prescription drugs that are likely to lead to a meaningful disruption in supply of those drugs in the U.S. These requirements helped FDA work with industry early on to address problems before shortages occur and resulted in decreasing numbers of new shortages in recent years.

FDA continues to make significant progress in reducing the number of drug shortages, from 251 new shortages in 2011 to 26 new shortages in 2016 and 39 new shortages in 2017. Specifically, in 2017, multiple hurricanes impacted drug manufacturing in Puerto Rico. In 2017 and early 2018, a large manufacturer made decisions resulting in discontinuances and delays for multiple medications, including IV opioid analgesic drugs.

FDA has been working with manufacturers to resume production and has expedited review of new submissions, helping to increase supplies. FDA was able to help prevent 145 shortages in 2017 and continues these important prevention efforts in 2018. To continue transparency on the Agencies processes, an update to the Manual of Policies and Procedures (MAPP 41901.1 Rev. 3) on CDER Drug Shortage Management was posted to our website on December 4, 2018.[31] To further address shortages, FDA has created a new Task Force, comprising senior leaders from FDA, the Centers for Medicare and Medicaid Services, and the Department of Veterans Affairs to identify the root causes and holistic solutions for this critical public health problem. A report on this issue will be delivered to Congress by the end of 2019.

On November 27, 2018 the Drug Shortages Task Force under a cooperative agreement with the Robert J. Margolis, MD, Center for Health Policy at Duke University held a public meeting with stakeholders on "Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions". This public meeting built on the earlier listening sessions and one-on-one stakeholder meetings and allowed FDA to obtain valuable feedback from additional stakeholder groups, including health care professionals, patients, manufacturers, wholesalers, pharmacists, insurers, academic researchers and the public.

[31] Updated MAPP is available at https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM079936.pdf.

Drug Pricing and Access - Biosimilars

In July 2018, FDA released the Biosimilars Action Plan[32] (BAP) to provide information about the key actions FDA is taking to encourage innovation and competition among biologics and the development of biosimilars. The BAP builds on the progress in implementing the approval pathway for biosimilar and interchangeable products. The BAP is focused on four key areas:

- Improving the efficiency of the biosimilar and interchangeable product development and approval process
- Maximizing scientific and regulatory clarity for the biosimilar product development community
- Developing effective communications to improve understanding of biosimilars among patients, clinicians, and payors
- Supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition.

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 3, 2018, 65 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 33 different reference products. As of December 3, 2018, FDA has licensed 15 biosimilar products. These accomplishments represent the next step to increasing treatment options for patients.

During June and July 2018, FDA issued two draft guidances and one final guidance for industry. The final guidance entitled, "Labeling for Biosimilar Products" provides FDA's recommendations for labeling for biosimilar products and is intended to assist applicants in developing prescription drug labeling for proposed biosimilar products.

In September 2018, FDA held a public hearing on FDA's approach to enhancing competition and innovation in the biological products marketplace, including by facilitating greater availability of biosimilar and interchangeable products. In December 2018, FDA hosted a webinar for health care professionals to provide an overview of the regulatory framework for biosimilar and interchangeable products, including the general approval requirements for biosimilars, the approach and scientific concepts used in the development of biosimilar products, and clinical and practical considerations when using biosimilar and interchangeable products.

In December 2018, FDA issued two draft guidances and two final guidances for industry. The final guidance entitled, "Biosimilars: Questions and Answers on Biosimilar Development and the BPCI Act of 2009" and the draft guidance entitled, "New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 2)" are companion guidance documents that through a question and answer (Q&A) format is intended to inform prospective applicants and facilitate the development of proposed *biosimilars* and *interchangeable biosimilars*, as well as to describe FDA's interpretation of certain statutory requirements added by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). The final guidance entitled, "Interpretation of the

[32] For additional information visit https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm613761.pdf

'Deemed To Be a License' Provision of the Biologics Price Competition and Innovation Act of 2009" and the draft guidance entitled, "The 'Deemed to be a License' Provision of the BPCI Act: Questions and Answers" describe and provide answers to common questions about FDA's interpretation of the statutory provision under which an application for a biological product approved under the Federal Food, Drug, and Cosmetic Act (FD&C Act) as of March 23, 2020, will be deemed to be a license for the biological product under the Public Health Service Act (PHS Act) on March 23, 2020.

Harnessing Real-world evidence

FDA uses real world evidence to monitor postmarket safety and adverse events, and to make regulatory decisions. This includes integrating evidence such as electronic health records, registries, and claims and billing data into regulatory decision making and to answer questions relevant to broader populations of patients.

Sentinel

Figure 3 Data used to support postmarket safety activities

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.

In FY 2018, the Sentinel System expanded surveillance to 292 million patients, which is an increase of 69 million patients from FY 2017. Each year, the Sentinel distributed database naturally grows as more data accumulates within the existing data partners. Effective in FY 2020, FDA will begin to assess performance of the Sentinel System according to the number of investigations of priority drug safety questions analyzed using the Sentinel ARIA System.

In February 2018, FDA held the Tenth Annual Sentinel Initiative Public Workshop to bring the stakeholder community together to discuss a variety of topics on active medical product surveillance and current and emerging Sentinel projects. 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.

FDARA and 21st Century Cures Act Implementation

FDARA provided the second authorizations of the Generic Drug User Fee Amendments (GDUFA II), the Biosimilars User Fee Act (BsUFA II), and the sixth authorization of the Prescription Drug User Fee Act (PDUFA VI). The five-year reauthorizations 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
- Enhancing FDA's capacity to fulfill its mission of bringing novel drug products to market.

Generic Drug Review

Many Americans face challenges with access to medically necessary drug products due the rising healthcare costs fueled largely by extravagant prescription drug pricing. The availability of safe and effective generic drugs can help reduce the cost of drug products. As such, generic drug review is a high priority for the Human Drugs Program. The review function supports the larger FDA mission of promoting and protecting public health.

GDUFA II includes important features to modernize the generic drug program. For example, under GDUFA II, certain applications may be eligible for a shorter review time, including applications for drug shortage products. Our GDUFA II commitment also included a pre-Abbreviated New Drug Application (pre-ANDA) program designed to support development of complex generic drug products under GDUFA II. The pre-ANDA program features meetings between FDA and sponsors at various stages of drug development to help clarify regulatory expectations early in product development and during application review.

Commitment to the GDUFA program led to a record number of combined approvals and tentative approvals in FY 2018.[33] FY 2018 was the third consecutive year that FDA set a combined approvals and tentative approvals record. FDA achieved these successes by providing greater predictability, transparency, and efficiency, along with improved timeliness, to the generic drug review process.

Under GDUFA II, FDA uses "real time" communications such as information requests and discipline review letters issued during the review of an original ANDA to give applicants an opportunity to correct certain deficiencies within the current review cycle. These communications help minimize the number of review cycles necessary for approval and promote transparency in the review process.

FDA has also taken several actions under the agency's Drug Competition Action Plan (DCAP) to help remove barriers to generic drug development and market entry to spur competition so that consumers can get access to the medicines they need at affordable prices. FDA has focused efforts under the DCAP on three key areas:

- Improving the efficiency of the generic drug development, review and approval processes
- Maximizing scientific and regulatory clarity with respect to generic versions of complex drug products
- Closing loopholes that allow brand drug companies to "game" the Hatch-Waxman Amendments in ways that forestall the generic competition that Congress intended.

[33] See the Activities Report of the Generic Drug Program (FY 2018) at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm625314.htm. During FY 2018, OGD approved or tentatively approved 971 ANDAs.

In FY 2018, FDA established policies under the DCAP to promote generic drug development in areas where there is inadequate competition. This included developing 208 new and revised drug development guidance documents. Of these, 74 address the development of generic versions of complex, difficult-to-copy, drugs. The agency also published two updates to the List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic. FDA maintains this list to improve transparency and encourage the development and submission of generic drug applications for products in markets with little competition.

The agency also approved the first three generic drugs designated as competitive generic therapies, which are a new category of drugs for which there is inadequate generic competition. In addition, FDA began prioritizing the review of generic drug applications for which there are no blocking patents or exclusivities and for which there are no more than three approved drug products. This prioritization policy is supported by data that shows a significant price decrease when there are at least three generic drugs on the market, which lowers the costs to consumers.

Under GDUFA II and the DCAP, FDA will continue modernizing the generic drug program and ensuring that Americans have timely access to safe, effective, high quality, and lower cost human generic drugs.

Generic 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.[34]

Product Category	Approved	Product Name	FDA-Approved Use on Approval Date
Opioid Dependence	Apr 2018	Hydromorphone Hydrochloride Injection (generic of Dilaudid)	For the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate
	Jul 2018	Morphine Sulfate Injection (generic of Infumorph)	For the management of pain severe enough to require use of an opioid analgesic by intravenous administration and for which alternative treatments are not adequate
Infections	Apr 2018	Ertapenem Sodium for Injection (generic of Invanz)	For the treatment of certain moderate to severe infections caused by susceptible bacteria
	Aug 2018	Cefepime Hydrochloride for Injection (generic of Maxipime)	For the treatment of infections caused by susceptible strains of microorganisms

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

Product Category	Approved	Product Name	FDA-Approved Use on Approval Date
Cancer	Aug 2018	Arsenic Trioxide Injection (generic of Trisenox)	For induction of remission and consolidation in certain patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy
	Sep 2018	Carmustine for Injection (generic of BiCNU)	For palliative therapy in certain brain tumors, multiple melanoma, relapsed or refractory Hodgkin's and non-Hodgkin's lymphoma
Other	Jan 2018	Potassium Chloride Extended-Release Tablets (generic of K-Tab)	For the treatment of patients with hyperkalemia, with or without metabolic alkalosis
	May 2018	Methylphenidate Hydrochloride for Extended-Release Oral Suspension (generic of Quillivant XR)	For the treatment of ADHD
	Oct 2018	Nitric Oxide Gas for Inhalation (generic of INOmax)	For improved oxygenation and to reduce the need for extra corporeal membrane oxygenation in term and near-term neonates with hypoxic respiratory failure

New Drug Review

With PDUFA V, FDA created 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 60 days review clock time for FDA to meet with the applicant as well as address review activities for these highly complex applications.

PDUFA VI contained many enhancements designed to build on the achievements of earlier agreements. One of the key programs continuing under PDUFA VI is the Enhanced Review Transparency and Communication for NME NDAs and Original BLAs (the Program). As of September 2018, FDA has received 355 applications through this Program since its inception on

October 1, 2012, which involves more communication and transparency between the applicant and the FDA review team during review of marketing applications. The FY 2018 Program cohort has received 75 applications to date.

FDA is using vital PDUFA resources to continue to support early and meaningful communication between FDA and drug sponsors, including through the popular, highly successful, and resource-intensive Breakthrough Therapy program. Seventy-two percent of the novel drugs approved in 2018 were approved in United States before any other country. Thirty-five percent of novel drugs approved in 2018 were first-in-class, which is one indicator of the drug's potential for strong positive impact on the health of the American people. Additionally, 72% of the novel drugs approval in 2018 were designated in one or more expedited categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval.

During FY 2018, FDA published 35 draft and final guidance documents including the submission procedures for human factors protocols for new drug, and biologics license applications and guidance on adaptive design for clinical trials. FDA also conducted 8 public meetings related to the process for the review of human drug and biologics license applications.

PDUFA VI continues to support drug development oversight and marketing application review for the new drugs regulatory program. Some 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
- Enhanced use of real-world evidence for use in regulatory decision making
- Additional postmarket funding for FDA's Sentinel system
- 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 (RTF) decision and have addressed the deficiencies that led to the RTF, received from October 1, 2017 through September 30, 2022.

New Product Approvals

Below are some of CDER's recent new product approvals. This list does not represent any degree of importance or priority ranking of products.[35]

Product Category	Approved	Product Name	FDA-Approved Use on Approval Date
Autoimmune Disease	May 2018	Olumiant	To treat moderately to severely active rheumatoid arthritis
Opioid Dependence	May 2018	Lucemyra	For the non-opioid treatment for management of opioid withdrawal symptoms in adults

[35] For more information on product approvals and designations visihttp://www.fda.gov/NewsEvents/ProductsApprovals//.

Product Category	Approved	Product Name	FDA-Approved Use on Approval Date
Liver Disease	Jul 2018	Mulpleta	To treat thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure
Infectious Diseases	Oct 2018	Nuzyra	To treat community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections
	Jul 2018	TPOXX	The first drug ever to treat smallpox and therefore help in the event of a bioterror attack with this virus
Other	Feb 2018	Erleada	To treat a certain type of prostate cancer using novel clinical trial endpoint
	Feb 2018	Lokelma	To treat hyperkalemia.
	Apr 2018	Crysvita	To treat adults and children ages 1 year and older with x-linked hypophosphatemia (XLH), a rare, inherited form of rickets.
	May 2018	Palynziq	To treat a rare and serious genetic disease known as phenylketonuria (PKU)
	Jun 2018	Epidiolex	To treat rare, severe forms of epilepsy
	Aug 2018	Pifeltro	To treat HIV-1 infection in adult patients
	Nov 2018	Yupelri	To treat patients with chronic obstructive pulmonary disease (COPD)
	Nov 2018	Daurismo	To treat newly-diagnosed acute myeloid leukemia (AML) in adult patients

21st Century Cures

The Cures Act supports our innovation and evidence framework to expedite the delivery, discovery, development, and evaluation of beneficial new medical products for the American public. The Cures Act authorizes FDA to prioritize and enhance ongoing activities including efforts to:

- Facilitate greater patient engagement in drug development
- Advance innovative clinical trials through adaptive designs and novel statistical modeling
- Foster the generation of evidence derived from real-world experience and evaluate its applicability to drug development
- Support the advancement of emerging manufacturing technologies
- Qualify new drug development tools.

Additionally, the Cures Act provides new hiring authorities to improve FDA's ability to compete with industry and academia in hiring and retaining scientific experts.

The Cures Act included authorization of the limited population pathway for antibacterial and antifungal drugs (LPAD). This facilitates development and approval of antibacterial and antifungal drugs intended to treat serious or life-threatening infections in a limited population of patients with unmet needs. In June 2018, FDA published draft guidance describing the recommended criteria, processes, and other general considerations for demonstrating the safety and effectiveness of drugs approved under the LPAD pathway. FDA is working to revise this draft guidance and meet the statutory deadline for publication of the final guidance by February 2020. The Cures Act clarified FDA's authority to:

- Remove the breakpoint information from antimicrobial drug labeling
- Leverage the work done by standards development organizations
- Take advantage of online tools to modernize and streamline the updating of breakpoints information for these antimicrobial drugs.

In December 2017, FDA launched the susceptibility test interpretive criteria ("breakpoints") webpages also required by the Cures Act to enable up-to-date breakpoints for the reports provided to physicians to inform appropriate treatment choices. In 2018, FDA opened a public docket to receive comments on the FDA-recognized breakpoints listed on the web page.

In accordance with the Cures Act, FDA is establishing an updated qualification process for drug development tools (DDT) including 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. For biomarkers, FDA's work is primarily focused in two distinct areas:

- Supporting use of surrogate endpoints in individual drug and biological product development programs, including by cataloguing those previously used as well as a process to develop novel surrogate endpoints
- Facilitating a public process to support biomarker qualification as a drug development tool.

In July 2018, FDA published a list of surrogate endpoints (SE) which were the basis of approval or licensure (as applicable) of a drug or biological product for both accelerated and traditional approval. FDA Collaborated with the Foundation at FNIH Biomarkers Consortium, Critical Path Institute, FDA CERCI program, National Biomarker Development alliance. The outcomes of these collaborations have been over six workshops and two White Papers. The Cures Act requires FDA to publish a guidance describing the standards, process, and timeframes for DDT qualification. FDA must also establish a taxonomy for the classification of biomarkers for use in drug development. These topics were discussed at a public workshop in December 2018.

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. In July 2018, FDA awarded new 3-year grants to Rutgers, Georgia Tech and MIT for studying and recommending improvements to the process

of continuous manufacturing of drugs and biological products and similar innovative monitoring and control techniques. This research is likely to advance FDA's regulatory science and facilitate production of high-quality, cost-effective complex drug products for the benefit of the public.

The Cures Act supports FDA'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. FDA is actively working to integrate RWE such as electronic health records, registries, and claims and billing data into regulatory decision making and to answer questions relevant to broader populations of patients. In December 2018 FDA developed and published a framework to evaluate the use of RWE gathered from industry, academia and patient advocacy stakeholders to support regulatory decisions.

International Harmonization

FDA leads and engages in work conducted by the International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) to pursue international harmonization of scientific and technical standards for drugs, including both innovator and generic drugs. Harmonizing the drug development process allows drug developers to implement a single global drug development program and utilize common elements of applications to file for approval in multiple markets. In the case of generic drugs, further harmonization of bioequivalence standards will offer particular opportunities. Harmonization could allow manufacturers to use the data submitted in support of a generic drug marketing application to meet other regions' regulatory requirements for approval. In addition, harmonization may increase the size of markets and thereby attract more competition from manufacturers, lower costs by increasing the number of market entrants, and expand patient access in jurisdictions in which generic drug manufacturers otherwise may have decided not to pursue marketing authority due to differences in scientific and technical standards that require additional expensive studies in each jurisdiction.

To advance this initiative, FDA submitted a proposal, or "reflection paper", to ICH outlining a new strategic approach for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for generic drugs. As part of this approach, this paper outlines recommendations to:

- Develop a series of ICH guidelines on bioequivalence standards for simple dosage forms
- Develop a series of ICH guidelines on bioequivalence standards for complex dosage forms
- Survey existing ICH Efficacy and Multidisciplinary guidelines for revision or modernization work
- Develop additional guidelines, as needed, that will advance the harmonization of standards for generic drugs
- Establish a generic drug discussion group

The paper was reviewed and endorsed by the ICH Assembly in November 2018. An ICH generic drug discussion group will soon be formed and the ICH-endorsed paper will soon be posted on the ICH website.

FDA continues to collaborate with regulatory authorities and the pharmaceutical industry under ICH to identify areas where there is a commonly recognized need for regulatory harmonization,

to develop guidelines to improve the quality and efficiency of drug development, manufacturing, and post-market safety oversight across multiple regulatory regions.

FDA believes that harmonizing scientific and technical standards for human drugs will help advance markets that drives product competition and increase patient access to high-quality drugs worldwide. FDA will continue pursuing other ways to harmonize international standards for both brand and generic drugs to lower barriers for global entry, expand the opportunities for U.S. drug developers and improve the economic framework for drug development and competition.

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 oral 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 an acute serious disease setting. 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. Furthermore, antibacterial products are challenging to develop because of limited economic returns.

Despite these considerable challenges in developing an antibacterial drug, FDA approved eight new antibacterial drugs over the past four years, all of which were designated as *qualified infectious disease products* pursuant to section 505E(d) of the FD&C Act. The antibacterial product pipeline nevertheless remains very fragile. The regulatory science research projects described below help to facilitate development and informed use of antibacterial drugs.

CDER has awarded external contracts, through FDA's Broad FDA Announcement, to fund the following research:

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

CDER has awarded Interagency Agreements to work with other federal agencies to fund the following research:

- CDC studies to understand the microbiome disruption potential for antibacterial drugs and CDC will generate data for antibiotic breakpoints decisions.

- ASPE studies to understand the market for antibacterial drugs, the incentives for developing new antibacterial drugs, and the social value of developing new antibacterial drugs.

CDER's coordinated activities address some important gaps in knowledge for antibacterial drug development. Other important areas of work are needed to provide dependable pathways for studying new antibacterial drugs.

Drug Quality and Security Act Implementation

Title I - Compounding

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. Seventy-four firms were registered with FDA as outsourcing facilities at the end of fiscal year 2018. The DQSA also amended section 503A of the FD&C Act to remove provisions that the U.S. Supreme Court held to be unconstitutional in 2002.

Following the enactment of the DQSA, FDA has acted quickly to increase its drug compounding oversight through inspections and enforcement, developing 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, FDA has completed the following actions:

- Conducted over 600 inspections of compounders, including over 160 inspections of compounders registered as outsourcing facilities
- Issued over 220 warning letters to compounders, including one warning letter that addressed violations identified at four facilities
- Issued over 100 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
- Issued over 200 recall notices regarding compounded drug products.

FDA has issued 24 draft and revised draft guidance documents regarding compounding and related activities, 16 of which have been finalized. FDA also issued three proposed rules, two of which have been finalized, a Federal Register Notice regarding the list of bulk drug substances that may be used in compounding under section 503B, and a draft and revised draft memorandum of understanding. The policy documents address many significant compounding and related 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, FDA continued 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 six sets of listening sessions with more than 75 stakeholder organizations. 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 seven such intergovernmental working meetings and has also held two teleconferences with state regulators to discuss emerging issues. FDA also held a meeting with its Federal partners on drug compounding in FY 2018. FDA also announced in FY 2018 its intent to hold a public meeting the following year on certain policy matters related to compounding. 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 will continue these efforts, which are critical to protect the public health.

Title II - Drug Supply Chain Security Act

The Drug Supply Chain Security Act (DSCSA) enhances FDA's ability to protect consumers from exposure to potentially harmful drugs through improved detection and removal of such products from the drug supply chain. DSCSA requires FDA to establish the regulatory framework to implement the law, and 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.

Two critical areas of DSCSA implementation are Product Identification and Tracing, and Licensing.

Product Identification and Tracing: FDA will collaborate with prescription drug manufacturers, wholesale distributors, repackagers, and many dispensers (primarily pharmacies) to develop the new system for enhanced drug distribution security by 2023. The 2023 system is expected to enable:

- Secure tracing of product at the package level
- Verification of product identifiers at the package level
- Prompt response to suspect and illegitimate products when found
- Improved efficiency of recalls
- Transparency and accountability in the drug supply chain.

Licensing: FDA is working on regulations to implement the new licensing standards set forth in the DSCSA for wholesale drug distributors and third-party logistics providers, as well as preparing to establish an FDA licensing and inspection program. FDA also issued guidance specific to reporting requirements for wholesale distributors and third-party logistics providers and will continue to engage stakeholders through stakeholder meetings, public comments on guidances, and through questions received by FDA staff.

Since enactment of the DSCSA, FDA has worked to develop regulations, standards, policies, and programs to implement the law.[36] FDA has issued ten draft guidance documents and six final guidances, including two final guidances to assist stakeholders in understanding when a product without a product identifier is grandfathered and when requirements will be enforced. FDA also continued its stakeholder outreach and communications holding six public meetings as well as multiple stakeholder meetings to increase awareness of the DSCSA. In 2018, FDA completed a series of three public meetings with stakeholders, including members of the supply chain, state authorities, standards organization, and solution providers, on various strategies and issues related to the enhanced drug distribution security provisions of the DSCSA.

FDA continues to develop a long-term program schedule for implementing the multiple statutory requirements of the law. As the phased in requirements of DSCSA go into effect over the next five years, FDA will continue to engage supply chain stakeholders as we develop the enhanced drug distribution security by 2023.

Guidances

Below are notable drug guidances recently issued by FDA. These guidances help address various issues. This list reflects notable guidances published most recently and does not represent any degree of importance or priority ranking among the published guidances.[37]

Date	Docket #	Title	Description
Apr 2018	FDA-2018-D-1334	Opioid Dependence: Developing Depot Buprenorphine Products for Treatment Guidance for Industry (Draft)	Addresses drug development and trial design issues relevant to the study of depot buprenorphine products
Aug 2018	FDA-2018-D-2382	Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Medication-Assisted Treatment	Intended to assist sponsors in developing drugs for medication-assisted treatment of opioid use disorder
Sep 2018	FDA-2014-D-2138	Adverse Event Reporting for Outsourcing Facilities under Section 503B of the FD&C	Communicates FDA's current thinking on adverse event reporting for outsourcing facilities
Dec 2018	FDA-2014-D-0779	Current Good Manufacturing Practice – Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act	Addresses considerations of how cGMP requirements should be applied according to the size and scope of an outsourcing facility's operations

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

[37] Full list of FDA guidance documents is available at http://www.fda.gov/RegulatoryInformation/Guidances.

Date	Docket #	Title	Description
Dec 2018	FDA-2011-D-0611	Biosimilars: Questions and Answers on Biosimilar Development and the Biologics Price Competition and Innovation Act	Describes FDA interpretation of certain statutory requirements and facilitates the development of proposed biosimilars and interchangeable biosimilars
Dec 2018	FDA-2018-D-4627	Biomarker Qualification: Evidentiary Framework	Discusses general considerations to address when developing a biomarker for qualification under the 21st Century Cures Act

Rules

Below are some 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.[38]

Date	Docket #	Purpose or Benefit
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
Dec 2016	FDA-2016-N-3464	List of Bulk Drug Substances That Can Be Used to Compound Drug Products in Accordance with Section 503A of the Federal Food, Drug, and Cosmetic Act; Proposed Rule
Dec 2017	FDA-2015-N-0101	Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use
Sep 2018	FDA-2017-N-6924	Repeal of Regulation Requiring an Approved New Drug Application for Drugs Sterilized by Irradiation

EMPOWER CONSUMERS AND PATIENTS

Patient-Focused Drug Development

Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. The primary goal of PFDD is to better incorporate the patient's voice in drug development and evaluation, including but not limited to:

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

- Facilitating and advancing use of systematic approaches to collecting and utilizing robust and meaningful patient and caregiver input to more consistently inform drug development and regulatory decision-making
- Encouraging identification and use of approaches and best practices to facilitate patient enrollment and minimizing the burden of patient participation in clinical trials
- Enhancing understanding and appropriate use of methods to capture information on patient preferences and the potential acceptability of tradeoffs between treatment benefit and risk outcomes
- Identifying the information that is most important to patients related to treatment benefits, risks, and burden, and how to best communicate the information to support their decision making.

Through the PFDD initiative FDA has been addressing the need to better enable patients to provide meaningful input into drug and biologic development. The Cures Act created a new subsection "Patient Experience Data". This requires reviewers to include a brief statement regarding patient experience data and related information if it is submitted and reviewed as part of an application. FDA has implemented an approach to record and track the submission and review of patient experience data. A new subsection called "Patient Experience Data" has been included in drug review documents, which will require reviewers to include a brief statement regarding patient experience data and related information that is submitted and reviewed as part of an application.

As described in the plan published in June 2017 FDA will issue a series of guidances to address methodological PFDD topics required by Section 3002 of the Cures Act, including how patient experience data and other relevant information from patients and caregivers can be collected and used for medical product development and regulatory decision-making.[39] To inform the first guidance, FDA conducted a public workshop in December 2017 to convene a stakeholder discussion on methodological approaches that can be used by a person seeking to collect patient experience data for submission to FDA to inform regulatory decision making. FDA issued the first draft guidance in June 2018, addressing sampling methods for collecting representative information on patient experience to inform the development and evaluation of medical products throughout the medical product lifecycle. This guidance also discusses methods to operationalize and standardize the collection, analysis and dissemination of patient experience data. It also includes a glossary of terms that will be used in one or more of the four draft guidance documents.

In October 2018, FDA hosted a two-day PFDD workshop with stakeholders including patients, expert practitioners, drug developers and other interested persons to obtain stakeholder feedback on methods to be addressed in the second and third PFDD guidance documents to:

- Identify what is important to patients regarding the burden of disease, treatment and the benefits and risks in the management of the patient's disease; and
- Select, develop or modify Fit-for-Purpose Clinical Outcome Assessments to measure the patent experience in clinical trials.

[39] Full plan is available at https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM563618.pdf

This two-day workshop included discussion of FDA discussion papers and public input received from the docket will inform the development of the second and third methodological PFDD guidance documents as outlined in the plan published in June 2017.[40]

In addition to the work related to the four methodological PFDD guidances, in December 2018, FDA also issued a draft guidance on developing and submitting proposed drug guidance relating to patient experience data.[41] This guidance, also required under Section 3002 of the Cures Act, is intended to assist stakeholders seeking to develop and submit a proposed draft guidance relating to patient experience data for consideration by FDA. To inform the development of this draft guidance, a public workshop was conducted in March 2018 to obtain input from external stakeholders.

To complement the PFDD guidance work and accomplishments outlined above, FDA plans to further advance the quality and utility of sponsor-submitted patient experience data for regulatory decision making by establishing a competitive grant program to begin in FY 2019.

STRENGTHEN SCIENCE AND EFFICIENT RISK-BASED DECISION MAKING

Improving the Efficiency of Medical Product Development and Regulation with In Silico Tools

FDA recognizes that science has enabled fundamental advances in our understanding of human disease. Furthermore, we recognize that efficient regulatory processes informed by the most up-to-date science enables us to develop treatments that target the underlying mechanisms that drive diseases. Applying in silico (computational) approaches - such as modeling and simulation - to drug development enables applicants to apply predictive models in early drug development and provides regulators with tools to conduct critical premarket and postmarket analyses.

In silico clinical trials use computer models and simulations to develop and evaluate drugs. Modeling and simulation play a critical role in organizing diverse data sets and exploring alternate study designs, enabling safe and effective new therapeutics to advance more efficiently through the different stages of clinical trials. CDER is currently using modeling and simulation to:

- Predict clinical outcomes
- Inform clinical trial designs
- Support evidence of effectiveness
- Optimize dosing
- Predict product safety
- Evaluate potential adverse event mechanisms
- Select appropriate endpoints
- Optimize clinical development programs (e.g., efficacy extrapolation based on PK matching in pediatric patients)
- Enrich patients.

CDER addresses a variety of drug development, regulatory, and therapeutic questions through modeling and simulation strategies. CDER's Office of Translational Sciences (OTS) uses these

[40] For additional detail, visit https://www.fda.gov/downloads/Drugs/NewsEvents/UCM620708.pdf

[41] Guidance available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM628903.pdf

same strategies in the review of Investigational New Drugs Applications (INDs) and New Drug Applications (NDAs). These approaches help assess the combined effect of drug interactions, renal impairment, and hepatic insufficiency in patients, with clinical management strategies described in drug labeling where appropriate.

CDER also uses modeling and simulation to support the creation of natural history databases to for model-based drug development. FDA is currently collaborating with scientists to develop such natural history models in Parkinson's disease, Huntington's disease, Alzheimer's disease, and muscular dystrophy to better evaluate the behavior of new treatments in rare disease populations that are inherently hard to study due to their small size.

Modeling and simulation is also used by CDER in the premarket setting for predictive safety assessments. This includes quantitative structure activity relationship (QSAR) to make predictions of whether a drug or drug impurity is likely to have mutagenic (cancer-causing) effects based on the chemical structure. In addition, quantitative systems pharmacology models are used for safety assessment. An example in CDER is the use of a cardiac physiology/pharmacology model to predict the risk of a drug to cause abnormal heart rhythms. An implementation working group with the ICH led by FDA is working toward global implementation of this approach to eliminate the need for certain cardiac safety clinical trials.

FUNDING HISTORY[42]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$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 Actual	$1,755,609,000	$495,384,000	$1,260,225,000
FY 2019 Annualized CR	$1,713,629,000	$495,395,000	$1,218,234,000
FY 2020 President's Budget	$1,980,030,000	$713,895,000	$1,266,135,000

[42] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

BUDGET REQUEST

The FY 2020 Budget Request is $1,980,030,000, of which $713,895,000 is budget authority and $1,266,135,000 is user fees. The budget authority is increased by $218,500,000 compared to the FY 2019 Continuing Resolution level and user fees increased by $47,901,000. The Center for Drug Evaluation and Research (CDER) amount in the request is $1,749,191,000. The Office of Regulatory Affairs amount is $230,839,000. The FY 2020 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 2020 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 2020 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 2020 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

Human Drugs - FY 2020 Budget Request

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. These novel initiatives will require new investments, 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.

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: + $25.0 million / 10 FTE

Center: + $25.0 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. This improved analytical framework would 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: + $12.0 million / 27 FTE

Center: +$ 10.0 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 2020 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: +$2.0 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.

Compounding: + $13.5 million / 30 FTE

Center: + $10.7 million / 20 FTE

FDA seeks funding to catalyze development of policies and regulations for the outsourcing facilities, including advancement of the list of bulk drug substances that outsourcing facilities may use in compounding and current good manufacturing practice guidance and regulation specific to outsourcing facilities.

Development of the List of Bulk Drug Substances

Development of the list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the FD&C Act ("the 503B Bulks List") is a laborious initiative. The number of bulk drug substances that will require evaluation is significant. In 2013 and 2014, FDA issued Federal Register notices soliciting nominations for bulk drug substances for inclusion on the 503B Bulks List and, in 2015, a Federal Register notice opening a docket for submission of new nominations or renominations. FDA has identified for evaluation approximately 300 unique bulk drug substances, and many of those substances have been proposed for multiple uses, dosage forms and routes of administration. In addition, bulk drug substances continue to be nominated and renominated.

The evaluation of bulk drug substances is complex. In March 2019, FDA issued a final guidance describing a two-part analysis that the Agency intends to use when determining whether to include a nominated bulk drug substance on the 503B bulks list because of a clinical need for an outsourcing facility to use it in compounding. The first part of the analysis involves pharmacists, medical officers, regulatory counsels, and other Agency staff conducting in-depth review of nominated substances, engaging with the nominators, researching the availability of FDA-approved drugs containing the bulk drug substance, and gathering information about whether a compounded drug is needed and whether it can be compounded from FDA-approved drugs.

The second part of the analysis draws on the expertise of medical officers, chemists, pharmacists, and other technical experts throughout the Agency. FDA's chemists evaluate physical and chemical characterization of substances; medical officers research and review any safety issues raised by the use of the substance in compounding and the available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists; and pharmacists research information about the historical use of the bulk drug substance in compounding. The experts produce extensive reviews detailing a thorough analysis of each bulk drug substance and the dosage forms and routes of administration the nominators proposed.

The process for developing the 503B Bulks List also involves other resource-intensive procedures and expertise. FDA must publish a notice in the Federal Register proposing bulk drug substances to be included on the 503B Bulks List, including the rationale for such proposal. FDA must then provide a comment period of at least 60 calendar days. After reviewing the public comments submitted in response to that notice, FDA may decide to consult with the Pharmacy Compounding Advisory Committee (PCAC). The Agency will then make a determination of which bulk drug substances will be placed on the list, and publish a notice in the Federal Register designating bulk drug substances for inclusion on the list. FDA is also identifying in the Federal Register bulk drug substances that will not be placed on the list. In March 2019, FDA issued its first Federal Register notice that two bulk drug substances had been evaluated and are not included on the 503B Bulks List.

Funding will enable FDA to hire staff with the relevant scientific, analytical, and regulatory expertise needed to evaluate substances and develop the 503B Bulks List. Timely establishment of the 503B Bulks List will provide outsourcing facilities and compounders considering registering as outsourcing facilities with more immediate certainty about the bulk drug substances that may be used in compounding and facilitate the compounding of drug products to meet the clinical needs of healthcare providers and patients.

Current Good Manufacturing Practice Guidance and Regulation for Outsourcing Facilities

The Drug Quality and Security Act of 2013 created outsourcing facilities to supply healthcare providers with compounded drugs made under current good manufacturing practice (CGMP) requirements. Before becoming outsourcing facilities, many entities were compounding drugs under a lower quality standard as state-licensed pharmacies and not yet accustomed to CGMP. Stakeholders, especially those currently registered as outsourcing facilities and compounders potentially interested in registering as outsourcing facilities, are awaiting FDA final guidance and regulations addressing the CGMP requirements applicable specifically to outsourcing facilities. In December 2018, FDA issued a revised draft guidance describing FDA's proposed policies regarding outsourcing facility compliance with the CGMP regulations in 21 CFR Parts 210 and 211. FDA's draft guidance explains that FDA intends to promulgate more specific CGMP regulations pertaining solely to outsourcing facilities. Funding would enable FDA to issue final guidance regarding compliance with 21 CFR Parts 210 and 211and proposed and final regulations relating specifically to the CGMP requirements for outsourcing facilities at a faster pace. This would give outsourcing facilities and those contemplating becoming outsourcing facilities clarity on CGMP requirements for outsourcing facilities, thereby assisting them in meeting healthcare providers' and patients' needs for quality compounded drugs.

Field: + $2.8 million / 10 FTE

Supporting Outsourcing Facilities' Efforts to Improve Compounding Quality

Outsourcing facilities would benefit from more frequent FDA inspections and site visits. These visits 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. Outsourcing facilities are distinct from conventional manufacturers in numerous ways and require specialized knowledge to inspect. Establishing a specialized group of investigators who would spend most their time on outsourcing facility inspectional activities would allow the investigators to develop a highly sophisticated expertise with cGMP requirements and policies specific to outsourcing facilities; become intimately familiar with the facilities, systems, and technologies that they routinely inspect; provide timely, consistent, substantive feedback when compliance issues are identified; and improve the efficiency of their inspections. It also would help FDA meet annual inspection targets and conduct additional facility visits when requested by the industry. In addition, further training can be provided to this specialized group of investigators, including cGMP requirements.

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: + $20.0 million / 2 FTE

Center: + $20.0 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, the 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 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 postmarket 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 2020 funding would 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. ln addition to accessing more detailed clinical data, this effort would apply modem 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 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. 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 would allow the optimization of human safety expert review while freeing resources to be redirected toward advancing product development, review, and approval. FY 2020 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: + $45.0 million / 5 FTE

Center: +$45.0 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 lag behind and inhibit innovation. Currently, FDA has several 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 would 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 would 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 could also enable safety issues to be monitored along all phases of the drug lifecycle from animal studies to premarketing clinical trials to postmarketing 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 2020 funding would 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 2020 funds requested would 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, the Agency 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 would 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 would 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 would 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: +$20.0 million / 5 FTE

Center: +$20.0 million / 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 2020 funding would 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 would 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 are identified on behalf of patients. FDA would 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: +$27.0 million / 5 FTE

Center: +$27.0 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 would 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 would 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 would 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 would support the capture and management of all the required information about a drug product, facilitate risk identification, mitigation and communication, and provide a structured template that would 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 would 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 would enable the automation of elements of the application review that are currently performed manually, reducing overall application review cycle times.

The funding request for this new generic drug review platform would 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 would support resources and costs for IT investments as well as, structure for data management, contracts and grants. Taken together, these programs would 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.

Opioids: + $55.0 million / 14 FTE

Center: +$33.2 million / 2 FTE

FDA requests $33.2 million to combat the opioid epidemic and to support the substantial work

that is needed to implement the SUPPORT Act, enacted in October 2018. The SUPPORT Act gives FDA new authorities to continue current epidemic-related efforts and develop and implement new actions to reduce the use, misuse, and abuse of opioid medicines. FDA will use the funding to develop and implement evidence-based actions targeted to:

- Decrease initial exposures to opioid medicines, thus preventing new addiction
- Support development and approval of treatments for individuals with opioid use disorder
- Foster the development of novel therapies without addictive properties to ensure that persons suffering from severe and chronic pain have the safe and effective medicines they need
- Improve enforcement and assess benefit-risk.

Critical areas related to the use and abuse of opioid drugs demand science-based study and analysis. For example, identified research studies include collecting, generating, and analyzing the pre-clinical, clinical, and real-world data needed to support safer analgesic packaging and rational prescribing through evidence-based treatment guidelines. FDA needs more information about pain and how to treat it more safely and effectively.

The requested funding will also support the development of surveillance programs that can help FDA assess the impact of its regulatory actions and treatment guidelines on opioid use, misuse, and abuse. FDA will use this evidence when developing regulatory policy, and targeted compliance and enforcement activities.

Funding will also support the development of a comprehensive systems model of the opioid crisis. This model is critical to harness the best available data to assess the potential effects and interdependencies of various interventions. FDA will also use funding to support development of studies to improve the evaluation of abuse-deterrent generic opioid products, and the development of mechanistic models and social and behavioral science research to help foster the safe use of opioids.

The FY 2020 Budget also requests funding to continue the activities critical to enhancing regulatory oversight of products entering the country through International Mail Facilities (IMF). With the requested resources, FDA will work to resolve a broad range of complex regulatory compliance and enforcement cases and issues related to importation of potentially unsafe medical products found at the IMFs. FDA will be required to respond to regulatory status consults on potential unapproved new drug and misbranding charges, follow up domestically on violative firms discovered from import surveillance and compliance work, and provide incident coordination and outreach related to imported products to protect public health.

FDA will also review and analyze imports data from the IMFs to identify trends and compliance issues for action to drive the IMF strategy. This includes the use of administrative destruction authority, establishing sampling plans, and deploying rapid screening technologies in the IMFs, and to ensure the effectiveness and consistency with risk-based imports policy and strategy to target higher risk products.

In addition, FDA will increase surveillance and cyber-driven intelligence based on drug information gathered at the IMFs. Also, ORA will compile the database of violative products and firms, and CDER will evaluate the products and websites and determine whether to issue a Warning Letter or other enforcement action to the person responsible for the website. The

requested resources will also support FDA's ability to have technical experts available to provide expert testimony in criminal trials.

Due to the complexity associated with the identification of these products, the wide range of natural and synthetic opioid drugs, FDA will need staff to sustain the critical efforts in this area.

The responsibilities of the additional staff will focus on supporting the IMFs and include but are not limited to:

- Method development, validation, development/maintenance of data libraries for current and future field instrumentation
- Confirmatory testing of samples
- Training of current and future import staff in the use of current and future field deployable instrumentation and methods
- Real time technical support to the IMFs remotely
- Participation as technical advisors during field operations
- Evaluation of new technology that can be applied to the analyses of opioids, drug products and supplements encountered daily in these facilities.

Field: + $21.8 million / 12 FTE

With the funding requested in the FY 2020 Budget, ORA will continue building out FDA presence at IMF facilities, improve product targeting, increase staff and safety, purchase equipment, and improve laboratory facilities.

After evaluating the needs of all IMFs, taking into consideration the corresponding divisions under program alignment, volume of parcel incoming by IMF and existing personnel, ORA began hiring to increase staffing to 125 FTE in support of the nine international mail facilities. The additional staff will provide the agency the manpower to increase its reviews from 15,000 to 100,000 per year. In addition, ORA is requesting additional staff and funds to support lab work related to the increased package screening.

Medical Countermeasures: +$1.0 million / 4 FTE

Center: + $1.0 million / 4 FTE

The FY 2020 Budget Request includes $1 million for FDA review and regulatory science capacity to facilitate the development and availability of MCMs to respond to CBRN and emerging infectious disease threats.

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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
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 2017: 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 2017: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
223212: Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt. *(Output)*	FY 2017: 99% 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 2017: 100% 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 2017: 96% Target: 90% (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
224221: Percentage of Human and Animal[43] Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (*Output*)	Baseline: 86% (New Measure)	80%	80%	Maintain

[43] Due to Program Realignment, ORA's Workplan now combines Human and Animal drug inspection activities together, so this combination performance goal is repeated in both the Human Drugs and Animal Drugs and Feed program narratives.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
224222: Percentage of Human and Animal[44] Drug follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (*Outcome*)	Baseline: 67% (New Measure)	55%	55%	Maintain
292202: Number of people for whom FDA is able to evaluate product safety through Mini-Sentinel/Sentinel system. *(Outcome)*	FY 2018: 292 million Target: 233 million (Target Exceeded)	N/A	N/A	N/A
292203: Number of medical product analyses conducted through FDA's Sentinel Active Risk Identification and Analysis (ARIA) System. *(Output) (New Measure)*	FY 2018: 74 (Historical Actual)	50	55	+5

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

REVIEW GOALS

The New Drug Review performance measures focus on ensuring that the public has access to safe and effective new treatments as quickly as possible. The goal of the PDUFA program is to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval. The Agency will continually work to meet or exceed the review performance goals when possible moving forward.

The goal of the GDUFA program is to enhance the efficiency of the generic drug review process, promote transparency between FDA and generic drug sponsors, and enhance access to high-quality, lower cost generic drugs. The value of this investment in the Generic Drug Review program is reflected by FDA's performance on its review goals under GDUFA and FDA's commitment to meet shorter review goals (8 months) for priority submissions under GDUFA II.

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, FDA is able to evaluate drug safety issues and inform regulatory decision making. To date, the Sentinel Initiative has contributed to multiple drug safety communications and labeling changes, providing vital information to patients and providers about the safety of drugs and vaccines.

[44] Due to Program Realignment, ORA's Workplan now combines Human and Animal drug inspection activities together, so this combination performance goal is repeated in both the Human Drugs and Animal Drugs and Feed program narratives.

Development of the Sentinel System has matured so that the number of people covered by the system is now sufficient to shift the focus of the performance goal to how the data are used to protect public health. Consequently, FDA has developed a new Sentinel performance measure that focuses on using the system to generate high quality evidence about the use of medical products and better understand their risks and benefits. The new measure leverages Sentinel's Active Risk Identification and Analysis (ARIA) system, which is comprised of pre-defined, parameterized, reusable routine querying tools, combined with the multi-site electronic data in the Sentinel Common Data Model. This enables safety analyses to be done more efficiently using a trusted distributed database that undergoes continuous quality checks and refreshes. The results of these analyses have been presented at FDA Advisory Committee Meetings, highlighted potential ways to intervene in the opioid crisis, informed responses to Citizens Petitions, and influenced numerous regulatory decisions.

The new goal is framed as the number of analyses conducted using the ARIA system. Given that this is a new goal, and that the analyses conducted each year can vary greatly in the number, timing, complexity and character of the safety issues, the initial targets have been set at 50 and 55 analyses for FY 2019 and 2020 respectively and will be reassessed periodically. These targets reflect the trend toward more complex analyses that employ more sophisticated analytical methods, which yield more meaningful inputs to public health and regulatory decision making.

NEW ORA FIELD PERFORMANCE MEASURES

ORA is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention and allows for a more robust analysis.

Program Activity Data

CDER Workload and Outputs	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	153	153	153
Efficacy Supplements	248	248	248
Manufacturing Supplements	2,001	2,001	2,001
Commercial INDs (Drugs and Biologics) with Activity	7,387	7,387	7,387
Sponsor Requests: IND-Phase Formal Meetings	2,887	2,887	2,887
Sponsor Requests: Review of Special Study Protocols	155	155	155
Submissions of Promotional Materials	107,108	114,000	116,500
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	70	70	70
Reviews: Standard NDA/BLA	141	141	141
Approvals: Priority NDA/BLA	56	56	56
Approvals: Standard NDA/BLA	89	89	89
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	9.5	9.5	9.5
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	19	19	19
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	7.9	7.9	7.9
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	11.9	11.9	11.9
Reviews: NDA Supplementals	3,095	3,095	3,095
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	6,033	6,335	6,652
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	193	193	193
Receipts: IND/IDE Amendments (Biologics Only)	23,648	23,648	23,648
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	16	16	16
Approvals: PLA/BLA	15	15	15
Reviews: License Supplement (PLA/ELA/BLA)	471	471	471
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	1,044	1,000	1,000
Outputs – Reviews/Approvals			
Actions – ANDA	4,225	4,000	4,000
Approval Actions - ANDA (both Tentative and Full Approvals)	971	975	1,000
Median Review Time from ANDA Receipt to Approval (months)	29.84	30	30
Actions - ANDA Supplementals (Labeling and Manufacturing)	5,786	5,700	5,800
Over-the-Counter Drug Review			
OTC Monographs Under Development*	25	25	25
OTC Monographs Published*	2	4	4
*Category includes Proposed Rules and Final Rules; OTC Monographs published in FY 2018: Health Care Antiseptic Final rule (FR 82, 243; 20 December 2017) and Withdrawal notice for Proposed Amendment to the TFM for ibuprofen (83 FR 22224; 14 May 2017)			

CDER Workload and Outputs	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information **	18	18	18
New Written Requests Issued**	22	21	22
Pediatric Exclusivity Determinations made**	13	9	9
Post Exclusivity Safety Report **	13	9	9
**Category includes Proposed Rules and Final Rules			
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	2,081,903	2,367,288	2,691,606
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	17,944	20,000	21,000
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,356	7,724	8,110
Number of drugs with Risk Communications	250	195	215
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	33	33	33
Number of FOI Requests	3,235	3,300	3,300
Number of FOI Requests Processed	3,229	3,325	3,325
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	116	123	123
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	202	190	190
Number of Citizen Petitions Completed [1] (excluding suitability petitions and OTC monograph-related petitions)	97	107	107

[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 2018 Actuals	FY 2019 Estimate	FY 2020 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,662***	***1,709***	***1,709***
Pre-Approval Inspections (NDA)	81	100	100
Pre-Approval Inspections (ANDA)	90	90	90
Bioresearch Monitoring Program Inspections	667	600	600
Drug Processing (GMP) Program Inspections	632	650	650
Compressed Medical Gas Manufacturers Inspections	42	50	50
Adverse Drug Events Project Inspections	73	88	88
OTC Monograph Project and Health Fraud Project Inspections	19	70	70
Compounding Inspections[1]	127	142	142
Domestic Laboratory Samples Analyzed	1,041	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1221***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	102	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	159	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	280	255	255
Foreign Drug Processing (GMP) Program Inspections	743	900	900
Foreign Adverse Drug Events Project Inspections	8	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,883***	***3,069***	***3,069***
IMPORTS			
Import Field Exams/Tests	8,607	10,000	10,000
Import Laboratory Samples Analyzed	735	620	620
Import Physical Exam Subtotal	**9,342**	**10,620**	**10,620**
Import Line Decisions	871,212	845,143	904,303
Percent of Import Lines Physically Examined	1.07%	1.26%	1.17%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,883***	***3,069***	***3,069***

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

[2] The FY 2018 actual unique count of foreign inspections includes 115 OIP inspections (48 for China and 67 for India).

3 ORA is currently evaluating the calculations for future estimates.

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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.

Leveraging Innovation

OOPD administers major provisions of the Orphan Drug Act and other relevant statutes, where Congress sought to provide incentives to promote the development of products for the treatment of rare diseases and for underserved populations. OOPD incentive program activities facilitate product development innovation and collaboration with private, public and academic entities. Further, the programs directly support the FDA's Strategic Policy Roadmap priority area to leverage innovation and competition to improve health care, broaden access, and advance public health goals.[45]

Orphan Product Grants Activity[46]

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

[45] https://www.hhs.gov/about/strategic-plan/strategic-goal-4/index.htmlhttp://www.hhs.gov/about/strategic-plan/strategic-goal-2/index.html"

[46] FY 20187 and FY 2019 each includes $1.2 million of OOPD program funds to support Orphan Product Grants

Clinical Trial Grants Program

Over 700 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. In FY 2018, OOPD received 79 clinical trial applications. OOPD funded 12 new grants, including studies to treat Stargardt Disease (a rare retinal disease that typically causes vision loss in childhood), and Head & Neck Squamous Cell Carcinoma. In addition, in FY 2018, OOPD provided funding or continued support for 75 other ongoing clinical study projects, including several Phase 3 trials.

OOPD published a new RFA for FY 2019 that will increase the impact of the program and allow for patient input into study designs.

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 appropriated grant funds, which are less than the $30 million congressionally authorized amounts, are covering less and less of the total cost for conducting clinical trials. 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

The Natural History Grant Program, launched in FY 2016 supports 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 in the first cycle of this new program, including 29 applications for Neurology focused studies and funded six new research grants for natural history studies in rare diseases, including studies for Friedreich's ataxia and sickle cell anemia. Two of the six grants were awarded through a partnership with the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS). OOPD published a new RFA for FY 2019. These 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.

Over 4,700 orphan drug designations OOPD issued since 1983 have resulted in over 700 marketing approvals, the 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. For FY 2018, OOPD received 521 new applications and designated 339 orphan drugs.

These included potential treatments for many kinds of rare cancers, sickle cell disease, and Ebola. FDA approved 88 orphan designated drugs for marketing indications in FY 2018 to date.

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.

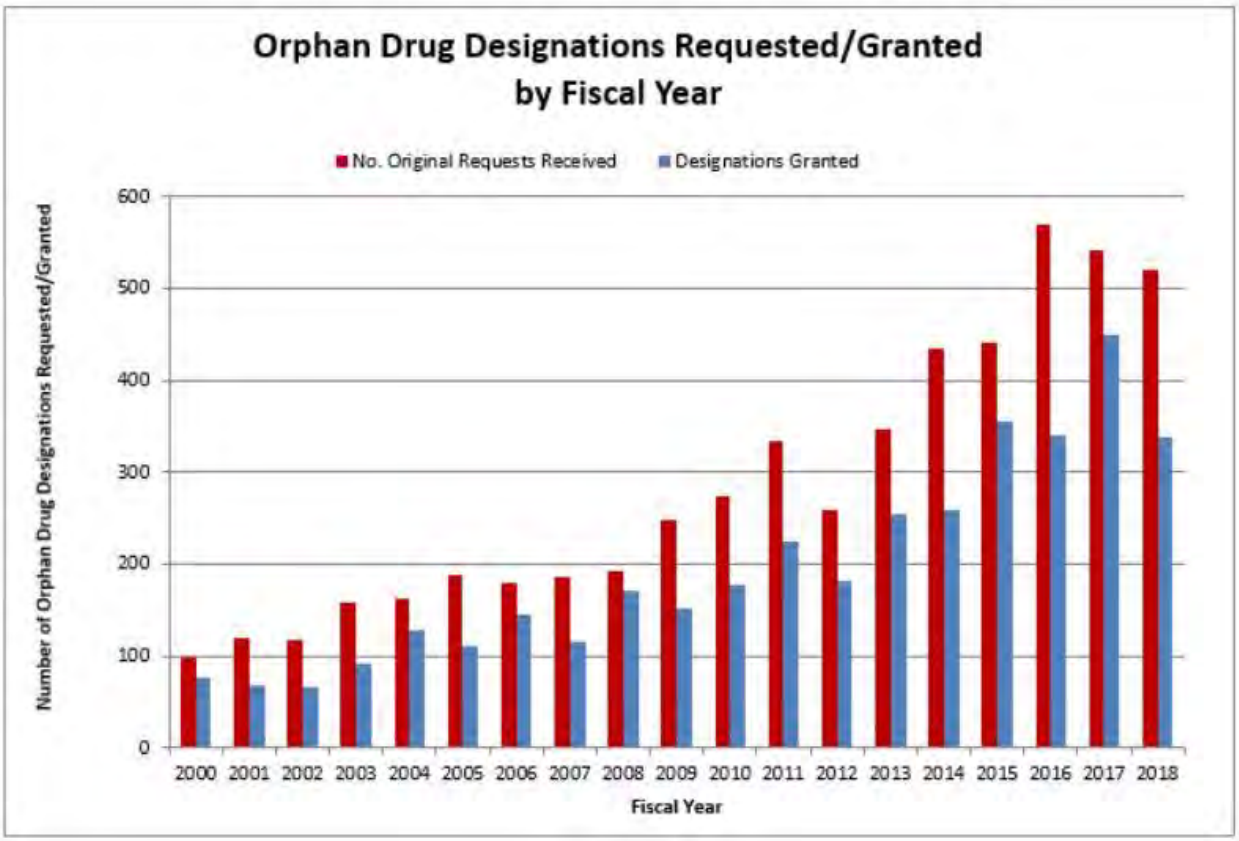

Figure 4 Orphan Drug Designations Requested/Designated by Fiscal Year

Product Designations

Below are examples of Orphan Product designations that occurred in 2018.[47]

Date	**Product**	**Purpose or Benefit**
July 2018	Gene Therapy	Treatment of Spinal Muscular Atrophy (SMA)
August 2018	Autologous Mesenchymal Stem Cells	Treatment of Amyotrophic Lateral Sclerosis (ALS)

Rare Pediatric Disease Priority Review Voucher Designation

The Food and Drug Administration Safety and Innovation Act (FDASIA) added Section 529 to the FD&C Act to encourage development of new drug and biological products ("drugs") for the prevention and treatment of qualifying rare pediatric diseases. This legislation created the Rare Pediatric Disease Priority Review Voucher (PRV) program wherein the sponsor of an approved

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

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. OOPD partners with the Office of Pediatric Therapeutics in making rare pediatric disease determinations. In FY 2018, OOPD received 51 new rare pediatric disease designation requests plus two consults from submitted marketing applications needing rare pediatric disease determinations. OOPD determined that 52 requests/consults 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. In FY 2018, a total of four rare pediatric disease priority review vouchers were issued.

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

Humanitarian Use Device Designation Activity

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

OOPD reviews applications from sponsors requesting HUD designation. A device that has received HUD designation is eligible for Humanitarian Device Exemption (HDE) approval if, among other criteria, the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of available devices or alternative forms of treatment. FDA approval of an HDE application authorizes the applicant to market the device. This marketing approval is subject to certain profit and use restrictions set forth in Section 520(m) of the FD&C Act. Since 1990, 74 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 FY2018, 16 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 2018, OOPD received 17 new HUD applications and designated 17 devices. Of the 17 devices that were designated, nine designations were based on HUD applications originally submitted in prior years. In FY 2018, two devices received an HDE approval from CDRH. Also, in FY 2018, one manufacturer who previously had 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,

11 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. The Consolidated Appropriations Act, 2017 (House and Senate Committee Reports) increased the appropriations of the program to a total of $6 million from $3 million. On August 18, 2017, FDA Reauthorization Act of 2017 extended the program through September 30, 2022.

On January 16, 2018, FDA posted a new Request for Applications for the Pediatric Device Consortia Grants Program, administered by OOPD, with the goal to facilitate the development, production, and distribution of pediatric medical devices through funding of pediatric device consortia. In FY 2018, FDA awarded five consortia funding $6 million per year over the next five years. Of the estimated $6 million granted this year, approximately $1 million will be used for real-world evidence projects to develop, verify, and operationalize methods of evidence generation, data use and scalability across device types in the pediatric device ecosystem. The consortia funded in this program are based out of Philadelphia, PA; Washington, DC; Houston, TX; Los Angeles, CA; and San Francisco, CA.

Since the program's inception in 2009, a total of $37.4 million has been awarded to the consortia. Collectively, the consortia have supported the development of more than 1000 potential pediatric devices, many of which are in the early stages of development. Over 20 new devices are now available for use in pediatric patients as a result of advisory assistance received from the consortia, including the PIVO, a needle-free blood collection device that attaches to peripheral IV systems; the JustRight Surgical Vessel Sealing System designed for use in open and laparoscopic general surgical procedures to seal blood vessels and vascular bundles; and the Lifeflow Rapid Infusion to deliver fluids to a patient's vascular system. The consortia collectively have also raised more than $150 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 2018, OOPD participated in 35 individual industry outreach and patient oriented meetings. In addition, OOPD received 60 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 25 of these meetings, often to explain how orphan drugs and humanitarian devices could be developed with ODA incentives and HDE provisions, as well as FDARA, the 21st Century Cures Act, and 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 2018 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. In FY 2019 through FY 2021, 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	User Fees
FY 2016 Actuals	$29,099,000	$29,099,000	$0
FY 2017 Actual	$29,099,000	$29,099,000	$0
FY 2018 Actual	$29,099,000	$29,099,000	$0
FY 2019 Annualized CR	$29,099,000	$29,099,000	$0
FY 2020 President's Budget	$29,099,000	$29,099,000	$0

Funding History table is not comparably adjusted.

BUDGET REQUEST

The FY 2020 Budget Request is $29,099,000. With this funding level, OOPD will fund approximately 10-12 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

Office of Orphan Products Development Program Activity Data			
Program Workload and Outputs	**FY 2018 Actual**	**FY 2019 Estimate**	**FY 2020 Estimate**
Grant Programs			
Total Orphan Product Grant (New and Continuations)	87	90	90
Total Pediatric Consortia Grants (New and Continuations)	5	5	5
Total Natural History Grants (New and Continuations)	6	7	7
Orphan Drug Designation Requests/Designations Granted/Orphan Drug Approvals			
New Orphan Drug Designation Requests	521	550	550
Drug Designations Granted	339	350	350
FDA Orphan Drug Marketing Approvals	88	90	90
HUD Requests and Designations			
New HUD Designation Requests	17	27	27
HUD Designations	17	20	20
Rare Pediatric Disease Priority Review Voucher Requests and Designations			
New RPD Requests	53	65	65
RPD Designations	52	55	55

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BIOLOGICS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
Biologics	**363,766**	**381,890**	**379,144**	**431,561**	**52,417**
Budget Authority	***217,138***	***217,135***	***217,138***	***262,138***	***45,000***
User Fees	***146,628***	***164,755***	***162,006***	***169,423***	***7,417***
Center	320,146	338,310	335,355	387,812	52,457
Budget Authority	175,132	175,131	175,132	220,132	45,000
User Fees	145,014	163,179	160,223	167,680	7,457
Prescription Drug (PDUFA)	130,171	151,195	144,529	151,782	7,253
Medical Device (MDUFA)	13,602	11,887	14,444	14,117	-327
Generic Drug (GDUFA)	1,055	78	1,072	1,085	13
Biosimilars (BsUFA)	186	19	178	696	518
Field	43,620	43,580	43,789	43,749	-40
Budget Authority	42,006	42,004	42,006	42,006	---
User Fees	1,614	1,576	1,783	1,743	-40
Prescription Drug (PDUFA)	1,410	1,370	1,566	1,532	-34
Medical Device (MDUFA)	204	206	217	211	-6
FTE	**1,434**	**1,434**	**1,394**	**1,422**	**28**

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 Institutes 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) biologics 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; and
- Strengthen CBER as a preeminent regulatory organization for biological products.

CBER's strategic plan contributes to the improvement of public health and provides 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. 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.

The Biologics Program accomplishments align with the CBER and Department of Health and Human Services' Strategic Plan, the FDA 2018 Strategic Policy Roadmap, and reflects implementation of new legislative mandates, expanded roles in addressing health needs, recent innovations in regulatory science and technology, and expanded opportunities for collaboration. The following selected accomplishments demonstrate the Biologics Program's delivery of its regulatory and public health responsibilities within the context of current priorities.[48]

Foster Competition and Innovation

FDA takes steps to facilitate efficient access to beneficial, safe and effective, and innovative products that can address existing, novel, and emerging health problems. 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 advance the development of innovative and complex biological products, including those representing ground breaking treatments, the exciting medical promise of precision medicine, and treatment options where very limited options exist. FDA also promotes innovation in manufacturing that can increase the reliability and safety of product supply, ensure the domestic supply of strategic biologics products, and potentially lower the cost of products through advances in how they are made.

Modernizing the Regulatory Process to Improve Innovation

FDA is taking steps to ensure the regulatory process is predictable, transparent, and scientifically modern, while also facilitating innovation by applying a risk-based regulatory approach. FDA has developed new policies and guidance for product regulation in key areas of novel medical science, with the goal of creating pathways that allow beneficial new technologies to efficiently reach patients while maintaining our standards for product safety and effectiveness. This work to modernize the regulatory process supports the strategy from the HHS Strategic Plan FY 2018-

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

2022 to leverage cutting-edge science to support product development strategies and regulatory evaluation.

Programs such as the Regenerative Medicine Advance Therapy (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 40 Breakthrough Therapy designations, with 28 of the 40 products being for rare diseases (Orphan Product designated). In FY 2018, FDA granted seven Breakthrough Therapy designations. The Agency has also granted 30 RMAT Designations since program inception in December 2016[49].

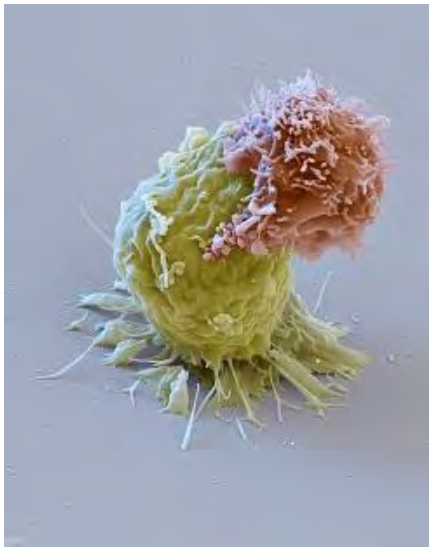

Figure 5 CAR-T Cell Attacking Cancer Cell

The FDA's 2017 approvals of the first three gene therapy products, two that use engineered immune T-cells to reprogram a patient's own cells to attack cancer and one directly administered gene therapy, are a result of decades of research. To support continued innovation in this field and provide clear recommendations to sponsors and researchers of novel therapies, FDA issued a suite of six human gene therapy guidances in July 2018. These guidances serve as the building blocks of a modern, comprehensive framework to help advance the field of human gene therapy while making sure new products meet the FDA's standards for safety and effectiveness. Three guidances are disease specific (hemophilia, retinal disorders and rare diseases) and three provide comprehensive updates to three existing guidances, originally published from 2006 and 2008, that address manufacturing issues related to human gene therapy.

FDA is working with the National Institute of Standards and Technology and other stakeholders to facilitate an effort to coordinate and prioritize the development of standards and consensus definitions of terms for regenerative medicine therapies, which include gene therapies. These standards and terms will help foster the development, evaluation, and review of such products.

FDA launched the INitial Targeted Engagement for Regulatory Advice on CBER producTs (INTERACT) meeting program in June 2018 for potential sponsors to engage with FDA early in the development process and obtain advice on a wide range of development-related topics. These meetings can be used to clarify CBER's expectations regarding product development programs and to help facilitate more efficient product development.

Ensure Availability of Novel Products

To improve innovation and help unlocking the full potential of novel technologies like cell and gene therapies, and new vaccines, FDA is working with industry on advanced manufacturing technologies. These technologies hold great promise for improvements in the reliability, flexibility and cost effectiveness of manufacturing for biological products. CBER awarded five grants to globally-recognized research institutions to study and recommend improvements for the continuous manufacturing of biological products, as well as innovative monitoring and control

[49] As of December 31, 2018

techniques. These grants help encourage the establishment of high tech manufacturing platforms in the U.S. and help bridge the knowledge and experience gaps in the adoption of emerging manufacturing technologies in the biological product sector.

FDA works to ensure the domestic supply of certain strategic products. For CY 2018, the Biologics Program has documented four new drug product shortages, 14 prevented shortages, five ongoing shortages, 44 notifications from 22 different manufacturers. CBER has used regulatory flexibility to prevent or mitigate one shortage and expedited 19 reviews to prevent or mitigate a shortage.

FDA developed a work plan in 2018 with the U.S. Department of Defense (DoD) to ensure that those products that are prioritized by DoD as important to the health of those involved in national defense receive the highest level of attention from the Agency, on par with breakthrough designated therapies. The plan was finalized, and a MOU was signed, in November 2018. This plan enhances collaboration and coordination and places initial priority on products regulated by CBER to help ensure safe and effective products are available to those protecting our Nation.

In July 2018, FDA granted an emergency use authorization (EUA) to DoD to enable the emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma. Under this EUA, the product is authorized for the treatment of hemorrhage or coagulopathy of U.S. Military personnel during an emergency involving agents of military combat when plasma is not available for use or when the use of plasma is not practical. Hemorrhage is the leading cause of preventable deaths among combat trauma casualties.

To further advance the development and availability of dried plasma, in October 2018, FDA issued a draft guidance titled, "Considerations for the Development of Dried Plasma Products Intended for Transfusion." The draft includes recommendations regarding starting materials for the preparation of dried plasma products, manufacturing and product quality, product characterization studies, packaging and reconstitution, clinical studies and devices for manufacturing dried plasma.

Real World Evidence to Evaluate Effectiveness and Safety

In December FDA released a new strategic approach, "the Framework for the Real-World Evidence Program," to leverage information from large medical databases from healthcare providers, insurance claims data, and other partners. FDA is developing new tools to collect data from routine medical care to gain a deeper understanding of a medical product's safety and benefits, additional treatment implications, and potential limitations. Real-World Evidence (RWE) captured throughout the totality of a product's post-approval lifecycle has been a significant aid in informing regulatory decisions, including the development of new products and changes to existing products. This initiative ties to the strategy from the HHS Strategic Plan FY 2018-2022 to identify and assess adverse events related to the use of regulated human medical products, including the development and more effective use of large, nationally representative database systems, electronic health records, common data models, and natural language processing (NLP).

FDA continued progress in launching the Biologics Effectiveness and Safety (BEST) Initiative, an expansion of the CBER Sentinel program. BEST provides access to electronic health record sources from over 20 million patients to conduct robust, rapid safety/effectiveness studies of blood, advanced therapeutics and vaccines. Though the BEST Initiative, CBER has successfully

implemented improved coding for biological products with three data partners, vastly improving our transfusion safety surveillance capabilities.

BEST has been used to perform several hundred queries related to safety and regulatory questions such as estimating blood usage, identifying reasons for transfusions, and identifying transfusion-related adverse events and estimating their rates. Leveraging the power of BEST, FDA developed individual clinical profiles for transfusion recipient patients and estimated adverse event rates for transfusion-related acute lung injury across three data partners for the period of spanning 2010 to 2018.

Further, BEST is harnessing innovative approaches such as machine learning, artificial intelligence and NLP to conduct queries and medical chart reviews of EHR records to improve FDA's ability to identify cases of Transfusion-Associated Circulatory Overload and Post-transfusion Sepsis, both very serious and life-threatening medical conditions.

FDA collaborated with the Center for Medicare and Medicaid Services to conduct a rapid response analysis of the relative effectiveness of cell-cultured and egg-based vaccines among Medicare beneficiaries ages greater than 65 years of age. This investigation showed a modest increase in effectiveness of cell-cultured vaccines as compared to egg-based vaccines.

FDA, in collaboration with the National Heart Lung and Blood Institute and the HHS Office of the Assistant Secretary launched the Transfusion Transmissible Infections Monitoring System (TTIMS) to help assure the continued safety of the U.S. blood supply and monitor the effects of FDA's policy changes regarding donor deferral. TTIMS contractors are actively monitoring over 60 percent of the U.S. blood supply by developing methods to calculate incidence/prevalence for HIV, hepatitis B virus and hepatitis C virus pre- and post-implementation of the men who have sex with men one-year donor deferral policy.

The contractors completed recency testing of all in-house HIV samples on 8.4 million blood donations collected from January 2017 through September 2018 by the American Red Cross. It was determined and reported at the 2018 AABB conference that it is too early to understand the impact of the blood deferral policy, since the number of donations from reinstated MSM donors (0.017 percent of the 8.4 million donations) is too small to assess any meaningful impact on national blood collections.

Improve Global Public Health Through International Collaboration

FDA provides scientific and regulatory advice to sponsors and stakeholders and collaborates with other agencies and international regulatory authorities such as NIH/National Institute of Allergy and Infectious Diseases, HHS, the Biomedical Advanced Research and Development Authority, and the Coalition for Epidemic Preparedness Innovations on prevention of emerging infectious diseases. International collaborations enable a rapid/effective response to public health emergencies using established communication channels, relationships, partnerships. Rapid response helps decrease the spread of infectious disease, which may be spread by travel to endemic areas.

In October 2018, FDA/CBER representatives participated in the World Health Organization (WHO) Expert Committee on Biological Standardization meeting to establish WHO Biological Reference Preparations and written standards relevant to the manufacturing, licensing, and control of biological products. FDA also participated with the Management Committee and

Assembly of the International Council for Harmonisation to discuss Multiregional Clinical Trials, Good Clinical Practices, and Continuous Manufacturing.

FDA collaborated with CDC and WHO to enable the availability of an investigational Ebola vaccine provided to individuals residing in the Democratic Republic of the Congo suffering from a current outbreak of this disease. In June 2018 CBER also participated in WHO's Global Advisory Committee for Vaccine Safety. This committee provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short or long-term national immunization programs.

FDA representatives 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. FDA also served as the Chair to the Asia-Pacific Economic Cooperation Regulatory Harmonization Steering Committee to continue efforts around establishing Centers of Regulatory Excellence for training regulators in best regulatory practices.

FDA hosted the 21st U.S.-Japan Cellular and Gene Therapy Conference on March 1, 2018, in conjunction with Japan's Ministry of Education, Culture, Sports, Science and Technology, under the U.S.-Japan Cooperative Research Program. Ideas were exchanged on cutting edge and diverse areas of biomedical research, and enhanced opportunities for collaborations, focusing on neurodegenerative diseases, growing challenges, therapeutic advances and barriers to progress in the research area.

To yield greater efficiencies for U.S. and E.U. regulatory systems by avoiding duplication of inspections and enable reallocation of resources towards inspection of manufacturing facilities with potentially higher public health risks across the globe, FDA signed a Mutual Recognition Agreement with the European Union on November 1, 2017. CBER has actively participated in conducting assessments resulting in fifteen-member states achieving positive capability assessments and has begun requesting inspection reports for firms under its auspices.

Strengthen Science and Efficient Risk-Based Decision Making

To modernize our regulatory toolbox, FDA is incorporating the best science and implementing policies that help new, beneficial innovations reach consumers efficiently. By adopting the most advanced science and risk management tools to inform our policies, FDA will facilitate product development by designing better ways of predicting the safety, purity, potency, and effectiveness of biological products early in their life cycle. These tools will help maintain FDA's gold standard for product review, and make sure that our approach to managing risk are efficient and up-to-date.

FDA also ensures the continued safety of the blood and tissue supply by keeping them free of infectious agents and contamination and approving safe and effective vaccines to prevent the spread of infectious diseases. This work is instrumental in decreasing the morbidity and mortality associated with these diseases as well as helping to halt the spread of the disease.

FDA's field work plays an integral role in helping to assure the safety of FDA-regulated products. The field staff provides additional surveillance through inspections at domestic and foreign manufacturing facilities and clinical study sites, including blood and tissue establishments, vaccine and allergenic facilities, device manufacturers, gene and cell therapy facilities, and plasma fractionators. Strengthening science and efficient based decision making

supports the HHS strategic plan strategy to "Improve surveillance, epidemiology, and laboratory services" to guide better decision making to target interventions more responsibly, and ultimately improve health.

Facilitate Product Development Through Applied Research

Incorporating the best science is a key part of promoting access to products that can help people improve their lives. 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 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. The applied research program supports development of new tools, models, standards, and methods, harnessing new technologies to expedite product development and provide effective regulatory responses to public health emergencies. This work supports the strategy from the HHS Strategic Plan FY 2018-2022 to conduct research to facilitate development and availability of innovative, safe, and efficacious medical products, including development of regulatory science.

In October 2018, FDA with the Centers of Excellence in Regulatory Science and Innovation, held a workshop, "Predictive Immunogenicity for Better Clinical Outcomes." The workshop included discussion on the advances in the development of technological approaches for predictions of immunogenicity and explored strategies for choosing appropriate tools and interpreting the results. Immunogenicity, the propensity of a therapeutic protein to induce immune responses, may affect safety and/or efficacy, and is thus an important concern in the development and regulation of cell and gene therapies and protein therapeutics, which are rapidly expanding therapies.

In May 2018, CBER convened the Vaccines and Related Biological Products Advisory Committee to discuss approaches for demonstrating effectiveness of group B streptococcus (GBS) vaccines intended for use in pregnant women to protect the newborn infant. GBS causes substantial infant morbidity and mortality globally. The development, licensure, and distribution of an effective vaccine that protects against invasive GBS disease in the newborn and young infant would be expected to significantly reduce disease. Currently, there no licensed vaccine to prevent GBS disease, however research is emphasizing the development of a vaccine that can be administered to pregnant women to prevent infant disease.

In September 2018, FDA and NIH/ National Institute of Allergy and Infectious Diseases held a public workshop entitled, "Science and Regulation of Live Microbiome-Based Products Used to Prevent, Treat, or Cure Diseases in Humans" to bring together the scientific community to discuss microbiome-based products and how they may be used to prevent or treat a variety of different diseases. Topics included the regulatory framework for live microbiome-based products; safety and effectiveness of live microbiome-based products used to prevent, treat, or cure diseases in humans; and strain selection for live microbiome-based products to prevent, treat, or cure diseases in humans.

Many diseases that used to be common in this country and around the world, including polio, measles, diphtheria, pertussis, rubella, mumps, tetanus, rotavirus and Haemophilus influenzae type b can now be prevented by vaccination. Vaccines have eradicated smallpox and prevented countless cases of disease and saved millions of lives.

While vaccines are highly effective, there have been small increases in Mumps and pertussis in the United States. Research conducted in coordination with CDC indicates that by college age, levels of anti-mumps virus antibodies had declined substantially. FDA is currently evaluating ways of improving the vaccine, such as optimizing the structure of the vaccine virus to trigger the production of longer-lasting, more robust antibodies. To determine why pertussis rates have been rising, CBER is studying pertussis vaccine in baboons, an animal model that closely reproduces the way whooping cough affects people and found that people immunized with acellular vaccines may be protected from whooping cough symptoms, they may still become infected and infect others, including infants.

Modernizing Clinical Data to Make Product Development More Efficient

FDA has been working to modernize the approach to the design of clinical trials for drugs and biologics to help make drug development more efficient and less costly and to increase information for providers and patients. To help modernize the process FDA held two joint public meetings in March 2018 to help gather feedback for the development clinical trial guidance documents and new pilot programs.

Two draft guidances were released in September 2018. The first guidance gives recommendations to sponsors to address the design and conduct of clinical trials intended to evaluate more than one investigational drug at the same time, or more than one cancer type or both within the same overall trial structure. For example, a trial could allow multiple rare B-cell malignancies to be tested with one therapy. The second guidance addresses adaptive trial designs that allows for planned modifications to one or more aspects of the design based on data collected from the study's subjects while the trial is ongoing, to improve efficiency.

FDA launched two new pilots for drugs and biologics: Complex Innovative Designs (CID) Pilot Meeting Program and Model-Informed Drug Development (MIDD). CID helps to solidify the science used to support novel approaches and promote their adoption in drug development programs. MIDD approaches facilitate the development and application of exposure-based, biological, mathematical and statistical models derived from preclinical and clinical data sources and use a variety of quantitative methods to help balance the risks and benefits of drug products in development. These pilots will help further the development of medical products.

Protect the Public Health from Infectious Disease

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 which can be spread through contact with infected individuals, travel to endemic areas, arthropod vectors, risk behaviors, and many other mechanisms. According to the Centers for Disease Control and Prevention, vaccines, which are regulated by FDA to ensure they are safe and effective, have reduced preventable infectious diseases to an all-time low and now few people experience the devastating effects of vaccine-preventable diseases. The following graphic compares vaccine-preventable diseases in the U.S. from the 1900's to present time.[50]

[50]Source: Adapted from the CDC Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition https://www.cdc.gov/vaccines/pubs/pinkbook/index.html and the March 2018 update at https://www.cdc.gov/vaccines/pubs/pinkbook/pink-errata.html.

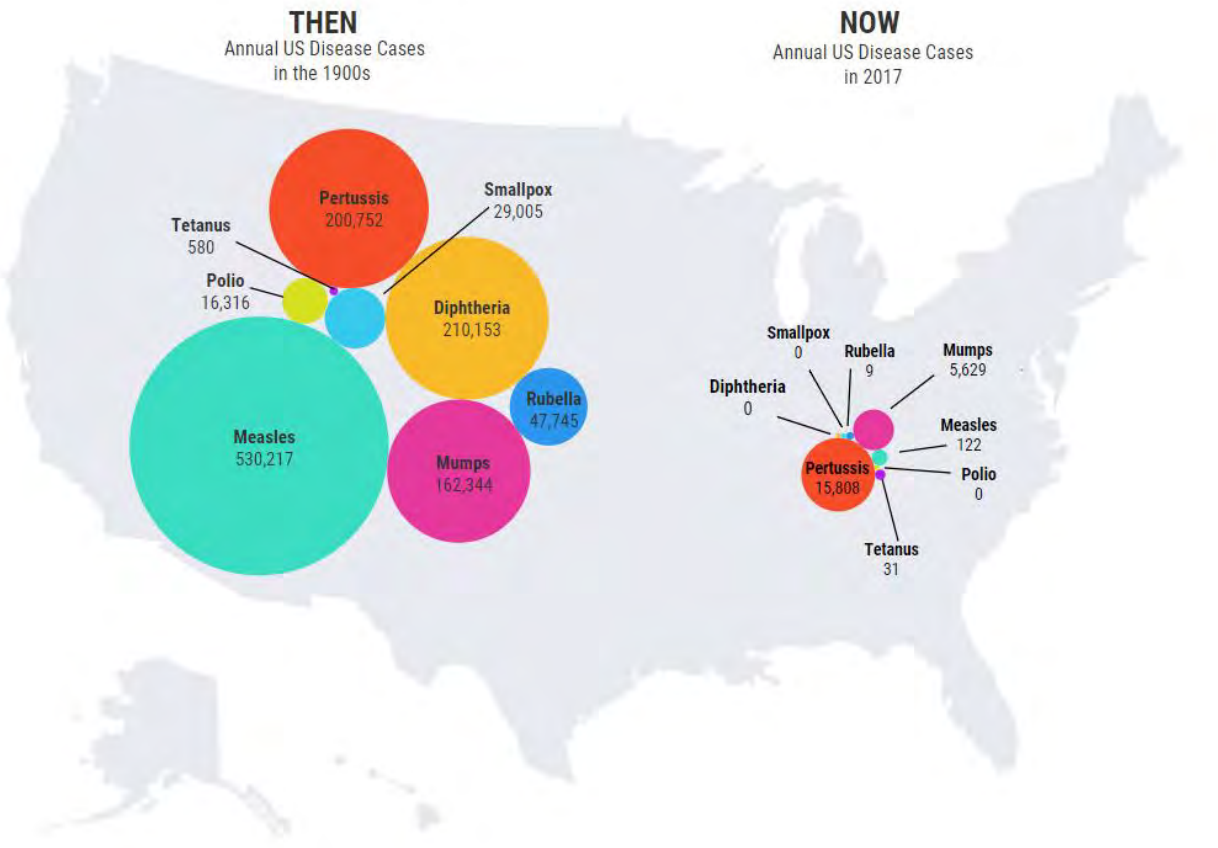

Figure 6 Impact of Vaccines in the 20th and 21st Centuries

FDA approved three influenza vaccines, expanding their approved use to include children as young as six months of age, in 2018. Previously only one influenza vaccine was approved for use in children as young as 6 months of age. Children younger than 5 years of age, especially those younger than 2 years, are at high risk of serious flu-related complications.

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 this information and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee, which met on March 1, 2018, FDA selected the strains for inclusion in the influenza virus vaccines for the 2018-2019 U.S. influenza season.

To promote the development and adoption of innovations that can ensure the continued safety of the U.S. blood supply, FDA released "Bacterial Risk Control Strategies for Blood Collections Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion" draft guidance in December 2018. The draft guidance incorporates feedback from discussions held during the July 2018 Blood Products Advisory Committee meeting and updates the previous draft guidance from 2016 and reflects broader FDA efforts to advance and encourage new developments to enhance product safety. This guidance also further advances the potential for technology to be used to reduce the risk of contamination of the blood supply from known and emerging pathogens, while ultimately reducing cost overall.

To ensure there are effective and efficient ways to screen for Zika in the blood supply, as well as in donated human cells and tissues, FDA published revised recommendations in July 2018 for testing blood donations for the Zika virus. When Zika virus first emerged, the unknown course of the epidemic and the observed severe effects from the disease indicated that individual donor testing was needed to ensure the continued safety of the blood supply. Given the significant decrease in cases of Zika virus infection in the U.S. and its territories, FDA now recommends testing pooled blood donations and switching to individual donor testing only in specific situations, based on guidelines in FDA published guidance.

Figure 7 Figure 3 Blood Donation

Current scientific knowledge continues to support the recommendation to screen living donors of cells or tissues for risks of infection with Zika virus based on geographical areas with risk.

FDA is working to protect the blood and tissue supply from tick-borne diseases; the Centers for Disease Control (CDC) has identified 18 tick-borne pathogens in the United States and additional pathogens associated with tick bites are emerging.

Transfusion-transmitted babesiosis has emerged as a significant risk to the U.S. blood supply. Human babesiosis is a disease transmitted primarily through tick vectors caused by Babesia microti (B. microti), which is a rodent parasite. In March 2018, FDA approved the first donor screening tests for the detection of antibodies to B. microti in human plasma samples and for the detection of B. microti DNA in human whole blood samples. In July 2018, FDA published a draft guidance providing recommendations for donor screening, donation testing, donor deferral, and product management to reduce the risk of transfusion-transmitted babesiosis from donors of blood and blood components. In January 2019, FDA approved the first nucleic acid amplification test (NAT test) for the detection of RNA from multiple Babesia species in whole blood specimens.

Pathogen reduction technology has the potential to improve blood safety by reducing or eliminating infectious organisms, including bacteria, viruses, and parasites, from blood components intended for transfusion. CBER continues to support the development and implementation of pathogen reduction technologies for blood components intended for transfusion. To help advance these technologies and explore expansion of their use from plasma and apheresis platelets for transfusion to whole blood and red blood cells, in November 2018, CBER hosted a two-day public workshop on Pathogen Reduction Technologies for Blood Safety.

Compliance and Oversight

Postmarket inspections are conducted after products are approved and 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. These inspections are performed to assure that products are manufactured in compliance with Current Good Manufacturing Practices and other applicable FDA regulations.

Surveillance is provided through inspections at domestic and foreign manufacturing facilities and clinical study sites, including blood and tissue establishments, vaccine and allergenic facilities, device manufacturers, gene and cell therapy facilities, and plasma fractionators. This work

supports the strategy from the HHS Strategic Plan FY 2018-2022 to "Improve surveillance, epidemiology, and laboratory services" to guide better decision making to target interventions more responsibly, and to identify and mitigate urgent and persistent threats to public health.

Though cell-based regenerative medicine holds significant medical promise, the marketing of unapproved treatments potentially puts patients' health at risk. As a part of FDA's comprehensive policy framework for the development and oversight of regenerative medicine products, FDA took action regarding three stem cell companies in 2018 for marketing products without FDA approval and for significant deviations from good manufacturing practice requirements, putting patients at risk. These actions included:

- Filing two complaints in federal court seeking permanent injunctions to stop two stem cell clinics from marketing stem cell products until, among other things, they obtain necessary FDA approvals and correct their violations of current good manufacturing practice requirements.
- Issuing a warning letter for marketing an adipose derived stem cell product without FDA approval and for significant deviations from current good manufacturing practice requirements.

EMPOWER CONSUMERS AND PATIENTS

FDA is also working to bridge early-stage efforts, such as the Patient Focused Drug Development meetings, to advance more systematic, methodologically-sound approaches to collect patient and caregiver input, such as burden of disease and treatment and the benefits and risks in the management of the patient's disease, so that it becomes data that can further inform regulatory decision-making.

In June 2018, CBER and CDER issued the draft guidance, "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input." It is the first of a series of four patient-focused drug development guidance documents to address, in a stepwise manner, how stakeholders (patients, researchers, medical product developers and others) can collect and submit patient experience data and other relevant information from patients and caregivers for drug and biological product development and regulatory decision-making.

To inform development of patient-focused drug development guidance in October 2018, FDA hosted a workshop to identify methodological approaches to develop and identify what is most important to patients and caregivers; and best practices for selecting, developing or modifying fit-for-purpose Clinical Outcome Assessments to measure the patient experience in clinical trials.

CBER initiated three patient experience data studies to collect patient preference information to inform regulatory decision-making. Patients are the people who will ultimately experience the benefits, risks, and daily impact of disease treatments. Patients have diverse circumstances and experiences that shape their preferences and their willingness to accept risks in pursuit of treatments that bring benefits to their lives. As FDA weighs treatments for approval, it is important to understand how different patient populations balance the benefits and risks of different treatment options.

SELECTED GUIDANCES TO SUPPORT MISSION AND PRIORITY AREAS

FDA guidances are documents that explain the agency's interpretation of, or policy on, a regulatory issue. Guidances are prepared primarily for industry, but also for other stakeholders and internal staff, and FDA uses them to address such matters as the design, manufacturing, and testing of regulated products; scientific issues; content and evaluation of applications for product approvals; and inspection and enforcement policies. Although guidances are not legally binding, they show stakeholders one way to reach their regulatory goal. However, stakeholders are free to use other approaches that satisfy the relevant law and regulations.

Below are other selected guidance documents recently issued by CBER, not discussed elsewhere in the Biologics Program Description and Accomplishments.[51]

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

Date	#	Title	Description
Dec 2018	FDA-2018-D-3380	Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products; Draft Guidance	Describes considerations for the development and labeling of in vitro companion diagnostic devices to support indicated uses of multiple biologic oncology when appropriate.
Oct 2018	FDA-2018-D-3090	Hematologic Malignancies: Regulatory Considerations for Use of Minimal Residual Disease in Development of Drug and Biological Products for Treatment; Draft Guidance	Assists sponsors planning to use minimal residual disease as a biomarker in clinical trials conducted under an investigational new drug application or to support marketing approval of biological products for treatment of specific hematologic malignancies.
Oct 2018	FDA-2018-D-3268	Rare Diseases: Early Drug Development and the Role of Pre-IND Meetings;Draft Guidance	Assists sponsors of biological products for the treatment of rare diseases in early development and in the planning of and participation in formal pre-investigational new drug application meetings with the FDA.
Sept 2018	FDA-2015-D-3438	Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use; Guidance	Provides industry FDA's recommendations on selection of appropriate package type terms and selection of appropriate discard statements for injectable medical products for human use, packaged in multiple-dose, single-dose, and single-patient-use containers.
Aug 2018	FDA-2018-D-3092	Hematologic Malignancy and Oncologic Disease: Considerations for Use of Placebos and Blinding in Randomized Controlled Clinical Trials for Drug Product Development; Draft Guidance	Provides recommendations to industry regarding use of placebos and blinding in randomized controlled clinical trials in development programs for biological products for treatment of hematologic malignancies and oncologic diseases.

SELECTED BIOLOGICS PRODUCT APPROVALS

New biological drugs such as vaccines, blood products, biotechnology products, and gene therapy and biological medical devices must be proven safe and effective before companies can put them on the market. FDA reviews the results of laboratory, animal, and human clinical testing done by companies to determine if the product they want to put on the market is safe and effective.

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

Disease	Approved	Trade Name	Proper Name	Purpose or Benefit
Certain cancers and diseases caused by nine HPV types	Oct 2018	Gardasil 9	Human Papillomavirus (HPV) 9-valent Vaccine, Recombinant	Expanded the approved use of the vaccine to include women and men aged 27 through 45 years
Transfusion reactions	Oct 2018	ID CORE XT	ID CORE XT (Reagents and Analysis Software)	Red blood cell typing provides significant advantages to patients requiring frequent transfusions helping to reduce transfusion reactions.
Thermal Burn Wounds	Sep 2018	RECELL Autologous Cell Harvesting Device	Mechanical and enzymatic autologous skin processor for preparing cell suspension, with applicator	Covers up to 80 times the area of the donor skin sample. Sprayed onto a burn for patients 18 years of age and older.
Hemophilia A	Aug 2018	JIVI	Antihemophilic Factor (Recombinant), PEGylated	Used to treat and control bleeding in previously treated adults and adolescents (12 years of age and older) with hemophilia A.
Zika	July 2018	cobas Zika	Procleix Zika Virus Assay	For detection of Zika virus RNA in plasma specimens from individual living human donors, in whole blood and blood components and to screen organ and tissue donors.
HCV, HIV-1, HIV-2 and HBV	July 2018	NGI UltraQual Multiplex PCR Assay for HCV, HIV-1, HIV-2 and HBV	UltraQual Multiplex PCR Assay for HCV, HIV-1, HIV-2 and HBV Hepatitis B Virus	First assay to detect and differentiate HIV-2 from HIV-1. For the detection of HCV RNA, HIV-1 RNA, HIV-2 RNA, and HBV DNA in pooled and individual Source Plasma specimens.

Disease	Approved	Trade Name	Proper Name	Purpose or Benefit
Reversal of Factor Xa Inhibitors	May 2018	ANDEXXA	coagulation factor Xa (recombinant), inactivated-zhzo	For patients treated with rivaroxaban and apixaban, for reversal of anticoagulation due to life-threatening or uncontrolled bleeding.

FUNDING HISTORY[52]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$329,156,000	$215,308,000	$113,848,000
FY 2017 Actual	$340,016,000	$215,443,000	$124,573,000
FY 2018 Actual	$381,890,000	$217,135,000	$164,755,000
FY 2019 Annualized CR	$379,144,000	$217,138,000	$162,006,000
FY 2020 President's Budget	$431,561,000	$262,138,000	$169,423,000

BUDGET REQUEST

The FY 2020 Budget Request for the Biologics Program is $431,561,000, of which $262,138,000 is budget authority and $169,423,000 is user fees. This level provides a net increase of $52,417,000. Budget authority increases by $45,000,000 compared to the FY 2019 Annualized Continuing Resolution level and user fees increase by $7,417,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is $387,812,000. The Office of Regulatory Affairs amount is $43,749,000.

The FY 2020 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, such as newly identified clinical biomarkers, innovative clinical trial designs, 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, Breakthrough Therapy Designation, Accelerated Approval, and Priority Review to expedite the approval and availability of important products for patients, when appropriate. These pathways will 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.

Through FDA's mission, the Agency will continue to protect the public against the threats of emerging infectious diseases and bioterrorism, including facilitating the development of

[52] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

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.

FDA will advance the use of real-world evidence including through use of 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. The use of real-world evidence captured throughout the totality of a product's post-approval lifecycle has been a significant aid in informing regulatory decisions, including the development of new products and changes to existing products.

BUDGET AUTHORITY

Medical Product Safety (+$45 million / 20 FTE)

Integrated Pathogen Reduction of the Blood Supply: +$20.0 million / 4 FTE

Center: +$20.0 million / 4 FTE

This funding would allow CBER to create a pilot program for pathogen inactivation technology which could help protect the blood supply from existing and emerging pathogens and potentially reduce or eliminate donor deferral and/or testing requirements. This project would optimize adaptation of existing technology for pathogen reduction and implement a moderately-sized pilot program to assess the feasibility of the widespread introduction of pathogen inactivation of all whole blood that is collected. The request would facilitate necessary preparatory laboratory work, purchase of the necessary equipment, and contracting for the blood banking services and clinical trials required for the demonstration of the feasibility of this approach.

Bacterial contamination of platelets is a leading risk of infection from blood transfusion. Bacterially contaminated platelets are associated with a higher risk of morbidity and mortality than any other transfusable blood component and are an example where these technologies can dramatically help the American public.

Existing and emerging infectious diseases present a continued risk to blood safety, as they are spreading faster and emerging more quickly. Continued vigilance against emerging threats is critical, including the introduction of new technologies to keep the blood supply safe in the event of rapidly emerging novel pathogens. Pathogen reduction technologies applied to whole blood that is then separated into red cells, platelets, and plasma could help ensure that the entire blood

supply continues to be safe in the face of existing and emerging pathogens and could also reduce cost while ensuring availability even in the face of emerging pathogens.

Medical Countermeasures Initiative (MCMi): +$2.0 million / 8 FTE

Center: +$2.0 million / 8 FTE

This funding would improve and sustain the FDA's ability to foster the establishment of clear, scientifically supported regulatory pathways for MCMs as well as to fill critical scientific gaps and advance platform and manufacturing technologies to facilitate the efficient development and availability of MCMs. In addition, it will help bolster FDA staffing to support MCM-related work, in particular regulatory review capacity and expertise in the medical review divisions responsible for evaluating MCMs, so that development programs move forward efficiently, and that the FDA is better prepared to handle the demands of responding to CBRN and emerging threats.

Promote Domestic Manufacturing: $10.0 million / 4 FTE

Center: +$10 million and 4 FTE

The FY 2020 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 advanced manufacturing of biological products, including vaccines and cell- and gene-based therapies. With these 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. 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.

Create a New Medical Data Enterprise: $13.0 million / 4 FTE

Center: +$13 million and 4 FTE

The 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. The FDA will establish a new capability, including the development of data and analytical tools, to conduct near-real-time evidence evaluation. The 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 the FDA's capacity to utilize real-world evidence to evaluate the pre- and post-market safety and effectiveness of medical products would potentially 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: +$7.4 million

Center: +$7.5 million / Field: -$0.1 million

The Biologics Program request includes an increase of $7,417,000 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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
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 2017: 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 2017:100% 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 2017: 100% Target 90% (Target Exceeded)	90%	90%	Maintain
233206: Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. *(Output)*	FY 2017: 99.5% 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 2017: 100% Target: 60% (Target Exceeded)	60%	60%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
234101: Increase manufacturing diversity and capacity for influenza vaccine production. *(Output)*	FY 2018: 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 2018: 100% Target 85% (Target Exceeded)	85%	85%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 75% (New Measure)	70%	70%	Maintain
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 71% (New Measure)	65%	65%	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 2018, 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 third international collaborative study comparing several alternative methods was completed in FY18. This study demonstrated that some alternative methods were sensitive to the methods used for inactivating the potency reference standard and suggested that additional criteria be defined for the selection of reagents to be included in new assays. Additional follow-up studies are being planned for FY 2019 that will continue to evaluate and compare alternative potency methods.

FDA continued work to develop improved candidate vaccine viruses. FDA produced a new influenza candidate vaccine virus (CBER-RG7C) for the high pathogenic H7N9 A/Guangdong/17SF003/2016 virus recently isolated from an infected human in China. The hemagglutinin (HA) antigen yield was further optimized by targeted mutations in the HA gene. The optimized vaccine virus, CBER-RG7D, shown much higher viral protein yields than those of CBER-RG7C virus (increased by 90 percent in cells and 150 percent in eggs). Both vaccine viruses are listed at WHO website: http://www.who.int/influenza/vaccines/virus/candidates_reagents/summary_a_h7n9_cvv_20181108.pdf?ua=1, and can be used for manufacturers to produce inactivated vaccines against highly pathogenic A/Guangdong/17SF003/2016 -like influenza viruses.

New ORA Field Performance Measures

ORA is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome-based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention and allows for a more robust analysis.

PROGRAM ACTIVITY DATA

CBER Workload and Outputs	FY 2018 Estimate	FY 2019 Estimate	FY 2020 Estimate
Original Biologics License Applications (BLA)			
Workload [1]	21	21	21
Total Decisions [2]	58	58	58
Approved	46	46	46
BLA Efficacy Supplements			
Workload [1]	21	21	21
Total Decisions [2]	16	16	16
Approved	13	13	13
BLA Manufacturing Supplements			
Workload [1]	1,181	1,181	1,181
Total Decisions [2]	1,368	1,368	1,368
Approved	1,266	1,266	1,266
BLA Labeling Supplements			
Workload [1]	193	193	193
Total Decisions [2]	142	142	142
Approved	117	117	117
Original New Drug Application (NDA)			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
NDA Efficacy Supplements			
Workload [1]	1	1	1
Total Decisions [2]	0	0	0
Approved	0	0	0
NDA Manufacturing Supplements			
Workload [1]	18	18	18
Total Decisions [2]	18	18	18
Approved	16	16	16
NDA Labeling Supplements			
Workload [1]	4	4	4
Total Decisions [2]	4	4	4
Approved	4	4	4
Original Abbreviated New Drug Application (ANDA)			
Workload [1]	0	0	0
Total Decisions [2]	1	1	1
Approved	1	1	1
ANDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0

CBER Workload and Outputs	FY 2018 Estimate	FY 2019 Estimate	FY 2020 Estimate
ANDA Manufacturing Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
ANDA Labeling Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
Device 510Ks			
Workload [1]	54	54	54
Total Decisions [2]	64	64	64
Final Decision - SE	45	45	45
Device Premarket Applications (PMA)			
Workload [1]	3	3	3
Total Decisions [2]	8	8	8
Approved	2	2	2
Device Premarket Applications (PMA) Supplements			
Workload [1]	70	70	70
Total Decisions [2]	85	85	85
Approved	18	18	18
Investigational New Drugs (IND)			
Receipts: IND (new)	676	676	676
Receipts: IND Amendments	12,085	12,085	12,085
Total Active IND [3]	2,850	2,850	2,850
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	13	13	13
Receipts: IDE Amendments	353	353	353
Total Active IDE [3]	161	161	161
Patient Safety			
Adverse Event Reports Received [4]	78,266	80,000	85,000
Biological Deviation Reports Received	46,971	50,000	50,000
Sponsor Assistance Outreach			
Meetings	525	525	525
Final Guidance Documents [5]	33	30	30
Admin/Management Support			
Advisory Committee Meetings Held	9	13	13
FOI Requests Processed	268	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 Activity Data (PAD)			
Field Biologics Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,849***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	75	100	100
Blood Bank Inspections	807	900	900
Source Plasma Inspections	243	190	190
Pre-License, Pre-Market Inspections	81	55	55
GMP Inspections	45	28	28
GMP (Device) Inspections	13	7	7
Human Tissue Inspections	625	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***70***	***47***	***47***
Bioresearch Monitoring Program Inspections	15	11	11
Foreign Human Tissue Inspections	1	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	6	7	7
GMP Inspections (Biologics & Device)	38	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,919***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	73	45	45
Import Line Decisions	170,575	179,104	188,059
Percent of Import Lines Physically Examined	0.04%	0.03%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,919***	***1,939***	***1,939***

[1]ORA is currently evaluating the calculations for future estimates.

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ANIMAL DRUGS AND FEEDS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
Animal Drugs and Feed	**200,465**	**210,732**	**220,030**	**239,515**	**19,485**
Budget Authority	***174,434***	***174,430***	***174,434***	***192,314***	***17,880***
User Fees	***26,031***	***36,302***	***45,596***	***47,201***	***1,605***
Center	133,595	145,181	152,942	166,904	13,962
Budget Authority	108,919	108,918	108,919	121,199	12,280
User Fees	24,676	36,263	44,023	45,705	1,682
Animal Drug (ADUFA)	16,095	24,865	27,267	27,706	439
Animal Generic Drug (AGDUFA)	8,469	11,375	16,644	17,882	1,238
Third Party Auditor Program	112	23	112	117	5
Field	66,870	65,551	67,088	72,611	5,523
Budget Authority	65,515	65,512	65,515	71,115	5,600
User Fees	1,355	39	1,573	1,496	-77
Animal Drug (ADUFA)	310	36	431	440	9
Animal Generic Drug (AGDUFA)	238	3	335	216	-119
Food Reinspection	807	---	807	840	33
Third Party Auditor Program	---	---	---	---	---
FTE	**944**	**944**	**956**	**983**	**27**

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 2018 (P.L. 113-14); Animal Generic Drug User Fee Reauthorization Act of 2018 (P.L. 113-14).

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

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Animal Drugs and Feeds Program began 50 years ago, 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 animal food. The Program is administered by the Center for Veterinary Medicine and the Office of Regulatory Affairs to protect and promote the health of humans and animals by ensuring:

- the safety of the American food supply
- the safety of animal food and devices
- the safety and effectiveness of animal drugs.

Specifically, the Program:

- evaluates new animal drug applications for safety and effectiveness
- monitors animal drugs, animal foods, and animal devices on the market
- evaluates animal food additives for safety and utility
- conducts applied research to further protect human and animal health.

The Program also helps promote and provide incentives for the availability of animal drugs to meet the needs of the large number and wide diversity of minor species, such as fish, honey bees, and birds, and for minor uses (infrequent and limited) in the major species: cattle, pigs, chickens, dogs, cats, horses and turkeys.

The Animal Drugs and Feeds Program leverages budget authority and user fees to protect human and animal health. Congress passed and the President signed the Animal Drug User Fee Act IV and Animal Generic Drug User Fee Act III reauthorization in FY 2018. 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. User fees are also authorized under the FDA Export Reform and Enhancement Act (Export Certificate program). The Export Certificate program helps support the export of products marketed in the U.S. that are acceptable to the importing country.

Foster Competition and Innovation

FDA protects and promotes public health by ensuring that medical products are properly tested for safety and efficacy, are known to be of reliable quality, and are properly labeled. Promoting public health also requires the Agency to take steps that can help facilitate efficient access to safe and effective, and innovative products that can address existing, novel, and emerging animal and human health challenges.

Fostering Innovation in Plants and Animal Drugs

FDA announced the availability of a Plant and Animal Biotechnology Innovation Action Plan on October 2018. Innovations in plant and animal biotechnology offer tremendous opportunities for advancing public health. Promising new technologies that can edit animal and plant genomes have the potential to improve human and animal health, animal well-being, and food safety and security.

The Agency is committed to supporting innovation in plant and animal biotechnology through a science and risk-based approach, while simultaneously advancing its public health mission and avoiding unnecessary barriers to future innovation. The Action Plan works to address questions FDA regularly receives from biotechnology stakeholders, including developers of these products and public health interest groups. This new plan identifies priorities in three important areas:

1. advancing human and animal health by promoting product innovation and applying modern, efficient and risk-based regulatory pathways
2. strengthening public outreach and communication regarding the FDA's approach to innovative plant and animal biotechnology
3. increasing engagement with domestic and international partners on biotechnology issues

Building on more than 25 years of world-class plant biotechnology evaluations, the FDA has reviewed public comments and begun drafting a guidance to clarify the regulatory approach for plant biotechnology products for human and animal food. The safety of food from more than 180

varieties of genetically engineered plants has already been evaluated and many of these products are consumed by Americans every day. The new guidance will provide the clarification necessary to help small and medium size firms understand their responsibilities under our regulatory framework so that they're better able to navigate the regulatory pathway toward bringing safe, innovative plant biotechnology products to market.

The Veterinary Innovation Program (VIP) pilot was launched in October 2018 to offer intensive technical and programmatic assistance to developers of certain innovative veterinary products, including animal biotechnology products. VIP is intended to enhance regulatory predictability and efficiency, improve Agency responsiveness, and enable early, sustained interactions with innovators.

This is a period of exceptional innovation in American agriculture with the increasing development and use of new technologies. These innovations present the FDA with the opportunity to provide sufficient flexibility to allow for a regulatory process that supports the development of significant and beneficial technology, while safeguarding human and animal health.

Animal Drug Review

FDA efficiently evaluates new animal drugs and determines whether these products are safe and effective for their intended use, manufactured to meet current good manufacturing practice requirements and properly labeled. These activities increase the availability of safe and effective animal drug products to support the health of pet (companion) animals and food-producing animals, while ensuring that food from treated animals is safe for humans to eat.

FDA consistently meets or exceeds the Animal Drug User Fee Act (ADUFA) and Animal Generic Drug User Fee Act (AGDUFA) performance goals. Based on current data, FDA exceeded these goals for all submission types for both pioneer and generic animal drugs in the FY 2017 reporting period. Both user fee acts require FDA to review and act on 90 percent of pioneer and generic new animal drug applications and other key submissions within specified time frames each fiscal year.

In FY 2018, Congress passed and the President signed the ADUFA IV and AGDUFA III reauthorizations for FY 2019 through FY 2023. These two user fee acts enhance the FDA's ability to maintain a predictable and timely animal drug review process, foster innovation in drug development, and increase access to new therapies for food-producing and companion animals.

The bipartisan legislation reauthorizing ADUFA and AGDUFA builds on the success of previous authorizations and includes several additional provisions, including a requirement to post on the Agency's website the number of pending animal food additive petitions and a requirement to report on the FDA's progress in bringing all approved antimicrobial animal drugs that are medically important under veterinary oversight. The Program also committed to working on implementing the U.S. - EU GMP Inspection Mutual Recognition Agreement for veterinary pharmaceuticals.

The Animal Drugs and Feed Program also continues to enhance harmonization and collaboration with international organizations, other countries' regulatory agencies and related industry. The Program simultaneously reviewed and approved 8 applications and is currently reviewing 19 additional applications through the U.S.- Canada Regulatory Cooperation Council. The Council

works to minimize regulatory differences and duplicative procedures in the two countries to help streamline the approval process. These collaborative efforts contribute to:

- increasing the availability of safe and effective animal drugs
- lowering the cost of drug development for drug sponsors
- reducing the number of animals used in research studies.

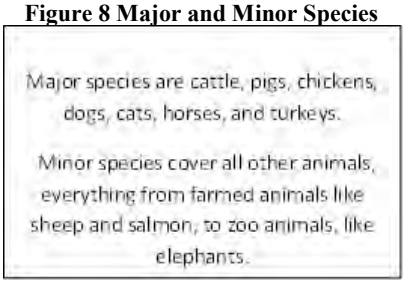
In November 2018, FDA proactively solicited public comments on proposed research to study the use of systemically and non-systemically absorbed drugs in certain types of dog bioequivalence studies. These studies would not result in euthanasia of the animals but instead would involve collection of blood samples from dogs, which is minimally invasive, after they have received oral tablets of two commonly used, generally well-tolerated medicines. The dogs taking part will be retired for adoption at the study conclusion. The FDA expects that the availability of this novel alternative approach will provide animal drug sponsors with a scientifically sound method to demonstrate bioequivalence of certain drugs and would support the replacement, reductions and refinement of use of animal in research.

Minor Use Minor Species

The Minor Use and Minor Species (MUMS) Animal Health Act, passed in 2004, helps make more animal drugs legally available to veterinarians and animal owners for use in minor animal species or for minor uses (rare diseases) in major species. Greater access to these "MUMS drugs" gives veterinarians more options.

MUMS drugs are needed for small markets that do not provide sufficient return on investment for sponsors seeking approval. FDA granted 144 MUMS drug "designations" over the last thirteen years to incentivize drug development for minor uses and minor species, and this has contributed to the approval of drugs such as antiparasitic drugs for sheep and goats, as well as drugs to treat heartworm disease in ferrets. "Designation" status for MUMS drugs gives sponsors eligibility to apply for grants to help defray the cost of their studies and provides seven years of exclusive marketing rights following approval or conditional approval.

Figure 8 Major and Minor Species



In April 2018, FDA published final GFI #210, *"The Index of Legally Marketed Unapproved New Animal Drugs for Minor Species,"* which describes an alternative to the drug approval process for non-food producing minor species. In some cases, like for zoo animals or ornamental fish, an animal drug is 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. In such cases, this process provides a faster and less expensive process for obtaining legal marketing status for eligible products. As of November 2018, the Index included a total of 13 animal drugs.

For many years, FDA has worked cooperatively with the USDA's Minor Use Animal Drug Program. This initiative funds safety and effectiveness studies, at land grant universities, that are intended to meet the requirements for new animal drug approval. These projects are limited to those needed for minor species of agricultural importance and has led to the approval of 29 MUMS products.

Selected Product Approvals in 2018

Below are some of the most recent Animal Drugs and Feeds Program significant product approvals during calendar year 2018. 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.

Date	Product Name	Purpose
November 2018	Experior	For reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter during the last 14 to 91 days of feed.
July 2018	NexGard	For the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.
June 2018	Cystorelin	For use with cloprostenol sodium to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows and beef cows.
May 2018	Semintra	For the control of systemic hypertension in cats.
May 2018	Mirataz	For the management of weight loss in cats.

Combatting Antimicrobial Resistance

In September 2018, FDA announced its Strategic Approach for Combating Antimicrobial Resistance. The risk-based and cross-cutting approach will contribute to national and worldwide efforts to slow the development of resistance and extend the useful life of antimicrobials. Antimicrobial drugs have been successfully and widely used in medicine for more than 60 years to effectively fight bacterial infections in humans and animals. When bacteria develop resistance to an antimicrobial drug, that drug may be less effective in fighting infections caused by those bacteria.

In September 2018, the FDA published "Supporting Antimicrobial Stewardship in Veterinary Settings" outlining key goals and objectives for FY 2019 – FY 2023. This strategy applies a risk-based approach to:

- evaluate new and currently approved antimicrobial products for animals
- collaborate with key stakeholders to support stewardship of these products by end users
- collect data on sales, resistance and antimicrobial use to monitor the effectiveness of these actions to slow the development of resistance.

The Animal Drugs and Feeds Program ensures the safety and effectiveness of animal drugs, including antimicrobials. The Program collaborated with key stakeholders in recent years to make significant public health progress to ensure that 95 percent of medically important antimicrobials (i.e. antimicrobials important for treating human disease) sold or distributed for use in food-producing animals are under veterinary oversight. The Program, as outlined in the 5-

year plan is committed to working with industry and other key stakeholders to bring the remaining 5 percent of medically important antimicrobials approved for use in animals under veterinary oversight.

The FDA needs access to scientifically-sound data on antimicrobial use and resistance to understand the drivers of resistance in veterinary settings and to assess the impact of interventions designed to limit the development of resistance. Efforts to support this include:

- enhancing the collection of antimicrobial drug sales and distribution data
- developing strategies and collaborating with others for collecting antimicrobial drug use data
- enhancing the collection and analysis of antimicrobial resistance data trends.

Antimicrobial Drug Sales

In December 2018, FDA published the sales and distribution summary report that represented the first full year of sales after nearly all medically important antimicrobials sold or distributed for food producing animals were transitioned under veterinary oversight. The report indicated a 41 percent decrease in the sales of medically important antimicrobials from 2014 (the year of peak sales) through 2017, and a 33 percent decrease from 2016 through 2017. While there are certain inherent limitations on how sales information may be appropriately interpreted and used, the additional sales data will further understanding about how antimicrobials are sold or distributed and will inform efforts to support the judicious use of medically important antimicrobials.

FDA published a final rule in May 2016 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). In June 2018, GFI #252, "Antimicrobial Animal Drug Sales and Distribution Reporting Small Entity Compliance Guide," was issued to help small business understand and comply with the new reporting requirements. Congress requires animal drug sponsors to report annually to FDA the amount of antimicrobial drug products they sell or distribute for use in food-producing animals and 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.

Antimicrobial Drug Use

In 2018, FDA funded for the third year two cooperative agreements with researchers from the University of Minnesota and Kansas State University to conduct pilot studies to characterize the use of animal drugs in food-producing animals. This information is being collected to improve FDA's understanding, at a national level, as to how antimicrobials are used in various animal production settings. Once the data from these projects are collected, analyzed, and aggregated, FDA intends to prepare and publish a summary report. The investigators for both cooperative agreements are required to utilize data collection methodologies that can capture detailed information on antimicrobial use, while protecting confidential information. They have reported significant progress, but noted important challenges, including the large range of farm recordkeeping and record storage procedures and differences in granularity of available records.

National Antimicrobial Resistance Monitoring System (NARMS)

The National Antimicrobial Resistance Monitoring System (NARMS) monitors antimicrobial resistance in enteric (intestinal) bacteria in food producing animals. FDA uses data from

NARMS and other sources to estimate the overall risk of antimicrobial resistance of an antimicrobial drug in food-producing animals when determining whether to approve the drug for the proposed use. A drug's conditions of use may be limited based on this risk estimation to mitigate the risk of antimicrobial resistance development.

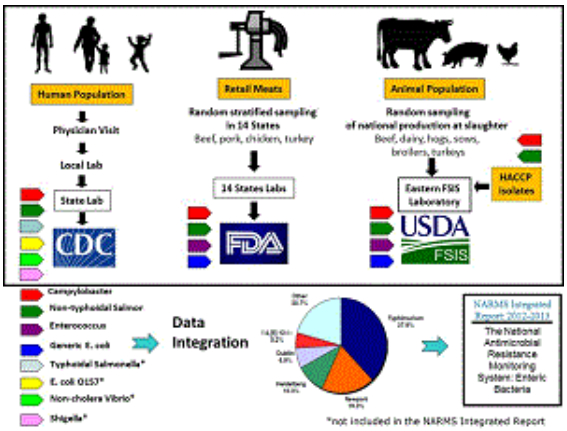


Figure 9 NARMS

In FY 2018 work began on implementing the FDA Science Board recommendations, including expanding NARMS surveillance to new commodities.In April 2018, NARMS launched its first pilot to conduct surveillance on veal at nine retail meat sites. These data will improve understanding about the post-approval impact of antimicrobial use in these animals. In November 2017, FDA developed and launched through NARMS a new publicly available tool, Resistome Tracker, to help in the global effort to address antibiotic resistance in foodborne pathogen. Resistome Tracker allows users to examine the distribution of antimicrobial resistance genes in all Salmonella genomes within the National Institutes of Health's National Center for Biotechnology Information (NCBI) system. Since its launch, new data has been added monthly and as of November 2018 the site has been viewed 8,500 times.

Making these data available to the public allows public health officials, academics, and researchers using new genomic technologies to:

- track infectious diseases
- identify potential sources antimicrobial resistant genes
- track the global spread of antimicrobial resistant genes.

FDA is collaborating with NCBI to build automatic analytical tools to predict antibiotic resistance based on WGS data alone, which demonstrates that WGS can predict resistance in more than 95 percent of Salmonella isolates. Advances in WGS are revolutionizing infectious disease diagnosis and surveillance by providing a complete picture of traits a microorganism has acquired over time, such as known virulence traits and antibiotic resistance genes.

Unapproved and Compounded Animal Drug Products

FDA 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. In FY 2018, scientific and public-health-based risk ranking criteria were developed to prioritize action against particular classes of products which the Agency believes present the greatest likelihood of safety concerns. The Program also revoked a draft Animal Drug Compounding Guidance after receiving comments from a variety of stakeholders and began finalizing a new draft Guidance. 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. The Animal and Veterinary compliance and enforcement webpage was also expanded to include unapproved animal drug Regulatory Actions and also 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. When firms violate the FDA requirements of the FD&C Act, FDA takes appropriate action to address the violations while ensuring that products of concern do not reach U.S. consumers. CVM is in the process of identifying and addressing policy and process changes to implement an inspection program that targets high-risk animal food establishments and products. FDA issued 17 warning letters in FY 2018 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 2018, FDA classified 29 Class I (most serious), 17 Class II, and 8 Class III recalls of regulated animal products.

Selected Guidance Issued in 2018

Below are some GFIs issued by the Animal Drugs and Feeds Program in calendar year 2018.

1Selected Guidances Issued in 2018

Date Issued	Docket #	Title	Description
November 2018	FDA-2016-D-4461	CVM GFI #243 (VICH GL56) *Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Species: Study Design Recommendations for Residue Studies in Honey for Establishing Maximum Residue Limits and Withdrawal Periods*	This guidance provides study design recommendations which will facilitate the universal acceptance of the generated residue depletion data to fulfill the national/regional requirement to establish MRLs or to justify withdrawal periods in honey; use of veterinary drug products in honeybee production is considered as a minor use in minor species in most jurisdictions.
July 2018	FDA-2018-D-2354	CVM GFI #257 (VICH GL57) *Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Species: Marker Residue Depletion Studies to Establish Product Withdrawal Periods in Aquatic Species*	This guidance provides study design recommendations which will facilitate the universal acceptance of the generated residue depletion data to fulfill the national/regional requirement. This is an extension of the parent residue guidance GFI #207/VICH GL48 and provides recommendations on what should be included in a marker residue depletion study for aquatic food-producing animals.

Date Issued	Docket #	Title	Description
June 2018	FDA-2005-D-0155	CVM GFI #3, *General Principles for Evaluating the Human Food Safety of New Animal Drugs Used in Food-Producing Animals*	This guidance describes the type of scientific data or information drug sponsors can provide to address the human food safety of new animal drugs used in food-producing animals.
May 2018	FDA-2009-D-0052	CVM Draft GFI #197, *Documenting Electronic Data Files and Statistical Analysis Programs*	This guidance provides a framework for drug sponsors to provide electronic data files and programs to support their safety and effectiveness submissions.
March 2018	FDA-2018-D-0943	CVM Draft GFI #255, *Elemental Impurities in Animal Drug Products Questions and Answers*	This guidance provides recommendations to drug sponsors to help them apply a risk-based control strategy for elemental impurities in new animal drug products.

Strengthen Science and Efficient Risk-Based Decision Making

Ensuring that human and animal food is safe from contamination is an essential element of promoting human and animal health. FDA faces unique challenges in the oversight of human and animal food safety driven in part by globalization and the increasing complexity of production and supply chains. The Animal Drugs and Feeds Program rises to this challenge by leveraging sound scientific data and risk-based decision making at all stages of a products lifecycle, from pre-market review of animal food ingredients to post-market response to food safety emergencies.

Animal Food Safety

One of the key responsibilities of the Animal Drugs and Feeds Program is to regulate animal food and ensure the safety of new animal food ingredients before they enter into the market. The health and safety of livestock, poultry, fish and other animals, including pets are ensured by:

- reviewing animal food additive petitions (FAP), generally recognized as safe (GRAS) notices, and animal food labels and labeling
- monitoring and taking action to reduce animal food contaminants
- reviewing, approving and maintaining medicated feed mill licenses
- evaluating the risk associated with hazards in pet food, including evaluation of consumer complaints and reportable food registry submissions
- collaborating with our state regulatory partners to oversee that the industry is meeting animal food standards

One of the unique aspects of animal food is that for most animals the diet provided to them constitutes the majority of, or their sole ration. Therefore, FDA's review of FAPs is critical to

ensure that the uses of the additives are safe for both the target animals and the humans eating the edible tissue from these animals, and that the additive functions as intended.

Over the past five years, submissions of FAPs have gone up by 150 percent. In FY 2018 FDA performed 103 animal FAP reviews and 107 reviews for investigational food additive files. 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.

FDA and the public benefit from having more information about the safety of the substances in the human and animal food supply as more GRAS notices are voluntarily filed with the Agency. In FY 2017, FDA's GRAS final rule went into effect. The final rule helps stakeholders draw more informed conclusions about whether the intended conditions of use of a substance in food for humans or animals is subject to the premarket approval requirements of the FD&C Act.

Modernizing Food Safety

FDA faces unique challenges in the oversight of human and animal food 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 Congress passed the Food Safety Modernization Act (FSMA). To minimize food safety hazards, FSMA directs FDA to enhance current food safety systems based on the public health principles of comprehensive prevention, risk-based resource allocation, and public-private partnerships.

As of September 2018, all business sizes reached their compliance dates for current good manufacturing practices (CGMPS), and both large and small business reached their compliance dates for hazard analysis and risk-based preventive controls (PCs). Very small businesses have until September 2019 to become compliant with the relevant PC requirements. FDA published the FSMA regulation, "Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Food for Animals," (PCAF regulation) in September 2015. This regulation requires facilities that manufacture, process, pack, or hold animal food to adhere to CGMPs and to implement PCs.

Training courses were developed for these regulations and input was provided to the Food Safety Preventive Controls Alliance course, which is the recognized standardized curriculum to help firms comply with the PCAF regulation. While this is the primary regulation impacting the animal food industry, three other FSMA regulations also apply to animal food:

- *Foreign Supplier Verification Programs for Importers of Food for Humans and Animals*
- *Sanitary Transportation of Human and Animal Food*
- *Accreditation of Third-Party Certification Bodies to Conduct Food Safety Audits and Issue Certifications*

FDA continues to develop relevant Guidance for Industry (GFI), develop resources to help the animal food industry comply with the new FSMA requirements, and publish guidance documents to assist with FSMA implementation. The following are some of the key guidance documents published in 2018, with a full list of FSMA related guidance documents available on FDA's FSMA website:

- Draft GFI #246, *"Hazard Analysis and Risk-Based Preventive Controls for Food for Animals; Supply Chain Program"* to help receiving facilities comply with PCAF

Requirements for establishing and implementing a supply-chain program for its suppliers. Published in June 2018.

- Draft GFI #245, *"Hazard Analysis and Risk-Based Preventive Controls for Food for Animals"* to help owners, operators, or agents in charge of a facility to develop a food safety plan that complies with PCAF requirements. Published in January 2018.
- Draft GFI, *"Foreign Supplier Verification Programs for Importers of Food for Humans and Animals"* to provide questions and answers to facilitate importers' understanding of the FSVP requirements. Published in January 2018.
- GFI, *"Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs."* Published in January 2018.

In FY 2018 the FDA continued to proactively engage with industry and regulatory partners on FSMA to foster a greater understanding and to educate stakeholders on how to comply with FSMA-related regulations and guidance documents. This was accomplished by conducting listening sessions, webinars, and meetings on FSMA-related regulations and guidance documents, as well as active participation in the FSMA Technical Assistance Network (TAN), a central source for information and questions related to FSMA rules, programs, and implementation strategies.

Preventing and Responding to Animal Food Emergencies

The Animal Drugs and Feeds Program provides funds to support the activities of the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), a network of 44 state and university veterinary diagnostic laboratories. The collaboration of veterinary diagnostic laboratories with FDA has helped the Agency prevent and respond to animal food emergencies by carefully investigating the clinical aspects of the reported illness. Such partnerships expand FDA's ability to protect animal and human health.

In FY 2018, FDA and the Vet-LIRN increased its capacity for conducting state-of-the-art susceptibility testing and genetic analysis. Vet-LIRN laboratories conducted dozens of investigations into consumer complaints of illness or death potentially due to animal food. They leveraged use of Whole Genome Sequencing (WGS) technology to contribute to the recall of several pet food products in 2018. Those products were contaminated with Salmonella, Listeria or E. coli all of which can cause disease in people as well as their animals. During 2018 Vet-LIRN also investigated multiple cases of hyperthyroidism in pets and found that the illness was caused by foods containing thyroid tissue, which should have been excluded.

WGS is a critical tool that helps FDA 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 routinely determine and interpret the complete DNA sequence obtained from microorganisms, enabling the Agency to more rapidly identify emerging patterns of resistance.

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. In 2018 Vet-LIRN continued implementation of a pilot project to monitor antimicrobial susceptibility and to sequence selected veterinary pathogens. Twenty Vet-LIRN laboratories are gathering data on antibiotic susceptibility for various Salmonella

species, E. coli and Staphylococcus pseudointermedius, and they are providing the isolates to four Vet-LIRN laboratories that have sequencing capabilities. Integrated monitoring by these veterinary diagnostic laboratories could inform risk-based intervention strategies for FDA.

Leveraging Real-World Adverse Event Data

The Animal Drugs and Feeds Program has the largest animal drug adverse event database in the world, containing real-world safety and effectiveness data from more than 840,000 cases, a case may include more than one animal, especially cases involving food producing animals which are often treated and managed as a group. The majority of cases reported, approximately 80 percent, involve companion animals. The data includes adverse events reported in more than 89,000,000 food animals, and approximately 800,000 companion animals. The Program uses a comprehensive adverse event reporting system to monitor the continued animal safety of animal food and drugs, human user safety, and the effectiveness of approved animal drugs.

In FY 2018, FDA received more than 100,000 adverse event reports. Onecase can include both initial and follow up reports. Some reports triggered drug safety communications. One example was an FDA warning alerting pet owners and veterinary professionals about the potential for neurological adverse events associated with certain flea and tick products. In FY 2017, drug safety reports triggered a warning about eye injury and irritation in both people and dogs following application of two canine ear medications.

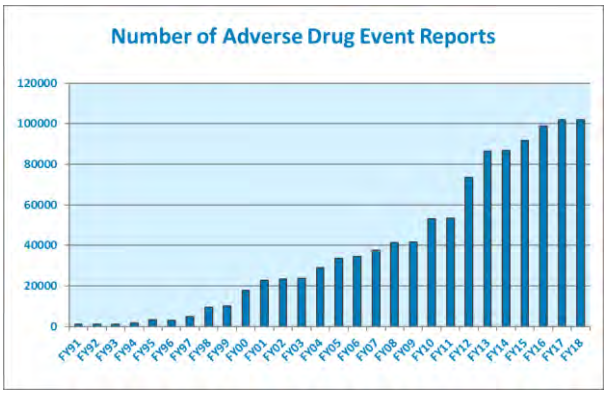


Figure 10 Adverse Drug Event Reports

The number of adverse event reports received each year continues to grow. The long-term trend of increased reporting may be attributed to both increases in the number of approved animal drug products and increased awareness of reporting.

Efforts continue to increase the functionality, utilization, and analysis of this pharmacovigilance database to improve animal drug safety. Adverse event signal detection and management strategies are under development to help identify 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. The Program is continuing efforts to harmonize pharmacovigilance internationally to enhance animal drug safety globally.

Animal Drug Inspections

FDA's Office of Regulatory Affairs (ORA) conducts preapproval inspections to support application reviews 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.

Accurate test results are essential to the review and approval of new animal drugs and help to ensure that the rights and welfare of animals are protected. Post-approval, ORA inspects 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.

FUNDING HISTORY[53]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$188,042,000	$158,629,000	$29,413,000
FY 2017 Actual	$190,879,000	$162,852,000	$28,027,000
FY 2018 Actual	$210,732,000	$174,430,000	$36,302,000
FY 2019 Annualized CR	$220,030,000	$174,434,000	$45,596,000
FY 2020 President's Budget	$239,515,000	$192,314,000	$47,201,000

BUDGET REQUEST

The FY 2020 Budget Request for the Animal Drugs and Feeds Program is $239,515,000, of which $192,314,000 is budget authority and $47,201,000 is user fees. Budget authority increases by $17,880,000 compared to the FY 2019 Annualized Continuing Resolution level and user fees increase by $1,605,000. The Center for Veterinary Medicine (CVM) amount in this request is $166,904,000. The Office of Regulatory Affairs amount is $72,611,000.

The Animal Drugs and Feeds Program is responsible for ensuring animal drugs and food 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 CVM 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 food additives for safety and utility, and ensuring food for animals is safe, made under sanitary conditions, and properly labeled. In addition, 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 and public health emergencies. The Program examines the safety and effectiveness of animal drugs on the market, reviews Adverse Drug Experience reports, monitors the safety of animal devices, investigates livestock and pet illnesses, provides outreach and education, and conducts compliance and enforcement actions when appropriate. Ongoing risk-based efforts to reduce the marketing and distribution of high-risk unapproved animal drugs will continue. FDA's efforts are ongoing to limit compounding to legitimate veterinary medical needs to treat animal health issues 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.

[53] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

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. The Animal Drugs and Feeds Program works extensively with state partners to continue building an integrated food safety system that supports animal food standards, response efforts, and enhanced surveillance and communication systems.

The Animal Drugs and Feeds Program will continue implementation of the five-year antimicrobial resistance action plan to advance antimicrobial steawardship in veterinary settings, reduce overuse of antimicrobial drugs, and combat the rising threat of resistance. The Program will also continue monitoring and surveillance efforts on antimicrobial resistance among enteric (intestinal) pathogenic bacteria via the National Antimicrobial Resistance Monitoring System (NARMS). Outbreak and response efforts will also continue to be strengthened by 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 and by investigating potential problems with animal food, including pet food, 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 2020 Budget Request support mission critical activities, and Presidential, HHS, and FDA human and animal health priorities.

Budget Authority

Food Safety (+$13.9 million / 23 FTE)

Advancing FSMA: (+$5.9 million / 1 FTE)

Center: +$0.3 million / 1 FTE

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct domestic animal food facility inspections required by FSMA. The FY 2020 Budget request will enhance compliance with the preventive control rules by funding cooperative agreements with state animal food regulatory programs enabling states to increase their capability to conduct FSMA related domestic inspections. In addition, CVM will be able to hire additional FTEs to provide technical expertise to support both FDA and state partners in the administration of the cooperative agreements and development of preventive controls programs within the state agencies.

Field Animal Drugs & Feeds: +$5.6 million/ 0 FTE

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct domestic food and feed facility inspections required by FSMA. FDA expects that states will continue to gradually increase the number of inspections they conduct as FDA transitions to prevention-oriented inspections. The National Association of State Departments of Agriculture (NASDA) and Association of American Feed Control Officials (AAFCO) requested funds for FDA to provide states to complete Preventive Control (PC) inspections by updating and building new state programs. The cooperative agreements will support work for states to implement the

recommendations of the NASDA PC Animal Food Framework that include evaluating and building infrastructure, updating inspection and enforcement programs, developing outreach and training programs, and shifting laboratory resources to focus on hazard analysis.

Strengthening Response Capabilities for Foodborne Outbreaks: (+$3.0 million / 10 FTE)

Center: +$3.0 million / 10 FTE

With this funding increase, the Animal Drugs and Feeds Program will increase surveillance and expand collaboration to more rapidly identify and respond to the growing number of outbreaks and other public health threats associated with animal food, including pet food contamination, and residues in the edible tissue of food producing animals. There has been an increase in the number of recalls for two reasons:

- industry has identified new hazards when complying with the FSMA preventive controls
- the increasing application of whole genome sequencing enhanced the sensitivity of our surveillance systems to identify foodborne outbreaks that previously would have gone undetected.

The Program will also increase its capacity to coordinate and communicate with other federal, state and local food safety partners to help ensure that unsafe products are removed from the marketplace as quickly as possible to limit exposure.

Promoting Innovation and Emerging Technologies While Maintaining Product Safety: (+$5 million / 12 FTE)

Center: + $5.0 million / 12 FTE

The Animal Drugs and Feeds Program will use this funding increase to strengthen its capacity to review biotechnology plants. The Program also will use this funding to enhance the pre-market animal food program to meet 80 percent of established timeframes for Food Additive Petitions (FAPs) and Generally Recognized as Safe (GRAS) notices, while working to eliminate the backlog of review requests for these products. With industry submissions of FAPs increasing by 150 percent in the last four years and submissions of GRAS notices increasing by 200 percent in FY 2017, this funding is critical for ensuring that new and innovative animal food ingredients that demonstrate safety and utility reach the market.

The Program will publish two guidance documents on ingredient pre-submission interactions and evaluation of genome edited plants to improve efficiency and effectiveness for industry before and during the submission process. The Program also will continue to conduct scientific reviews of animal food ingredients to ensure they are safe for the target animals and for the humans eating the edible tissue from these animals.

Medical Product Safety (+ $4 million / 4 FTE)

New Medical Data Enterprise: (+ $4.0 million / 4 FTE)

Center: + $4.0 million / 4 FTE

With this funding increase, the Animal Drugs and Feeds Program would 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 would 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 would 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.

USER FEES

Current Law User Fees: +$1.6 million

Center: +$1.682 million / Field: -$0.077 million

The Animal Drugs and Feeds Program request includes an increase of $1,605,000 for user fees, 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 2019 Target	FY 2020 Target	FY 2020+/- FY 2019
243201: Complete review and action on original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. *(Output)*	FY 2017: 100% 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	FY 2017: 100% w/in 270 day Target: 90% w/in 270 days (Target Exceeded)	90% w/in 240 days	90% w/in 240 days	Maintain

Measure	Year and Most Recent Result / Target for Recent Result(Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020+/- FY 2019
applications received during the fiscal year. *(Output)*				
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 2018: 63% 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
244302: Respond to consumer complaints related to animal food safety issues by initiating in-depth Vet-LIRN investigations within 30 days of receipt. *(Output)*	FY 2018: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
214221: Percentage of Human and Animal[54] Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. *(Output)*	Baseline: 90% (New Measure)	80%	80%	Maintain
224221: Percentage of Human and Animal[55] Drug significant inspection violations which receive	Baseline: 86% (New Measure)	80%	80%	Maintain

[54] Due to Program Realignment, ORA's Workplan now combines Human and Animal food inspection activities together, so this combination performance goal is repeated in both the Foods and Animal Drugs and Feed program narratives.

[55] Due to Program Realignment, ORA's Workplan now combines Human and Animal drug inspection activities together, so this combination performance goal is repeated in both the Human DrugsFoods and Animal Drugs and Feed program narratives.

Measure	Year and Most Recent Result / Target for Recent Result(Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020+/- FY 2019
appropriate follow-up after regulatory action was taken. *(Output)*				
214222: Percentage of Human and Animal[56] Food follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. *(Outcome)*	Baseline: 78% (New Measure)	65%	65%	Maintain
224222: Percentage of Human and Animal[57] Drug follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. *(Outcome)*	Baseline: 67% (New Measure)	55%	55%	Maintain

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

Reauthorization of ADUFA and AGDUFA

ADUFA IV and AGDUFA III have been reauthorized for FY 2019 through FY 2023. ADUFA IV includes two new performance goals: commencing tissue residue method demonstrations within 120 days, and conducting pre-submission conferences within 60 days. ADUFA IV also reduces review times on two performance goals from 180 days to 60 days for categorical exclusions and Animal Drug Availability Act (ADAA) Combinations. Additionally, CVM committed to working on implementation of the U.S. - EU GMP Inspection Mutual Recognition Agreement. AGDUFA III includes a significant reduction in performance goal review times

[56] Due to Program Realignment, ORA's Workplan now combines Human and Animal food inspection activities together, so this combination performance goal is repeated in both the Foods and Animal Drugs and Feed program narratives.

[57] Due to Program Realignment, ORA's Workplan now combines Human and Animal drug inspection activities together, so this combination performance goal is repeated in both the Human DrugsFoods and Animal Drugs and Feed program narratives.

across all submission types. Both ADUFA IV and AGDUFA III require electronic submission to improve efficiency, and require all approved drugs to include the NADA or ANADA number on the labeling to allow veterinarians and consumers to know it is an FDA approved product.

New Vet-LIRN Performance Measure

The Veterinary Laboratory Investigation and Response Network (Vet-LIRN) rapidly responds to consumer complaints related to animal food safety issues. The Network's 44 state and university veterinary diagnostic laboratories contributed to the initiation of nearly 300 case investigations in FY 2018 where there was compelling indication of harm caused by a regulated product and where animal diagnostic samples were available for testing. These laboratories provided pivotal data that led to 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 is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome-based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention, and allows for a more robust analysis.

PROGRAM ACTIVITY DATA

Animal Drugs and Feeds Program Activity Data (PAD)

Animal Drugs & Feeds Program Activity Data (PAD)			
CVM Workload and Outputs	**FY 2018 Actual**	**FY 2019 Estimate**	**FY 2020 Estimate**
New Animal Drug Applications (NADAs) [1]			
Received	19	23	23
Completed	23	20	21
Approved	14	16	17
Pending [2]	14	17	19
New Animal Drug Application Supplements [1, 3]			
Received	591	575	600
Completed	536	560	590
Approved	438	475	500
Pending [2]	157	172	182
Abbreviated New Animal Drug Applications (ANADAs) [1]			
Received	23	23	26
Completed	19	21	22
Approved	6	16	18
Pending [2]	15	17	21
Abbreviated New Animal Drug Application Supplements [1, 3]			
Received	315	325	335
Completed	298	300	305
Approved	208	200	215
Pending [2]	151	176	206
Investigational New Animal Drug (INAD) Files [4]			
Received	2,885	3,400	3,600
Completed	2,840	3,400	3,500
Pending [2]	354	354	454
Generic Investigational New Animal Drug (JINAD) Files [4]			
Received	669	635	645
Completed	551	615	640
Pending [2]	223	243	248
Food (Animal) Additive Petitions Completed	104	100	100
Investigational Food Additive Petitions Completed	107	110	110
Adverse Drug Event (ADE) [5]			
ADE Reports Received	102,100	105,000	107,000
Post-Approval ADE Data Reviews	161	190	210

[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.

[5] This measure tracks the number of "Post-approval ADE data reviews" completed each fiscal year. A Post-approval ADE Data Review is a comprehensive report by product of multiple ADE reports (in some cases this could be hundreds or thousands of individual reports).

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 2018 Actuals**			**FY 2019 Estimate**			**FY 2020 Estimate**		
	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	***1,436***	***160***	***1,276***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	33	33	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	120	120	0	175	175	0	175	175	0
BSE Inspections	746	0	746	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	5	0	5	25	0	25	25	0	25
Illegal Residue Program Inspections	322	0	322	450	0	450	450	0	450
Feed Manufacturing Program Inspections	179	0	179	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,223	13	1,210	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***74***	***70***	***4***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	20	20	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	51	51	0	33	33	0	33	33	0
Foreign Feed Inspections	2	0	2	5	0	5	5	0	5
BSE Inspections	1	0	1	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,510***	***230***	***1,280***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	3,557	868	2,689	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	963	0	963	867	2	865	867	2	865
Import Physical Exam Subtotal	**4,520**	**868**	**3,652**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	456,684	65,887	390,797	479,518	69,181	410,337	503,494	72,640	430,854
Percent of Import Lines Physically Examined	0.99%	1.32%	0.93%	0.97%	0.72%	1.02%	0.93%	0.68%	0.97%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***3,050***	***0***	***3,050***	***3,396***	***0***	***3,396***	***3,396***	***0***	***3,396***
State Contract Inspections: BSE	2,713	0	2,713	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	549	0	549	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	85	0	85	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	$3,369,732	0	$3,369,732	$3,470,824	0	$3,470,824	$3,574,949	0	$3,574,949
State Contract Tissue Residue Funding	$0	0	$0	$0	0	$0	$0	0	$0
Total State Funding	**$3,369,732**	**$0**	**$3,369,732**	**$3,470,824**	**$0**	**$3,470,824**	**$3,574,949**	**$0**	**$3,574,949**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***4,563***	***230***	***4,333***	***5,134***	***367***	***4,799***	***5,134***	***367***	***4,799***

[1] The FY 2018 actual unique count of foreign inspections includes 5 OIP inspections (4 for China and 1 for India).

[2] The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number is expected to decrease in the future until there are no planned State Partnership inspections.

[3] The State cooperative agreement BSE inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number along with the funding for these inspections are expected to decrease in the future until there are no planned State Cooperative Agreement BSE inspections.

4 Tissue residue funding has ended in FY18 and state contract illegal tissue residue inspections are no longer being conducted.

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DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
Devices and Radiological Health	**512,901**	**479,930**	**522,838**	**631,718**	**108,880**
Budget Authority	***332,893***	***332,885***	***332,893***	***423,893***	***91,000***
User Fees	***180,008***	***147,045***	***189,945***	***207,825***	***17,880***
Center	411,791	381,463	421,598	529,978	108,380
Budget Authority	247,888	247,884	247,888	338,888	91,000
User Fees	163,903	133,579	173,710	191,090	17,380
Prescription Drug (PDUFA)	1,320	987	1,460	4,272	2,812
Medical Device (MDUFA)	156,148	126,998	165,815	180,125	14,310
Mammography Quality Standards Act (MQSA)	6,435	5,594	6,435	6,693	258
Field	101,110	98,467	101,240	101,740	500
Budget Authority	85,005	85,001	85,005	85,005	---
User Fees	16,105	13,466	16,235	16,735	500
Medical Device (MDUFA)	2,110	2,086	2,240	2,179	-61
Mammography Quality Standards Act (MQSA)	13,995	11,380	13,995	14,556	561
FTE	**2,159**	**2,159**	**2,328**	**2,399**	**71**

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 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 program operates with appropriations and user fees.

Advances in material science, digital technology, and advanced manufacturing are contributing to an unparalleled period of invention in medical devices and more opportunities to improve health than at any other time. FDA's Devices Program fosters this innovation in order to spur the development of safer, more effective technologies and assure timely patient access, while maintaining FDA's gold standard.[58] The Devices Program oversees development of new devices that make less-invasive treatments possible and provide new options to patients whose conditions

[58] The FDA's gold standard for product review strives to maximize benefits, and minimize risks and significant uncertainties in meeting our principal obligation to make sure that new products are safe and effective.

would have been considered untreatable in the past – all while providing the assurances patients depend upon. The foundation of this program is medical device safety.

Providing patients with access to safe and effective medical products to meet their health care needs is central to the FDA's mission, and the Devices Program remains committed to both encouraging innovation to improve safety and detecting safety risks earlier. This is about fostering a transparent and efficient system so that devices are able to meet the standard to come to market when they are safe, effective, and have the assurances patients depend on. As such, evidentiary requirements must be clear and well understood, and the means to meet these requirements is efficient and enables patients to have access to safe, innovative technologies.

The FDA regulates more than 190,000 different devices, which are manufactured by more than 18,000 firms in more than 21,000 medical device facilities worldwide. On average, FDA approves, clears, or grants marketing authorization to approximately 12 new or modified devices every business day after carefully determining, based on sound science, whether the benefits of the device outweigh its risks to the patient.

The Devices Program is responsible for the regulation and oversight of a wide range of medical devices that patients and their health care providers use every day. These devices range from simple tongue depressors to complex instruments that help save and sustain life, such as heart valves, artificial pancreas, programmable pacemakers with micro-chip technology, medtech alternatives to opioid products, and laser surgical devices, among others. Medical devices also include in vitro diagnostic products, such as next generation sequencing tests and complex multivariate assays that help diagnose conditions and help determine which treatments patients should pursue based on their individual genetic makeup.

In addition, the Devices Program regulates radiation-emitting electronic products such as X-ray equipment, medical ultrasounds, and MRI machines, as well as monitors mammography facilities to make sure the equipment is safe and properly operated. The Devices Program also works with federal partners, hospitals, and industry to mitigate cybersecurity threats from medical devices by encouraging an approach of vigilance, responsiveness, resilience, and recovery. The Devices Program tailors its oversight of medical devices according to the degree of risk presented, so it can focus its resources on those products that pose the most risks to patients. FDA has also been a world leader in harmonizing review and oversight practices to spur development of higher quality devices all over the world. The Agency engages heavily with international counterparts to share information about potential safety concerns with medical devices, and to identify and take action to protect patients and the public health where possible.

Figure 11 Devices Program Mission & Vision

Mission

The Devices Program mission is to protect and promote the public health by assuring that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. This provides consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products it oversees, and helps support the development of new and innovative products to continue to come to market and meet patient needs. The Devices Program facilitates medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and provides the assurances patients in the U.S. depend upon.

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. First in the world" is not about a competition between countries, but rather a measure of timely patient access. 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.

To achieve this vision, the Devices Program ensures manufacturers have a better understanding of the requirements for devices to come to market in the United States. This is accomplished through transparency about FDA's process and earlier interactions with manufacturers of promising treatments regarding the evidence that FDA will need to ensure safety and effectiveness. In addition, FDA has taken actions to make evidence generation more timely, efficient, and robust. These efforts better serve the needs of patients, who are at the heart of everything the Devices Program does. The Devices Program strategic priorities are:[59]

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

- Employee Engagement, Opportunity, and Success, which recognizes the connection between taking care of our employees and achieving our vision. Engaged employees are the most productive, creative, motivated, less likely to leave, and committed to the mission and vision. However, engagement requires work life balance, open dialogue, and opportunities for professional growth and success.
- Simplicity, which is about how the Devices Program addresses the challenges achieving its mission and vision —although issues are often complex; solutions and processes do not necessarily have to be.
- Collaborative Communities, which acknowledge that we serve the American public better and achieve our vision when stakeholders in the medical device ecosystem, including the Devices Program staff, proactively work together to solve both shared problems and problems unique to others.

By applying these three approaches more systematically, the Devices Program will arrive at the threshold of achieving its vision in the next three years. As two important measures of success, the Devices Program:

- aims to have more than 50 percent of manufacturers of novel technologies meet FDA's standards to bring their devices to the U.S. first or in parallel with other major markets by December 31, 2020, and
- continues implementing new practices to ensure that it is consistently first in the world to identify and act upon new safety risks associated with medical devices.

Full and consistent implementation of strategic priorities alongside ongoing efforts to make the Devices Program even more efficient will enable it to achieve its vision that U.S. patients have access to high-quality, safe, and effective medical devices of public health importance first in the world. It will also facilitate continued improvement to the U.S. health care system as a whole. Recent accomplishments of the Devices Program that demonstrate its commitment to improving the safety and quality of life for patients include:

Each year, the Devices Program carefully reviews medical devices to assure that they meet FDA's high standards for safety and effectiveness and approves, authorizes or clears thousands of products for entry into the market. FDA has been focused on taking steps to better clarify requirements– to communicate better about the evidence needed to demonstrate regulatory standards for marketing – and this work has helped to reduce the time and cost of the total product life cycle of medical devices.

As evidence of FDA's continued efforts to make the requirements for meeting US marketing standards clearer, devices are being introduced to the market more quickly, more and more companies are bringing their technologies to the U.S. to market first before they do so in other countries, and more products that go through the Devices Program's premarket process are being approved, cleared, and authorized for marketing. The increase in cleared, approved, and authorized medical devices that meet FDA's high standards provides patients more options to improve and extend their lives than they have had in the past.

- Approved 95 novel medical devices in 2017—the highest number since the advent of the medical device user fee program in 2003. This followed the second highest number from 2016 and continued an 8-year trend that has resulted in a marked increase in the annual number of novel device approvals since 2009.

- The Devices Program has been at the forefront of engaging with patients. For instance, the Devices Program made partnering with patients one of its strategic priorities, and by the end of 2017 over 96% of the Devices Program staff had engaged with a patient or patient organization. Additionally, the Devices program established FDA's first advisory committee comprised solely of patients, care partners, and those who represent their needs.
- At the close of FY 2018, FDA designated 96 devices as breakthrough, cleared two 510(k)s, authorized two De Novo classifications, and approved four PMAs for designated breakthrough devices
- The number of early feasibility studies approved per year more than doubled—from 21 in FY 2014 to 52 in FY 2018.
- The Devices Program reduced the time it takes to approve an Investigational Device Exemption (IDE) application by more than 1 year, from 442 days in FY 2011 to 30 days in FY 2018.
- In June 2018, FDA expanded the approval of the MiniMed 670G hybrid closed loop system, expanding use of an artificial pancreas to include individuals aged 7 to 13 with Type 1 diabetes and approved a continuous glucose monitoring system with a fully implantable glucose sensor and compatible mobile app.
- In March 2018, FDA expanded the approval of a heart valve to include a size small enough to be used in newborn pediatric patients to treat heart defects, making it the smallest mechanical heart valve approved in the world.

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Strengthen Science and Efficient Risk-Based Decision Making

Investing in New Tools, Policies and Resources to Enhance Post-Market Safety

On November 20, 2018, FDA set an important and ambitious new goal when it comes to device safety: Ensuring that the FDA is consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices. This is an important milestone - a culmination of steps that the agency has taken in recent years to strengthen and implement new post-market monitoring tools to adequately assess device performance and patient safety in real-time. In many cases, FDA has already been the first to act on or identify and act on safety signals.

FDA is evolving beyond current post-market surveillance system – which is largely passive and relies on device users to report problems to us, sometimes resulting in underreporting – and moving to an active surveillance system that relies on real-world evidence and timely receipt of robust safety information. The Agency has long recognized the systemic weaknesses of the passive system – a challenge faced by other countries as well – and FDA has prioritized this area for regulatory reform efforts.

In 2012, FDA announced a vision for the medical device program that reflected the importance of safety, by looking to establish a "U.S. post-market surveillance that quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearances."

Soon thereafter, FDA issued a strategy for establishing a national medical device post-market surveillance system that employs active surveillance. Active medical device surveillance will better protect patients by continuously generating, accessing, and evaluating large data sets on device performance and clinical outcomes associated with device use in routine clinical practice. It also improves the FDA's ability to link adverse events with specific devices, so the Devices Program can act quickly with manufacturers and healthcare providers to make timelier, evidence-based decisions to mitigate device problems and keep patients safe.

Implementing a national surveillance system would not be possible without the FDA's establishment in recent years of a unique device identification (UDI) system, in which medical devices are marked on their labels with a unique code that can be used to track the device through its distribution and use in patients. These identifiers are stored in a public database, which now contains more than 1.5 million device records, that enables patients and health care providers to download information about their devices. Patient registries also utilize UDIs to help quickly identify safety signals tracked to specific devices.

FDA has also taken steps to advance the use of real-world evidence in pre- and post-market decision-making. FDA believes that including the device identifier in electronic data more broadly, including in insurance claims, will advance FDA's efforts to leverage real-world data to support the development of more effective post-market surveillance tools. A key element of implementing this strategy is the multi-stakeholder effort to establish the new national system for gathering real world evidence through the National Evaluation System for health Technology (NEST). Based on early activities, FDA has evidence that NEST will help improve the breadth and quality of real-world evidence that can be accessed and analyzed.

National Evaluation System for health Technology (NEST)

NEST leverages a wide range of data systems that could provide crucial information on medical devices, including data from patient registries, Medicare claims and electronic medical records. Moreover, it was designed from the very beginning to serve as a resource for the entire community, which is why the Governing Board for NEST's independently-run public-private coordinating center (called NESTcc) is comprised of members representing the key community stakeholders, including patients and providers.

Delivering on the goal to be first in the world to consistently identify and act on medical device safety signals will rest in part on FDA's ability to fully leverage NEST as an active surveillance and evaluation system that complements the approaches currently in use by more quickly detecting emerging safety signals through active surveillance, supporting timely evaluation of

these signals to determine if they represent a real risk to patients, and ensuring timely responses to new and increased risks.

The Devices Program provided the seed funding that helped establish the NESTcc and secured partial industry funding for NEST as part of the latest Medical Device User Fee Agreement (MDUFA IV) with industry. To date, the NESTcc has entered into agreements this year with 12 organizations that represent more than 195 hospitals and almost 4,000 outpatient clinics with access to more than 495 million patient records – which will all be a part of the early data network.

Despite all of the progress FDA has made and the promise of this system, NEST will require considerably more funding to fully meet its tremendous potential. The FDA will continue to put resources available have into building out this system. In September 2018, the Devices Program allocated an additional $3 million in agency funding to the NESTcc. This new funding for NEST, which was provided in addition to the annual funding allocated by the latest user fee agreement, will allow FDA to continue supporting demonstration projects for building out active surveillance capabilities.

However, for NEST to become fully functional and fulfill its promise of helping to ensure safer devices for patients, additional resources are essential. Funding is the principal barrier to establishing this system.

As FDA works to secure additional funding, the Devices Program continue to do whatever possible to build out NEST now. With the FDA's support, the NESTcc has initiated eight test case demonstration projects using real world data. Some examples of projects to conduct post-market surveillance include testing the feasibility of using patient registries and claims data to evaluate the safety and effectiveness of total joint and knee replacement surgeries; to compare the safety and effectiveness of different tissue closure techniques (staples, sutures, skin adhesives) from wounds resulting from trauma or surgery; and to evaluate the safety of intervertebral body fusion devices used to treat spinal conditions like degenerative disc disease.

The promise of NEST is clear: real-time device safety information means better outcomes for patients who depend on devices to improve their health. FDA is committed to making the promise a reality by prioritizing NEST's development and ensuring it's set up for long-term success to advance public health.

Specifically, NEST will help provide the following benefits for patients and the ecosystem:

- NEST can help facilitate reimbursement (the Center for Medicare and Medicaid Studies (CMS) serves on the NEST Governing Committee)[60] as improved data collection can help establish coverage with evidence development (CED)
- The system will help improve the quality of real-world evidence that FDA can use to detect emerging safety signals quickly and take appropriate actions.
- NEST will provide another source of information for medical device manufacturers to assess the safety and effectiveness of their devices and continue to develop innovative improvements.

[60] https://nestcc.org/about/governance/

- NEST will help healthcare providers and patients be better informed about the evolving benefit-risk profile of devices on the market and enable them to make more informed decisions.
- NEST 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.
- As a complement to NEST, FDA aims to improve evidence generation about the safety and effectiveness of health technologies in clinical areas that are unique to women by continuing to work with external stakeholders to build the Women's Health Technologies Strategically Coordinated Registry Network (CRN), through the Medical Device Epidemiology Network Initiative (MDEpiNet) Public-Private Partnership.

Women's Health Technologies Strategically Coordinated Registry Network

As FDA implements an active surveillance system to quickly detect new safety signals, FDA will continue efforts to strengthen the Coordinated Registry Networks (CRN), which link different real-world data sources to generate clinical evidence about medical products used by patients. In particular, the Devices Program is focusing on addressing clinical questions on device therapies that are unique to women, such as treatment of uterine fibroids, pelvic floor disorder, female sterilization and long-acting reversible contraception. The FDA partnered with the American College of Obstetricians and Gynecologists, the American Urogynecologic Society, the National Library of Medicine and others on this, known as the Women's Health Technologies CRN, or WHT-CRN. FDA targeted part of the additional $3 million in funding for NESTcc for this effort.

Notable successes of the WHT-CRN include the development and international harmonization of core data sets in four clinical areas – stress urinary incontinence (SUI), pelvic floor disorders, uterine fibroids, and long-acting, reversible contraception and sterilization therapies. The Devices Program is tapping into anonymous payer claims data from New York State and data from the New York Clinical Data Research Network to enable us to answer crucial clinical questions, such as the long-term safety and efficacy of urogynecologic mesh for stress urinary incontinence. The next step is to develop an implementation guide for the participating registries so they can develop tools to efficiently extract clinical data from electronic health records.

Additionally, to help inform the health care community's understanding of how the WHT-CRN could ultimately be more broadly applied, the FDA has initiated surveillance pilot projects using payer claims data and will undertake a pilot assessing the feasibility of using electronic health records (EHR) to study mesh.

Similar to NEST, the WHT-CRN holds great promise as FDA advances new tools and approaches for using data to improve outcomes for women and ensure they have access to safe, effective and innovative devices.

Modernize FDA's 510(k) program to advance the review of the safety and effectiveness of medical devices

As part of FDA's Medical Device Safety Action Plan, FDA committed to strengthen and modernize the 510(k) program. This is a pathway used for clearance of low- to moderate-risk devices that are substantially equivalent to a device already on the market – otherwise known as a predicate device.

The most impactful way that FDA can promote innovation and improved safety in the 510(k) program is to drive innovators toward reliance on more modern predicate devices or objective performance criteria when they seek to bring new devices to patients.

Older predicates might not closely reflect the modern technology embedded in new devices or the more current understanding of device benefits and risks. In some cases, the predicate could be decades old. Data show that nearly 20 percent of current 510(k)s are cleared based on a predicate that's more than 10 years old. That doesn't mean the products are unsafe. But it does mean that some devices may not be continually improving, which is the hallmark of health technologies.

FDA believes that newer devices should be compared to the benefits and risks of more modern technology; that is why the Devices Program is looking at ways to promote the use of more recent predicates. To advance these goals, the Devices Program is considering making public on its website those cleared devices that demonstrated substantial equivalence to older predicate devices - potentially focusing on predicates that are more than 10 years old as a starting point, so that the public is aware of those technologies. The Devices Program's goal in focusing on older predicates is to drive sponsors to continually offer patients devices with the latest improvements and advances.

Before proceeding, FDA will seek public feedback on whether the Devices Program should make public those devices or those manufacturers who make technologies that rely on predicates that are more than 10 years old, whether other criteria should inform FDA's point of reference, and whether there are other actions FDA should take to promote the use of more modern predicates. Encouraging product developers to use more modern predicates would give patients and their doctors a choice among older and newer versions of a type of device, promote greater competition to adopt modern features that improve safety and performance, and help make sure that newer devices reflect more modern technology and standards that can improve patient care and outcomes. It would help the overall product environment continue to evolve in the direction toward more modern performance standards.

This market-based approach will promote the right kind of innovation for patients. Innovation that reflects the most modern principles. Among other steps, FDA is developing proposals to potentially sunset certain older predicates and promote the use of more modern predicates. FDA will consider whether this approach should become a requirement in the future. To achieve some of these public health goals, FDA may need to seek additional guidance from Congress.

The Devices Program is considering this approach because the products FDA reviews through the 510(k) program are increasingly complex. They often involve different technological features from the predicates on which they're based. Newer devices are more often interconnected and interoperable, increasing cybersecurity threats. Miniaturization of device components has allowed devices to become smaller and more portable. Devices more frequently use automation and robotics, and advanced materials, changing the way healthcare providers and patients interact with them.

FDA is proposing these changes after accounting for all of the improvements to the Devices Program 510(k) review in recent years. FDA has also posted a performance report that highlights some of the key achievements of the past decade, including the measures taken to increase the predictability and transparency of the 510(k) review process. These efforts include the more than 50 final guidance documents on important medical device policy issues that we've issued since 2009.

Importantly, FDA has increased expectations for the quality and quantity of information required in 510(k) submissions, resulting in a more than doubling of the size of submissions – now, an average of 1,185 pages, compared to 475 pages in 2009. While the Devices Program reviewers have spent more time reviewing applications during this same period – an increase of about 32 percent – the average total time for the agency to reach a decision has decreased, reflecting a more robust and efficient program. These metrics reflect not only the strengthening of the medical device review program, but also the dedication of the talented Devices Program career staff in carrying out FDA's public health mission and continuing to drive forward critical program enhancements.

Modernizing the 510(k) Pathway

To keep pace with these developments and advance these goals, in early 2019, FDA intends to finalize guidance establishing an alternative 510(k) pathway that allows manufacturers of certain well-understood device types to rely on objective safety and performance criteria to demonstrate substantial equivalence as a way to make it more efficient to adopt modern criteria as the basis for the predicates that are used to support new products. The Devices Program's goal in finalizing this pathway is to expand its use broadly across the 510(k) program and make it the primary pathway for devices eligible for 510(k) review.

The Devices Program believes this approach is the future of the 510(k) program. Rather than looking to the past as a baseline for safety and effectiveness – and rely on predicate devices that are sometimes decades old as FDA's point of comparison – the Devices Program premarket review would be based on a contemporary baseline that looks to the future and a baseline that can be updated as technologies advance. Sometimes, by relying on old predicates, it can actually make it more difficult for more advanced technology to reach patients since it's harder for an innovative product to bridge to an outdated technology reflected in a decades-old predicate. FDA's new proposed approach enables us to help improve safety and performance, as appropriate, and ensure new products can more easily reflect beneficial new advances.

FDA is planning to rename this new approach the "Safety and Performance Based Pathway" to reflect its focus on advancing improved safety and performance of new products. Through this new path, a company would demonstrate that a novel device meets modern performance-based criteria that have been established or recognized by the FDA and reflect current technological principles. These criteria would reflect the safety and performance of modern predicate devices. This efficient new pathway could eventually supplant the practice of manufacturers comparing their new device technologically to a specific, and sometimes old, predicate device.

This modern framework is a direct and transparent approach to demonstrating the safety and effectiveness of low to moderate risk devices. This alternative pathway to substantial equivalence would provide more direct evidence of the safety and performance of a device and better information for patients and providers to make well-informed health care decisions. In addition, with this new approach, the FDA may drive greater market competition to develop safer devices. Manufacturers would be able to demonstrate that their products meet or exceed objective safety and performance criteria that are based on modern technological principles. And companies could also, for the purposes of supporting coverage decisions, more readily demonstrate to payors that their products perform better than other devices on the market.

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 device problems more quickly, and better target recalls to improve patient safety. Establishment of the UDI system has been a tremendous milestone in building a stronger, more modernized medical device safety net. The UDI provides a standard and clear way to document device use, including in electronic health records, clinical information systems, claims data sources, and registries. It allows more accurate reporting, reviewing, and analyzing of adverse event reports so that new and increased known safety issues can be identified and corrected more quickly.

In addition, UDI provides a mechanism to reduce medical errors by enabling healthcare professionals and others to more rapidly and precisely identify a device and obtain important information concerning the device's characteristics, which also prevents confusion between similar devices that can lead to device misuse. UDI provides a mechanism to help device manufacturers, distributors, and healthcare facilities manage device recalls more effectively. UDI also provides a foundation for a global, secure distribution chain, helping to address counterfeiting and diversion and prepare for medical emergencies.

By providing a standard and clear way to document device use, incorporating UDI as a standard in EHRs, clinical information systems, billing systems, and registries will enable NEST to perform enhanced analyses of devices on the market to better understand device performance in diverse populations. As of June 2018, there are more than 1.7 million records representing submissions from more than 4,300 labelers to the Global UDI Database (GUDID), and these records are made publicly available through an FDA-funded NLM portal, AccessGUDID.

The benefits offered by the UDI system can only be fully realized with the adoption and use of UDIs by the medical device ecosystem—manufacturers, distributors, payers, providers, patients, health care systems and other stakeholders with important roles to play throughout the medical device lifecycle. The Learning UDI Community (LUC), which is sponsored by the Association for Healthcare Resources and Materials Management (AHRMM), involves all members of the medical device ecosystem in developing a common understanding and approach to UDI adoption within the health care setting. Its work has significantly informed and accelerated UDI adoption.

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. 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 GUDID.

Cybersecurity

The Devices Program's goal is to encourage a coordinated approach of vigilance, responsiveness, resilience, and recovery with respect to cybersecurity that fits FDA's culture of continuous quality improvement. This means taking a total product lifecycle approach, starting at the product design phase when FDA builds 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. Specifically, FDA 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.

FDA has published guidances – recommendations for manufacturers and others – that contain recommendations for comprehensive management of medical device cybersecurity risks throughout the total product life cycle. This includes closely monitoring devices already on the market for cybersecurity issues. To enable more expedient actions, the Devices Program's overall approach incentivizes industry to make changes to marketed and distributed medical devices to reduce risk.

Medical devices, like other computer systems, can be vulnerable to security breaches, potentially impacting the safety and effectiveness of the device. This vulnerability increases as medical devices are increasingly connected to the Internet, hospital networks, and other medical devices. In recent years, FDA, manufacturers, and healthcare entities have made tremendous strides to improve the cybersecurity of medical devices and FDA remains committed to continual improvements to keep pace with emerging threats and vulnerabilities.

FDA continues to coordinate its cybersecurity efforts with other agencies. FDA participates in the HHS Cybersecurity Working Group and works collaboratively with the Industrial Control Systems Cyber Emergency Response Team (ICS-CERT) of the Department of Homeland Security (DHS). FDA also works with the FTC in the Cybersecurity Forum for Independent and Executive Branch Regulators. FDA actively participates in Department of Commerce-led initiatives on multi-stakeholder engagement in coordinated vulnerability disclosure and patchability of Internet of Things (IoT) devices. In addition, FDA is taking steps to help build on the work that the Devices Program and FDA stakeholders have already achieved. Specifically, the Devices Program plans to:

- Build capability to update and patch device security into a product's design and to provide appropriate data regarding this capability to FDA as part of the device's premarket submission.
- Support the development of a "Software Bill of Materials" that would be provided to FDA as part of a premarket submission and made available to medical device customers and users, so that they can better manage their networked assets and be aware of which devices in their inventory or use may be subject to vulnerabilities.
- Update premarket guidance on medical device cybersecurity to better protect against moderate risks, such as ransomware campaigns that could disrupt clinical operations and delay patient care, and major risks such as exploiting a vulnerability that enables a remote, multi-patient, catastrophic attack.

The Devices Program recognizes that a key to the adoption of proactive postmarket cybersecurity is the sharing of cyber risk information and intelligence within the medical device community. FDA routinely collaborates with the Department of Homeland Security (DHS) on potential cybersecurity vulnerabilities and exploits that could impact medical devices or the healthcare sector. FDA also continues to work with external partners to advance the state of cybersecurity in the medical device ecosystem through several initiatives, including supporting the establishment of additional medical device vulnerability Information Sharing Analysis Organizations (ISAOs).

With so many devices dependent on software and internet access today, having a plan in place to address cybersecurity risks is as essential to the device development process as coming up with a novel new product. Working with the medical device industry and other federal agencies, FDA will continue its work to ensure the safety and effectiveness of medical devices at all stages of their lifecycles against potential cyber threats.

Mammography Quality Standards Act Program

According to the Centers for Disease Control and Prevention, breast cancer is the most common cancer in American women. FDA's mammography program — authorized by the Mammography Quality Standards Act (MQSA) — helps to ensure that 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 that they can understand.

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 (DBT) 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.

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 2018, 84 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.[61]

The MQSA program recently enhanced the inspection process with an Enhancing Quality Using the Inspection Program (EQUIP) initiative, which adds inspection questions related to existing regulations about image quality. The initiative ensures that facilities have processes in place to maintain image quality and detect issues early so that they can be rapidly corrected. The first year of inspections was focused on educating facilities about the new EQUIP program. Analysis of citations from this year's inspections will inform efforts to help facilities achieve full compliance with EQUIP.

FDA's mammography quality program promotes public health by maintaining quality standards for the latest breast cancer screening technology while allowing FDA resources to be focused on activities for which FDA involvement is value-added.

During year two of the initiative, which began in March 2018, inspection violation citations began to be issued to facilities. Beginning in March 2019, facilities that have a repeat EQUIP violation will be referred to their accrediting bodies for a review of mammograms they performed, to assess whether image quality was affected.

On October 18, 2018, FDA announced that The Office of Management and Budget has indicated it is reviewing a proposed rule from the FDA to amend its regulations governing mammography. The proposed a new rule would modernize mammography quality by recognizing new technologies, making improvements in facility processes and updating reporting requirements.

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

The agency is proposing updates that incorporate current science and mammography best practices, including addressing breast density reporting by mammography facilities to patients and health care providers. These updates are intended to improve the delivery of mammography services.

The FDA believes there are tremendous public health benefits to this rule, including the potential for earlier breast cancer detection that benefits patient survival and wellness, reduces cancer treatment costs, and promotes more informed decision-making by strengthening the communication of health care information between patients and their providers.

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. For years, FDA has administered a comprehensive program for oversight of radiology devices. The Agency 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 and 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.

Participation in consensus standards development is a key component of the radiological health program, both to address safety issues and to reduce burden on industry by recognizing standard performance requirements and testing methods that are used worldwide. Recent standards successes include incorporation of pediatric safety features in standards for computed tomography (CT), fluoroscopy, and general and dental radiography.

Through the Council of Radiation Program Control Directors (CRCPD), FDA supports and collaborates with state agencies on projects to promote and protect public health, including working to better understand current levels of radiation exposure. The Nationwide Evaluation of X-ray Trends (NEXT) recently completed a survey on patient exposures during dental radiography and is planning a next survey on chiropractic and outpatient facilities where minimal information on current radiation dose information exists. 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. FDA collaborates with stakeholders, including the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO), to promote action

on a list of priorities for radiation protection in medicine for the next decade called the Bonn Call for Action.

Promoting a Culture of Quality and Organizational Excellence

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 focus on continuous improvements, organizational excellence and quality management promotes simplicity. Quality and excellence require the Devices Program engage in continuous improvement, leaning, and improving processes to better serve all customers, reducing unnecessary burdens, and increasing quality and predictability. 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.

For example, 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. In 2018, FDA launched the Voluntary Manufacturing and Product Quality Pilot, through which an appraiser evaluates a medical device manufacturer's quality maturity and compliance with regulatory requirements.

FDA has engaged with 38 manufacturing sites that have undergone the quality maturity appraisal across 18 companies, both domestic and international. By moving the organizational focus beyond the compliance baseline to improving patient outcomes, improving product quality, and aligning with business value, the pilot has demonstrated significant performance outcomes. A small manufacturer participating in the program was able to improve their clinical intake process from 8 months to less than 28 days, an 857% improvement, allowing the manufacturer to complete their clinical trial ahead of schedule.

One of the larger class III manufacturers has implemented 18 out of 22 improvement opportunities identified and has improved production yield, demonstrated 7% production improvement, and is expanding capacity for product production and delivery by 30%; increasing the quality of their class III product and increasing access through improved production and capacity. The improvements have also demonstrated financial value that has been reinvested in expanding US production capacity.

FDA has also been able to modify manufacturing submissions towards a least-burdensome submission that reduces the 30-Day review timeline to a target of 5 business days. FDA has received 35 submissions as October 29, 2018 and has reviewed 97% in the target 5 days or less. The pilot has also demonstrated that the information provided in the streamlined submission provides sufficient information for the review team to evaluate the impact of the change to safety and effectiveness. Participant sites have also reported resource savings from the maturity appraisal in comparison to a compliance audit.

Additionally, through engagement with MDIC, 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 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. To support this effort, in September

2018 the Devices Program released a guidance document, Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics, that clarifies current thinking on the validation efforts and requirements for these systems. The recommendations in this guidance are intended to promote consistency, predictability, and transparency in the device submission review process when determining substantial equivalence for devices that have different technological characteristics, which do not raise different questions of safety and effectiveness, then a recognized predicate.

Case for Quality

The Devices Program advanced manufacturing and product quality through its Case for Quality Program and Voluntary Maturity Appraisal Pilot. Appraisal results are focused on assessing firm capability to successfully meet business objectives, increasing value to stakeholders, and achieving public health outcome objectives. The goal of the program and pilot is to drive quality and continuous improvement within the device industry.

Over the course of 2017, the Devices Program engaged industry and other stakeholders through external forums and a public meeting, culminating in publication of a Federal Register (FR) notice on December 28, 2017. The FR announced the details and solicited industry participation for a Voluntary Manufacturing and Product Quality Pilot that will run through calendar year 2018. The Pilot will assess resource utilization at participating industry sites and within FDA, monitor improvement projects at the companies, and evaluate impact of the pilot on submission burden on industry and FDA (i.e., reduction in number or type of submissions and review time).

Shifting from a compliance focus to a continuous improvement focus enables manufacturers to identify opportunities to reduce costs and improve medical device quality, improving patient safety. The streamlined submissions reduce the review effort by the Devices Program, accelerating product improvements and innovations.

Current Pilot Results:

- Industry participants have reported cost savings by using a quality appraisal rather than a regulatory audit. Savings reported by participants have been in the range of $65,000 - $350,000, depending on the site size and complexity.
- Industry participants have started various improvement projects based on the appraisal output. For example, a small manufacturer improved clinical trial intake times from 6 months to 28 days.

The Devices Program has conducted several streamlined manufacturing 30-Day notice reviews and has been able to reduce the acceptance time from 30 days to less than 5 business days. A large manufacturer participating in the pilot estimated the financial benefit of the Devices Program accelerated review at $1.2 million.

Reduce the Burden of Addiction Crisis that are Threatening American Families

Devices to Prevent and Treat Opioid Use Disorder Challenge

On May 30, 2018, the FDA announced the launch of the Devices to Prevent and Treat Opioid Use Disorder Challenge to spur the development of medical devices, including digital health and diagnostic devices, to help combat the opioid crisis and to help prevent and treat Opioid Use Disorder—a serious health condition which can be a devastating outcome of opioid drug use.

Despite recent advances in some of these areas, there are still many opportunities to advance new technologies and bring new products to market to meet this urgent public health need. This challenge will provide those companies that are selected by the FDA under this new program with the opportunity to work closely with the agency to accelerate the development and review of their innovative products. The goal is to provide additional incentives for product developers to invest in products that can address aspects of the addiction crisis, and advance the development of promising technologies. FDA received more than 250 applications from medical device developers and based on these criteria, eight submissions were selected.

This new effort builds on the success of previous work to take a collaborative approach to promoting medical device innovation and safety, such as the 2012 challenge that led to multiple new approaches to treat life-threatening, end-stage renal disease. The FDA stands ready to provide significant assistance and expedite premarket review of applications to help bring innovative devices that, if properly instituted, could help those at risk for addiction or treat those who might develop opioid use disorder. The Devices Program also hopes that in turn these novel products may also help pave the way for the development of future products that build on the latest technologies.

The engagement and participation from so many developers is indicative of the dire need we face for new ways to treat this disease, and that medical devices, including digital health technologies, like mobile medical apps, will play a critical role in the FDA's all hands on deck approach to confronting the opioid epidemic.

Foster Competition and Innovation

Real World Evidence

The Devices Program is already relying on real-world evidence 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. Further, the Devices Program spearheaded the work of 15 National Coordinated Registry Networks and four 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.

Between 2016 and 2018, the Devices Program set — and exceeded — goals to increase access to, and use of, real-world evidence to support regulatory decision-making. Real-world evidence derived from multiple sources outside typical clinical research settings (e.g., electronic health records, claims and billing activities, product and disease registries, or and health-monitoring devices) provides immense amounts of information about medical devices and it plays an increasing role in health care decisions. To realize the full promise of real world evidence, FDA has sought to clarify what it is, what it can reveal, and how it can be used most effectively at various stages of the device life cycle – including when it can be used for regulatory decision-making to meet FDA's gold standard.

In 2017, FDA issued final guidance titled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," which describes how FDA evaluates real-world data (the raw information about patient health status and/or delivery of health care collected from a variety

of sources) and determines whether such data are of sufficient quality for generating the types of real-world evidence that can be used in FDA decision-making for medical devices at various stages of the device life cycle. The guidance describes the characteristics that FDA considers in assessing the relevance and reliability of the data, as well as specific examples in which real world evidence may be used.

FDA's use of real-world evidence to support regulatory decision-making for medical devices will continue to accelerate by leveraging more robust sources of device safety and effectiveness made available through NEST. Under the right conditions, real world evidence may be suitable to support clearance or approval of a new device, or the expansion of indications for the use of devices that are already on the market, in less time and at lower cost than ever before.

Breakthrough Devices Program

FDA's Breakthrough Devices Program has delivered important results for patients since it was established in late 2016 by the 21st Century Cures Act. This program helps patients gain timely access to breakthrough medical devices when they have few or no treatment alternatives and their needs would otherwise go unmet. Eligible devices must provide more effective treatment or diagnosis for life-threatening or irreversibly debilitating diseases than existing options. In addition, there must be no approved or cleared treatment, or the device must offer significant advantages over existing approved or cleared alternatives. Organizations such as the National Organization for Rare Disorders (NORD)[62] supported inclusion of this provision in the 21st Century Cures Act. Additionally, organizations including the Juvenile Diabetes Research Foundation (JDRF) support FDA's breakthrough devices program in general as, when appropriate, it helps patients have access to safe and effective medical devices earlier when they may not have other options.

FDA's Breakthrough Devices Draft Guidance proposed to employ "sprints" in which the sponsor of a breakthrough device identifies a regulatory challenge they need to solve and FDA works interactively with the sponsor to address that challenge within a short timeframe—often just a few weeks.

For example, Second Sight Medical Products Inc.'s Orion Cortical Visual Prosthesis System recently qualified for the FDA's voluntary Breakthrough program. The Orion is a brain implant for patients with blindness caused by damage to the optic nerve. With the designation, Second Sight qualified for more interactive and timely communication with FDA, which is a key feature of the Breakthrough Devices Program. These early interactions resulted in the development of a flexible clinical study design, more FDA review team support, and senior management engagement, all of which are intended to allow FDA and the sponsor to evaluate the innovative device more efficiently.[63]

At the close of FY 2018, FDA had designated 96 devices as breakthrough, cleared two 510(k)s, authorized two De Novos, and approved four PMAs for designated breakthrough devices. FDA received twice as many breakthrough designation requests at the close of FY 2018 than in all of 2017. This program shows how changes to FDA's regulatory paradigm made with appropriate

[62] For more information visit https://rarediseases.org/wp-content/uploads/2015/06/NORD-Comments-on-the-21st-Century-Cures-Act.pdf

[63] For more information visit https://medtech.pharmaintelligence.informa.com/MT123026/Two-Roche-Alzheimers-Assays-Win-US-FDA-Breakthrough-Device-Status

safeguards and implementation improve patient access to novel technologies and can enhance quality of life when treatments might not otherwise be available.

Clinical Trial Enterprise and Early Feasibility Studies

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.

FDA has made efforts to expedite the safe initiation of clinical trials in the U.S., and these policies should result in clinical studies being conducted in the U.S. earlier in the device development process than has historically occurred. FDA issued guidance and started a pilot program to facilitate the early clinical evaluation of novel device technologies in the U.S., using risk-mitigation strategies that appropriately protect human subjects.

In addition, FDA implemented process changes to the Investigational Device Exemption (IDE) program. For example, the percentage of IDE submissions that received an approval decision authorizing study initiation (i.e. an IDE conditional approval or full approval decision) within two IDE cycles increased from 46 percent in FY 2011 to 77 percent in FY 2017, while the median time to full IDE approval was reduced from 435 days to 30 days. Additionally, the number of early feasibility studies that received an approval decision authorizing study initiation in the U.S. within two IDE cycles increased from 24 in FY 2014 to 45 in FY 2017, which represents an increase of more than 87 percent.

In addition, FDA continues to improve the clinical trial ecosystem in the U.S. through collaborative efforts, such as the Medical Device Innovation Consortium's (MDIC) Clinical Trial Innovation and Reform Project, which have the potential to improve the efficiency of the clinical study process leading to earlier access in the U.S. to beneficial innovative technologies for patients. Recently, under the MDIC, a public-private partnership focused on advancing the science of evaluating devices, FDA has been working with health care providers, health care systems and companies to create a consortium of clinical sites for device early feasibility studies. This effort is intended to reduce challenges to conducting clinical trials in the U.S., such as the long delays in negotiating contracts, receiving institutional review board approvals for studies, and enrolling patients into a trial, all of which can delay patient access to innovative medical devices. The number of early feasibility studies approved per year has more than doubled—from 21 in FY 2014 to 52 in FY 2017 and 54 approved in 2018 alone —providing evidence that the EFS Program remains robust and permits efficient clinical trial progression in the U.S. while providing appropriate human subject protections.

The Medical Device Single Audit Program (MDSAP) and Global Harmonization

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 manufacture audits and inspections across various nations. 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. This supports the Devices Program continued efforts to better focus resources and oversight on those areas that pose the most risk to patients.

MDSAP continued to experience significant growth in firm participation over fiscal years 2017-2018, from approximately 515 firms participating by the end of FY17 to 2,718 firms at the end of FY18. During this time, the Devices Program accepted 2,203 new establishments into MDSAP. Since participating facilities are required to be audited at least annually through MDSAP, FDA can remove these establishments from its inspection work plan without losing confidence that they were being evaluated to ensure compliance.

Additionally, the Devices Program reviewed and classified 754 audit reports submitted by Auditing Organizations participating under MDSAP. Audit reports received under the program are viewed as equivalent to FDA establishment inspection reports and are processed and classified consistent with FDA compliance operations. Further, the Devices Program participated in 21 of 30 assessments to evaluate the quality and consistency of MDSAP audits for 14 auditing organizations, which directly provides confidence in the MDSAP audit model and the auditing organizations conducting the audits of the manufacturers.

Empower Consumers and Patients

Digital Health

FDA is a world-leader in fostering development of new and innovative digital health technologies and has made balanced oversight of these products one of its chief priorities. Providing patients with access to safe and effective medical products to meet their health care needs is central to the FDA's mission, and the Devices Program committed to finding new ways to deliver on a complementary mission of encouraging innovation to improve safety and detect safety risks earlier – particularly for medical devices. As a critical part of its mission, FDA has a vital role to enable patients in the United States to realize the promise of digital health products that it regulates as medical devices.

The Device Program is committed to implementing policies, adding expertise, and exploring a software precertification pilot program to bring clarity and efficiency to how FDA regulates digital health products. Consistent with the 21st Century Cures Act, which defined categories of software not subject to FDA regulation, FDA has created a risk-based approach to digital health, including exercising enforcement discretion with respect to its device authorities for low risk software that could be classified as a device.

Examples of low risk software includes software that automates simple health care tasks for providers or helps consumers track and organize their medical information. This approach allows FDA to focus oversight on products that pose the greatest risks to patients – particularly those products that are novel and not as well understood. This It also enables FDA to foster technology innovations, while, at the same time, providing consumers and clinicians with better information and greater assurances that mobile medical apps and other digital health medical devices that fall within the agency's regulatory purview are safe and effective.

FDA continued progress on its "Software Precertification (PreCert) Pilot Program" that will enable it to develop a tailored approach toward regulating software by evaluating the software developer and/or digital health technology developer. The purpose of FDA's Software Pre-Cert pilot is to leverage customer input to develop a program that can help reduce the time and cost of market entry for software developers that FDA determines reliably manufacture high-quality, safe, and effective digital health devices while providing appropriate patient safeguards.

The goal of the Pre-Cert program is to develop a tailored and pragmatic regulatory framework that trusts the excellence of organizations, but also continually verifies the safety, effectiveness, and performance, tailoring the regulatory approach to the software development cycle while maintaining regulatory standards of safety and effectiveness. The process FDA is using to build this program is incremental, responsible, and innovative. As you know, FDA is currently working with nine pilot participants to gain valuable feedback on getting the right information from these new technologies, to answer the same questions that the Devices Program has always asked to assess safety and effectiveness.

Since launching the Pre-Cert pilot with nine pilot participants in September 2017, FDA has built on its initial strategy and released the second draft of the Pre-Cert program in June 2018. In 2018, FDA developed the appraisal elements and methodology for evaluating digital health technology developers. In addition, FDA developed a risk framework for evaluating digital health devices and a new approach to product review that would be tailored to product risk and streamlined, while continuing to establish reasonable assurance of safety and effectiveness for medical devices. FDA identified the real-world data to evaluate the developers, the PreCert program, and the digital health product and put forward ideas on how this real world data could be used to support device modifications. FDA's digital health team continues to work with participants and other stakeholders to assemble the essential building blocks of this unique and innovative program.

For digital health technologies to reach their fullest potential, it is critical that FDA be forward-leaning in making sure that FDA has implemented the right policies and regulatory tools and communicated them clearly to encourage safe and effective innovation, while assuring the safeguards patients depend upon.

Precision Medicine

The Devices Program has a unique role in advancing precision medicine. Precision medicine generally means tailoring treatments to specific characteristics, such as a patient's genetic makeup or the genetic profile of a tumor. Targeting treatments based on genetic information can improve the success of the treatment and minimize exposure to adverse effects. To fully realize the potential of precision medicine, next generation sequencing (NGS) tests that the Devices Program oversees used for risk assessment, diagnosis, and treatment must be accurate and reliable.

NGS works by looking at a person's DNA to detect genomic variations that may determine whether a person has or is at risk of developing a genetic disease and, in certain cases, may help to inform treatment decisions. Unlike traditional diagnostics that typically detect chemical changes associated with a single disease or condition, NGS can look at millions of DNA changes in a single test to help determine the cause of a person's disease or condition. Availability of these types of tests plays an important role in the advancement of the field of precision medicine.

As NGS technologies continue to evolve, the FDA remains dedicated to adapting regulatory review capabilities and leveraging authorities to the fullest extent in order to make innovative and accurate testing technologies available to patients as efficiently as possible. To this end, on April 12, 2018, FDA finalized two guidances to drive the efficient development of a novel technology that scans a person's DNA to diagnose genetic diseases, which are usually hereditary, and guide medical treatments. The guidances provide recommendations for designing, developing, and validating NGS tests, and will play an important role in the continued advancement of

individualized, genetic-based medicine. Among other things, the final guidances encourage data sharing and the accumulation in public databases of evidence supporting the clinical validity of genomic tests, which will help provide an even more efficient path to market for these groundbreaking technologies that, at the same time, ensures patients can continue to rely upon their results.

Patient Preference Initiative

FDA has made it a priority to work with companies and other stakeholders on gathering information from patients about their views and needs, and on building the tools that are needed to capture patient input in a way that provides meaningful data. In considering the patient perspective, the FDA remains committed to assuring that medical devices meet the rigorous standards the agency uses to ensure the benefits of each product outweigh the risks for their intended use. Some patients' personal treatment goals and values may make them more willing to accept certain risks related to a medical product, especially in disease areas where treatment options may be limited. Patient preference studies, when well-designed and conducted, can add important information to the benefit-risk profile of certain medical devices. When assessing whether valid scientific evidence shows that a device's probable benefit outweighs its likely risks, the FDA can also consider rigorous, systematically gathered patient preference information as a part of the totality of the evidence from clinical and nonclinical testing.

Patients have a unique role in deciding what treatments should be available for them and FDA has worked to establish a strong, evidence-based approach for when and how the regulatory process should take their preferences into account when making decisions on marketing authorization The FDA encourages medical device manufacturers to include in their premarket submissions information about how patients consider tradeoffs between benefits and risks, and to consult with the agency early when considering patient preference studies.

FDA launched its Patient Preference Initiative as part of the medical device regulatory decision-making process and has seen increasing evidence of the benefits of soliciting patient feedback. The initiative is designed to identify and develop methods for assessing patient valuations of benefit and risk and outcomes that matter most to patients related to specific device types and specific illnesses and conditions that can be used to inform product review decisions. These efforts help assure a systematic and thorough approach to help patients understand how a disease or condition impacts their daily lives and the types of treatment benefits and risks that matter most to them. Due to FDA's efforts to improve available tools and apply a methodical approach, 100 percent of Premarket approval, de novo, and Humanitarian Device Exemption decisions made by FDA now include a public summary of available and relevant patient perspective data.

Patient preference is an evolving area of regulatory science, supported in part by the nonprofit Medical Device Innovation Consortium (MDIC), and FDA encourages further research in this field. In October 2017, the Devices Program held the inaugural meeting of the Patient Engagement Advisory Committee (PEAC)—the first-ever advisory committee comprised of patients – and focused on the patient perspective. PEAC discussed and made on how FDA can leverage patient-driven platforms, such as social media and registries, to better engage patients and consumers as empowered partners in the work of protecting public health and promoting responsible innovation.

Collaborative Communities

The Devices Program collaborates across the total product lifecycle of a medical device and believes better outcomes in protecting public health can be achieved when FDA integrates different perspectives, experiences, resources, and expertise from the medical device ecosystem. With this in mind, last January the Devices Program announced the strategic priority of Collaborative Communities with the vision of encouraging the formation of continuing forums where public and private sector members proactively work together to achieve common objectives and outcomes, to solve shared challenges, and to leverage collective opportunities in an environment of trust, respect, empathy, and openness.

The Devices Program's commitment to Collaborative Communities acknowledges that the FDA serves the American public better when stakeholders in the medical device ecosystem, including the FDA, work together. Collaborative Communities can contribute to improvement in areas affecting U.S. patients and healthcare and result in wide-ranging benefits for public health. In fact, FDA is so committed to this concept that the Devices Program included it in feedback to Congress on potential legislation for in vitro diagnostic regulatory reform.

The Devices Program recognizes the potential benefits Collaborative Communities could offer for the future of these healthcare products, which are lab tests used to help detect and monitor the treatment of diseases and other health conditions. In this context, the Devices Program sees opportunities for Collaborative Communities to help evaluate evidence to support new clinical claims and new technologies, as well as develop performance criteria that would create efficiencies in the FDA's oversight approach to more established tests. The Devices Program believes that Collaborative Communities could serve to further accelerate solutions to broad public health challenges leading to innovation in many areas of the medical device landscape, while providing the safety assurances patients depend on.

The Devices Program will apply the collaborative community approach to both domestic and international regulatory activities. The role of the Devices Program will be to foster a community spirit and responsible choice through the creation of collaborative communities with broad and fair representation to solve problems and proactively build for the future. The Devices Program will enable customers to take a more active role in the advancement of smart regulation. Collaborative communities will also help FDA respond to the rise of Patient Scientists—those scientists, health care professionals, engineers and others who focus on serving the unmet and developing needs of patients and who incorporate their own experiences as or with patients into their work in industry, health care, and government.

In the next three years the Devices Program will make building collaborative communities a standard practice. In addition, the Devices Program will consider whether a collaborative community approach could be adopted across two or more countries. The International Medical Device Regulators Forum (IMDRF), whose mission is to advance the convergence and harmonization of medical device regulation and of which the U.S. is a co-founder and active member, could serve as a catalyst for the establishment of global collaborative communities.

By December 31, 2020, the Devices Program intends to establish at least 10 new collaborative communities and have laid the groundwork for establishing several Collaborative Communities to more efficiently generate better evidence for medical device evaluation and regulatory decision-making through a number of efforts including work with the following: National Evaluation System for health Technology (NEST); Case for Quality, which allows the FDA to

identify device manufacturers that consistently produce high-quality devices to better focus resources to help manufacturers raise their level of quality; and pediatric medical device innovation, to support the development and availability of safe and effective pediatric medical devices.

Guidance Documents

The Devices Program guidance documents serve as valuable resources for developers who are working to bring new and innovative devices to market, and Congress has asked FDA to issue many such guidance documents to enable development in many important areas of technology. This list does not represent any degree of importance or priority ranking among the published guidances. This list demonstrates FDA's continuing efforts to support the development of a wide range of novel technologies that are safe for patients.[64]

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

Date	#	Title	Description
Apr 2018	FDA-2016-D-1270	Considerations for Design, Development, and Analytical Validation of Next Generation Sequencing (NGS) - Based In Vitro Diagnostics (IVDs) Intended to Aid in the Diagnosis of Suspected Germline Diseases	This guidance outlines key considerations for designing, developing, and establishing analytical validity of NGS-based tests used for DNA sequencing intended to aid in the diagnosis of symptomatic individuals with suspected germline diseases or other conditions.
Apr 2018	FDA-2016-D-1233	Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics Unique Device Identification: Direct Marking of Devices	This guidance discusses FDA's considerations for analytical validation of NGS-based tests intended to help diagnose suspected hereditary diseases.
Nov 2017	FDA-2015-D-2245	Unique Device Identification: Direct Marking of Devices	This guidance assists industry, particularly labelers, in understanding the requirements for direct marking of devices for unique device identification purposes and defines terms used in FDA's regulations pertaining to unique device identifier (UDI) direct marking requirements.
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.

Product Approvals

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

Date	Product Name	Description
Jun 2018	MiniMed 670G hybrid closed looped system	The first FDA-approved device that is intended to automatically monitor glucose (sugar) and provide appropriate basal insulin doses was expanded to include patients with diabetes aged 7 to 13 years old.
Jun 2018	Senseonics Eversense CGM System	The first fully implantable device to measure glucose in people with diabetes for up to 90 days.
May 2018	Imagen Technologies Inc's OsteoDetect	Computer assisted detection and diagnosis software that analyzes wrist radiographs using machine learning techniques to identify and highlight distal radius fractures during the review of posterior-anterior (PA) and lateral (LAT) radiographs of adult wrists.
Feb 2018	Banyan Biomarkers, Inc. Banyan BTI	An in vitro diagnostic test to aid in the evaluation of patients 18 years of age and older with suspected traumatic brain injury.
Aug 2017	Quantitative Insights Inc's QuantX	Computer-aided diagnosis software used to assist radiologists in the assessment and characterization of breast abnormalities using MR image data. The software automatically registers images, segments, and analyzes user-selected regions of interest (ROI) via an artificial intelligence algorithm.

FUNDING HISTORY[65]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$447,605,000	$323,157,000	$124,448,000
FY 2017 Actual	$450,799,000	$329,764,000	$121,035,000
FY 2018 Actual	$479,930,000	$332,885,000	$147,045,000
FY 2019 Annualized CR	$522,838,000	$332,893,000	$189,945,000
FY 2020 President's Budget	$631,718,000	$423,893,000	$207,825,000

BUDGET REQUEST

The FY 2020 Budget Request for the Devices Program is $631,718,000 of which $423,893,000 is budget authority and $207,825,000 is user fees. The budget authority increases by $91,000,000

[65] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

compared to the FY 2019 Annualized Continuing Resolution level and user fees increase by $17,880,000.

FDA's historic mission is to both protect and promote public health by assuring timely patient access to devices that are high-quality, safe and effective - such technologies as those that make less-invasive treatments possible and provide new options to patients whose conditions would have been considered untreatable in the past. The FDA is equally committed to advancing medical device innovation that can address unmet medical needs to reduce or prevent the adverse health effects from disease. Both objectives are essential to meeting FDA's public health mission, resulting in more lives saved and improved quality of life. The foundation of this program is medical device safety.

FDA's Devices Program fosters innovation to spur the development of safer, more effective technologies and assure timely patient access, while maintaining FDA's gold standard.

Providing patients with access to safe and effective medical products to meet their health care needs is central to the FDA's mission, and FDA remains committed to both encouraging innovation to improve safety and detecting safety risks earlier. This is accomplished by fostering a transparent and efficient system so that devices are able to meet the standard to come to market when they are safe, effective, and have the assurances patients depend on. As such, evidentiary requirements must be clear and well understood, and the means to meet these requirements must be efficient and enable patients to have timely access to safe, innovative technologies.

The FY 2020 Budget Request enables the Devices Program to make historic leaps in patient safety and digitization of government services that will reduce the time and cost of market entry for new products that patients need while enhancing safeguards. The success of FDA in providing patients with new treatments and diagnostics, and more options for effective health care, is not coming at the expense of the robust non-clinical and clinical science on which FDA can rely on to make our regulatory decisions. Rather, due in part to FDA efforts to strengthen the clinical trial enterprise and leverage real world data, in some cases FDA is receiving clinical evidence that is more informative more quickly and more efficiently and answering postmarket questions FDA would not have been able to address in the past.

The Devices Program is also seeing an increasing number of companies choosing to market their devices in the U.S. first, and FDA also continues to see more first in the world approvals here in the U.S. than in the past. The Devices Program has worked for years to improve the predictability, efficiency and transparency of FDA regulatory systems so evidentiary requirements to bring devices to market are clear and understood. This ensures that patients ultimately benefit from more safe and effective devices on the market because more companies are able to understand and meet the FDA's gold standard. Changes the Devices Program policies and processes have resulted in an improved medical device pipeline and innovative, safe and effective technologies.

In addition, the FDA has taken actions to make evidence generation more timely, efficient and robust. By continuing to enhance and implement the right tools and foster an environment that lets industry be innovative, while prioritizing patient safety, the Devices Program will continue to deliver on FDA's public health mission.

The FY 2020 funding will enable the Devices Program to continue to support such critical advances. 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 that meet FDA's standards first in the world.

BUDGET AUTHORITY

Medical Product Safety (+$91.0 million / 26 FTE)

Transform Medical Device Safety, Cybersecurity, Review, and Innovation: +$55.0 million / 13 FTE

Center: $55.0 million / 13 FTE

Innovative and complex device technologies have been driving a revolution in health care. Although FDA has been issuing new and revising existing policies and processes to address these scientific and technological advances, as well as enhancing the safety of medical devices, and working to be consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices, its information technology systems, tools, and approaches are not designed to support these activities, which are critical to protecting patients and fostering innovation for safe and effective devices.

Funding for the necessary IT systems will allow for creation of an integrated device innovation platform that will make the review of device applications, postmarket surveillance, and cybersecurity efforts significantly more efficient and informative, which can help support shorter review cycles, the ability to more quickly identify and address safety signals and cyber vulnerabilities, and spur the development of more timely patient access to innovative, safer, more effective devices. Failure to improve its device information management systems and methods of review are slowing the regulatory process and limiting FDA's ability to make better informed decisions, support new product developments, mitigate cybersecurity threats, and optimally assure patient safety throughout the total product life cycle.

Currently, FDA's premarket device review and postmarket surveillance processes use information from many legacy IT systems that are aging and disconnected. These critical components of FDA's existing IT infrastructure are time-consuming to use, have increasing maintenance costs, and are built on older platforms that can no longer be upgraded, which significantly increases the risk of threats and vulnerabilities until the functionality is replaced with current, supported technology. For example, with over 30 data systems in the Devices Program, reviewers need to access up to 10 different systems during the review process. FDA's decision-making relies on the scientific expertise of its staff who are navigating these fragmented systems and their ability to have access to and use data. It would be facilitated through the Digital Transformation to create an integrated knowledge management system that would allow FDA experts to efficiently access and analyze information and data in current and new ways to be better able to address the rapidly evolving and increasingly complex technologies, safety risks, and cybersecurity threats the FDA is encountering. More challenges require modern systems that enhance decision making and reduce inefficiencies.

Through the Devices Program's Digital Transformation, FDA will build an integrated knowledge management system and portal using modern, agile information technology systems with secure cloud-based data storage. This investment will enable safety issues to be monitored along the total life cycle of the device from bench testing to premarket clinical trials to postmarket adverse events and real-world evidence. FDA will also expand its capability to quickly evaluate new

questions, using laboratory research or other appropriate methods. This capability to better leverage pre-existing and new data in near real time is essential for implementing FDA's new approaches for digital health technologies, breakthrough devices, use of real-world evidence, and cybersecurity.

As part of this transformation, FDA will establish customer-friendly interfaces with industry, patients, and providers. These platforms will foster greater and more transparent interactions between FDA and its customers, including providing industry with the ability to track their premarket submissions. Funding for this initiative would also support building reliable, connected environments that allow reviewers and users access to integrated data, tools, and knowledge. This transformation will reduce duplicative efforts and create one integrated environment for reviewers to analyze complete information to more efficiently process applications and respond to regulatory questions. Funding will also be used to recruit technical experts to ensure the integrity of data and IT systems while making FDA data management more holistic. Advancements in this area will improve the quality of incoming data, fix data errors when they occur, and protect privacy of existing data.

FDA's Digital Transformation will further enable the Devices Program to integrate, redesign, and streamline at least 80 percent of its core business processes. This, in turn, could generate additional time and cost savings to industry and FDA, improve FDA's ability to more quickly identify and address safety signals, and spur the development of innovative, safer, more effective devices. By consolidating data systems and migrating to a reliable hybrid cloud environment, FDA can move closer to the speed of industry in streamlining workflows, reducing the cost of maintaining data and network security, and improving the timeliness of delivery of services.

Additionally, this investment will support digital health technologies, which offer the opportunity to improve patient care, empower consumers, and reduce health care costs. Recently, 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 ease regulatory burdens and reduce uncertainty, FDA will continue to develop a regulatory paradigm for these products, build greater 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.

Implementing these technology and regulatory improvements are essential for advancing technologies to improve the health and quality of life of patients while assuring critical safeguards. Overall, these investments will make the review of device applications and postmarket surveillance significantly more efficient and provide more timely patient access to innovative and safer devices.

Create a New Medical Data Enterprise for Safety and Modernizing Device Oversight: +$23.0 million / 5 FTE

Center: $23.0 million / 5 FTE

Real-time device safety information means better outcomes for patients who depend on devices to improve their health. FDA will advance the use of real-world evidence to better inform patient care, identify and address safety signals more quickly, and provide more efficient, robust, and

potentially lower-cost ways to develop clinical evidence that can inform medical device review and promote innovation for new devices that help improve and extend the lives of patients as well as fund postmarket safety studies. 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, and help NEST fulfill its promise of ensuring safer devices for patients. 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.

Active Surveillance

Delivering on the goal to be first in the world to consistently identify and act on medical device safety signals will rest in part on FDA's ability conduct active surveillance and complements the approaches currently in use by more quickly detecting emerging safety signals through active surveillance, supporting timely evaluation of these signals to determine if they represent a real risk to patients, and ensuring timely responses to new and increased risks. And 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 identification and responses to public health risks.

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.

Bring MedTech Manufacturing Home: +$12.0 million / 4 FTE

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.

Medical Countermeasures Initiatives: +$1.0 million / 4 FTE

Center: +$1.0 million / 4 FTE

The FY 2020 Budget Request includes $1.0 million for FDA review and regulatory science capacity to facilitate the development and availability of Medical Countermeasures (MCMs) to respond to chemical, biological, radiological and nuclear (CBRN) and emerging infectious disease threats.

CURRENT LAW USER FEES

Center: +$17.4 million / Field: +$0.5 million

The Devices Program request includes an increase of $17.9 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 so patients have more treatment and diagnostic options. This funding will enable FDA to hire more clinical and scientific experts which improves the ability to make well-informed and timely decisions about premarket submissions. The net benefit for patients from the increase in user fee funds is access, as soon as is appropriate, to innovative devices that are also high-quality, safe and effective, which can improve, extend, and in many cases, save their lives while maintaining FDA's regulatory standards and reliance on robust science.

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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
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: 80% 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 2016: 99% in 180 days Target: 95% 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)	55% in 150 days	60% in 150 days	+5%
253221: Percentage of Bioresearch Monitoring (BIMO) follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. *(Outcome)*	Baseline: 90% (New Measure)	65%	65%	Maintain
252203: Percent of total received Code Blue MDRs reviewed within 72 hours during the year. *(Output)*	FY 2018: 92% Target: 90% (Target Exceeded)	90%	90%	Maintain
254202: Percentage of time CDRH meets the targeted deadline of 120 working days to review GMP information and issue Device Warning Letters. *(Output)*	FY 2018: 25% Target: 50% (Target Not Met)	75%	75%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
254203: Percentage of time CDRH meets the targeted deadlines for on-time recall classification *(Output)*	FY 2018: 89% Target: 85% (Target Exceeded)	85%	85%	Maintain
252101: Number of technical analyses of postmarket device problems and performance. *(Output)*	FY 2018: 54 Target: 50 (Target Exceeded)	50	50	Maintain
253207: Number of technical reviews of new applications and data supporting requests for premarket approvals. *(Output)*	FY 2018: 2,305 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 2018: 99.2% Target: 97% (Target Exceeded)	97%	97%	Maintain
254221: Percentage of Medical Device and Radiological Health significant inspection violations which receive appropriate follow-up after regulatory action was taken. *(Output)*	Baseline: 89% (New Measure)	80%	80%	Maintain
254222: Percentage of Medical Device and Radiological Health follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. *(Outcome)*	Baseline: 81% (New Measure)	65%	65%	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.

Warning Letters Recall Classifications

Warning letters are issued to prompt voluntary compliance with FDA requirements, including medical device GMP requirements described in 21 CFR 820. A warning letter is reserved for firms with major violations or for those who fail to implement adequate corrective actions. To ensure the applicability of evidence to the present situation, the agency strives to issue Warning Letters within four months from conclusion of the inspection. Some of this time is consumed by preparation of exhibits and the establishment inspection report, the remainder of which is reserved for review and action on inspectional findings. CDRH did not meet the FY 2018 target of issuing warning letters within 60 days of receipt. Beginning in FY 2019, the targets will be adjusted to align more closely with the statutory time frame of 120 days.

New ORA Field Performance Measures

ORA is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention, and allows for a more robust analysis.

PROGRAM ACTIVITY DATA TABLES

Devices and Radiological Health Program Activity Data (PAD)

CDRH Workload and Outputs	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Original PMAs and Panel-Track Supplements (without Advisory Committee input)			
Workload [1]	70	67	67
Total Decisions [2]	62	64	64
Approved [3]	44	48	48
Original PMAs and Panel-Track Supplements (with Advisory Committee input)			
Workload	4	5	5
Total Decisions [2]	4	4	4
Approved	2	3	3
Modular PMAs			
Workload	79	91	91
Actions [4]	87	107	107
180-day PMA Supplements			
Workload	205	245	245
Total Decisions [5]	198	236	236
Approved	179	223	223
Real Time PMA Supplements			
Workload	343	340	340
Total Decisions [6]	334	330	330
Approved	317	311	311
510(k) Premarket Notifications			
Workload	3,592	3,854	3,854
Total Decisions [7] (SE & NSE)	3,241	3,347	3,347
Cleared [9] (SE)	3,113	3,195	3,195
Humanitarian Device Exemptions (HDE)			
Workload	-	3	3
Total Decisions [2]	3	3	3
Approved	2	3	3
Investigational Device Exemptions (IDE)			
Workload	307	309	309
Total Decisions [8]	299	299	299
Approved	176	179	179

CDRH Workload and Outputs	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Investigational Device Exemption Supplements			
Workload	1,848	1,846	1,846
Closures [10]	1,850	1,851	1,851
Pre-Submissions			
Workload	2,786	2,922	3,064
Closures [11]	2,646	2,775	2,910
De Novo			
Workload	56	60	60
Total Decisions [14]	24	51	51
Granted	16	25	25
Standards			
Total Standards Recognized for Application Review	1,262	1,300	1,350
Medical Device Reports (MDRs) [12]			
Reports Received	1,285,059	1,349,312	1,416,777
Analysis Consults [13]	552	580	610

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

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

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

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

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

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

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

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

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

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

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

[12] MDRs' include individual and summary Medical Device Reports.

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

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

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Activity Data (PAD)			
Field Devices and Radiological Health Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,550***	***2,498***	***2,498***
Bioresearch Monitoring Program Inspections	308	300	300
Pre-Market Inspections	48	60	60
Post-Market Audit Inspections	35	60	60
GMP Inspections	1,350	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	834	700	700
Domestic Radiological Health Inspections	102	50	50
Domestic Field Exams/Tests	43	100	100
Domestic Laboratory Samples Analyzed	174	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***626***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	14	14	14
Foreign Pre-Market Inspections	25	30	30
Foreign Post-Market Audit Inspections	19	20	20
Foreign GMP Inspections	557	550	550
Foreign MQSA Inspections	11	14	14
Foreign Radiological Health Inspections	59	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***3,176***	***3,111***	***3,111***
IMPORTS			
Import Field Exams/Tests	25,499	19,800	19,800
Import Laboratory Samples Analyzed	624	670	670
Import Physical Exam Subtotal	**26,123**	**20,470**	**20,470**
Import Line Decisions	22,291,902	23,852,335	25,521,999
Percent of Import Lines Physically Examined	0.12%	0.09%	0.08%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,663***	***7,880***	***7,880***
Inspections (MQSA) by State Contract	7,614	6,800	6,800
Inspections (MQSA) by State non-Contract	1060	1,060	1,060
GMP Inspections by State Contract	49	20	20
State Contract Devices Funding	$76,674	$270,000	$278,100
State Contract Mammography Funding	$10,591,706	$10,803,540	$11,019,611
Total State Funding	**$10,668,380**	**$11,073,540**	**$11,297,711**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,839***	***10,991***	***10,991***

[1] The FY 2018 actual unique count of foreign inspections includes 8 OIP inspections in China.

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

3 Domestic MQSA Non-VHA and VHA Inpsections have been combined into one output line.

[4] ORA is currently evaluating the calculations for future estimates.

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020	
				President's Budget	+/- FY 2019 Annualized CR
National Center for Toxicological Research (BA Only).....	64,512	64,512	64,512	66,512	2,000
FTE.....	301	301	301	301	—

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 1) Protect and Promote the Safety and Health of Families, 2) Foster Competition and Innovation, 3) Empower Consumers and Patients, and 4) Strengthen Science and Efficient Risk-Based Decision Making. NCTR enhances FDA's basis for science-based regulatory decisions by conducting collaborative research to:

- expedite the translation of laboratory findings to the clinic and regulatory application
- identify adverse effects earlier in product development and understand the risks and benefits of nanomaterials used in FDA-regulated products
- provide strategies to reduce and rapidly detect contaminants in FDA-regulated products
- use biomarkers—biological indicators of disease—to foster precision medicine
- accelerate FDA's capability to manage and analyze research data using bioinformatics
- reduce costly and dangerous surgeries by expanding minimally invasive imaging capabilities.

The following selected accomplishments demonstrate NCTR's delivery of its regulatory and public-health responsibilities.

Foster Competition and Innovation

Public health protection is the core driver of the NCTR research which aims to ensure that medical products are properly tested for safety and efficacy. 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, examples of NCTR research include text mining to help facilitate efficient access to data that can help resolve public-health issues and participating in global scientific collaborations to foster and leverage novel approaches and research standards.

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 conduct projects to limit the emergence and 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 have demonstrated that when certain *Salmonella* strains were exposed to different concentrations of specific antibiotics, there was an increase in the rate of resistance. In collaboration with FDA's Center for Veterinary Medicine (CVM), NCTR scientists used techniques to better understand the diversity of organisms. NCTR scientists also studied the presence of plasmids—independent DNA molecules commonly found in cells—that can contribute to AMR and enhanced disease-causing ability. NCTR and CVM continue their efforts in this vastly understudied area of research and are developing a database and analysis tool to better understand and control *Salmonella enterica* in foods and feed. A publication describing NCTR's and CVM's research in this area can be found in the *International Journal of Food Microbiology*[66].

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 human exposure 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 important research area for FDA.

In FY 2018, NCTR published an article, in collaboration with CVM, related to antimicrobial drug residues and the human intestinal microbiome permeability in *Anaerobe*[67]. This research involved:

- studying the effects of tetracycline (a common antimicrobial drug) on the human intestinal microbiome
- analyzing the slight differences in these effects between individuals
- accumulating more data to contribute to the knowledge-base on the impact of tetracycline.

The study was extended to assess if the gut bacteria degrades or inactivates the antibiotic. This data was presented at the 2018 Annual Meeting of American Society of Microbiology and a manuscript was submitted to *Regulatory Toxicology and Pharmacology*.

Figure 12*Salmonella* is one of the most widely studied bacteria on Earth.

[66] For more information please visit: http://For more information please visit: https://www.sciencedirect.com/science/article/pii/S0168160518300345?via%3Dihub

[67] For more information please visit: https://www.sciencedirect.com/science/article/pii/S1075996417302342?via%3Dihub

In support of pathogen reduction, NCTR is starting a research study that explores and provides research data on how fecal microbial transplant is an effective treatment for bacterial infections such as *Clostridium difficile*.

Text Mining

Text-mining methods apply computation approaches to text for word recognition, frequency of use, and association—identifying similarities between documents, such 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 by FDA reviewers. 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 description of this research effort was published in June 2018 and can be found in *Drug Discovery Today.*[68]

NCTR recently started a collaborative bioinformatics project with CDER to 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 diseases interact with the same functional protein domain and will look for correlation among the data. In other words, the database will theoretically detect if a person with a rare disease is more likely to develop cancer or vice versa.

In 2018, to enhance available bioinformatics tools, NCTR implemented technical assistance avenues. Additionally, other mechanisms, such as surveys and trainings, have been developed and implemented for FDALabel to improve the tool by collecting user feedback, usage data, and communicating directly with FDALabel customers.

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 and 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. Now in its ninth year, the Global Summit's goal is to engage the global community and

[68] For more information please visit: https://www.sciencedirect.com/science/article/pii/S1359644617305858

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 2018 Global Summit on Regulatory Science was held September 26-27, 2018, in Beijing, China. The theme was Risk/Benefit of Dietary Supplements and Herbal Medicine in the Era of Data Science. The Summit had representatives from FDA and over 20 countries. The Summit reinforced the need for and initiation of scientific exchange and collaboration.

The 9th Annual 2019 Global Summit for Regulatory Science (GSRS19) will be held in Italy, in September 2019, at the Joint Research Centre – European Commission in Ispra. The meeting will focus on nanotechnology and nanoplastics. Additional details are forthcoming. For updates, abstract guidelines, agenda, and more visit www.fda.gov/globalsummit.

Bioinformatics Collaborations

NCTR and the Arkansas state university system held the fourth annual Arkansas Bioinformatics Consortium conference in April 2018 to leverage statewide bioinformatics capabilities. The conference—organized by NCTR, Arkansas Research Alliance, and the Arkansas Bioinformatics Consortium—focused on the "Data Analytics: Genomics and Beyond."

NCTR scientists led two of the four workshops and two of the breakout sessions at the 14th Annual Mid-South Computational Biology and Bioinformatics Society Conference. The theme of the 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.

On March 20, 2018, two Research Collaboration Agreements (RCA) were signed between FDA/NCTR and the Food Safety Commission of Japan (FSCJ) to work on two joint research projects. Today's consumer products are increasingly globalized, impacting public health worldwide and posing new challenges for regulatory authorities. Descriptions of these two research projects are shown below:

- The first project will develop knowledge-based tools that can help international risk-assessment agencies who work on chemical toxicological prediction.
- The second project will provide the most appropriate tools for use in risk assessment of contaminants in food (e.g. acrylamide, furan, bisphenol A, and arsenic species).

NCTR conducted research, in collaboration with CDER on 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. Scientists worked on DILI caused by bile acids for which CDER scientists have great interest based on their review process of new drug candidates. In collaboration with CDER, an article was published in *Alimentary Pharmacology & Therapeutics*. Another manuscript entitled "The influence of drug properties and host factors on delayed onset of symptoms in drug-induced liver injury" in collaboration with the Spanish DILI registry and Duke University was recently accepted by *Liver International*.

Nanotechnology Collaborations

The NCTR/ORA 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 conduct regulatory science research 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. Nanocore develops standards in collaboration with the National Toxicology Program and international standards development organizations to ensure data quality and minimize iterations for industry submissions, speeding up the review process.

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 study continues into FY 2020.

Empower Consumers and Patients

NCTR's research allows FDA to focus on promoting public health by empowering patients and consumers to make well-informed choices about their medical care including patient-focused medical product development. Within this area, NCTR will implement a Perinatal Health Center of Excellence and conduct research through a Memorandum of Understanding with CDER on over-the-counter drug review. Additionally NCTR will:

- identify human cancer mutations that can be used as biomarkers to potentially speed the development of effective personalized cancer treatments
- finalize research regarding the toxic potential of silver nanoparticles in feminine-hygiene products using 3D mucosal models and animal models.

With Congressional support, NCTR will fully implement the Virtual Center of Excellence for Perinatal and Maternal Pharmacology and Toxicology – also known as the FDA Perinatal Health Center of Excellence (PHCE). In FY 2018, the PHCE was accepted by the FDA Centers and ORA representatives with the goal to strengthen the scientific bases of decision making of FDA-regulated products used during pregnancy and in premature infants, newborns, and children. The PHCE council, with representatives from all FDA Centers and ORA, developed and accepted a framework for the development, review and selection of research projects. This critical area will be able to move forward with sustained Congressional support.

Over the Counter (OTC) Drug Review

In FY 2018, NCTR in collaboration with CDER, completed thorough literature searches and reviews for the following OTC drugs:

- the six potential Food Handler Antiseptics Active Ingredients
- impurities/degradants in selected United States Pharmacopeia (USP) Monograph drug product - Tetrahydrozoline Hydrochloride Ophthalmic Solution.

This research effort involved summarizing 2274 relevant references, providing relevant articles, a list of irrelevant references, the search tables, and by late 2018 NCTR scientists will have also summarized ~300 relevant references on chlorine safety.

Strengthen Science and Efficient Risk-Based Decision Making

NCTR's research provides FDA 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. Within this area, examples of NCTR research include perinatal opioid exposure; detection of bacterial and microbial contamination; antimicrobial resistance and the human microbiome; and pathogen reduction.

Perinatal Opioid Exposure

The FDA Opioid Action Plan[69] provides comprehensive guidance for reestablishing safe-use standards for these products. In support of the plan, NCTR completed a methods-development protocol that gave FDA hands-on-experience in neural stem-cell growth. This experience will allow scientists to conduct lab-based *in vitro* research rather than relying solely on whole animal (*in vivo*) research. NCTR scientists are conducting research to assess perinatal opioid exposure, a concern shared in the perinatal-related FDA Drug Safety Communication.[70] NCTR, in collaboration with CDER, is finalizing the data on opioid exposure to brain cells during perinatal development.

Rapid Detection of Bacterial and Microbial Contamination

NCTR scientists significantly improved a method for rapidly detecting low levels of harmful bacteria such as *E-coli O157:H7* in various foods. This method measures single bacterial cells without requiring a time-consuming growth period in a Petri dish. This method is proven to be superior to the current FDA regulatory method. A publication describing the application of this method in raw spinach was published in *Frontiers in Microbiology*[71].

Figure 13*E. coli* is one of the most commonly found bacteria in foods

NCTR scientists demonstrated RAPID-B—a field portable, ultrasensitive, and selective real-time detector of bacteria in food, such as *E. coli O157, Salmonella*, and *Listeria monocytogenes*—at a national government conference. The scientists demonstrated its portability by transporting the instrument by car from Arkansas to the 2018 USDA Food Safety Inspection Service and Agriculture Research Service Annual Conference in West Virginia. As part of the conference, the NCTR scientists demonstrated RAPID-B and described how it can detect different bacterial pathogens and the "mad cow" disease-causing agent. Collaborations between NCTR and USDA are planned in this area. USDA has identified portable, real-time detection of *Listeria* and *Salmonella* in food as a priority.

Ongoing collaborative research efforts by NCTR and the Center for Food Safety and Nutrition (CFSAN) scientists include:

- detecting *Listeria monocytogenes* faster using genetic tags

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

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

[71] For more information please visit: https://www.frontiersin.org/articles/10.3389/fmicb.2017.01493/full

- improving the ability to detect low levels of *Listeria* cells in foods, such as cantaloupe, avocado, or carrots
- expanding the scalability to identify the source of a contamination
- detecting microbial contaminants—including mycobacteria—in tattoo inks.

NCTR and CFSAN's collaborative tattoo research aims 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. The dramatic increase in tattooing and the use of permanent makeup have made this study relevant to the mission of FDA. A manuscript describing the progress of this study was published in FY 2018 in the *Journal of Applied Microbiology*. [72] This study continues with the goals of:

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

Artificial Intelligence (AI) System — DeepSafe

The Office of Regulatory Affairs (ORA) reviews import entry from foreign countries with over 40 million entry lines each year. This big data represents a critical regulatory challenge, but also offers tremendous opportunity to develop artificial intelligence capable of preventing the entry of adulterated, misbranded, or other violative goods. The current screening uses various rules to determine a risk score that determines if the goods will require a manual review. In collaboration with ORA, NCTR is conducting research using AI for screening and assessing FDA-regulated food imports. This research aims to develop an intelligent system by applying deep learning for screening and assessing import entry known as DeepSAFE. This AI system will make the product evaluation and risk-assessment process at the ports of entry more robust.

Strengthen Science and Efficient Risk-Based Decision Making

NCTR's research supports FDA to use regulatory science to strengthen risk-based decision making. NCTR brings modern scientific tools into FDA to maintain FDA's gold standard for product review, and to ensure FDA risk management is efficient and up-to-date. As the products that FDA is asked to review become more complex and specialized, there is a larger demand to develop innovative technologies and methods. Some of the research that supports this area includes informing standards development and using *in silico* tools for improving medical product development and making regulation more efficient. Within this area, examples of NCTR research include perinatal, pediatric, and maternal medicine; cancer-drug toxicity; precision medicine; biomarkers; nanotechnology; bioimaging; and bioinformatics.
In support of this priority, NCTR will:

- develop novel *in silico* (computer-based) methods to supplement animal models
- in collaboration with CDER, deploy an updated scientific database containing Marketing Application information on new molecular entities and biologics, and incorporating additional data about Breakthrough Therapy Designations

[72] For more information please visit: https://onlinelibrary.wiley.com/doi/abs/10.1111/jam.13713

- facilitate the development of a high-throughput and high-content genotoxicity assessment to evaluate the safety of FDA-regulated products.

Perinatal, Pediatric, and Maternal Medicine

NCTR is providing the infrastructure to stimulate robust research efforts through faster, less expensive, and more predictive approaches and models, leading the way to improved safety and/or efficacy of FDA-regulated products in susceptible populations. These susceptible populations include pregnant women and infants—focusing on the perinatal period—the period-of-time including pregnancy, child birth, and infant/child development. Many drugs and other medical products provided to pregnant women, neonates, and infants are used off-label because of the difficulties with performing clinical trials needed for drug approval in these populations. Therefore, these populations represent a vastly understudied stage of development.

Advancements at NCTR's bio-imaging facility allow FDA to translate imaging technologies from the laboratory animal to the clinical setting and to gather information not previously obtainable. This information helps the medical community understand pediatric-anesthetic use and reduce 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. NCTR research on pediatric anesthetics led to an FY 2017 FDA Drug Safety Communications where FDA approved label changes for the use of general anesthetics and sedation drugs in young children to include a warning about cumulative exposures that may affect the developing brain. A pediatric anesthetic-related ongoing study is evaluating the utility of neural stem-cell models to predict the effects of pediatric anesthetics sevoflurane and isoflurane in combination with nitrous oxide.

Scientists from NCTR; the Mayo Clinic in Rochester, Minnesota; and Baylor College of Medicine in Houston, Texas recently published results from neuropsychological tests that were conducted on school-age children who were given anesthesia during one or more surgeries that occurred before their third birthday. This study determined whether 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 summary of this research was published in July 2018 and can be found at *Anesthesiology*.[73] NCTR also conducted research to evaluate the methods used to measure growth of *S. aureus* and the production of toxic shock syndrome as influenced by menstrual tampons. The manuscript titled, "Assessment of the Syringe Method for Testing Tampon-associated *Staphylococcus aureus* Growth and Toxic Shock Syndrome Toxin-1 Production" is undergoing internal review. The research concluded August 31, 2018 and should improve CDRH's review of tampon devices, provide a safer product, and increase consumer confidence.

Cancer-Drug Toxicity

Despite two decades of worldwide intensive research efforts to understand cancer biology for advancing anticancer-drug development, only ~200 anticancer drugs have been made available to cancer patients. This low throughput is in large part due to anticancer-drug development suffering high failure-rates during the later phases of clinical development.

[73] For more information visit: http://anesthesiology.pubs.asahq.org/article.aspx?articleid=2679328

NCTR, in collaboration with scientists from University of Birmingham in the United Kingdom and University of Arkansas at Little Rock summarized both successful and failed attempts in anticancer-drug development over the past 20 years. This collaborative review helped to identify why the current development model may be less than ideal. Furthermore, potential strategies for improvement of anticancer-drug development are offered in the publication, available in *Trends in Pharmacological Sciences.*[74] In FY 2018, NCTR scientists and CDER demonstrated that direct liver-cell toxicity may contribute to the mechanism of kinase inhibitor (KI)-induced liver damage.KIs are a relatively new type of drug that has played an increasingly important role in the treatment of cancer and inflammation.NCTR examined the toxicity of 34 FDA-approved KIs in cultured rat- and human-liver cells (hepatocytes).The hepatocytes were treated with KIs at 10 concentrations that reflect maximum therapeutic clinical blood levels.The data from this study helps FDA develop a better understanding of why some KIs result in liver damage.Furthermore, the results suggest that *in vitro* models may be useful in predicting clinical liver toxicity.A manuscript describing the study is available in *Toxicology Letters.*[75]

NCTR also conducted research to 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. One article was published in April 2018 in *Toxicological Sciences* and one article has been accepted for publication in *Food and Chemical Toxicology*. This research utilized a much faster method to identify potentially cancerous substances as opposed to classical 2-year animal methods.

In FY18, NCTR completed a study that will promote women's health by facilitating the development of personalized approaches to treat breast cancer. NCTR, in collaboration with the Office of Women's Health, completed a study to quantify genetic markers in difficult to treat breast cancers. An invited manuscript is in preparation for the Special Issue "Molecular Biology and Pathology of Breast Cancer" in the *International Journal of Molecular Scie*nces.

NCTR is conducting research to identify new clinical biomarkers that predict chemotherapy-induced cardiotoxicity prior to the occurrence of overt cardiac-tissue damage. NCTR published findings related to the identification of biomarkers that may predict chemotherapy-induced cardiotoxicity. The results were published in the February 2018 issue of *Experimental Biology and Medicine*. NCTR also identified additional biomarkers with the potential to predict cardiotoxicity before patient treatment or during early stages of chemotherapy. An abstract of the recent results has been accepted and will be presented in the Global Cardio-Oncology Summit 2018 as a poster.

Doxorubicin Research

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 studying DOX using various research approaches.

[74] For more information please visit: https://www.frontiersin.org/articles/10.3389/fmicb.2017.01493/full

[75] For more information please visit: https://www.sciencedirect.com/science/article/pii/S0378427418301395?via%3Dihub

A continuing DOX-related study involves scientists from NCTR, National Cancer Institute, Korea University, and CDER. In a previously completed study, it was found that males may be more susceptible than females to DOX toxicity. This current study specifically seeks to understand the molecular basis for different susceptibility to DOX toxicity between males and females. Further investigations will involve detection methods to determine where DOX and its metabolites may be localized in the heart. The most recent information about this research was presented at the 2018 Society of Toxicology[76] meeting. This study continues into FY 2019.

NCTR completed a study aimed at testing cardiotoxicity of various drugs including those used in chemotherapy. The goal of this preliminary study was 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 is designed to mimic the delayed cardiotoxicity observed in human cancer survivors. This study may give rise to a larger study using the same model of cardiotoxicity.

Cyclophosphamide Research

Cyclophosphamide is a drug used to treat cancers and autoimmune diseases, by quickly controlling disease. However, 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.

Scientists from NCTR, CDER, and the University of Arkansas for Medical Sciences have demonstrated that the two commonly used chemotherapeutics discussed above (cyclophosphamide and doxorubicin), administered alone or in combination, did not induce behavioral alterations in a female-mouse model reflective of human breast-cancer patients. The study, which was completed in FY 2018, investigated the memory and attention problems that some female breast-cancer patients experience after chemotherapy—sometimes known as "chemo" brain. Thus, the selected chemotherapeutics were administered intravenously at clinically-relevant doses and the mice were assessed using a comprehensive test battery to detect effects on learning and memory, general activity, and motor coordination. The study results show no significant behavioral alterations and provide new insights into two commonly used chemotherapeutics. The NCTR lead author of the article was awarded the Developmental Neurotoxicology Society's "2018 Richard Butcher New Investigator Award" for this publication. The article is available online at *Toxicological Sciences.*[77]

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. NCTR scientists continue research to identify new biomarkers—a biological indicator of a biological state or condition—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

[76] For more information please visit: http://www.toxicology.org/pubs/docs/Tox/2018Tox.pdf

[77] For more information please visit: https://academic.oup.com/toxsci/article/162/2/462/4706007

- improve therapeutic patient treatments.

Examples of NCTR biomarker-development research to improve therapeutic patient treatments are shown below.

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.

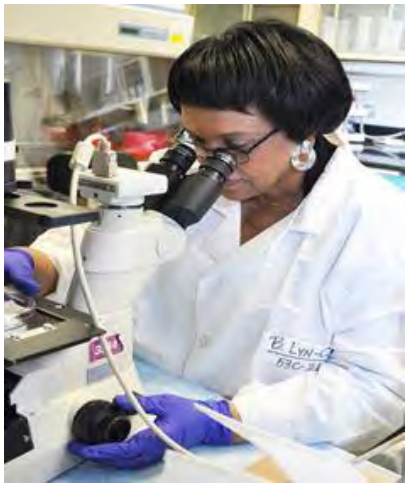

Figure 14 NCTR scientist looks at cells through a microscope.

In an FY 2018 consortium effort with the Health and Environmental Sciences Institute, NCTR scientists collaborated with experts from other government agencies, academia, and industry to search for non-invasive biomarkers of neurotoxicity that can be evaluated in circulating biofluids, such as serum, plasma, urine, and cerebrospinal fluid. In the first set of studies, several unique biomarker candidates were identified, and an initial summary of these findings was published in *Experimental Biology and Medicine*[78]. Preliminary findings from this work were presented at the 2018 Society of Toxicology Annual Meeting. This collaborative study continues.

NCTR scientists used a well-known chemical that is toxic to the liver—thioacetamide—which could be a liver carcinogen (cancer-causing agent) in humans, to discover microRNA biomarkers of liver toxicity. They also 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*[79] and research on this topic continues.

In support of precision medicine, NCTR scientists presented a webcast lecture titled, “Ethnicity- and Gender-Related Differences in Alzheimer’s Disease (AD),” as part of the FDA Grand Rounds series. AD has a higher incidence in women at later ages and poses a greater threat to African-American and Hispanic communities. This presentation discussed NCTR’s novel research into proteins implicated in AD and their levels in post-mortem African-American and Caucasian brain tissues from both genders to explore ethnicity- and gender-related differences. Research studies like these are crucial to a precision-medicine approach treating neurodegenerative diseases like AD. A recording of the presentation and a brief synopsis can be found on FDA.gov.

NCTR is conducting a study specifically tailored to precision-medicine solutions for FDA entitled, "Sequencing Quality Control Phase 2 (SEQC2): A Consortium Effort to Assess Next-Generation Sequencing (NGS) for Enhanced Regulatory Science Research and Precision

[78] For more information please visit: http://journals.sagepub.com/doi/full/10.1177/1535370217739859

[79] For more information please visit: http://www.nature.com/articles/s41598-017-02798-7.pdf

Medicine." This effort seeks to develop quality metrics and standard analysis protocols for NGS and other similar technologies frequently encountered in regulatory applications and research. Thus, the outcome from SEQC2 has the potential to significantly impact FDA projects and practices and to prepare FDA for the effective use and review of NGS data. Three recent publications related to this research can be found in *Pediatric Investigation*[80], *Nature Biotechnology*[81], and *Experimental Biology and Medicine*[82].

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.

Research being conducted at the NanoCore to better understand the attributes of these emerging materials, their safety, and efficacy are listed below.

- With CDER, NCTR is studying how nanomaterial-containing drug distribute to different parts of the body, to determine their safety and efficacy, using rodent animal models.
- With OWH, NCTR is evaluating the potential migration and toxicity to the vaginal tissue of silver nanoparticles when used in feminine-hygiene products.
- With the National Toxicology Program, NCTR is developing documentation standards to shorten FDA review times for industry submissions of scientific nanomaterial data.

A continuing study at NCTR involves determining the effect of silver nanoparticles on the intestinal virome—the collection of viruses in and on the human body. The virome is thought to affect the overall human microbiome which is an integral part of understanding toxicity of regulated products. The rise in use of nanoparticles in many types of regulated products has made this issue vital to FDA. The most recent publication related to this study can be found in the *International Journal of Nanomedicine.*[83]

Another ongoing NCTR study deals with the impact that nanomaterials may or may not have on the formation of biofilm on the surface of teeth. Nanomaterials are being considered to combat the dental formation of biofilms which are precursors to tooth decay. Initial data reveals that low-concentrations of each of the tested nanomaterials have minimal effect on the growth of biofilms. This research was presented in June 2018 at the 118th General Meeting of the American Society of Microbiology. Further research is needed to study other nanomaterial candidates and their effect on biofilms.

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. NCTR continues the development of minimally-invasive diagnostic methods for identifying nervous system-tissue

[80] For more information please visit: https://onlinelibrary.wiley.com/doi/epdf/10.1002/ped4.12044

[81] For more information please visit: https://www.nature.com/articles/nbt.4029.pdf

[82] For more information please visit: http://journals.sagepub.com/doi/pdf/10.1177/1535370217750087

[83] For more information please visit: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5961469/pdf/ijn-13-2857.pdf

anomalies. This technology, derived from FDA-regulated MRI instruments, is called magnetic resonance spectroscopy (MRS).

NCTR, in collaboration with Huntington Medical Research Institute, 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. The data obtained from these studies are being readied to support the qualification of MRI signals as brain-toxicity biomarkers. Recent publications highlighting this approach can be found in: *Journal of Magnetic Resonance in Medicine*[84], *Experimental Biology and Medicine*[85], and *Neurotoxicology*[86].

NCTR, in collaboration with FDA Product Centers, is studying 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[87] on May 22nd, 2017 about gadolinium-based contrast agents (GBCAs) and their retention in the brain and will continue through FY 2019.

New and continuing imaging research at NCTR includes:

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

Other imaging advancements include:

- Multi-center study completed in collaboration with Amgen, AstraZeneca, and GlaxoSmithKline on non-invasive MRI biomarkers of DILI. Publication in *PLoS One*[88]
- Initiated a collaboration with University of Arkansas-Fayetteville to use MRI scans of porcine mitral valve to optimize human-valve replacement. Publication in *PLoS One*[89]
- Validated a three-dimensional MRI technique to more accurately evaluate brain neurotoxicity. It will allow for minimally-invasive detection of brain lesions.

Bioinformatics

Bioinformatics uses computer software tools to develop and improve methods for storing, managing, and analyzing large quantities of biological data. NCTR develops, provides training for, and makes bioinformatics tools available to FDA and the global research community. FDA must have the software and database tools to manage the large amount of scientific data generated by new technologies required to improve product development, safety assessments, and risk analysis. Computer-based methods (*in silico*) are also important since they can, in some cases, be used as an alternative to animal methods (*in vivo*). Below are examples of NCTR's bioinformatics program.

[84] For more information please visit: https://onlinelibrary.wiley.com/doi/pdf/10.1002/jmri.25378

[85] For more information please visit: http://journals.sagepub.com/doi/abs/10.1177/1535370217739859?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

[86] For more information please visit: https://www.sciencedirect.com/science/article/pii/S0161813X18300330?via%3Dihub

[87] For more information please visit: https://www.fda.gov/Drugs/DrugSafety/ucm455386.htm

[88] For more information please visit: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0197213

[89] For more information please visit: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0184042

Publicly Available Dataset/Database Name	Description
DILIrank	Largest publicly available annotated dataset listing 1,036 FDA-approved drugs ranked by potential to cause drug-induced liver injury (DILI). The drugs were defined and verified as shown below: • 192 "Most-DILI" concern • 278 "Less-DILI" concern • 312 "No-DILI" concern • 254 "Ambiguous-DILI" concern DILIrank is used by FDA reviewers, industry for drug development, and researchers for adverse drug reaction studies and to build scientific models. More informationcan be found at *Drug Discov ery Today*[90]
Endocrine Disruptor Knowledge Base (EDKB)[91]	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)[92]	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[93]	NCTR created and maintains two FDALabel versions that make previously unavailable information easy to access—one for the public and one for FDA staff who review drug labeling. FDALabel, allowing customizable searches of over 99,000 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 • physicians and consumers for drug-safety information. Labeling documents with information about product indications, target populations, and adverse drug reactions are added weekly. In

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

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

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

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

	collaboration with CDER, NCTR is developing a version that will allow multiple products to be searched at the same time for use by CDER and CBER reviewers

FUNDING HISTORY[94]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$63,329,000	$63,329,000	$0
FY 2017 Actual	$63,331,000	$63,331,000	$0
FY 2018 Actual	$64,512,000	$64,512,000	$0
FY 2019 Annualized CR	$64,512,000	$64,512,000	$0
FY 2020 President's Budget	$66,512,000	$66,512,000	$0

BUDGET REQUEST

The FY 2020 Budget Request is $66,512,000, which is all Budget Authority. Budget Authority increases by $2,000,000 compared to the FY 2019 Annualized Continuing Resolution level. The FY 2020 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 to better understand and interpret diverse data submissions generated using new methodologies and techniques.
- inspire innovation and knowledge sharing through collaboration.

These research areas include, but are not limited to, the advancement of bioinformatics technologies, precision medicine, biomarkers, bio-imaging, perinatal health, 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, benefit the American public. These funds will allow such efforts to continue and will give the programs and associated projects the opportunity to develop.

[94] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

BUDGET AUTHORITY

Medical Product Safety ($2.0 million)

Promoting Domestic Manufacturing: +$2.0 million

NCTR 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, developing and testing of these technologies. NCTR will be able to pursue the following activities to focus on supporting FDA's highest priorities for FY 2020.

Virtual Center of Excellence for Perinatal and Maternal Pharmacology and Toxicology

As part of FDA's FY 2020 initiative to advance safe and effective medical products, NCTR will implement the newly established FDA Virtual Center of Excellence for Maternal and Perinatal Pharmacology and Toxicology, also known as Perinatal Health Center of Excellence (PHCE).

Participants from across the FDA Centers and ORA, along with the researchers from across the agency have already demonstrated a great deal of interest in the PHCE with NCTR receiving 20+ peer-reviewed research proposals in the planning phase. The additional funds will be used to stimulate more perinatal research efforts across FDA. FDA expertise in the field of pediatric medicine has already led to advancements in the field through faster, less expensive, and more predictive approaches and models. The virtual center will enhance the effort by harnessing the collective talents and resources of the agency and serve as a hub for research and collaborations internally and externally. The importance and potential for the PHCE is tangible and realistic given the current knowledge gaps and rapidly evolving technology. It will improve the safety and/or efficacy of FDA-regulated products in understudied populations, including pregnant women and infants — focusing on the perinatal period (the period-of-time including pregnancy, child birth, and child development).

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 2019 Target	FY 2020 Target
263103: Conduct translational and regulatory research to advance the safety of products that FDA regulates (Output)	FY 2018: In collaboration with CDER, an article was published in Alimentary Pharmacology & Therapeutics on drug-induced liver toxicity caused by bile acids. (Target Met) FY 2018: Optimized differentiation conditions of neural precursor cells to investigate the effects of opioid exposure on prenatal development. Investigation of the individual effects of opioids on neural precursor cell viability and toxicity are on-going.(Target Met)	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 perinatal development	Develop methodology that can be used to detect *Burkholderia cepacia* in non-sterile pharmaceutical products and pharmaceutical water Gather data regarding the toxicity of 40 FDA approved small molecule kinase inhibitors—highly effective cancer fighting molecules—on the liver and heart
263201: Develop science base for supporting FDA regulatory review of new and emerging technologies (Output)	FY 2018: Findings published in Toxicological Sciences on research utilizing a much faster method to identify potentially cancerous substance as opposed to classical 2-year animal methods (Target Met)	Finalize research regarding the toxic potential of silver nanoparticles in feminine-hygiene products using 3D mucosal models	Develop a safety assessment for gene editing therapies that are pending clinical trials

Measure	Most Recent Result / Target for Recent Result	FY 2019 Target	FY 2020 Target
262401: Develop biomarkers to assist in characterizing an individual's genetic profile in order to minimize adverse events and maximize therapeutic care (Output)	FY 2018: Completed a study to quantify genetic markers in difficult to treat breast cancers. Manuscript in preparation for invited Special Issue "Molecular Biology and Pathology of Breast Cancer" in the International Journal of Molecular Sciences. (Target Met)	Identify human cancer mutations that can be used as biomarkers to potentially speed the development of effective personalized cancer treatments	Construct a database of information on how genetics effect drug efficacy and toxicity (pharmacogenomic data) in understudied minority populations that will aid in the clinical application of biomarkers In collaboration with the University of Arkansas for Medical Sciences, develop biomarkers of the heart to predict and mitigate radiation-induced heart disease
264101: Develop risk assessment methods and build biological dose-response models in support of food protection (Output)	FY 2018: NCTR published findings related to antimicrobial drug residues and their effects on human intestinal microbiome and epithelial cell permeability/wound healing in the February 2018 issue of *Anaerobe* and the November 2017 issue of *Food and Chemical Toxicology*. CVM and NCTR also presented related data at the NIH-FDA Joint Agency Microbiome meeting in December 2017. (Target Met)	Explore and provide results of research on how fecal microbial transplant is an effective treatment for bacterial infections such as *Clostridium difficile*	In collaboration with CVM, develop a database and analysis tool to better understand and control Salmonella enterica in foods and feed

Measure	Most Recent Result / Target for Recent Result	FY 2019 Target	FY 2020 Target
263104: Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates (Output)	Investigators found that antibiotic-coated catheter inhibited growth of antibiotic-sensitive Staphylococcus aureus and Enterococcus faecium but not antibiotic-resistant bacteria isolated from patients. Silver-coated catheter prevented growth against both antibiotic-sensitive and -resistant bacteria.(Target Met)	Discover and validate early biomarkers of cardiotoxicity associated with an effective chemotherapy drug utilizing a variety of methods including whole RNA genome sequencing	Develop parameters to assist reviewers when evaluating applications submitted to FDA for genome assembly-based devices, products, and services
263102: Develop computer-based models and infrastructure to predict the health risk of biologically active products (Output)	FY 2018:Novel data mining and visualization methods resulted in a total of 63,082 drug adverse event pairs were identified from FAERS as the significant association between 936 drugs and 10,316 adverse events. New safety signals were identified when comparing with the currently available information in various sources. Results were presented in the Society of Toxicology 2018 Annual Meeting. (Target Met)	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	Examine the utility of In Vitro (lab-based) to In Vi*vo* (animal-based) Extrapolation (IVIVE) as a new tool for FDA safety assessments

Advance the Safety of FDA-Regulated Products

NCTR research is vital to ensure the safety and effectiveness of the products that FDA regulates. Two specific examples include research regarding opioids and gadolinium—a heavy metal commonly used as a contrasting agent during MRI procedures. In FY2018, in support of the FDA Opioid Action Plan, the NCTR initiated a study to investigate opiod exposure during

prenatal development. Final data on this study should be available in FY 2019. Additionally, in FY 2019, NCTR will continue to advance the safety of FDA-regulated products by providing data on the bioaccumulation of gadolinium in the brain and, in FY2020, will gather toxicity data on FDA-approved cancer fighing molecules, called kinase inhibitors.

Develop Science Base for New and Emerging Technologies

NCTR continues to develop the science base to help FDA in its regulatory review of new and emerging technologies. In FY 2018, NCTR published research utilizing a faster method to identify potentially cancerous substances than the current 2-year animal methods. In FY 2019, NCTR research regarding the toxic potential of silver nanoparticles in feminine-hygiene products using 3D mucosal models will be finalized. In FY 2020, scientists plan to develop a safety-assessment for gene editing therapies that are pending clinical trials.

Precision Medicine

NCTR continues to support FDA in its pursuit for precision medicine solutions through cutting-edge research that uses genetic information from an individual or demographic group to tailor treatment regimens to increase safety and effectiveness. NCTR investigates post-market chemotherapy drugs and new alternative drugs and methods available to cancer patients. In FY 2018, NCTR completed a study on genetic markers for difficult to treat breast cancer. Manuscripts and publications are currently in development. Work in precision medicine will continue in FY 2019 with research to identify human cancer mutations to help speed the development of personalized cancer treatments. In FY 2020, NCTR will work in collaboration with the University of Arkansas for Medical Sciences, to develop biomarkers of the heart to predict and mitigate radiation-induced heart disease.

PROGRAM ACTIVITY DATA

National Center for Toxicological Research Program Activity Data (PAD)			
Program Workload and Outputs	**FY 2018 Estimate**	**FY 2019 Estimate**	**FY 2020 Estimate**
Research Outputs			
Research Publications	170	165	160
Research Presentations	135	145	150
Patents (Industry)	5	5	5
Leveraged Research			
Federal Agencies (Interagency Agreements)	3	3	3
Nongovernmental Organizations	28	30	32
Active Research Projects	159	165	176

OFFICE OF REGULATORY AFFAIRS - FIELD ACTIVITIES

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
Office of Regulatory Affairs	**1,171,116**	**1,152,189**	**1,173,404**	**1,223,992**	**50,588**
Budget Authority	***1,061,799***	***1,061,760***	***1,061,799***	***1,110,861***	***49,062***
User Fees	***109,317***	***90,429***	***111,605***	***113,131***	***1,526***
Prescription Drug (PDUFA)	9,511	9,123	10,569	10,333	-236
Medical Device (MDUFA)	2,314	2,292	2,457	2,390	-67
Generic Drug (GDUFA)	55,915	55,355	56,808	57,430	622
Biosimilars (BsUFA)	1,150	1,158	1,100	1,363	263
Animal Drug (ADUFA)	310	36	431	440	9
Animal Generic Drug (AGDUFA)	238	3	335	216	-119
Family Smoking Prevention and Tobacco Control Act	14,684	10,612	14,684	14,684	---
Mammography Quality Standards Act (MQSA)	13,995	11,380	13,995	14,556	561
Food and Feed Recall	1,000	---	1,000	1,040	40
Food Reinspection	5,382	---	5,382	5,600	218
Voluntary Qualified Importer Program	4,320	---	4,320	4,495	175
Third Party Auditor Program	144	---	144	150	6
Outsourcing Facility	354	470	380	434	54
FTE	**4,898**	**4,898**	**4,939**	**4,997**	**58**

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 on FDA regulated products to ensure their safety,

effectiveness, and quality. As FDA's lead office for all agency field activities, ORA is responsible for a wide range of mission critical activities including:

- inspections and investigations (including criminal investigations)
- sample collection and analyses
- examination of FDA-regulated products offered for import into the United States
- oversight of recalls and execution of enforcement actions
- response to consumer complaints and emergencies
- development and promotion of state and local partnerships.

FDA regulated products account for about 20 cents of every dollar spent in the United States. ORA protects consumers and enhances public health by maximizing compliance and minimizing risk of all FDA-regulated products including:

- human and animal foods, cosmetics, and dietary supplements
- human and veterinary drugs
- vaccines, blood products, tissue, tissue products, allergenics, cellular and gene therapy products
- medical devices and products that emit radiation
- tobacco products.

ORA has staff in 227 offices across 49 states, including the U.S. Virgin Islands and the Commonwealth of Puerto Rico, with staff both temporarily and permanently assigned to foreign posts. ORA manages 13 scientific laboratories including two colocated medical product labs, and one tobacco lab that conducts applied research and performs highly specialized analyses of domestic and imported products. ORA also develops and maintains information technology systems used across FDA that support information sharing and risk-based decision making. In addition, ORA promotes an Integrated Food Safety System (IFSS) by providing resources to state, local, tribal, and territorial (SLTT) regulatory jurisdictions to conduct inspections, collect samples, and enhance program capacity and infrastructure by advancing conformance with national regulatory program standards.

Recent Accomplishments

Three of ORA's most significant accomplishments from the past year are as follows.

Enhanced Presence at International Mail Facilities (IMFs)

In response to the current opioid crisis, ORA prioritized support to increase personnel and improve space and infrastructure at IMFs. In FY 2018, ORA increased our presence at the IMFs by hiring 40 import investigators, which resulted in an increase in examinations at the IMFs to 27,000, which was three times more than FY 2017 levels. In addition, ORA doubled the Office of Criminal Investigations(OCI) Port of Entry program staff by hiring 12 special agents and two senior operations managers to oversee the program, as well as 8 chemists to perform scientific testing and assist in the development of a standard set of tools to aid in investigations and parcel review. Improvements at IMFs will continue, as ORA implements new authorities included in the the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (the SUPPORT Act), signed into law on October 24, 2018. The SUPPORT Act will enhance ORA's ability to work in partnership with Customs and Border Protection (CBP) and U.S. Postal Service to prevent the importation of unsafe, unapproved, and

misbranded products by providing new enforcement tools and additional resources, equipment and analytical instrumentation for the IMFs.

Integrated Food Safety System (IFSS)

ORA continues to support a Food Safety Modernization Act (FSMA) mandate to strengthen the food safety capabilities of SLTT agencies that FDA relies on to meet the increased inspection mandate. ORA offers resources through contracts, grants, and cooperative agreements to promote the development of partnerships among other federal and SLTT agencies. In addition, to support the design and management of IFSS regulatory programs, FDA works with its SLTT agencies and association partners to develop and implement national standards.

European Union (EU) Mutual Recognition Agreement

The amended Pharmaceutical Annex of the 1998 U.S. – European Union (EU) Mutual Recognition Agreement (MRA) was implemented on November 1, 2017. The Mutual Recognition Agreement allows us to utilize each other's good manufacturing practice inspections of pharmaceutical manufacturing facilities. This collaborative effort increases efficiency across U.S. and EU regulatory systems by avoiding duplicative inspections, allowing the reallocation of resources to areas with higher public health risks, and thereby enabling greater market access and improving international harmonization.

ORA continues to work with the Centers on successful implementation and operationalization of the MRA by participating in European assessments organized by the European Medicines Agency. As of December 1, 2018, FDA has recognized 20 European drug regulatory authorities as capable of conducting inspections of manufacturing facilities that meet FDA requirements. To date, ORA has completed its review of 42 inspection reports from EU capable countries.

Strengthen Science and Efficient Risk-Based Decision Making

Surveillance of FDA-Regulated Products

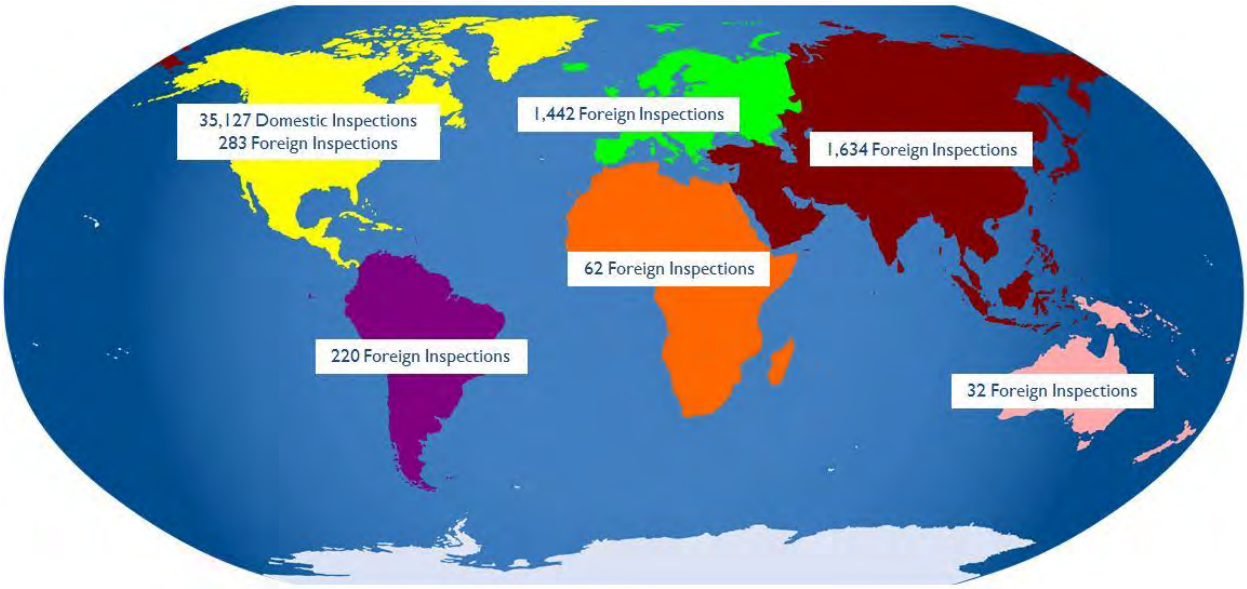

Figure 15 FY 2018 FDA Inspections by Continent. *Numbers as of December 2018

ORA works with each FDA Center to develop and implement a work plan that outlines assignments for over 500 activity areas across FDA's regulated commodities while maintaining flexibility to respond to unplanned activities, such as product recalls, emergencies, and outbreak investigations, to ensure quick containment and mitigation. ORA accomplishes the FDA mission through a highly skilled professional staff including:

- Consumer safety officers (CSOs)
- Compliance officers
- Laboratory analysts
- Recall coordinators
- Occupational Safety and Health Officers
- Consumer complaint coordinators
- Criminal investigators
- State cooperative program specialists

FDA's foreign inspections are a critical component of protecting the health and safety of U.S. citizens. These inspections ensure that products produced in foreign countries intended for the U.S. market meet the same regulatory standards as those manufactured domestically.

ORA enhances the overall coverage of the foreign establishment inventory by leveraging the work of its dedicated foreign inspections cadre, the inspection staff located at FDA's foreign offices, and domestic-based investigators. In addition, through enhancements to technology systems, FDA has increased transparency and access to importers and other government agencies to improve the efficiency of the review of products offered for entry into the U.S.

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 food products. ORA's investment in training and the mobilization of joint ORA and state Rapid Response Teams increases consumer protection, and minimizes the loss of consumer confidence, while lessening the economic impact on industry.

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
- stakeholder outreach.

In FY 2018 alone, ORA conducted 130 inspections of compounding facilities. Many belong to the category of compounders called outsourcing facilities created by the Drug Quality and Security Act of 2013. Outsourcing facilities are a new sector of drug compounder intended to provide a safe and reliable supply of compounded drugs needed by hospitals, clinics and other providers. ORA Occupational Safety and Health Officers have provided advisement and training to safely handle and ship active pharmaceutical ingredients.

The FDA Reauthorization Act of 2017 (FDARA) requires the Food and Drug Administration (FDA) to publicly report information related to inspections of facilities necessary for approval of a drug or a device. FDARA section 902 requires that the FDA make a report regarding facility

inspections related to drug and device approvals available on an annual basis through the Agency's website. The report contains data on inspections necessary for the approval of specified human drugs and medical devices. The inaugural report was published March 1, 2018. The information and metrics contained in this report provide benchmark data to industry stakeholders regarding inspections related to product application approvals.

Enforcement of FDA Authorities

ORA's Office of Criminal Investigations (OCI) has the primary responsibility for criminal investigations conducted by FDA and for all law enforcement and intelligence issues pertaining to threats against FDA-regulated products. Through July of FY 2018, the criminal investigative work of OCI resulted in:

- 283 domestic arrests
- 34 foreign arrests
- 215 convictions
- Approximately $2.3 billion in forfeiture, fines, and restitutions.

FDA continues to move aggressively toward targeting worldwide organized criminal groups involved in the distribution of illicit FDA-regulated products. As part of a larger Agency-wide strategy to combat this threat, OCI will assign two additional OCI Special Agents overseas. These two postings will be based out of U.S. Embassies and act as the single point of contact for embassy personnel in all matters relating to the law enforcement jurisdiction of the FDA.

Further, they will serve in a diplomatic role representing the FDA and the U.S. Government with foreign partner agencies. Currently, OCI has Special Agents stationed at Europol, in the Netherlands, and the Interpol Global Complex for Innovation (IGCI) in Singapore. These new positions enhance OCI's capabilities to share and receive criminal intelligence, plan and execute enforcement operations, and the further development of viable international partnerships.

OCI's ongoing Import Operations Program (IOP) is intended to detect violative shipments of FDA-regulated commodities entering our national ports and mail systems. There are 12 full-time and six part-time OCI IOP Special Agents overseen by two Senior Operations Managers. Their priorities include responding to international mail facilities, fast parcel carriers, ports, and mail hubs. This initiative enables OCI Special Agents to collaboratively work with their regulatory colleagues from FDA, CBP, and other Federal law enforcement agencies to stop the flow of violative or counterfeit human and animal drugs, vaccines, medical devices, and other biologic and tobacco products into the United States. During FY 2019, OCI anticipates doubling the size of IOP.

In recognition of the global supply chain, OCI has continued to place a strong emphasis upon international engagement. For example, OCI plays leading coordinating roles in the annual Operations Pangea and Opson. Operation Opson targets counterfeit and substandard food and beverages. Operation Pangea targets illicit medicines. Demonstrating the seriousness of the threat posed by illicit medicines, Operation Pangea X involved 123 of Interpol's 193 member countries. Further, Operation Pangea X was responsible for:

- over 400 arrests
- 470,000 seizures valued at over $51 million
- 3,524 websites being taken down worldwide.

OCI also maintains a leadership position within the Permanent Forum of International Pharmaceutical Crime, thereby placing its Special Agents in direct contact with their law enforcement counterparts from around the world. During FY 2018, OCI strengthened its Cybercrime Investigations Unit (CcIU) by assigning five additional full-time Special Agents to this program. Currently, there are 11 full-time CcIU Special Agents whose activities are managed by a Senior Operations Manager and supported by dedicated analytical staff. Their priorities include the strategic targeting of transnational criminal groups misusing the internet and those that support them by attempting to penetrate the FDA regulated supply chain, or by intentionally misrepresenting the nature of their products. Looking forward to FY 2019, OCI anticipates doubling the size of CcIU.

During FY 2018, OCI facilitated several workshops including

- one in Santo Domingo, Dominican Republic, involving representatives from more than 8 countries, titled "Measures against trade in illicit counterfeit health and safety products;" and
- one in Bangkok, Thailand, involving representatives from more than fifteen countries, Interpol, and regulated industry, targeting counterfeit goods being sold online.

IFSS and Program Standardization

To support an IFSS and protect the nation's food supply through domestic oversight, FDA relies on the strength and capability of federal and SLTT public health regulatory programs. FDA provides resources to SLTT public health regulatory agencies to build infrastructure, provide education to industry, complete regulatory inspections, and implement national regulatory program standards. FDA currently has 48 human manufactured food contracts covering 44 states and Puerto Rico. FDA also has 32 animal food contracts and 5 eggs contracts. Through FDA Contracts, over 11,000 inspections, 1,600 site visits, and 9,700 sample collections are planned in FY19.

FDA collaborates with SLTTs and numerous regulatory and public health associations to develop guidance, training, and standards to ensure uniformity in the regulation and approach taken by our food safety partners. FDA also works with the Partnership for Food Protection (PFP) and 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)
- Voluntary National Retail Food Regulatory Program Standards (VNRFRPS).

National standards establish a uniform foundation for the design and management of human and animal food regulatory SLTT programs. One of the key principles of FSMA is to rely on partner agencies to meet inspection mandates. National regulatory standards increase consistency and uniformity among partner agencies, and promote interagency confidence for effective, and efficient action to protect public health. As of October 2018, we have 43 SLTT programs enrolled in the MFRPS, 22 in the AFRPS, and 839 in the VNRFRPS.

FDA has awarded produce safety cooperative agreements to 46 states and 1 territory to increase their capacity and training efforts. By funding states to establish or expand produce safety resources FDA is able to leverage resources and advance the Produce Safety Rule. FDA is committed to working with state partners and other stakeholders to develop educational materials for inspections and outreach. In FY18, FDA collaborated with external stakeholders to develop plans and documents to ensure national consistency for the implementation of produce inspections, compliance, and enforcement. Produce inspections are set to begin nationwide in 2019.

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

IMPORT LINES BY PROGRAM AREA
FY 2014-FY 2020 (Est.)

Program Area	2014	2015	2016	2017	2018	5 Yr Actual Percent Growth*	2018 Percent of Total Lines	Estimate 2019	Estimate 2020
Foods	12,180,223	13,080,429	13,952,537	15,251,687	16,859,790	8%	38.62%	17,702,780	18,587,918
Cosmetics	2,596,057	2,930,682	2,939,034	2,625,555	2,729,584	3%	6.25%	2,866,063	3,009,366
Human Drugs	641,908	688,208	739,309	789,853	871,212	8%	2.00%	914,773	960,511
Animal Drugs & Feeds	391,388	416,860	434,384	426,484	456,684	4%	1.05%	479,518	503,494
Biologics	82,710	150,673	151,911	157,080	170,575	21%	0.39%	179,104	188,059
Medical Devices & Rad Health	16,668,422	17,252,283	18,757,725	20,584,138	22,291,902	9%	51.06%	23,852,335	25,521,999
Tobacco Products	20,161	16,680	32,972	199,066	281,097	126%	0.64%	295,152	309,909
Total	32,580,869	34,535,815	37,007,872	40,033,863	43,660,844	8%	100.00%	46,289,724	49,081,257

*Percentage growth based off a 5 year average (FY 2014 - FY 2018)

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 and 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 target high-risk shipments and increase compliance with Federal standards and regulations.

FDA and CBP continue to work together to assess recommendations from Commercial Operations Advisory Committee (COAC) for implementation. COAC is a 20-member council that meets quarterly and advises government agencies on the commercial operations of CBP and related functions. Taken into consideration are such issues 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
- protection of intellectual property rights.

ORA continues to implement the Voluntary Qualified Importer Program (VQIP). The FDA VQIP portal launched this year and is open to accept VQIP applications for importer benefits that begin in FY 2020; with review of applications to begin in January 2019. VQIP is a fee-based program that provides an 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. As part of the application, importers must submit certifications issued under the FDA Accredited Third Party Certification program. Expedited entry incentivizes importers to adopt a robust system of supply chain management and allows FDA to focus its resources on food entries that pose a higher risk to public health.

FDA has developed and implemented an account management system, the Industry Trade Auxiliary System (ITACS), for bilateral communications with importers and other industry stakeholders. ITACS is voluntary and allows additional information to be requested by FDA on entries and submitted from trade. Additionally, and perhaps just as importantly, ITACS generates an electronic notification to trade rather than requiring the information to be sent out through traditional mail. The system went live in September 2017 and has received accolades from industry.

Premarket Medical Product Activities

To ensure products are produced as outlined in medical product application, ORA inspects manufacturing facilities. Implementation of GDUFA allows FDA to complete inspections of establishments which have not been previously inspected, those 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 and coordinates inspections of generic drug manufacturing facilities with Center application reviews. In addition, ORA and CDER are working to decrease the amount of time required to complete domestic and foreign inspections of establishments conducting bioequivalence analytical and clinical studies. To reduce the time from application to review decision, tighter timeframes have been applied. In addition, ORA and CDER have reached an agreement to allow CDER to conduct some analytical site inspections. This arrangement allows 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, thru our concept of operations (Con-Ops) strategic framework. This framework

discusses how the Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA) will work together regarding application review, inspections, and the compliance activities associated with them. These activities directly supports the assessment of marketing applications by assuring that the data in the applications is accurate, complete, and any manufacturing facility named in the application conforms to Current Good Manufacturing Practice (cGMP) requirements. In addition, CDER and ORA have developed a streamlined approach involving aligned, patient-focused, and risk-based drug product quality recommendations inclusive of drug substance, drug product, manufacturing, and facilities.

Strengthen Science and Efficient Risk-Based Decision Making

Risk-Related Prevention Focus

ORA supports a risk-related preventive focus. For example, ORA uses a risk-based model to focus inspection efforts, in conjunction with FDA Centers, to prioritize resources on the highest risk firms both domestically and abroad. In addition, ORA advocates for enhanced collaboration with federal, SLTT, and global public health regulatory partners.

To improve coverage of the domestic inventory FDA provides support and funding to SLTT food safety partners to support an IFSS. Strengthening the domestic network of regulators allows ORA to apply its investigators to the areas of regulation that pose the highest risk to the public, including the increase in unsafe, unapproved, and misbranded FDA regulated products imported from the global marketplace.

Over the years, sampling approaches have evolved to help FDA 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. The process also serves as a mechanism to actively identify risks and areas where preventive controls should be placed to protect public health. As FDA increases its understanding of contamination sources in high risk commodities and practices, resources can be effectively allocated to address public health risks through compliance sampling, targeted sampling or other risk mitigation strategies.

The Center for Food Safety and Applied Nutrition (CFSAN) and ORA have developed a model where various information sources, including those from our regulatory partners and external stakeholders, can be used to shape sampling assignments. For example, if a state or external stakeholder has done research on a certain product, FDA may include that data to inform its decision making on assignments.

The Center for Drug Evaluation and Research (CDER) and ORA 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 has streamlined FDA's process for inspections and compliance to reduce the time to issue advisory and enforcement actions. For example, as of July 2018, 81% of our enforcement/advisory actions were issued within six months of the close of the inspection.

Additionally, CDER and ORA are continuing to work together to develop a new and 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),

uses standardized electronic inspection protocols, templates and semi-automated inspection reports. Following four years of developing, pilot testing and refinement, the first two NIPP protocols, one covering sterile drug surveillance inspections and the other sterile pre-approval drug inspections, were fully implemented starting on October 29, 2018. The new protocols will not change the role of the investigator. Instead they will provide a more structured tool for completing inspections and completing the establishment inspection report. Additional protocols are being developed and will be piloted for implementation through 2020. It is expected that as NIPP data is collected, analysis will reveal anomalies, patterns and correlations, which will help drive decision-making and further reduce risks related to drug quality.

ORA and CDER are also working together to implement, the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54), which 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 wholesale distributors (WDDs) and third-party logistics providers (3PLs) to improve drug supply chain security. The DSCSA also created a new licensing scheme for WDDs and 3PLs that will license in states that don't have a licensing program in accordance with federal standards. The licensure program, still under development, can be categorized into three primary areas: accreditation, licensing, and inspection. These three areas must include: accepting and reviewing applications; developing a program for accrediting third parties to conduct inspections; developing an inspection program; and accepting user fees. Regulations to implement the licensing provisions are currently undergoing final review and are expected to be proposed in the first half of CY2019.

In order to maximize ORA's medical device inspectional resources, and mitigate the harm to consumers, the Center for Devices and Radiological Health (CDRH) and ORA incorporated a risk-based model for the identification of facilities to be inspected each year. For surveillance purposes, ORA focuses their medical device inspectional staff of approximately 120 investigators on products and facilities identified as highest risk through CDRH's risk-model.

Mammograms are critical to early detection of breast cancer. Each year, FDA and inspectors in 44 states evaluate the level of compliance at more than 8500 mammography facilities. Rad Health Representatives (RHR) within ORA work directly with the states to ensure that every mammography clinic is inspected yearly. The RHRs communicate with CDRH and with the states to ensure consistent compliance scrutiny and enforcement.

In addition, FDA participates in the Medical Device Single Audit Program (MDSAP) which allows an Auditing Organization to conduct a single regulatory audit of a medical device manufacturer in five (5) countries: the US, Australia, Brazil, Canada and Japan. Approximately 2900 facilities around the world are participating in the MDSAP program. ORA works closely with CDRH to ensure any signals of significant public health risk are communicated and appropriate "For Cause" inspections are initiated.

In FY19, ORA will conduct inspections of over 800 U.S. blood establishments. By providing this oversight, ORA plays an important role in maintaining the safety of the US blood supply. According to the 2015 National Blood Collection and Utilization Survey, 16 Million units of red cells, platelets and plasma were transfused in the US in 2015.

ORA conducts inspections of domestic and foreign vaccine manufacturers to help ensure the safety and availability of vaccines for U.S. children and adults. In the 2017-2018 flu season, 155.3 million doses of influenza vaccine were distributed in the U.S.

Under the Bioresearch Monitoring program, ORA conducts over 1100 domestic and 315 foreign inspections each fiscal year. These inspections are driven by risk-based selection models developed in each of FDA's six product centers to ensure that the rights, safety, and welfare of human and animal subjects are protected during participation in trials. In addition, inspections are conducted of postmarket adverse event reporting and risk evaluation and mitigation strategies (REMS) to ensure patients continue to be protected after products are available on the market.

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 enables ORA to adapt to meet challenges and improve our efforts to protect public health. Program Alignment (PA) was implemented in May 2017 and 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 FDA. ORA laboratories have also specialized and been aligned into Human and Animal Foods Labs or Medical Product, Tobacco and Specialty Labs.

The FDA PA initiative moved the agency toward a more collaborative program-based model. PA allows employees to become 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. PA modernizes and strengthens the FDA workforce to improve public health response in a way that keeps pace with the acceleration of scientific innovation, global expansion of markets, and modern legal authorities. For those regulated by FDA, the new organizational model will result in uniformity in both process and policy across the organization and coordinated interactions within FDA between the field and the centers.

Workforce and Leadership Development

Training and development of ORA staff is critical. Increasingly complex inspections, along with new regulations and legislation, require employees completing inspections to have specialized knowledge in each regulatory program area. Under PA, staff training and development have been elevated in the reporting structure to raise its visibility and cross-organizational importance.

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. The program curriculum provides

participants with successively complementary leadership and management skills that lead to the Executive Core Qualifications necessary for senior agency leaders.

ORA continues to complete Job Task analyses which deconstructs job functions to determine the knowledge skills and abilities needed to complete work in each focus area. In FY 2018 Job Task Analyses were completed in Pharma and Tobacco for investigators, and Chemistry for Analysts. In FY 2019, new Job Task Analyses will be completed for Microbiology (both Food and Medical Products) and State Liaisons, with updates to those already existing in Biologics, Clinical BIMO, and Medical Devices. Using previously collected data, ORA is redesigning the pharmaceutical investigator training to reflect the changing industry landscape. This redesign will provide for flexible and specialized workforce with the project carrying through FY2020 and FY2021. Similar development project work is already underway for the bioresearch monitoring, medical devices, and radiological health program areas with new courses being piloted in FY2019 and FY2020.

Reduce the Burden of Addiction Crises that are Threatening American Families

Tobacco Enforcement

On May 10, 2016, the "Deeming Rule" was published in the Federal Register giving FDA the authority to "deemed" tobacco products such as electronic cigarettes, cigars, hookah, and pipe tobacco and their components and parts. The Tobacco Operations Staff completed 71 inspections of tobacco product manufacturers (66 Domestic and 5 Foreign), 33 investigations and investigated 7 free sample events in FY 2018. The FDA sent letters to several companies requiring them to submit important documents to better understand the reportedly high rates of youth use and appeal of their electronic cigarette products. In addition, ORA inspected companies for the purposes of collecting evidence and documentation to determine the establishment's compliance with the relevant provisions of the Food Drug and Cosmetic Act (FD&C Act). CTP requested that ORA conduct an initial comprehensive evaluation to collect inspectional documentation to evaluate complaints regarding the sale of tobacco products to under age youth, illegal sales, and improper samples of products prohibited by the FD&C Act. CTP is currently reviewing these documents and may notify firms of their potential violations based on ORA's evidence. In fiscal year 2019, ORA's Tobacco Operations Staff will be performing at least 200 manufacturing inspections and investigating a minimum of 7 free sample events.

Foster Competition and Innovation

Cultivating a Global Regulatory Network

FDA continues to increase its regulatory presence globally to ensure that the human and animal food and medical products available in the United States meet U.S. regulatory requirements. FDA fosters this global product safety net by enhancing existing partnerships, encouraging new partnerships, and developing cross-agency coalitions with domestic and foreign partners. ORA continues to improve and increase information sharing and joint work planning and compliance collaborations with SLTT, federal, and global regulatory partners.

FDA recognizes that it must embrace new approaches to enhance the safety of imported foods and fulfill its public health mission in a global age. Recognizing the value in leveraging the expertise of foreign food safety systems, FDA continues to pursue systems recognition arrangements as a tool to:

- set regulatory priorities
- establish closer regulatory partnerships
- improve efficiency
- strengthen the nation's food safety supply.

Systems recognition determines if a foreign country's food safety system and food safety authority/authorities provide similar oversight and monitoring for food produced under its jurisdiction. Systems recognition assists the FDA to prioritize the scope and frequency of its oversight activities including foreign facility inspections, import field exams, and import sampling. FDA has established systems recognition with New Zealand, Australia, and Canada and is working to evaluate a system recognition agreement with member states in the European Union.

FDA continues to participate as an active member of Pharmaceutical Inspection Cooperation Scheme (PIC/S), the multinational organization that now contains 52 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. ORA has Increased their participation in PIC/S by joining the Joint Visits Programme (JVP) for Good Clinical Practice (GCP) and Good Pharmacoviligelence Practice (GVP). Under the JVP, ORA is conducting joint inspections with PIC/S members to compare inspectional focus and practices, with the goal of regulatory confidence building and information sharing with international partners. In September 2018, FDA hosted the annual PIC/S Training Seminar: Management of Risk Through the Product Life-Cycle, in Chicago, Illinois. The seminar was attended by over 200 inspectors from 46 countries.

The U.S. FDA – Mexico Produce Safety Partnership (PSP), is a bilateral partnership that focuses on the safety of produce traded across our respective borders. The goal of the PSP is to implement preventive practices and verification measures that support high rates of compliance with produce safety standards and best practices to reduce risk of foodborne illness or death associated with produce. The PSP collaboration reinforces preventive practices and allows both countries to respond rapidly in the event of a potential or actual outbreak. Mexico and the U.S. have cooperated on joint inspections, joint traceback investigations and root-cause-analysis environmental assessments, in addition to enhancing laboratory capacity.

Leveraging Laboratory Capabilities

ORA provides oversight of regulatory science standards in laboratories through the use of programs, systems, and cooperative agreements. FDA works with external partners, including states, foreign government regulatory authorities, and industry, to provide input on laboratory standards and on the identification of sampling assignments. This strategy gains cooperation up front, allows stakeholders to take part in developing assignments, and strengthens the surveillance of FDA-regulated food products.

ORA funds the Food Emergency Response Network (FERN) cooperative agreements designed to assist state laboratories build their capability and capacity to respond to large-scale food contamination events. Currently there are 33 FERN network laboratories, including 14 microbiological, 14 chemical, and 5 radiological laboratories. In addition, ORA provides cooperative agreements to 45 state human and animal food testing laboratories to meet and

maintain the International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC) 17025:2005.

Figure 16 Figure 2 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

ORA labs are standing up specialized pharmaceutical testing research programs to develop regulatory methods to evaluate new biotech drugs in the cancer and auto-immune therapy sectors. There are two groups that specialize in pharmaceutical testing research programs on each side of the country, one located at Pacific Southwest Laboratory and the other at Northeast Laboratory. ORA is acquiring advanced instrument platforms such as Nuclear Magnetic Resonance Spectroscopy and Mass Spectrometry systems for these laboratories to probe the critical quality attributes of protein-based or nanoparticle-based drugs.

ORA continues to expand its analytical repertoire by developing and using cutting-edge technology to respond to public health needs. Employing a newly integrated technology called Whole Genome Sequencing (WGS), an ORA lab contributed to the first recall in FDA history that was primarily based on WGS results. The regulatory outcome was built on a solid scientific case that represented effective federal-state collaboration, communication, and use of new technology. To promote this technology further, ORA works with state regulatory partners to initiate and use WGS in state laboratories on a national level.

IT systems and Initiatives

ORA is committed to increasing productivity and maintaining program integrity through our information technology systems and initiatives. Capabilities of ORA operational and reporting systems were enhanced to develop functionality specifically: Import Certification and Third Party Accreditation; Voluntary Qualified Importer Program; and Foreign Supplier Verification Program Preventive Controls for Human and Animal Food.

In collaboration with the U.S CBP and 46 partner government agencies, ORA has transitioned to the Automated Commercial Environment/International Trade Data System (ACE/ITDS) which enhances capabilities and productivity to ensure the safety of imported products under FDA's regulatory authorities. ACE/ITDS is a single access point where industry can electronically submit all data required by various government agencies involved in international trade and receive dispositions on the goods they present for import.

ORA established importer Industry account management functionality which allows electronic communications between importers, filers and FDA staff thus saving both postage and staff resources. In addition, the application programming interface (API) developed by ORA for industry to access product code information, allows external users to check for product codes or validate them prior to submission to FDA to ensure entries are not held or rejected due to inaccurate product code information.

ORA developed an FDA Data Dashboard providing greater transparency to the public about FDA's inspectional, enforcement, recall, and compliance activities. The Dashboard has also been expanded to support the FSMA requirement to provide industry with information needed to support the FSVP program.

FUNDING HISTORY[95]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$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 Actual	$1,152,189,000	$1,061,760,000	$90,429,000
FY 2019 Annualized CR	$1,173,404,000	$1,061,799,000	$111,605,000
FY 2020 President's Budget	$1,223,992,000	$1,110,861,000	$113,131,000

BUDGET REQUEST

The FY 2020 Budget Request is $1,223,992,000, of which $1,110,861,000 is budget authority and $113,131,000 is user fees. The budget authority increases by $49,062,000 compared to the FY 2019 Annualized Continuing Resolution level and user fees increase by $1,526,000.

The FY 2020 President's Budget allows FDA to continue to ensure that the food, feed, and medical products available to the American public are safe and effective.

[95] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

BUDGET AUTHORITY

Medical Product Safety (+$26.6 million / 32 FTE)

Opioids: +$21.8 million / 12 FTE
Field Human Drugs: +$21.8 million / 12 FTE

ORA is increasing FDA presence at International Mail Facilities (IMF) facilities, while taking into consideration the corresponding divisions under program alignment, incoming IMF parcel volume as well as existing personnel. With one-time funding from the FY 2018 Omnibus, ORA is hiring an additional 125 FTE in support of the nine IMFs and will increase the number of reviews from 15,000 to 100,000 per year. In addition, ORA is requesting additional staff and funds to support lab work related to the increased package screening.

Compounding: +$2.8 million / 10 FTE
Field Human Drugs: +$2.8 million / 10 FTE

Outsourcing facilities are working to ensure that their facilities and compounding practices result in compounded drugs of acceptable quality. With additional resources, FDA would be able to provide additional assistance to outsourcing facilities in their efforts to meet this important public health objective. FDA investigators, experts, and other staff would be able to dedicate more time and attention to facility inspections, reviewing the evidence collected, evaluating the corrective actions, and take appropriate measures to ensure that patients receive drugs compounded under appropriate conditions. Outsourcing facilities would benefit from more frequent and in-depth information-sharing meetings with FDA experts and correspondence with the Agency regarding quality improvements. Purchasers of compounded drugs would also have access to more up-to-date information regarding the outsourcing facilities so that they can make informed sourcing decisions. State and federal regulatory partners would also benefit from the availability of more timely and robust outsourcing facility information.

New Domestic Drug Industry: +$2.0 million / 10 FTE
Field Human Drugs: +$2.0 million / 10 FTE

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.

Food Safety (+$22.4 million / 23 FTE)

Advancing FSMA: +$10.3 million
Field Human Foods: +$10.3 million

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct domestic food and feed facility inspections required by FSMA. ORA will enhance its oversight of industry's compliance with the human food preventive control rules by expanding funding of cooperative agreements with state food regulatory programs.

To ensure effectiveness and efficiency, FDA expects that states will continue or increase their number of inspections as FDA transitions to prevention-oriented inspections and determines industry compliance with the new FSMA standards and rules. NASDA and AFDO also have requested funds for FDA to provide states to complete Preventive Control (PC) inspections.

Field Animal Drugs & Feeds: +$5.6 million

FDA provides state regulatory programs with contract and cooperative agreement funding to conduct [IS11] domestic food and feed facility inspections required by FSMA. FDA expects that states will continue to gradually increase the number of inspections they conduct as FDA transitions to prevention-oriented inspections. NASDA and AAFCO have requested funds for FDA to provide states to complete Preventive Control (PC) inspections by updating and building new state programs. The cooperative agreements will support work for states to implement the recommendations of the NASDA PC Animal Food Framework that include evaluating and building infrastructure, updating inspection and enforcement programs, developing outreach and training programs, and shifting laboratory resources to focus on analysis of hazards.

Strengthening Response Capabilities for Foodborne Outbreaks: +$6.5 million / 23 FTE
Field Human Foods: +$6.5 million / 23 FTE

In recent years FDA has refined its traceback methods to increase speed and efficiency during outbreaks and recalls. Additional resources are required to ensure that, as soon as possible, contaminated food is detected and removed from the marketplace and that consumers are alerted.

FDA is requesting additional FTEs to support new procedures for collecting, reviewing, and posting retail consignees for certain Class I and Class II recalls. To ensure we have complete information, FDA will expend significant resources collecting consignee lists throughout the distribution chain (recalling firm, distributors, etc.) and then reviewing them to identify retailers that may have sold the recalled product. The list of retailers will be consolidated into one master list and posted onto FDA's website. This will protect public health by allowing consumers to recognize whether they have purchased recalled products."

USER FEES

Current Law User Fees: +$1.5 million

The ORA request includes an increase of $1,526,000 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 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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 90% (New Measure)	80%	80%	Maintain
224221: Percentage of Human and Animal Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 86% (New Measure)	80%	80%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 75% (New Measure)	70%	70%	Maintain
254221: Percentage of Medical Device and Radiological Health significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	Baseline: 89% (New Measure)	80%	80%	Maintain
214222: Percentage of Human and Animal Food follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 78% (New Measure)	65%	65%	Maintain
224222: Percentage of Human and Animal Drug follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 67% (New Measure)	55%	55%	Maintain
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 71% (New Measure)	65%	65%	Maintain
254222: Percentage of Medical Device and Radiological Health follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 81% (New Measure)	65%	65%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
253221: Percentage of Bioresearch Monitoring (BIMO) follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	Baseline: 90% (New Measure)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2018: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
214305: Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). *(Outcome)*	FY 2018: 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
214212: Percentage of planned import food field exams. (Output)	FY 2018: 123% Target: 95% (Target Exceeded)	NA	NA	NA
214209: As required by the FSMA Legislation, cover all of the High Risk domestic inventory every three years. (Output)	FY 2018: 75% Target: 66% (Target Exceeded)	NA	NA	NA
224211: Percentage of planned foreign and domestic high-risk human drug inspections. (Output)	FY 2018: 70% Target: 70% (Target Met)	NA	NA	NA
234212: Percentage of planned domestic blood bank and biologics manufacturing inspections. (Output)	FY 2018: 105% Target: 95% (Target Exceeded)	NA	NA	NA

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
234213: Percentage of planned human foreign and domestic tissue establishment inspections. (Output)	FY 2018: 105% Target: 85% (Target Exceeded)	NA	NA	NA
244212: Percentage of planned domestic and foreign high-risk animal drug and feed inspections. (Output)	FY 2018: 97% Target: 95% (Target Exceeded)	NA	NA	NA
244203: Cover targeted prohibited material BSE actual inventory. (Output)	FY 2018: 92% Target: 95% (Target Not Met)	NA	NA	NA
253211: Percentage of work plan issued Medical Device Bioresearch Monitoring (BIMO) inspections. (Output)	FY 2018: 106% Target: 91% (Target Exceeded)	NA	NA	NA
254211: Percentage of planned domestic and foreign device inspections. (Output)	FY 2018: 88% Target: 80% (Target Exceeded)	NA	NA	NA

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

New ORA Field Performance Measures

ORA is embarking on an initiative to move from output focused performance goals such as inspection counts to public health outcome based performance goals. This initiative seeks to provide more meaningful performance goals for internal and external stakeholders, and to showcase more direct public health impacts for ORA. The new performance goals introduced for FY 2019 measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention, and allows for a more robust analysis.

Since these targets are 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 percent. This is particularly true for import food field exams because even when import investigators meet their work plan target, they are still required to continue exams for incoming high-risk products being flagged for review by a risk-screening tool for imports called PREDICT.

Coverage of Targeted Prohibited Material BSE Actual Inventory Goal Target Not Met

The only goal not met this year was the coverage of targeted prohibited material BSE inventory coverage. This goal fell short by three percentage points. Similar to last year, resource constraints and shifting priorities (e.g.: response to natural disasters) impacted the full completion of this goal. BSE coverage is also a collaborative effort between FDA and State partners and as such, inspection coverage may vary given differing fiscal year timeframes. The ability for FDA to track BSE inventory and BSE work conducted by the States is problematic due to IT constraints and FDA continues to work on infrastructure improvements for future success.

New ORA Field Performance Measures

PROGRAM ACTIVITY DATA TABLES

Field Foods Program Activity Data (PAD)

Field Foods Program Activity Data (PAD)			
Field Foods Program Workload and Outputs	**FY18 Actuals**	**FY2019 Estimate**	**FY2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***8,629***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	5,876	**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	162		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	234		
Domestic Fish & Fishery Products (HACCP) Inspections	809		
Import (Seafood Program Including HACCP) Inspections	191		
Juice HACCP Inspection Program (HACCP)	149		
Interstate Travel Sanitation (ITS) Inspections	1,046		
Domestic Field Exams/Tests	3,059	2,500	2,500
Domestic Laboratory Samples Analyzed	15,470	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,638***	***1,400***	***1,400***
All Foreign Inspections	1,638	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***10,267***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	185,761	168,200	168,200
Import Laboratory Samples Analyzed	20,895	35,300	35,300
Import Physical Exam Subtotal	**206,656**	**203,500**	**203,500**
Import Line Decisions	16,859,790	17,702,780	18,587,918
Percent of Import Lines Physically Examined	1.23%	1.15%	1.09%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	84,113	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***8,073***	***9,062***	***9,062***
State Contract Food Safety (Non HACCP) Inspections	7,210	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	788	1,000	1,000
State Contract Juice HACCP	57	100	100
State Contract LACF	117	100	100
State Contract Foods Funding	$13,620,000	$13,756,200	$13,893,762
Number of FERN State Laboratories	33	33	33
Annual FERN State Cooperative Agreements/Operations Funding	$15,865,891	$15,865,891	$15,865,891
Total State & Annual FERN Funding	**$29,485,891**	**$29,622,091**	**$29,759,653**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***18,340***	***18,462***	***18,462***

[1] The FY 2018 actual unique count of foreign inspections includes 171 OIP inspections (120 for China, 38 for India, & 13 for Latin America).

[2] ORA is currently evaluating the calculations for future estimates.

3 State partnership inspections have been removed from the PAD as they have been phased out. All state inspections are now accounted for under the "state contract" inspection category.

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Activity Data (PAD)			
Field Cosmetics Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***71***	***100***	***100***
Domestic Inspections	71	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***6***	***0***	***0***
Foreign Inspections	6	0	0
IMPORTS			
Import Field Exams/Tests	6,195	1,600	1,600
Import Laboratory Samples Analyzed	335	400	400
Import Physical Exam Subtotal	**6,530**	**2,000**	**2,000**
Import Line Decisions	2,729,584	2,866,063	3,009,366
Percent of Import Lines Physically Examined	0.24%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***77***	***100***	***100***

1 ORA is currently evaluating the calculations for future estimates.

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2018 Actuals	FY 2019 Estimate	FY 2020 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,662***	***1,709***	***1,709***
Pre-Approval Inspections (NDA)	81	100	100
Pre-Approval Inspections (ANDA)	90	90	90
Bioresearch Monitoring Program Inspections	667	600	600
Drug Processing (GMP) Program Inspections	632	650	650
Compressed Medical Gas Manufacturers Inspections	42	50	50
Adverse Drug Events Project Inspections	73	88	88
OTC Monograph Project and Health Fraud Project Inspections	19	70	70
Compounding Inspections[1]	127	142	142
Domestic Laboratory Samples Analyzed	1,041	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1221***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	102	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	159	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	280	255	255
Foreign Drug Processing (GMP) Program Inspections	743	900	900
Foreign Adverse Drug Events Project Inspections	8	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,883***	***3,069***	***3,069***
IMPORTS			
Import Field Exams/Tests	8,607	10,000	10,000
Import Laboratory Samples Analyzed	735	620	620
Import Physical Exam Subtotal	**9,342**	**10,620**	**10,620**
Import Line Decisions	871,212	845,143	904,303
Percent of Import Lines Physically Examined	1.07%	1.26%	1.17%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,883***	***3,069***	***3,069***

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

[2] The FY 2018 actual unique count of foreign inspections includes 115 OIP inspections (48 for China and 67 for India).

3 ORA is currently evaluating the calculations for future estimates.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Activity Data (PAD)			
Field Biologics Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,849***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	75	100	100
Blood Bank Inspections	807	900	900
Source Plasma Inspections	243	190	190
Pre-License, Pre-Market Inspections	81	55	55
GMP Inspections	45	28	28
GMP (Device) Inspections	13	7	7
Human Tissue Inspections	625	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***70***	***47***	***47***
Bioresearch Monitoring Program Inspections	15	11	11
Foreign Human Tissue Inspections	1	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	6	7	7
GMP Inspections (Biologics & Device)	38	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,919***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	73	45	45
Import Line Decisions	170,575	179,104	188,059
Percent of Import Lines Physically Examined	0.04%	0.03%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,919***	***1,939***	***1,939***

[1]ORA is currently evaluating the calculations for future estimates.

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 2018 Actuals**			**FY 2019 Estimate**			**FY 2020 Estimate**		
	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	***1,436***	***160***	***1,276***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	33	33	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	120	120	0	175	175	0	175	175	0
BSE Inspections	746	0	746	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	5	0	5	25	0	25	25	0	25
Illegal Residue Program Inspections	322	0	322	450	0	450	450	0	450
Feed Manufacturing Program Inspections	179	0	179	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,223	13	1,210	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***74***	***70***	***4***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	20	20	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	51	51	0	33	33	0	33	33	0
Foreign Feed Inspections	2	0	2	5	0	5	5	0	5
BSE Inspections	1	0	1	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,510***	***230***	***1,280***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	3,557	868	2,689	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	963	0	963	867	2	865	867	2	865
Import Physical Exam Subtotal	**4,520**	**868**	**3,652**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	456,684	65,887	390,797	479,518	69,181	410,337	503,494	72,640	430,854
Percent of Import Lines Physically Examined	0.99%	1.32%	0.93%	0.97%	0.72%	1.02%	0.93%	0.68%	0.97%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***3,050***	***0***	***3,050***	***3,396***	***0***	***3,396***	***3,396***	***0***	***3,396***
State Contract Inspections: BSE	2,713	0	2,713	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	549	0	549	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	85	0	85	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	$3,369,732	0	$3,369,732	$3,470,824	0	$3,470,824	$3,574,949	0	$3,574,949
State Contract Tissue Residue Funding	$0	0	$0	$0	0	$0	$0	0	$0
Total State Funding	**$3,369,732**	**$0**	**$3,369,732**	**$3,470,824**	**$0**	**$3,470,824**	**$3,574,949**	**$0**	**$3,574,949**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***4,563***	***230***	***4,333***	***5,134***	***367***	***4,799***	***5,134***	***367***	***4,799***

[1] The FY 2018 actual unique count of foreign inspections includes 5 OIP inspections (4 for China and 1 for India).

[2] The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number is expected to decrease in the future until there are no planned State Partnership inspections.

[3] The State cooperative agreement BSE inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number along with the funding for these inspections are expected to decrease in the future until there are no planned State Cooperative Agreement BSE inspections.

4 Tissue residue funding has ended in FY18 and state contract illegal tissue residue inspections are no longer being conducted.

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Activity Data (PAD)			
Field Devices and Radiological Health Program Workload and Outputs	**FY 2018 Actuals**	**FY 2019 Estimate**	**FY 2020 Estimate**
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,550***	***2,498***	***2,498***
Bioresearch Monitoring Program Inspections	308	300	300
Pre-Market Inspections	48	60	60
Post-Market Audit Inspections	35	60	60
GMP Inspections	1,350	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	834	700	700
Domestic Radiological Health Inspections	102	50	50
Domestic Field Exams/Tests	43	100	100
Domestic Laboratory Samples Analyzed	174	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***626***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	14	14	14
Foreign Pre-Market Inspections	25	30	30
Foreign Post-Market Audit Inspections	19	20	20
Foreign GMP Inspections	557	550	550
Foreign MQSA Inspections	11	14	14
Foreign Radiological Health Inspections	59	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***3,176***	***3,111***	***3,111***
IMPORTS			
Import Field Exams/Tests	25,499	19,800	19,800
Import Laboratory Samples Analyzed	624	670	670
Import Physical Exam Subtotal	**26,123**	**20,470**	**20,470**
Import Line Decisions	22,291,902	23,852,335	25,521,999
Percent of Import Lines Physically Examined	0.12%	0.09%	0.08%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,663***	***7,880***	***7,880***
Inspections (MQSA) by State Contract	7,614	6,800	6,800
Inspections (MQSA) by State non-Contract	1060	1,060	1,060
GMP Inspections by State Contract	49	20	20
State Contract Devices Funding	$76,674	$270,000	$278,100
State Contract Mammography Funding	$10,591,706	$10,803,540	$11,019,611
Total State Funding	**$10,668,380**	**$11,073,540**	**$11,297,711**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,839***	***10,991***	***10,991***

[1] The FY 2018 actual unique count of foreign inspections includes 8 OIP inspections in China.

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

3 Domestic MQSA Non-VHA and VHA Inpsections have been combined into one output line.

[4] ORA is currently evaluating the calculations for future estimates.

TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020	
				President's Budget	+/- FY 2019 Annualized CR
Tobacco	**626,663**	**625,406**	**626,663**	**761,739**	**135,076**
Center	**611,979**	**614,794**	**611,979**	**747,055**	**135,076**
Family Smoking Prevention and Tobacco Control Act	**611,979**	614,794	611,979	647,055	35,076
Expand tobacco product (Proposed)	**---**	---	---	100,000	100,000
Field	**14,684**	**10,612**	**14,684**	**14,684**	**---**
Family Smoking Prevention and Tobacco Control Act	**14,684**	10,612	14,684	14,684	---
FTE	**874**	**874**	**991**	**1,053**	**62**

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, including underage youth, 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.

FDA's comprehensive plan for tobacco and nicotine regulation serves as a multi-year roadmap to protect youth 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. Key features of the comprehensive plan include:

- regulatory policies on addiction, appeal and cessation
- Youth Tobacco Prevention Plan: announced April 24, 2018, to reduce access to - and use of - tobacco products, particularly e-cigarettes
- science-based review of tobacco products.

Almost 90% of adult smokers start smoking by the age of 18,[96] and nearly 2,500 youth smoke their first cigarette every day in the United States.[97] By lowering nicotine levels in cigarettes to minimally addictive or non-addictive levels, we could decrease the likelihood that future generations become addicted to cigarettes and allow more currently addicted smokers to quit.

REDUCE THE BURDEN OF ADDICTION CRISES THAT ARE THREATENING AMERICAN FAMILIES

The following selected accomplishments demonstrate FDA's commitment to reducing the burden of the addiction crises that are threatening American families by protecting youth and helping addicted adult smokers quit, and by significantly reducing tobacco-related disease and death in the U.S. in the years to come.

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 (ENDS) - such as e-cigarettes and vape pens - cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels.

This rule helps implement the goals of 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.

[96] 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.

[97] undefined

Figure 17

As part of the Agency's comprehensive plan for regulation of nicotine and tobacco, FDA has begun a public dialogue about lowering nicotine levels in combustible cigarettes to minimally addictive or non-addictive levels through a tobacco product standard regulation. 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 unintended consequences of limiting nicotine in cigarettes to minimally-addictive or non-addictive levels.

Further, FDA indicated that it is seeking public input on other tobacco regulatory issues. 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 published on March 26, 2018, an 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 deeming rule for certain products. Specifically, in August 2017, the FDA posted a revised guidance, Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule, which deferred enforcement of deadlines to submit tobacco product applications for newly regulated tobacco products that were on the market as of August 8, 2016.[98] Under these revised timelines, applications for newly regulated combustible products, such as cigars, pipe tobacco and waterpipe tobacco, would be submitted by August 8, 2021, and applications for non-combustible products such as ENDS would be submitted by August 8, 2022.

When Commissioner Gottlieb announced FDA's comprehensive plan for tobacco and nicotine regulation in 2017, the deadlines for certain deemed products were extended, in part, so FDA could issue guidance and foundational rules for submission of product applications and to allow manufacturers more time to prepare product applications. Commissioner Gottlieb made clear FDA's concerns about kids' use of e-cigarettes, especially those products marketed with obviously kid-appealing flavors. At the time, however, the trends in youth use appeared to be changing in the right direction – reported e-cigarette use among high school students, which peaked at 16.0 percent in 2015, had decreased to 11.3 percent in 2016 and held steady in 2017. What FDA did not predict was that, in 2018, youth use of e-cigarettes and other ENDS products

[98] https://www. fda. gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM557716. pdf

would become an epidemic. According to findings from the 2018 National Youth Tobacco Survey (NYTS), there has been a dramatic increase in youth use of e-cigarettes and other ENDS: from 2017 to 2018, there was a 78 percent increase in current e-cigarette use among high school students and a 48 percent increase among middle school students.[99]

Therefore, on November 15, 2018, Commissioner Gottlieb outlined updates to our policy framework to address the large increase in youth use of tobacco products. Our focus is on what appear to be the central issues—youth appeal and youth access to flavored tobacco products. FDA will be taking steps on the following product categories:

- flavored ENDS products (other than tobacco, mint, and menthol flavors or non-flavored products) that are not sold in an age-restricted, in-person location;
- flavored ENDS products (other than tobacco, mint, and menthol flavors or non-flavored products) that are sold online without heightened age verification processes;
- flavored cigars;
- ENDS products that are marketed to kids; and
- menthol in combustible tobacco products, including cigarettes and cigars.

FDA intends to provide additional details, including what the agency might consider an "age-restricted" location, what it might consider "heightened" age-verification online, and timelines for when FDA intends to implement these policies. This policy reflects FDA's aim of striking the right balance between closing the on ramp for kids to become addicted to nicotine while maintaining access to potentially less harmful forms of nicotine delivery for adult smokers seeking to transition away from combustible tobacco products.

FDA's Tobacco Program is accomplished by issuing regulations and guidance that explain FDA's expectations to regulated industry and 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 underage youth through the use of compliance inspections, warning letters, civil money penalties, and no-tobacco-sale-orders.

Product Review and Evaluation

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 submitted for FDA review under one of these three marketing pathways:

- premarket tobacco product application (PMTA)
- report demonstrating substantial equivalence (SE Report) to certain commercially marketed products
- request for exemption from demonstrating substantial equivalence (Ex Req).

[99] https://www. fda. gov/NewsEvents/Newsroom/PressAnnouncements/ucm625917. htm

On October 22 and 23, 2018, FDA held a public meeting to improve public understanding and seek feedback on the policies and processes for the submission and review of tobacco product marketing applications, including the general scientific principles relevant to various application pathways, in order to assist applicants considering submitting marketing applications for tobacco products.

PMTA and Substantial Equivalence

Under the 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, including users and non-users of tobacco products.

Alternatively, 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.

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[100] 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[101] 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 regulatory and statutory requirements
- notification and predicate eligibility phase – for provisional SE Reports only the applicant is notified when scientific review will begin
- substantive scientific review phase and issuance of a decision.

All regular SE Reports received are immediately entered into review. In FY 2018, FDA met all performance goals for Regular SE Reports and Exemption Requests. Additionally, as part of a re-examination of the review queue of "Provisional SE Reports," FDA announced new performance measures for these reports which will take effect in FY 2019. These performance measures are similar to those used for Regular SE Reports but are tailored for the unique circumstances of provisional SE reports.

[100] http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm#3

[101] 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.

On July 19, 2018, FDA issued for the first time SE orders on regular SE Reports for two non-combusted cigarettes tobacco products, demonstrating that the SE premarket review pathway is viable for non-combustible cigarettes. In addition, each of these products could serve as predicate products for future SE Reports.

FDA is also actively continuing scientific review of provisional SE Reports.[102] FDA announced on April 5, 2018, removal of certain provisional SE applications from review because those products are less likely to raise different questions of public health. Over 1,100 reports have been removed from review, but FDA estimates 1,500 provisional products may ultimately be removed from review, depending on additional information provided by the applicant. This new approach allows for increased efficiency, better use of resources, and greater transparency - while ensuring those products with the greatest potential to raise different questions of public health undergo a full multi-disciplinary scientific review.

Products removed from review can continue to be legally marketed so long as they do not undergo further changes or do not fall under certain other exceptions that would pull the products back into the review queue. As part of re-examining the review queue of "Provisional SE Reports," FDA also announced performance measures for these reports. These new performance measures will guide FDA's efforts and allow for all interested stakeholders to stay up-to-date on progress in reviewing these applications as of FY 2019.

On August 14, 2018, FDA announced the agency is improving transparency regarding certain review documents for provisional SE tobacco products. FDA will proactively provide applicants certain reviews with underlying data to facilitate understanding of a provisional Not Substantially Equivalent (NSE) decision. Applicants are no longer required to file a Freedom of Information Act request to obtain these documents following a decision.

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.

Modified Risk Products

In addition to the three marketing pathways, before marketing legally marketed tobacco products with claims that explicitly or implicitly represent the product is for use to reduce harm or the risk of tobacco-related disease, manufacturers must submit a Modified Risk Tobacco Product Application (MRTPA) and receive an FDA order authorizing that the product reduces harm or the risk of tobacco-related disease.

The following table is a summary of tobacco product applications received through October 31, 2018.

[102] 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.

Application Status	Product Class	Cumulative through 10/31/2018			
		Regular SE Reports	**Provisional SE Reports**	**Premarket Tobacco Applications**	**Modified Risk Tobacco Applications**
Received	Cigarettes	1,184	2,351	6	10
	RYO	976	642	3	0
	Smokeless	332	588	14	19
	Other	274	18	(Deemed) 373	(Deemed) 8
	Total	**2,766**	**3,599**	**396**	**37**
Pending	Cigarettes	44	669	3	3
	RYO	23	67	0	0
	Smokeless	36	185	6	7
	Other	3	0	(Deemed) 4	(Deemed) 0
	Total	**106**	**921**	**13**	**10**
>Closed[103]	Cigarettes	1,140	1,682	3	7
	RYO	953	575	3	0
	Smokeless	296	403	8	12
	Other	271	18	(Deemed) 369	(Deemed) 8
	Total	**2,660**	**2,678**	**383**	**27**

Research

FDA invests in research to inform regulatory actions by addressing gaps and adding to the evidence base. The regulatory research informs FDA's tobacco regulatory activities and helps FDA better understand tobacco use and associated risks which supports FDA's mandate to reduce the public health burden of tobacco product use in the United States. In FY 2018, FDA invested more than $182 million in scientific research with a focus on reducing youth initiation of tobacco use, reducing tobacco product harms, and encouraging those who already use tobacco products to quit. Research priorities address the following Scientific Domains:

- Toxicity: understanding how tobacco products and changes to tobacco product characteristics affect their potential to cause morbidity and mortality
- Addiction: understanding the effect of tobacco product characteristics on addiction and abuse liability
- Health Effects: understanding the short- and long-term health effects of tobacco products

[103] Closed includes refuse-to-accept, refuse-to-file, remove from review, issuance of an order, special advice/information request, response, withdrawn, or closure due to administrative issues.

- Behavior: understanding the knowledge, attitudes, and behaviors related to tobacco product use and changes in tobacco product characteristics
- Communications: understanding how to effectively communicate to the public and vulnerable populations (including underage youth) regarding nicotine and the health effects of tobacco products, including media campaigns and digital media
- Marketing Influences: understanding why people become susceptible to using tobacco products (both classes of products and products within classes) and to transitions between experimentation and initiation to regular use and dual use
- Impact Analysis: understanding the impact of potential FDA regulatory actions.

In addition to conducting independent research to support regulatory science, CTP partners with several other FDA Centers including the National Center for Toxicological Research (NCTR) and Center for Food Safety and Nutrition (CFSAN), 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 Tobacco Regulatory Science Program (TRSP)

FDA avoids duplication of resources and enhances scientific research capability by collaborating with NIH and tapping into its well-established infrastructure. In FY 2018, FDA funded 114 research projects via NIH. These research projects include grants and contracts which will address important FDA research priorities.

FDA funds NIH 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 2018, FDA funded 53 new grants to support regulatory science research on tobacco products in the fields of biomedical, behavioral, and social sciences.

FDA collaborates with NIH to fund the Tobacco Centers of Regulatory Science (TCORS). In September 2018, nine TCORS grants were awarded. This second round of funding covers FY 2018-2022. The objective of the Centers is to conduct multidisciplinary research that will inform and assess FDA's prior, ongoing, and potential regulatory activities. TCORS investigators also have the flexibility and capacity to respond to FDA's research needs as issues are raised in today's rapidly evolving tobacco marketplace.

FDA also collaborates with NIH to fund the Center for Coordination of Analytics, Science, Enhancement and Logistics (CASEL). Its objective is to facilitate synthesis, coordination, and communications of research and career enhancement within the scientific program by FDA.

FDA funds the Population Assessment of Tobacco and Health (PATH) Study via NIH's Nation

al Institute on Drug Abuse (NIDA) and works collaboratively with them on the scientific aspects of the study. The PATH Study is an ongoing national, longitudinal, cohort study of users of tobacco products and those at risk for tobacco use with a national sample of U.S. civilian, non-institutionalized persons ages 12 and older. It follows approximately 46,000 never, current, and former users of tobacco products. Research topics in the PATH study related to reducing harm include evaluating patterns of tobacco use such as switching products and using multiple products, as well as seeking to understand perceptions, knowledge, attitudes and use of modified risk tobacco products.

Figure 18 Population Assessment of Tobacco and Health logo

Data is collected in "Waves" and the questionnaire data is released to the public and to researchers. 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 on youth was launched in December 2017. Additionally, a sub-study of adult e-cigarette users was launched in December 2017 to better understand their e-cigarette use; data collection for this study was completed in August 2018.

Laboratory Analyses

FDA partners with CDC to address priority research needs and 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 harmful and potentially harmful constituents (HPHCs).

CDC is also providing the analyses of tobacco exposure biomarkers from research data collected in the PATH Study.

CTP partners with NCTR to research:

- the toxicology of compounds and cigarette smoke
- the toxicity of tobacco products via cell culture and animal models
- developmental bioinformatics projects.

In FY 2017, CTP partnered with CFSAN to develop an in vitro buccal (mouth) membrane model to determine absorption of HPHCs found in smokeless tobacco.

National Surveys

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. On November

15, 2018, data published from this survey indicated a 78 percent increase in current e-cigarette use among high school students and a 48 percent increase among middle school students from 2017 to 2018. NYTS survey data allows FDA to monitor youth awareness of, susceptibility to, experimentation with, and use of, a wide range of tobacco products.

FDA has worked with CDC National Center for Health Statistics (NCHS) and other federal partners to develop and include non-cigarette tobacco use questions on the National Health Interview Survey (NHIS).

In FY 2017, CTP partnered with the NIH's National Cancer Institute (NCI) 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.

Compliance and Enforcement

FDA has a comprehensive compliance and enforcement program to monitor industry compliance with regulatory requirements, and to restrict access and marketing of tobacco products, including e-cigarettes and vape products, to youth.

As part of the Youth Tobacco Prevention Plan, FDA has recently taken the following actions to stop youth use of, and access to, JUUL and other e-cigarette products:

- conducted multiple nationwide blitzes to crack down on the sale of e-cigarettes to minors at both brick-and-mortar and online retailers
- issued more than 1,300 warning letters and civil money penalty complaints to retailers who illegally sold e-cigarette products to minors
- partnered with the Federal Trade Commission (FTC) to issue warning letters to e-liquid manufacturers whose products used misleading, kid-appealing imagery such as candy
- requested e-cigarette manufacturers submit documents that will help FDA better understand the reportedly high rates of youth use and youth appeal of e-cigarette products
- issued letters to the manufacturers of five top-selling vape product brands asking each company to submit plans addressing youth access and use of their products
- investigated 21 e-cigarette companies that may be illegally marketing their products to youth
- took steps to foreclose online sales of e-cigarette products to minors.

Figure 19 Example of misleadingly labeled e-liquids resembling kid-friendly food products

Tobacco Retailer Inspection

As of October 31, 2018, FDA had contracts for tobacco retailer compliance check inspections in 56 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 general, inspections are conducted by officers and employees from the states and territories under contract. FDA commissions and trains these officials to conduct inspections on the Agency's behalf. FDA currently utilizes more than 800 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-Orders when violations are found. The following table lists the different enforcement actions that have resulted from these inspections.

CTP Tobacco Retailer Inspection Program

Enforcement Action	FY 2018 Actuals	FY 2019 (as of 10/31/2018)	Total Since the Program's Inception (as of 10/31/2018)
Retailer Inspections	146,398	10,841	1,000,029
Warning Letters	14,032	1,153	79,630
ENDS Products Only	2,929	39	6,126
Civil Money Penalties	3,537	368	19,195
ENDS Products Only	460	17	781
No-Tobacco-Sale-Orders	48	0	143

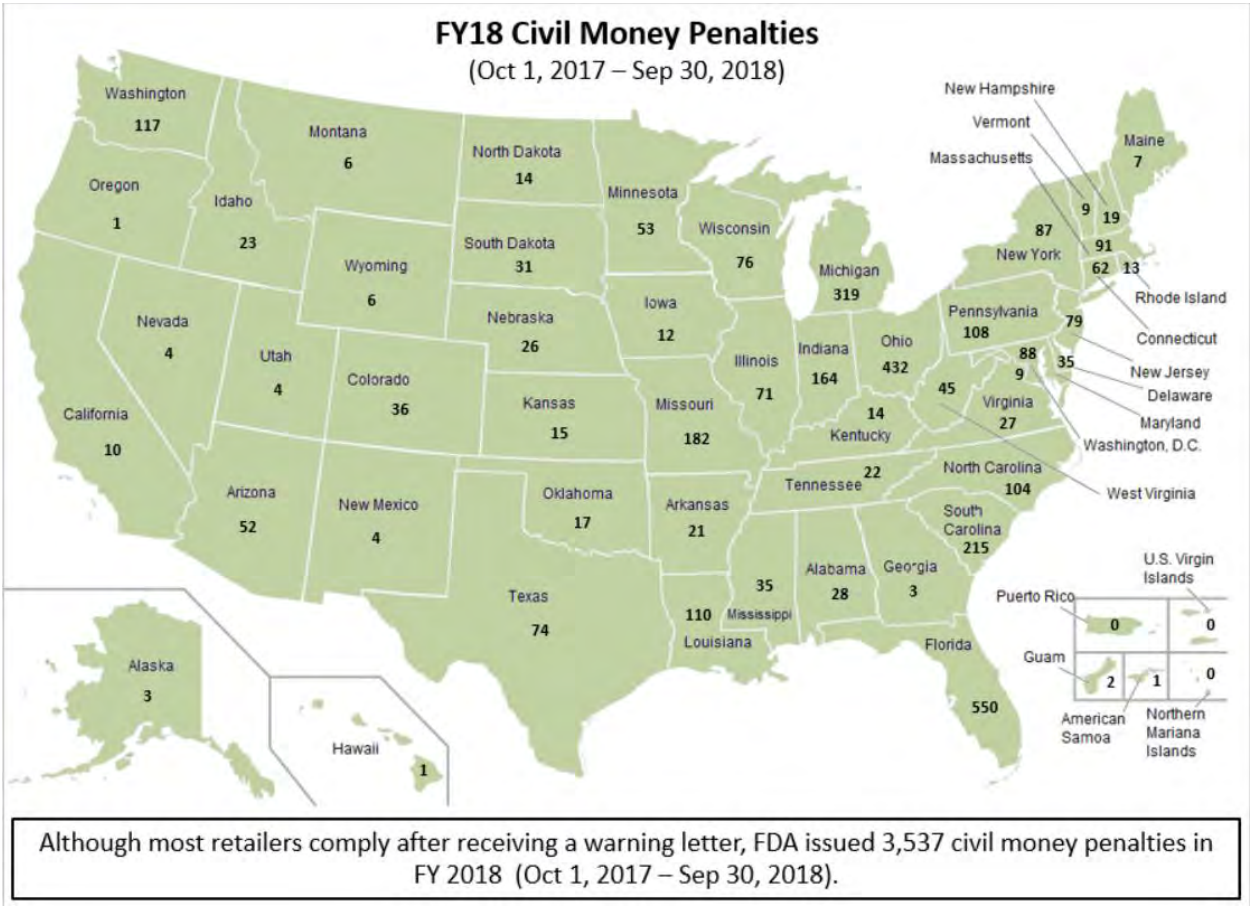

Figure 20 The number of Civil Money Penalty Complaints filed by the Center for Tobacco Products in FY 2018 by state.

Tobacco Retailer Education Program

"This Is Our Watch," is a voluntary national retailer education program designed to educate retailers on how to comply with federal tobacco laws, including deemed tobacco products. The program includes a free set of resources, such as a programmable calendar, designed to support retailers' efforts to educate staff on enforcing federal laws and regulations.

Tobacco Manufacturer Inspections

FDA regularly inspects registered establishments that manufacture or process tobacco products to determine compliance with existing laws and regulations. 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 October 31, 2018, CTP has overseen the completion of more than 900 inspections of vape shops to verify whether they were engaged in manufacturing activities, and ORA has completed over 400 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, including e-cigarettes and other ENDS products, in the U.S. market, and takes enforcement action when violations are found. As of October 31,

2018, FDA has issued over 690 warning letters as a result of these surveillance activities. In FY 2018, more than 115 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. CTP has produced over 65 compliance training webinars that explain in detail important requirements for industry manufacturers, importers, and retailers 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.

Public Education Campaigns

FDA's public education campaigns help educate the public—especially youth—about the dangers of regulated tobacco products. Achieving the FDA's mission to reduce tobacco-related death and disease requires a comprehensive, scientific, and innovative approach. FDA's tobacco use prevention campaigns focus on changing knowledge, attitudes and beliefs that lead to tobacco use, by following an evidence-based process to develop messages and tactics, including:

- identifying the problem to address
- researching the target audience and the best way to reach them
- testing messages and materials with the target audience
- sharing the messages using a variety of media
- assessing how effectively the messages reached the target audience and changing the messages if necessary.

FDA's current public education campaigns:

Campaigns	Launch date	Description
"The Real Cost" Campaign	February 2014	Educate at-risk youth aged 12 to 17 about the harmful effects of tobacco use.
"The Real Cost" Smokeless Campaign	April 2016	Educate at-risk male youth aged 12 to 17 about the harmful effects of smokeless tobacco use.
"The Real Cost" E-Cigarette (ENDS) Campaign	September 2018	Educate at-risk youth aged 12 to 17 about the harmful effects of e-cigarette use.
"Fresh Empire" Campaign	May 2015	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.
"This Free Life" Campaign	May 2016	Prevent and reduce tobacco use among Lesbian, Gay, Bisexual, and Transgender (LGBT) young adults aged 18 to 24.
"Every Try Counts" Campaign	January 2018	Encourages cigarette smokers to quit through messages of support that underscore the health benefits of quitting. Targets smokers ages 25-54 who have attempted to quit smoking in the last year but were unsuccessful.

The Real Cost

FDA's award-winning youth tobacco prevention campaign, "The Real Cost," continues to seek 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.

In its first two years, research shows the campaign has achieved its stated goals: "The Real Cost" prevented an estimated 350,000 teens ages 11 to 18 from initiating smoking between 2014 and 2016, half of whom might have gone on to become established adult smokers. Ultimately, preventing these kids from becoming established smokers has saved them, their families, and the country more than $31 billion by reducing smoking-related costs like early loss of life, costly medical care, and lower productivity.

Figure 21 "The Real Cost" campaign logo

These results not only reinforce the importance of our public education efforts in reducing the public health and financial burden of tobacco use, but also highlight the importance of investing in tobacco-related education campaigns. Investment in tobacco prevention can have huge returns: the campaign has a cost savings of $128 for every dollar invested in the first two years of the campaign. The campaign continues to air nationally across TV, radio, print, web, and social media, and new advertising will launch in January 2019.

"The Real Cost" smokeless campaign aims to shift rural teen boys' knowledge, attitudes, and beliefs about the dangers of smokeless tobacco. The campaign most recently launched new advertising in August 2018.

While evaluation of the smokeless campaign is still underway, preliminary data indicates that 85.9% of the target audience is aware of at least one of the campaign's videos. Data are also showing increased agreement with specific campaign targeted attitudes and beliefs that are correlated with reduced odds of smokeless use. For instance, agreement with several negative health consequence attitude and belief statements about smokeless tobacco are moving in the desired direction.

In September 2018, FDA expanded "The Real Cost" campaign to educate the nearly 10.7 million youth aged 12-17 who have ever used e-cigarettes or are open to trying them about the potential

risks of e-cigarette use. Campaign messages focus on educating youth that using e-cigarettes, just like cigarettes, puts them at risk for addiction and other health consequences.

Advertising and other prevention materials are delivered where teens spend most of their time—online and in school—including:

- online video ads
- additional content on "The Real Cost" campaign's youth-targeted website
- digital and social media content
- materials for use in high schools nationwide (e.g., posters for school bathrooms).

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.

Fresh Empire

"Fresh Empire" educates the nearly five million multicultural youth are open to sm

oking or are already experimenting with cigarettes about the harms of tobacco use. FDA launched new advertising in market in August 2018 to keep the target audience engaged with campaign messages.

Figure 22 "Fresh Empire" campaign logo

The 2018 Telly Awards named the "Fresh Empire" campaign the Bronze winner for both the Motivational category for Video / Shows / Segments, and Campaign for Social Responsibility categories. The Telly Awards honor excellence in video and television. In addition, the campaign earned the 2018 Platinum award for Event Marketing, and a Gold award for the effectiveness of its website. The Hermes is an international competition that honors excellence in communications and marketing.

This Free Life

FDA's "This Free Life" campaign targets LGBT young adult tobacco users because

they 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 two 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 signage, and local events to help prevent tobacco-related death and disease in the LGBT community.

Figure 23 "This Free Life" campaign logo

New advertising launched in Spring 2018, focusing on the 7,000 toxic chemicals found in cigarette smoke and how smoking harms nearly every part of your body.

The 2018 Telly Awards also named the "This Free Life" campaign the Gold winner in the Public Interest and Awareness category, and a Bronze winner in the Public Service and Activism category. Additionally, the campaign earned Platinum awards in three categories: YouTube video, social video and social marketing campaign.

Every Try Counts

In January 2018, FDA launched its first adult cessation campaign, "Every Try Counts." Approximately two out of three adult smokers, more than 22 million people, say they would like to quit.[104]

Figure 24 "Every Try Counts" campaign logo

However, in 2015, of the 55% of adult smokers who made a quit attempt, only seven percent were successful.[105] The "Every Try Counts" campaign is aimed at encouraging cigarette smokers to quit through messages of support that underscore the health benefits of quitting. These messages will be displayed in and around gas stations or convenience stores – retail locations where smokers face a multitude of triggers and that typically feature cigarette advertisements. The "Every Try Counts" campaign targets smokers ages 25-54 who have attempted to quit smoking in the last year but were unsuccessful. Ongoing research is planned for use in local campaign markets. Select campaign print ads are also available for use via the Centers for Disease Control and Prevention (CDC)'s Media Campaign Resource Center (MCRC). The MCRC provides access to advertisements for use by states and/or other public health organizations and agencies.

Outcome Evaluations

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 NCI 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 original Cohort and now Cohort 2 of "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.

"The Real Cost" Cohort 1 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, ultimately saving these kids, their families, and the country more

[104] Centers for Disease Control and Prevention (CDC). Quitting smoking among adults – United States, 2000-2015. Morbidity and Mortality Weekly Report. 2017;65(52):1457-1464.

[105] Centers for Disease Control and Prevention (CDC). Quitting smoking among adults – United States, 2000-2015. Morbidity and Mortality Weekly Report. 2017;65(52):1457-1464.

than $31 billion by reducing smoking-related costs like early loss of life, costly medical care, lost wages, lower productivity, and increased disability.

FDA is also conducting separate outcome evaluations of "The Real Cost" smokeless campaign messaging, the "Fresh Empire" campaign, the "This Free Life" campaign, and the "Every Try Counts" campaign to measure whether exposure to campaign messaging creates positive changes in tobacco-related knowledge, attitudes, beliefs, and intentions among the target audiences.

FUNDING HISTORY[106]

Fiscal Year	Program Level	Budget Authority	User
FY 2016 Actuals	$476,525,000	$0	$476,525,000
FY 2017 Actual	$754,076,000	$0	$754,076,000
FY 2018 Actual	$625,406,000	$0	$625,406,000
FY 2019 Annualized CR	$626,663,000	$0	$626,663,000
FY 2020 President's Budget	$761,739,000	$0	$761,739,000

BUDGET REQUEST

The FY 2020 Budget request is $761,739,000 all from user fees. This amount is $100 million above the FY 2020 level authorized in the Tobacco Control Act less the amounts for GSA Rent, FDA Headquarters, FDA White Oak Consolidation, and Other Rent and Rent Related, which are shown in their own sections of the budget request. This amount is $135,076,000 above the FY 2019 Annualized CR.

The Center for Tobacco Products amount in this request is $747,055,000. Currently, the Tobacco Control Act does not provide a means for FDA calculation of user fees for ENDS products and certain other deemed products. These products represent an increasing share of the tobacco marketplace as well as FDA's tobacco regulatory activities. This proposal includes a request to enable FDA to include all deemed products in the tobacco user fee assessments. FDA requests an additional $100 million and requests authority to include manufacturers and importers of all deemed products among the tobacco product classes for which FDA assesses tobacco user fees. To ensure that resources keep up with new tobacco products, the proposal would also index future collections to inflation.

In FY 2020, CTP will continue implementing the FDA-wide Comprehensive Plan for Tobacco and Nicotine Regulation, which the Center has incorporated into its six strategic priorities:

- Comprehensive Nicotine and Tobacco Regulatory Policy
- Premarket and Postmarket Controls: Regulations and Product Reviews
- Product Standards
- Public Education
- Compliance and Enforcement
- Investing in Human Capital

[106] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

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. Most recently, in November 2018, Commissioner Gottlieb announced several new steps being taken to advance the comprehensive plan for tobacco and nicotine regulation and protect youth by preventing access to flavored tobacco products and announcing plans to ban menthol in combustible tobacco products, including cigarettes and cigars.

FDA will continue to implement the comprehensive plan by:

- holding a public hearing on January 18, 2019 to discuss our efforts to eliminate youth e-cigarette use, focusing on the potential role of drug therapies to support cessation
- considering regulatory guidance on premarket review policy based on the principle of relative toxicity and risk
- working on foundational rules such as proposed rules on Substantial Equivalence, Tobacco Product Manufacturing Practices, PMTAs and MRTPs.

FDA is continuing efforts with the Nicotine Steering Committee, in conjunction with FDA's Center for Drug Evaluation and Research (CDER) and FDA's Office of the Commissioner to include:

- examining the science behind the Agency's evaluation of nicotine replacement therapies (NRTs)
- examining the types of safety and efficacy studies FDA requires and how these products are used and labeled.

Comprehensive Nicotine and Tobacco Regulatory Policy

FDA will continue pursuing the nicotine work mentioned above, as well as:

- continuing a national dialogue on nicotine to increase knowledge and understanding of the addictive nature of nicotine to better protect the public's health
- developing opportunities for global collaboration to learn from other governments' research, experiences, and challenges to inform our domestic efforts.

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 obtain FDA authorization before marketing new[107] tobacco products:

- by demonstrating they are appropriate for protection of public health, or
- by demonstrating substantial equivalence[108] to certain commercially marketed products.

[107] New tobacco product includes products with any modification after February 15, 2007.

[108] An alternative to new product applications where the characteristics are the same as predicate products (which is a product that was commercially marketed in the United States as of February 15, 2007, or a product previously found to be substantially equivalent) or the characteristics are different, but the product does not raise different questions of public health.

To help industry better understand expectations and aid them in preparing complete applications, CTP is exploring developing additional rules and guidances for product review pathways, tobacco product manufacturing practices, and registration and product listing. This will improve transparency and provide consistent submission guidelines which will facilitate industry's preparation of applications and speed application review by FDA staff. In addition to developing rules and guidances, CTP will continue to monitor performance measures for product reviews, including new performance measures added in FY19 for provisional SE Reports. In addition to working on foundational rules for application pathways, CTP is reviewing the process for review of SE Reports to identify areas where process improvements could enhance CTP work efficiencies. CTP is also hiring additional scientific staff to review product applications.

Product Standards

Section 907 of the Federal Food, Drug, and Cosmetic Act gives FDA the authority to issue, via notice-and-comment rulemaking, tobacco product standards that are appropriate for the protection of the public health. This authority is one of the most powerful tools that FDA has to regulate tobacco. CTP is advancing a product standard strategy to yield strong standards to improve public health, by exploring potential standards for addictiveness, toxicity, and appeal.

FDA is actively considering the need for other product standards. In July 2017, Commissioner Gottlieb announced FDA's intent to develop product standards to protect against known public health risks such as ENDS battery issues and concerns about children's exposure to liquid nicotine. FDA also is pursuing a product standard for establishing limits on the level of toxicants and impurities found in certain ENDS ingredients. And in November 2018, FDA announced its intention to move forward with proposed rulemaking to ban menthol in cigarettes and all flavors, including menthol, in cigars, on an expedited timeline.

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. 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.

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 2020, 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

- continue to use our communication tools (website, social media, email marketing, and stakeholder outreach) to reach consumers, public health stakeholders, and industry.

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.

FDA is currently revising its compliance policy that sets a compliance deadline of August 2022 for submission of premarket applications for ENDS. This revision means that ENDS products that are marketed to children and/or appealing to youth will no longer be subject to the compliance policy, and all flavored ENDS products (other than tobacco, mint and menthol flavors or non-flavored products) will no longer be subject to the policy unless they are sold in age-restricted, in-person locations or sold online with heightened age verification processes. The effect of not being subject to this compliance policy is that products must come off the market unless they submit a premarket application and receive marketing authorization from FDA. Continued planned activities include:

- reviewing FDA's current compliance policy to determine whether it can better account for manufacturers that are not successfully preventing widespread youth use of their products
- indefinitely stepping up enforcement actions with a sustained campaign to monitor, penalize, and prevent ENDS sales in convenience stores and other retail sites
- closely evaluating manufacturers' internet storefronts and distribution practices and taking enforcement actions if violations of the restrictions on sales to minors are found
- investigating whether manufacturers of certain ENDS products may be marketing new products that have not gone through premarket review
- conducting compliance check inspections via the Tobacco Retailer Inspection Program[109]
- coordinating with ORA to conduct inspections of tobacco manufacturing facilities
- coordinating inspections of vape shops to determine whether they conduct manufacturing activities
- providing outreach, education, and assistance to small tobacco manufacturers and retailers via CTP's OSBA
- enforcing promotion, advertising, and labeling requirements
- conducting surveillance, inspections, and investigations
- identifying criminal violations in tobacco-related cases.

Investing in Human Capital

FDA will continue to invest 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 Federal Employee Viewpoint Survey. FDA also promotes employee diversity and inclusion to cultivate an engaged workforce that reflects the country it serves.

[109] 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

Additional FY 2020 Support Activities

FDA will continue to:

- partner with other agencies, including NIH, CDC, and FDA's NCTR 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
- fund PATH Study analyses and sub-studies via NIH to more comprehensively examine new and emerging issues related to tobacco use behavior and health
- collect and analyze PATH Study participant responses and biomarker data to assess tobacco use transitions over time
- explore the addition of questions to the National Health Interview Survey cancer control supplemental questionnaire
- conduct priority research with research contract organizations.

PERFORMANCE

The Tobacco Control Act Program's performance measures focus on activities in order to achieve public health goals, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
280005: Total number of compliance check inspections of retail establishments in States under contract. *(Outcome)*	FY 2018: 146,398 Target: 130,000 (Target Exceeded)	130,000	130,000	Maintain
280006: Review and act on Regular SE Reports within 90 days of FDA receipt (applies to cigarettes, cigarette tobacco, smokeless tobacco, and roll-your-own tobacco products) *(Output).*	FY 2018: 95% Target: 80% (Target Exceeded)	80%	80%	Maintain
280007: Educate at-risk general market 12-17 year olds about the harmful effects of tobacco use. *(Output)*	FY 2018: Reached 75% of general market at risk 12-17 year olds with campaign	Reach 65% of 12-17 year olds with campaign messaging	Reach 65% of 12-17 year olds with campaign messaging	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
	messaging. (Target Met)	within 1 year.	within 1 year.	

COMPLIANCE CHECK INSPECTIONS

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 146,000 compliance check inspections of retail establishments in FY 2018. Although this number was much higher than the expected FY 2018 full year target of 130,000, 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 2019, 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 2019 and FY 2020 targets consider these challenges and will therefore remain at the FY 2018 target levels.

REGULAR SE REPORTS

Review and act on includes issuing a Deficiency letter (e.g. Advice/Information Request letter, Preliminary Finding letter), Cancellation, Closure, SE Order or NSE Order.

EDUCATE AT-RISK GENERAL MARKET 12-17 YEAR OLDS

"The Real Cost" reach target has changed for FY 2019 because the e-cigarette prevention campaign is limited to airing on age-verified digital media only, which limits the amount of reach possible. This strategy was driven by research that indicated adult smokers who saw "The Real Cost" e-cigarette ads may be less likely to use e-cigarettes to attempt to quit smoking.

PROGRAM ACTIVITY DATA

CTP Workload and Outputs	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget
Tobacco Retailer Inspections			
Number of Inspections	146,398	130,000	130,000
Tobacco Manufacture Inspections			
Number of Inspections [1]	96	200	300
Substantial Equivalence Reviews			
Number of Regular SE Reports	104	100	100

[1] Outyear estimates are based on the number of firms registered with FDA. FDA works to inspect each registered firm biennially.

FDA HEADQUARTERS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
FDA Headquarters	**290,638**	**315,684**	**299,587**	**320,164**	**20,577**
Budget Authority	***171,195***	***171,001***	***171,195***	***180,195***	***9,000***
User Fees	***119,443***	***144,683***	***128,392***	***139,969***	***11,577***
Prescription Drug (PDUFA)	50,082	60,244	56,391	59,194	2,803
Medical Device (MDUFA)	7,811	7,297	8,463	9,209	746
Generic Drug (GDUFA)	34,489	27,947	35,243	35,784	541
Biosimilars (BsUFA)	706	1,393	632	1,022	390
Animal Drug (ADUFA)	446	828	1,004	734	-270
Animal Generic Drug (AGDUFA)	63	73	785	26	-759
Family Smoking Prevention and Tobacco Control Act	24,491	46,921	24,491	30,867	6,376
Mammography Quality Standards Act (MQSA)	92	-20	92	102	10
Food and Feed Recall	75	---	75	78	3
Food Reinspection	480	---	480	499	19
Voluntary Qualified Importer Program	277	---	277	288	11
Third Party Auditor Program	39	---	39	41	2
Outsourcing Facility	392	---	420	225	-195
Innovative Food Products (Proposed)	---	---	---	1,900	1,900
FTE	**943**	**943**	**1,001**	**1,018**	**17**

*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.

FDA reduces the burden of addiction crises that are threating American families by working to:

- reduce harms from opioid addiction and abuse
- implement a Comprehensive Nicotine Strategy and Youth Use/Enforcement Strategy.
- monitor post market safety of drugs.

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.[110]

Foster Competition and Innovation

FDA HQ fosters competition and innovation by:

- continuing to implement FDARA and 21st Century Cures Act
- pricing/access with biosimilars
- supporting biotech innovation
- harnessing real-world evidence

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

- supporting international harmonization.

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 competition and innovation 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.

21st Century Cures Act and Food and Drug Administration Reauthorization Act (FDARA) of 2017

As part of the 21st Century Cures Act and the Food and Drug Administration Reauthorization Act (FDARA) of 2017, Congress is considering potential legislation that could impact medical product approval standards and regulatory pathways in an effort to expedite getting innovative products onto the market. FDA's work with respect to the initiatives has involved consolidating input from Centers and Offices across the Agency. Implementation of the 21st Century Cures Act and FDARA are priorities for FDA's authorizing committees, and the Agency has worked diligently to provide timely feedback to Congressional offices.

21st Century Cures Act and Human Subject Protection Harmonization

The 21st Century Cures Act (Cures Act) Section 3023 requires harmonization of the HHS and FDA human subject protection regulations. FDA is continuing to harmonize differences between its regulations and the Common Rule, that was revised January 19, 2017[111], 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 further refine FDA's compliance program for the HHS regulations requiring clinical trial registration and results reporting on ClinicalTrials.gov (42 CFR part 11). FDA HQ continues to provide consultation to NIH to support reports required under the Cures Act related to ClinicalTrials.gov

[111] https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf The compliance date of the revised Common Rule has been delayed until January 21, 2019; see https://www.gpo.gov/fdsys/pkg/FR-2018-06-19/pdf/2018-13187.pdf

Regulatory Policy and Guidance

FDA HQ led the development of FDA's regulations on acceptance of clinical data for medical devices.[112] FDA developed a guidance to accompany the final rule; both were issued in February 2018.

FDA HQ led the development of a notice of proposed rulemaking (NPRM) to allow an exception from the requirements to obtain informed consent when a clinical investigation poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of human subjects.[113] This proposed rule, if finalized, would implement a provision of the 21st Century Cures Act and harmonizes with the revised Common Rule. FDA issued the NPRM in November 2018.

Guidance Documents – Human Subject Protection and Good Clinical Practice

Below are selected guidance documents on human subject protection issued by FDA HQ in 2018. This list does not represent any degree of importance or priority ranking among those items.

Publication Date	Formal Title	Description
October 2018	Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations[114]	This level 2 guidance clarifies the impact of certain provisions of the HHS revisions to the Common Rule regarding informed consent, expedited review, and continuing review, on FDA-regulated clinical investigations.
May 2018	IRB Written Procedures[115]	This joint final guidance with HHS describes regulatory requirements for IRB written procedures and provides recommendations on operational details to comply with the requirements.
February 2018	Acceptance of Data from Clinical Investigations for Medical Devices – Frequently Asked Questions[116]	This guidance provides recommendations for submission of information when clinical data from device investigations conducted within or outside the US are submitted to support research or marketing applications or other submission.

[112] 83 FR 7366; https://www.gpo.gov/fdsys/pkg/FR-2018-02-21/pdf/2018-03244.pdf

[113] 83 FR 57378; https://www.gpo.gov/fdsys/pkg/FR-2018-11-15/pdf/2018-24822.pdf%20

[114] https://www.fda.gov/RegulatoryInformation/Guidances/ucm623197.htm

[115] https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM512761.pdf

[116] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm597273.pdf

Publication Date	Formal Title	Description
January 2018	Payment and Reimbursement to Research Subjects – Information Sheet Guidance[117]	This information sheet guidance clarifies that reimbursement for human subjects' travel expenses to and from the clinical trial site and associated costs (e.g., parking, lodging) would not raise issues regarding undue influence.

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 https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm.

Geographic Information System Mapping

In FY 2018 the FDA HQ Geographic Information System (GIS) team conducted risk modelling and incident preparedness and recovery support for incidents including real-time support for the 2018 Hurricane Season. FDA HQ completed maps for 100 GIS project requests involving FDA regulated firms.

Global Health Security and Counterterrorism

FDA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security, counterterrorism efforts, and address emerging threats. FDA HQ:

- serves as point of entry on policy and planning matters
- serves 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
- coordinates 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 a robust regulatory science research program to improve FDA's ability to perform science-based review of MCMs designed to lessen the effects of CBRN and emerging infectious disease threats. Accomplishments in FY 2017 and FY 2018 include:

- 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
- sponsoring nonclinical research studies to help inform FDA recommendations regarding potential transmission of Zika virus via organs and tissues

[117] https://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm

- developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during public health emergencies.
- expanding a database of regulatory-grade nucleic acid sequences to include antimicrobial-resistant organisms as well as Ebola- and Zika-related sequences
- developing Zika virus RNA reference materials that were distributed to manufacturers to validate nucleic acid based diagnostic tests and blood screening testing methods
- making available a Zika serological reference panel to aid in the regulatory evaluation of serological tests for the specific detection of recent Zika virus infection
- continuing the development of improved small animal models for Ebola and Zika
- developing a toolkit to assess efficacy of Ebola vaccines and therapeutics
- conducting survivor studies to better understand Ebola's after-effects, to help find new treatments
- addressing potential production bottlenecks for seasonal and pandemic influenza vaccines by developing novel alternative methods to measure influenza vaccine potency and generate reagents needed for vaccine standardization.

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 2017 and FY 2018 that support MCMs include:

- issuing 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
- issuing draft guidance on implementation of the Material Threat Medical Countermeasure Priority Review Voucher program
- using the expiry dating extension authority to authorize use of MCMs beyond their labeled expiry date to prevent shortages of critical products
- advancing efforts to create a national capability to track, collect, analyze, and evaluate information related to MCMs used during public health emergencies to inform real-time decisions about the safety and effectiveness of these MCMs
- addressing issues related to use of expanded access mechanisms and EUAs to make available unapproved MCMs for CBRN and other emerging infectious disease threats
- clarifying regulatory issues around building frameworks for conducting clinical studies during public health emergencies

FDA HQ facilitated coordination of response activities to emerging public health threats including the Ebola outbreak in the Democratic Republic of Congo 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 8 diagnostic tests for Zika virus under the EUA authority (in addition to 12 similar EUAs issued

for Zika virus diagnostic tests issued in FY2016) and a rapid, single-use diagnostic test for the detection of Ebola virus,which is the second Ebola rapid antigen fingerstick test available under EUA, but the first that uses a portable battery-operated reader, which can help provide clear diagnostic results outside of laboratories and in areas where patients are likely to be treated.

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:

- 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.

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
- 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 (FDA has subsequently approved this product).

FDA HQ also continued to advance efforts to facilitate the development and availability of medical products to support American military personnel. For example, FDA issued an EUA to enable the emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma for the treatment of hemorrhage or coagulopathy of U.S. Military personnel during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. FDA HQ also established a Memorandum of Understanding with the DoD setting forth a framework for the ongoing partnership with DoD and the creation of a robust program that can better serve the health care needs of American military personnel.

FDA HQ also continued to provide public information and education on FDA preparedness and response activities via events, press releases and interviews, the FDA website and social media.

International Inspections, Information Sharing, and Strategic Engagement

FDA HQ works with its regulatory counterparts and stakeholders abroad to ensure that products coming to the US market are safe, effective and of high quality. FDA HQ through its Office of Global Policy and Strategy, oversees four FDA country and regional offices, China, Europe, India, and Latin America, in seven locations abroad, with additional countries and regions

covered by HQ. Interactions with foreign regulators and stakeholders that benefit American public health include: expanding FDA inspectional capacity and making improvements to inspections; partnering to share information and expertise to strengthen foreign regulatory systems; strategic engagement and outreach to our foreign counterparts; and continued implementation of the China Safety Initiative.

During FY 2018, according to data as of November 1, 2018, investigators based in-country or on short-term assignments to China, India and Latin America from ORA conducted 536, 443, and 389 inspections respectively, slightly increasing its capacity from the previous year. FDA country and regional office staff, as well as investigators based in country or on short-term assignment to those offices, conduct foreign inspections that provide invaluable in-country insight and lead to improved future inspections. An example of improvements to inspections occurred this past fiscal year when the India Office developed a Foreign Export Inspection Guidance for CSOs. After its FY 2018 analysis of inspectional trends, and India export data and seasonality harvesting information, the Office added Guar Gum inspections to its inspection workplan for FY 2019. Guar gum is the second highest (by value) food commodity exported by India to the US, but there was minimal inspection data on these firms in the past. This action by the India Office will provide more targeted inspections on an important commodity.

The Office of Global Policy and Strategy's foreign offices often collaborate with regulatory authorities to create solutions to issues found in inspections. For example, in FY 2018, the India Office participated in a Canada/EU/India/FDA Workshop entitled "Indian Food Exports: Understanding Regulatory & Safety Requirements." The India Office provided information on FDA food facility inspections, food safety issues, and FSMA. Relevant to the region, over 350 participants gained information on seafood HACCP. The workshops were held in Delhi, Chennai, and Mumbai and provided opportunities for strategic partnership-building with counterparts from the Canada, the EU and India.

An example of FDA's foreign offices partnering to share information and expertise occurred in in FY 2018 in the FDA's China and Europe Offices. The China Office planned and conducted an inspection workshop between the China Food and Drug Administration and FDA. It shared FDA important inspection practices with attendees in Beijing. The Europe Office organized a bilateral conference with the European Medicines Agency to promote regulatory cooperation and alignment. The conference included sessions on generic drugs and tobacco regulation and included attendance and participation from international leads and FDA Center leadership. The conference sessions led to better understanding of FDA's regulatory requirements and positions on key issues by EU counterparts and the identification of strategic areas for future cooperation.

During FY 18, FDA established 3 new 21 CFR 20.89 Confidentiality Commitments with:

- The Health Canada Regulatory Operations and Regions Branch (RORB) regarding Drugs, Biologics, Medical Devices, Radiation-Emitting Products, Tobacco, Foods, Animal & Veterinary regulated products as part of cooperative law enforcement or cooperative regulatory activities.
- Chile National Director of Fisheries and Aquaculture Service (SERNAPESCA) regarding seafood regulated products as part of cooperative law enforcement or cooperative regulatory activities.
- South African Health Products Regulatory Authority (SAHPRA) regarding Drugs, Biologics, Medical Devices (including in vitro diagnostics and radiological health

products), Cosmetics and Dietary Supplements as part of cooperative law enforcement or cooperative regulatory activities.

FDA also established 23 new trade secret information confidentiality commitments pursuant to section 708c of the Food, Drug, and Cosmetic Act, to help advance the goals of the Mutual Reliance Agreement (MRA). Eighteen of these were signed with EU member states to facilitate the exchange of non-public information related to FDA regulated human drugs, while five of them were signed to facilitate the exchange of non-public information related to FDA regulated veterinary drugs. In addition, FDA signed one Cooperative Arrangement in October 2017 to facilitate regulatory activities. This research MOU with the Canadian Food Inspection Agency promotes sharing information and data. Specifically, it facilitates collaborative research projects related to the research, development, and validation of microbiological and chemical detection methodologies, and the evaluation of novel and innovative technologies.

In-country relationships with foreign regulatory counterparts enable FDA to leverage their respective regulatory capabilities, ensuring safer regulatory programs throughout the world, and ultimately protecting public health in the US. A demonstration of the FDA engaging its foreign counterparts and therefore leveraging that authority can be seen from late 2017 through early 2018 in Mexico during an investigation of a U.S. Salmonella outbreak. After learning from its regulatory counterparts in Mexico of suspected salmonella stemming from Mexican papaya, the FDA's Latin America Office's in Mexico City provided feedback to FDA's CORE network. This intel was used by CORE to change their list of possibly-suspect firms. FDA's 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 for 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 to identify the appropriate type of such investigation for a specified firm.

In other engagement activities, FDA Europe and China Offices, working with CFSAN and Office of Food Policy and Response (OFPR) supports, 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 late 2017, the parties met to discuss import and export controls, e-Commerce, and risk communication, all important topics to implementing existing legislative authorities.

In addition, in 2017 and 2018 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. 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.

FDA's India Office engaged in a series of in-person Seafood HACCP and U.S. Food Labeling workshops in Mumbai and Nellore in late 2017. These workshops improved participants' understanding of sanitation and prevent seafood safety hazards, and in turn, protect American public health. Almost 100 individuals were trained, providing the India government and industry participants with this important information.

In another engagement example, the Latin America Office collaborated with the Chilean Agriculture Commission (SAG) and ANASAC Chile (pesticide manufacturer) to identify potentially adulterated table grapes, wine grapes, and tomatoes from Chile. The testing results were shared with FDA through their International Arrangement and demonstrated SAG's commitment to providing safe food products, which is then passed on to the American consumer. In this case, the Latin American Office was able to act in coordination with the SAG when a Chilean pesticide manufacture notified it that one of its products was incorrectly formulated.

Engagement and outreach also includes interaction with international organizations. For example, at HQ the Office of Regional and Country Affairs (ORCA) established a new Cooperative Agreements (CoAg) with WHO to strengthen regulatory systems and ensure the safety and quality of food and medical products in FY 2018. The CoAg supports well-established collaborations between WHO and FDA in support of data-driven and science-based public health, research strategies, and approaches that align with FDA domestic and global goals. This agreement contributes to the knowledge base of the current regulatory efforts in support of global efforts to ensure quality of food and medical product quality and safety.

Continued Implementation of the China Safety Initiative International Partnerships

The China Safety Initiative (CSI) continues to allow FDA to expand its efforts to regulate the quality, safety and efficacy of FDA-regulated products exported to the United States from China. The primary focus of CSI was the expansion of the number of in-country FDA investigators, which was accomplished through a negotiated agreement with the Chinese government. In FY 2018, the China office completed 226 inspections focused on foods, animal feed, and animal drugs. The China Office conducted all assigned FDA food facility inspections in China.

To protect US consumers and enhance public health, inspections conducted by foreign office consumer safety officers (CSOs) the China Office conducts High Risk, For Cause, Follow-up priority inspections, collects regulatory information, and conducts regulatory trend analysis in conjunction with its CSOs and International Relations Specialists. It also ensures timely reporting via existing regulatory systems, as appropriate. This includes eNSPECT, FACTS, and/or Global Watch. This reporting allows the Agency to make informed decisions based on significant risk and provide critical regulatory intelligence to Centers and ORA that will assist in better risk-based regulatory decision making and work planning. This effort maximizes regulatory compliance and minimizes risk associated with those products from China exported to the US.

China also provides its Chinese regulatory counterparts with training to ensure the safety of its products being exported. In FY 2018, FDA's China Office also conducted a regulator-to-regulator workshop with the China National Drug Administration (CNDA)'s Center for Food and Drug Inspection (CFDI) in Beijing, China, focused on promoting and enhancing mutual understanding of how inspections are conducted by each regulatory authority. In collaboration with the India Office, FDA headquarters, and high-level representatives from U.S. FDA's Office of Regulatory Affairs (ORA), the China Office planned and conducted the workshop ensuring participants had opportunities to share their inspection experiences with others.

Leveraging the Regulatory Capabilities of Foreign Counterparts, Leading FDA's Engagements with the Government Accountability Office (GAO) and the Office of the Inspector General (OIG)

FDA HQ staff coordinates the Agency response to all requests from GAO and OIG. For each of the several dozen ongoing engagements, FDA HQ staff complete the following:

- identify appropriate subject matter experts
- coordinate and develop of FDA responses
- collect and submit data in response to requests
- assemble and edit Agency responses to draft reports
- ensure consistency with Agency legal and policy positions.

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, a greater number of these recommendations have been closed, and a greater proportion have been closed as implemented.

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

In FY 2018, FDA HQ:

- received 410 first-time requests for orphan drug designation and designated 289 promising drugs and biological products for rare diseases
- received 14 first-time requests for Humanitarian Use Device designations and designated 16 promising devices for rare diseases and conditions
- received 45 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 39 drugs and biologics for rare pediatric diseases
- funded 11 new clinical trial grant awards and 75 ongoing grants funding clinical studies of promising therapies for rare diseases
- funded 6 natural history grant awards to inform medical product development by better understanding how specific rare diseases progress over time
- funded 5 new pediatric device consortia with 3 real world evidence projects to provide multidisciplinary advice and funding to assist pediatric device innovators.

Premarket and Postmarket Support

In FY 2017, with respect to combination products, FDA HQ provided clarification and support for approximately 560 premarket applications, 1,419 inter-center consults and 74 post market activities. FDA HQ issued 8 formal requests for designation decisions (5 for combination products and 3 for non-combination products) with 100 percent of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also provided timely informal jurisdictional assistance for 78 separate Pre-RFD submissions (informal inquiries) and 48 FDA center-requested classification and assignment consultations. In FY 2017, FDA HQ also responded to 525 requests for product-specific assistance, the responses to which contributed to ensuring the timely and effective review of combination products.

In FY 2018, FDA HQ issued guidance on How to Prepare a Pre-Request for Designation (Pre-RFD) and on Postmarketing Safety Reporting for Combination Products Draft. As required by the 21st Century Cures Act (Cures Act), the FDA proposed a list of alternative or streamlined mechanisms for complying with the current good manufacturing practice (CGMP) requirements

for combination products. The FDA also proposed to amend 21 CFR Part 3 concerning the classification and assignment of medical products. The proposed rule clarifies the scope of the regulations, streamlines and clarifies the appeals process, and aligns the regulations with more recent legislative and regulatory measures. The Agency also issued Staff Manual Guide (SMG) 4101 entitled Combination Products Inter-center Consult Request Process and SMG 4103 entitled Expectations and Procedures for Engagement Among Medical Product Centers and Office of Combination Products on Regulations and Guidance Pertaining To Combination Products. Both SMGs are intended to promote inter-center collaboration and enhance efficiency and consistency in combination products regulation.

In late 2017, FDA HQ hosted an EMA fellow's visit to FDA to learn more about how FDA regulates combination products and also to share experience between EMA and FDA on regulatory, development and assessment challenges of different kinds of combination products. FDA also shared how the medical product Centers and the Oncology Center of Excellence collaborate in regulating oncology products including combination products. Subject matter experts from CBER, CDER, CDRH, and OCE participated in this effort.

In FY 2017, FDA HQ provided clarification and support for approximately 560 premarket applications, 1,419 intercenter consults and 74 combination product post market activities. FDA HQ issued 8 formal requests for designation decisions (5 for combination products and 3 for non-combination products) with 100 percent of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also provided timely informal jurisdictional assistance for 78 separate Pre-RFD submissions (informal inquiries) and 48 FDA center-requested classification and assignment consolations.

Pediatric Coordination

FDA HQ, working in conjunction with Center subject matter experts through the Pediatric Cluster, met to discuss pediatric scientific issues with European Medicines Agency (EMA) on 170 issues in FY 2018. Of the 170 issues discussed with the EMA, harmonization was achieved for 70 percent. Examples of the most frequent issues discussed included scope of pediatric development, dosing, regulatory issues/actions, safety and study design.

FDA HQ promoted high standards of scientific integrity by providing expert ethical opinions to agency Centers and Offices on a variety of ethical issues, with the completion of more than 50 consult reviews in FY 2018. These ethical issues included:

- study design considerations in pediatric rare disease populations
- gathering Pediatric Advisory Committee and patient and caregiver input on ethical and scientific issues related to the development of appropriate study endpoints
- review of research involving the exceptions from informed consent requirements for emergency research.

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)

- initiating research studies with colleagues across the FDA Centers as well as with external scientific researchers
- providing neonatal-perinatal medicine consultations across the FDA Centers with 31 consults completed in FY 2018
- co-organizing an expert workshop with the Duke-Margolis Center for Health Policy on "Advancing Endpoint Development for Preterm Neonates with Pulmonary Morbidities"
- co-developing a draft Guidance document on Neonatal Clinical Pharmacology studies.

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).

In FY 2018, these efforts included:

- completed 67 pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews) that were reviewed by FDA's PAC in comparison to 34 in FY2017.

This is a direct result of the risk-based assessment process in which the low safety risk products now have their mandated pediatric-focused safety reviews posted on FDA's website. The new pediatric safety review process has resulted in a profound reduction in the backlog of mandated safety reviews. FDA HQ, enhanced international pediatric collaborations by working in conjunction with Center subject matter experts through the Pediatric Cluster to discuss pediatric scientific issues with European Medicines Agency (EMA), Health Canada, PMDA, and TGA.

In FY 2018, these efforts included discussion of 188 issues, where a number of issues could be discussed with respect to an individual product. Out of the 188 issues discussed, harmonization was achieved for 70 percent. Examples of the most frequent issues discussed included scope of pediatric development, dosing, regulatory issues/actions, safety and study designs.

Empower Consumers and Patients

FDA is committed to empowering consumers and patients to make better and more informed decisions about their diet and health and to expand opportunities to use nutrition to reduce illness and death from disease.

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[118]

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

Communication with Stakeholders - Improvements to FDA.gov

FDA is working to improve the usability of FDA.gov, our public-facing web site, by transitioning to Drupal, a new state-of-the-art content management system (CMS), in February 2019. The Drupal platform will offer visitors better navigation tools to more easily find and share FDA content through web sites, mobile applications, and social media channels. In addition, the new platform will make it easier for the agency to highlight priority content and most requested content on our home page and topic landing pages, which reflects feedback from visitors to FDA.gov. To prepare for this transition, the FDA has archived over 65,000 old and outdated content items. In addition, the FDA is working to improve the information architecture across 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.

FDA is also working to specifically enhance the For Patients webpages to best meet informational needs of patients, family members, and advocates that will assist them in locating medical product information and opportunities to engage with FDA. For example, HQ has developed a table summarizing several of the agency's patient engagement initiatives. In addition, HQ has initiated the development of a centralized point of entry into FDA for inquiries and meeting requests from patients, family members, and patient advocates. The central entry point will streamline routing processes to ensure inquiries are received and responded to in an effective and efficient manner. Finally, an education video series about the agency's mission, patient engagement initiatives and how to begin navigating the agency is also part of these web enhancements and improvements.

Communicating with Stakeholders -Eloqua Email Delivery Service

FDA HQ has implemented the Eloqua email delivery system to send priority agency announcements/content to stakeholders who opt-in to receive these notifications. The FDA uses Eloqua to send device-friendly emails on important topics to keep stakeholders informed and drive traffic to FDA.gov. Currently, the FDA has 140 content topics available and over 1.5 million stakeholders who have subscribed to receive information. The topic of Recalls currently has more than 405,000 subscribers.

Meetings with Stakeholders (non-media)

Since May 2017, FDA HQ has conducted nearly 685 meetings or interactions with a wide range of stakeholders representing trade associations, consumer groups, healthcare professional organizations, research and policy institutions, and patient/disease-specific groups.

FDA HQ has also used social media to engage with our stakeholders, via Facebook, multiple Twitter accounts, Instagram, YouTube, and other channels. The agency conducted two Twitter chats, including one targeting a bilingual (English- and Spanish-speaking) audience.

The agency has also recruited and trained over 40 new patient representatives, selected for their experience and advocacy with specific medical conditions and diseases. The new representatives, who serve as special government employees to the FDA's Advisory Committees, bring the total number of patient representatives to approximately 200. In July 2017, the FDA conducted a workshop for patient representatives, providing them with an opportunity to learn about the FDA regulatory process and understand their responsibilities in this valuable collaboration.

Additionally, the FDA HQ co-chairs 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.

In collaboration with the Clinical Trials Transformation Initiative, FDA HQ established the Patient Engagement Collaborative, comprised of external patient community stakeholders, who will offer their experiences and perspectives on patient engagement in FDA's regulatory processes. Following an official call for nominations, a selection committee chose 16 individuals to serve as the first slate of members. An emphasis was placed on ensuring involvement of representatives with a variety of perspectives and inclusion of patients, caregivers, and representatives from a diversity of patient communities. The first slate begins their 2-3 year terms in August 2018.

Stakeholder Outreach Activities

MedWatch Product Safety Communications: FDA HQ issued over 221 MedWatch Safety Alerts since May 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, including one in Spanish. 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. 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 May 2017.

Healthcare Practitioners: FDA HQ has six stakeholder engagement related MOUs currently in place to facilitate interaction with health care provider groups, which allows the agency to leverage relationships to extend communication and learning opportunities for providers across the county, designed to ultimately benefit patients and improve outcomes. For example, as part of a Memorandum of Understanding (MOU) with the American Nurses Association, HQ conducted a joint webinar on November 16, 2017, "An Opioid Primer: Legislative, Policy, & Practice Implications." The 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 nurse's associations and its organizational affiliates.

Rural Health Symposium: FDA HQ held its inaugural Rural Health Symposium on October 26, 2017. The Symposium provided 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).

Rare Disease Listening Sessions Pilot: FDA HQ also established a Memorandum of Understanding (MOU) with the National Organization for Rare Disorders to help conduct outreach (e.g., pilot listening sessions) on ways to expand the inclusion of patient-related experience into FDA regulatory decisions on rare diseases and conditions. HQ has identified therapeutic areas to help foster early and iterative engagement on key clinical and regulatory issues. The first therapeutic area is genetic disorders.

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, the FDA acquired 300 artifacts, saw to the preservation through digital conversion of 33,000 pages of textual documents, and just over 2,900 pages of graphic rich materials from the 1940s to the 1980s, and arranged for the preservation through digital conversion of over 6,450 historical images and 200 historical videotapes in an antiquated format. The FDA also promoted on social media 5 history video blogs and 19 written stories about historically significant FDA artifacts.

Thus far in FY 2019, the FDA produced three important exhibits on different aspects of the agency's history to inform staff and the public about critical turning points in the agency's evolving regulatory powers, and is currently finalizing a contract on a fourth but more prominent Smithsonian quality exhibit. The FDA arranged for the preservation through digital conversion of approximately 100 historical film reels in various states of deterioration, and promoted on social media 2 history video blogs and 13 written stories about historically significant FDA artifacts. The FDA also coordinated efforts to accept a gift of approximately 4,500 historically significant pharmaceutical artifacts.

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, health care professionals, patients, news media, policymakers, regulated industry and others.

From May 1, 2017 through November 2018 FDA HQ issued:

- 221 MedWatch Safety Alerts (FDA's second largest e-list) to more than 425,000 subscribers;
- More than 400 News Releases and other press announcements in English and/or Spanish with a total reach of more than 89,000 subscribers;
- 161 FDA Voice Blogs with more than 53,000 subscribers;
- 449 Consumer Updates (both new and updated content) in English and Spanish to more than 117,000 subscribers; and
- more than 100 newsletters, which reach approximately 700,000 patients and health care professionals.

FDA Office of Women's Health (OWH) responds to key agency priorities regarding women's health by delivering credible, accurate, and easy-to-understand health information on a variety of health topics related to FDA regulated products and safety and health alerts.

These materials help women and their families make informed health decisions. The materials include fact sheets, brochures, purse cards, and medication discussion guides. Select materials are available in multiple languages and all are free and written at a 4th through 6th grade reading comprehension level. To date, in partnership with other national organizations, more than 100 million publications have been distributed nationwide. Notable

FY 2017 and 2018 accomplishments include:

- Reaching more than 14 million people via special promotions and stakeholder engagement initiatives using print and digital outreach
- Distributing approximately 1.7 million print and electronic patient education materials in 19 languages
- Disseminating FDA safety alerts and health information via the OWH twitter account to approximately 70,000 followers, of which 58% are health professionals and researchers, and approximately 2,500 are Pinterest followers
- Conducting webinars, conference presentations, and consumer outreach to over 20 national health professional and women's advocacy organizations.

Support for FDA's Priority Rulemakings

In 2018, FDA HQ continued to support the agency's public health mission by issuing a final regulation to classify Blood Establishment Computer Software into Class II subject to special controls with premarket review. This ensures that the special controls established and imposed by this final rule, together with general controls, will provide a reasonable assurance of safety and effectiveness of these medical devices.

FDA also finalized the extension of the compliance date for Nutrition Food Labeling and Serving Sizes requirements. This action provides manufacturers with additional time to reconfigure their food labels to reflect amounts of food customarily consumed at one eating occasion, furthering the Administration's deregulatory initiative and providing industry with additional time to comply with this nutrition requirement.

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 on 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.

Since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 378 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 398 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

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. The results include:

- A Research Impact and Outcomes (RIO) Framework, which is a first of its kind, to measure the impact of the Women's Health research program.
- Published a historic study in JAMA examining "Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs" which included 224,000 patients, supporting 36 drug approvals, over a ten-year period (2005-2015).

FDA HQ implemented the Research Impact and Outcomes (RIO) Framework to measure the impact of the Women's Health research program. This first of its kind framework is currently in use by FDA HQ and two FDA product Centers. FDA HQ is hosting three virtual workshops for national and international scientists and their organizations to facilitate the adaptation and application of the FDA RIO Framework.

In addition, since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 378 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 398 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

In May 2018, the Office of Women's Health published a decadal review titled "Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs, 2005-2015" in the Journal of the American College of Cardiology. This manuscript is the largest study to date. Given the large gaps in information about participation, FDA wished to add updated data on cardiovascular clinical trials participation, based on data collected over a large time-period and highlighted the data analyses that FDA performs on participation by gender for new drug applications to ensure safety and efficacy of products that are approved for use in both men and women. This study also evaluated the detail inclusion exclusion of individual screens across 5 clinical trials and found that inclusion exclusion criteria minimally impacted enrollment by gender.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ established a new 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 2018 program accomplishments are described below.FDA hosted a quarterly Scientific Speaker Series to provide 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 percent knowledge gain by attendees across topics such as insilico research, opioid use disorder, and sex differences in cardiovascular disease.

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.

In honor of Women's Health Week 2018, FDA HQ led a scientific session focusing on the science and statistics of including women in cardiovascular clinical trials. In addition to a robust discussion and debate, this session served to expand FDA transparency and communications to an audience of clinicians, scientists, women's health advocacy and patient representatives. Over 1200+ attendees participated in-person or via remote viewing.

Along with CDER and CTP, OWH is sponsoring a public meeting entitled "Opioid and Nicotine Use, Dependence, and Recovery: Influences of Sex and Gender" on September 27-28, 2018. This public meeting will feature researchers, clinicians, and policy experts discussing sex and gender influences on substance use, misuse, and recovery

OpenFDA

OpenFDA is an FDA initiative to provide software developers and researchers Application Programming Interfaces (APIs) to several high-value structured datasets, including adverse events, product labeling, and recall enforcement reports.

Since its launch, on June 2, 2014, OpenFDA has received more than 120 million data calls. Many of the calls came from outside the US. There are more than 6,600 registered users, tens of thousands connected systems worldwide, and dozens of new software applications that the community has built. Within a year's time, FDA plans to conduct an app-a-thon to encourage more users to develop healthcare information apps which utilize openFDA as a data source.

OpenFDA provides access to:

- Drug Adverse events – over 9.1 million records
- Device classifications – over 6,400 records
- Structured Product Labeling for FDA-regulated human drugs – prescription or over the counter– and biologics with over 132,000 records
- Medical device adverse event reports – 7.7 million records
- Food adverse event reports – over 76,000
- Food enforcement reports over 16.9 records
- Unique Device Identifiers – over 1.9 million records
- 510Ks – over 151,000 records
- Device pre-market approvals – over 39,000 records
- Drug enforcement reports – over 9,000 records
- Device registration and listing – over 256,000 records
- Device recalls – over 58,000 records
- Device enforcements – over 18,000 records
- medical device adverse event reports – over 6.1 million records
- unique device identifiers – over 1.3 million records

Strengthen Science and Efficient Risk-Based Decision Making

FDA is committed to strengthening its scientific workforce and tools for efficient risk management. This includes:

- advancing new tools and policies to improve FDA's ability to combat diversion and counterfeiting of drug products.
- expanding the use of high performance computing to make product review more efficient and advanced
- strengthening food safety
- strengthening the scientific workforce.

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.[119]

The FDA Food Safety Modernization Act (FSMA)

The FDA Food Safety Modernization Act (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 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. 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 heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. To date, FDA has awarded 46 states and 1 territory a total of $85 million in cooperative agreements to develop produce safety programs that will enable them

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

to deliver education and technical assistance to farmers and create infrastructure to provide inspection, compliance and oversight. FDA also issued a cooperative agreement with the National Association of State Departments of Agriculture (NASDA) to develop a national consortium of state and federal regulators to further states' implementation of their produce safety programs.

In 2018, FDA worked with NASDA to finalize resource materials and to train states to implement the On-Farm Readiness Review (OFRR) program, which allows farms to request a review by regulators of the readiness of their operations for produce safety rule (PSR) implementation.

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 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 rotating Late Duty Officer coverage by Emergency Coordinators for issues arising after-hours, weekends, and holidays. FDA HQ also provides surveillance and signal monitoring, including FDA's Emergency Operations Network Incident Management System, and Consumer Complaint reporting and monitoring functions.

In FY 2018, FDA HQ coordinated the emergency response to 94 significant incidents including:

- 20 serious adverse or injury event incidents
- 52 natural disasters
- 21 man-made disasters
- 1 National Special Security Event.

In FY 2018, FDA HQ also established four Incident Management Groups (IMG) to provide headquarters coordination for:

- three separate hurricane responses for Hurricanes Maria, Lane, and Florence
- IMG for the 2018 Cyclospora Outbreak.

FDA HQ evaluated 3,799 consumer complaints (including 34 reports of suspected product tampering), 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 emergency response.

In FY 2018, FDA HQ:

- coordinated 18 Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products.
- addressed three draft notices of Public Health Emergency of International Concern (PHEIC) from the HHS International Health Regulations Program.

- responded to and coordinated 200 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.
- conducted, evaluated and reported Table Top and Full Scale Exercises, for two Center Select Agent Laboratory facilities, included a medically downed patient in a High Containment Laboratory.
- A second Table Top exercised actions involved with a fire in the high containment area, with the resulting after action reports emphasized the need for additional training.
- created and presented three trainings for laboratory researchers on patient assessment, monitoring, movement and turn over to medical authority.
- trained key emergency response staff on how to better respond to complex incidents and make informed decisions during an event.
- supported The Gotham Shield Functional Exercise (a mandated Federal Emergency Management Agency-led exercise that examined tribal, local, state and federal capabilities multiple mission areas through a series of linked exercises involving numerous federal and state partner agencies).

Economic Analysis and Support for Medical Product Regulations Published

In 2018, along with the publication of the proposed or final rules themselves, FDA published the economic analyses for rules related to medical device products (Acceptance of Data from Clinical Investigations for Medical Devices; Classification of Blood Establishment Computer Software and Accessories; Medical Device Submissions: Amending Premarket Regulations that Require Multiple Copies and Specify Paper Copies to be Allowed in Electronic Format) and human drug products (Repeal of Regulation Requiring an Approved New Drug Application for Drugs Sterilized by Irradiation; Removal of Certain Time of Inspection and Duties of Inspector Regulations for Biological Products). 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 proposed and final rules that will clarify regulatory uncertainty among the regulated industry.

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.

In FY 2015 through FY 2017, FDA received a total of $155.2 million from the HHS Non-Recurring Expenses Fund (NEF) to replace one owned laboratory, significantly renovate two owned laboratories, address other urgent owned facilities and infrastructure needs, and relocate two aged and deteriorated leased labs. These NEF resources have allowed FDA to replace the Office of Regulatory Affairs' (ORA) functionally obsolete owned laboratory at FDA's Winchester Engineering and Analytical Center in Winchester, Massachusetts, with an efficient, modern laboratory and to renovate laboratory Buildings 14 and 53A as well as an animal research processing area in Building 53B for the National Center for Toxicological Research (NCTR) located at FDA's owned Jefferson Laboratories Complex (JLC), in Jefferson, Arkansas. These resources have also allowed FDA to relocate ORA's aged, leased laboratories in Kansas City, Kansas, and Atlanta, Georgia, into new, modern, and efficient laboratories designed to meet ORA's mission. Without the NEF resources received for these leased lab relocations, ORA would have had to cut critical items in its foods programs, such as delaying hiring, which would possibly reduce ORA's ability to train staff and conduct inspections, and/or delaying lab-equipment purchases required to keep up with changing technology.

The $89 million FY 2019 NEF resources that were received will advance the ongoing laboratory relocation project at the Southeast Regional Laboratory in Atlanta. Funding will also support construction and facilities needs at ORA's Denver Laboratory, FDA's owned San Juan Complex, and infrastructure projects at FDA's owned Pacific Southwest Laboratory in Irvine, California. Funds will also be used for building and site infrastructure improvements, such as renovations, building system upgrades, roadway/drainage repairs, and building equipment replacement at FDA owned locations.

FDA HQ continues to work to:

- identify ongoing laboratory replacement, relocation, repair, and improvement projects;
- prioritize these projects
- develop resource requests to implement the highest priority projects.

FUNDING HISTORY[120]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$301,574,000	$191,374,000	$110,200,000
FY 2017 Actual	$302,146,000	$187,063,000	$115,083,000
FY 2018 Actual	$315,684,000	$171,001,000	$144,683,000
FY 2019 Annualized CR	$299,587,000	$171,195,000	$128,392,000
FY 2020 President's Budget	$320,164,000	$180,195,000	$139,969,000

BUDGET REQUEST

The FY 2020 Budget Request is $320,164,000 of which $180,195,000 is budget authority and $139,969,000 is user fees. This level provides a net increase of $20,577,000 compared to the FY 2019 Annualized Continuing Resolution level. Budget authority increases by $9,000,000 and user fees increase by $11,577,000.

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 (+$10.5 million)

New Platform for Drug Development - Oncology Center of Excellence: +$5 million / 25 FTE

The FY 2020 Request includes $5 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

[120] Numbers reflect comparability adjustments for FY 2018, FY 2019, and FY 2020 consistent with budget figures.

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: +$1.5 million / 4 FTE

As part of FDA's 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 2020 Request includes $1.5 million for the Office of Laboratory Safety (OLS), 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. These funds will be used to support the development and implementation of a new electronic standardized laboratory safety audit/inspection program and an FDA laboratory quality management program across the Agency.

Medical Countermeasures Initiatives

OCS/OCET: +$3.0 million

Supporting the development and availability of medical countermeasures (MCMs) to counter chemical, biological, radiological and nuclear threats as well as emerging infectious diseases, such as pandemic influenza and Zika virus, remains a high priority for FDA. MCM development often presents unique and complex challenges with respect to generating the data necessary to support regulatory decision-making, such as a lack of animal models to support MCM development or insufficient biomarkers to enable the extrapolation of data generated in animal models to humans. Without such tools, it is difficult to generate the data necessary to support regulatory decision making. FDA supports cutting-edge regulatory science research under the Medical Countermeasures Initiative (MCMi) Regulatory Science Program to help develop these tools and promote innovation in the development of MCMs. The requested increase of $3.0 million for the MCMi Regulatory Science Program would allow FDA HQ to support intra- and extramural collaborative research to create the tools that support regulatory decision-making and help facilitate the development of advances in science and technology, including platform technologies and manufacturing processes, into safe and effective medical countermeasures (MCMs).

Office of Laboratory Safety

OLSS: +1.0 million

The $1.0 million request increase will enable OLSS to continually improve IT solutions for efficient Occupational Safety and Health program management (via contractual services), improve FDA-wide training programs, enhance communication efforts, laboratory safety programs, biological safety programs, establish a safety and engineering contract, and enhance the industrial hygiene program. The funding will support improvements to the enterprise Safety, Inventory, and Protocol System (SIPS) and establish, improve, and sustain FDA-wide training programs. In addition, the funding will support communication services, laboratory safety management, oversight and resources for biological safety, and the FDA-wide industrial hygiene (IH) program.

Food Safety (+1.9 million UF)

Promoting Innovation and Emerging Technology While Maintaining Product Safety

OFPR: +$1.9 million

FDA supports industry as it develops and implements new technologies in food, cosmetics, and veterinary products, including biotechnology products. This initiative will ensure that FDA keeps pace with how changes in the marketplace affect the human and animal food supply. This includes modernizing the regulatory system for biotechnology products (consistent with the administration's Agriculture and Rural Prosperity Task Force Report) to improve transparency, coordination, and predictability of the system. It also includes:

- supporting public confidence by assessing products in a risk-based manner;
- providing predictable pathways for commercialization; and
- increasing capacity for the scientific review of human and animal food ingredients to foster innovative products getting to market and improve nutrition.

FDA's goal is to promote and support industry innovation in the growing biotechnology space while also assuring consumers of the safety of these products.

FDA HQ will provide oversight and coordination of these crosscutting innovation and emerging technology activities. For example, FDA HQ develop a platform to track performance measures and evaluate metrics to understand program effectiveness. FDA HQ will also support and ensure policy alignment for new data analytic and risk prioritization activities.

USER FEES

Current Law User Fees (+$9.8 million / -12 FTE)

FDA HQ will utilize the requested increase in current law user fees to provide support to the FDA Centers and Offices. FDA HQ will provide strategic coordination, direction, and oversight across FDA UF programs.

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 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products. *(Output)*	FY 2018: Develop 50 mapping products to support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinated 20 incidents involving FDA regulated products during the year. Participated in four exercises during the year. (All Targets Met or Exceeded)	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in five exercises during the year.	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in seven exercises during the year.	+2 exercises
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 2018: FDA completed annual milestones for 7 additional projects, for a total of 45 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)	52 CORES projects with completed annual milestones	58 CORES projects with completed annual milestones Complete review of 80% of Medical Product nanotechnology standards	+6 projects
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship	FY 2018: 53% Target: 50% (Target Exceeded)	50%	50%	Maintain

programs. (Outcome)				
293205: Percentage of requests for combination product designations processed within the 60 day statutory requirement. *(Output)*	FY 2018: 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 2018: 188 Target: 45 (Target Exceeded)	90	90	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 2018: 67 Target: 30 (Target Exceeded)	30	30	Maintain
291306: The number of targeted engagements, which are strategic interactions between FDA and stakeholders that produce a tangible	FY 2018: 49 Target: 25 (Target Met)	25	27	+2

result in support of FDA's global mission. *(Outcome)*				
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2018: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain

Nanotechnology

The Office of the Chief Scientist is adding a new target in FY 2020 to reflect the additional work this office does in reviewing Medical Product nanotechnology standards like ISO TC 229 and ASTM E56. Standards are an invaluable resource for industry and FDA staff. Effective and meaningful participation in standards development organizations (SDOs) for the products FDA regulates are critically important in the emerging area of nano technology. The use of standards can increase predictability, streamline premarket review, and facilitate market entry and use for safe and effective regulated products. For example, standards can help address certain aspects of the evaluation of nano medical products safety and effectiveness, such as material specifications, testing methods, pass/fail performance criteria, and processes to address areas, such as risk management and usability.

Fellowship Program

To support the Department's mission and FDA's scientific expertise, FDA is expanding its fellowship efforts by launching a new FDA Traineeship Program while continuing other Fellowship programs. This performance goal focuses on FDA's efforts to retain a targeted percentage of the scientists who complete these programs. The size and focus of the new agency-wide Traineeship program will be greater in number and scope than the current Fellowship, and FDA will be resetting the retention target in FY 20 and beyond when the new FDA Traineeship Program is launched. Additionally, whether "graduates" from these programs continue to work for FDA or choose to work in positions in related industry and academic fields, they are trained in using an FDA-presented understanding of the complex scientific issues in emerging technologies and innovation, which furthers the purpose of HHS Strategic Objective 4.2: Expand the capacity of the scientific workforce and infrastructure to support innovative research.

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INFRASTRUCTURE - GSA RENT, OTHER RENT, AND WHITE OAK

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019 Annualized CR
FDA White Oak Consolidation	**50,559**	**49,453**	**50,772**	**58,926**	**8,154**
Budget Authority	***43,044***	***43,044***	***43,044***	***50,927***	***7,883***
User Fees	***7,515***	***6,409***	***7,728***	***7,999***	***271***
Prescription Drug (PDUFA)	3,597	3,597	3,810	3,848	38
Medical Device (MDUFA)	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	3,918	2,812	3,918	4,151	233
Other Rent and Rent Related	**121,919**	**121,530**	**123,881**	**146,251**	**22,370**
Budget Authority	***71,943***	***71,943***	***71,943***	***93,444***	***21,501***
User Fees	***49,976***	***49,587***	***51,938***	***52,807***	***869***
Prescription Drug (PDUFA)	24,672	26,163	26,127	26,389	262
Medical Device (MDUFA)	5,187	8,672	5,239	5,291	52
Generic Drug (GDUFA)	12,946	9,426	13,075	13,206	131
Biosimilars (BsUFA)	805	766	1,070	1,081	11
Animal Drug (ADUFA)	720	720	790	797	7
Animal Generic Drug (AGDUFA)	273	261	264	266	2
Family Smoking Prevention and Tobacco Control Act	4,898	3,579	4,898	5,283	385
Food and Feed Recall	43	---	43	45	2
Food Reinspection	204	---	204	212	8
Voluntary Qualified Importer Program	170	---	170	177	7
Third Party Auditor Program	24	---	24	25	1
Outsourcing Facility	34	---	34	35	1
GSA Rental Payments	**238,487**	**219,283**	**241,024**	**240,928**	**-96**
Budget Authority	***170,208***	***170,208***	***170,208***	***171,570***	***1,362***
User Fees	***68,279***	***49,075***	***70,816***	***69,358***	***-1,458***
Prescription Drug (PDUFA)	33,373	20,205	35,341	35,695	354
Medical Device (MDUFA)	8,229	8,229	8,312	8,395	83
Generic Drug (GDUFA)	12,594	12,594	12,720	12,847	127
Biosimilars (BsUFA)	339	339	451	455	4
Animal Drug (ADUFA)	522	522	839	847	8
Animal Generic Drug (AGDUFA)	376	304	307	310	3
Family Smoking Prevention and Tobacco Control Act	12,030	6,882	12,030	9,960	-2,070
Food and Feed Recall	73	---	73	76	3
Food Reinspection	348	---	348	362	14
Voluntary Qualified Importer Program	290	---	290	302	12
Third Party Auditor Program	47	---	47	49	2
Outsourcing Facility	58	---	58	60	2

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 directly supports FDA's priorities by providing secure, modern, and cost-effective office and laboratory space that empowers FDA's workforce to protect and promote the safety and health of families; to foster the competition and innovation that will improve healthcare, expand access to medical products, and advance public health goals; to empower consumers and patients to make better choices; and to strengthen science and efficient risk-based decision making. The Infrastructure Program consists of:

- General Services Administration (GSA) Rental Payments
- Other Rent and Rent Related Activities
- White Oak.

The Infrastructure Program supports FDA's offices and labs across the country and its headquarters White Oak Campus in Silver Spring, Maryland. The program provides the infrastructure and scientific facilities necessary for FDA's workforce to effectively protect and promote the safety and health of families. Therefore, the program directly affects the productivity and efficacy of the workforce, its ability to grow and strengthen, and its ability to empower consumers and patients to make informed health choices. Without adequate investment, FDA would be unable to respond to food safety, medical product, and public health emergencies, such as opioid addiction and abuse, tobacco use by American youth, and antimicrobial resistance. 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 that effectively support FDA's public health priorities, optimize the use of taxpayer

dollars, enhance workforce productivity, and ensure efficient operations. FDA promotes the efficient use 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.

Additionally, FDA's energy saving projects decrease long-term energy usage and operating and maintenance costs, while increasing facility life spans and efficiency to support Executive Order 13834, Efficient Federal Operations.

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, including FDA-owned and GSA-owned locations, as well as leasing space close to Campus to continue FDA's geographic consolidation. In addition, a new master plan has been developed for the Federal Research Center to finalize the housing strategy and ensure that environmental impacts have been considered. The new master plan was completed in November 2018 and was approved by the National Capital Planning Commission on December 6, 2018.

GSA Rental Payments

The GSA Rental Payments account includes rental payments for FDA's GSA-managed office and laboratory facilities. These facilities enable FDA to protect consumers and patients by keeping contaminated, adulterated, counterfeit, and defective food and medical products from reaching the marketplace and by swiftly and effectively addressing food safety, medical product, and public health emergencies that arise. Without these strategically located facilities FDA staff could not conduct boots on the ground work including:

- Conducting inspections of approximately 40,000 regulated products and manufacturers annually
- Collecting and analyzing more than 45,000 samples of regulated products annually
- Recalling unsafe products, like the 9,199 recalls in FY 2017 alone
- Reviewing more than 40 million distinct product lines offered for entry into the U.S.
- Swiftly identifying the causes of foodborne illnesses that affect more than 48 million Americans each year, like the recent outbreaks caused by Duncan Hines cake mixes contaminated by Salmonella Agbeni and the multistate outbreak of E. coli O157:H7 infections linked to romaine lettuce from the Yuma growing region, to save lives
- Interdicting opioids at International Mail Facilities (IMFs) to combat the addiction crisis, which is the dominant public health problem in the U.S., killing an average of 115 Americans daily
- Keeping the U.S. drug supply safe; in FY 2017, 86 percent of packages that the FDA reviewed at IMFs contained illegal, illicit, unapproved, counterfeit and potentially dangerous drugs

- Reviewing medical products to improve health outcomes, such as the 200 devices FDA cleared, granted, or approved in the past few years that treat or manage pain and reduce the need to administer opioids
- Conducting criminal investigations, which resulted in 283 arrests, 226 convictions, $205 million of assets forfeited and seized, and $461 million in fines and restitution in FY 2017 alone.

FDA occupies almost 6.6 million rentable square feet of GSA-owned and GSA-leased office, laboratory, warehouse, and border/inspection-station 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 approximately 265 buildings, including district offices, laboratories, resident posts, border stations, and field offices 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 2018, FDA:

- continued coordinating the design and construction for the relocation of two ORA laboratories to replace aging facilities and improve operations that protect the American food supply: one near Kansas City, Kansas, responsible for planning, processing, and analyzing food items, including infant and toddler foods; and one near San Francisco, California, responsible for sensory and microbiological analyses of foods, elemental analysis, food chemistry, and product sterility
- coordinated a prospectus lease acquisition for the relocation and replacement of an aging facility that will improve operations of the ORA laboratory near Atlanta, Georgia, that houses the Southeast Food and Feed Lab, with expertise in pesticide residues, chemotherapeutics, metals, entomology, nutrient analyses, colors, food additives, filth and decomposition, pathogens, molecular biology, and bacterial toxins; this location also houses the Southeast Tobacco Laboratory
- coordinated design and construction of two new leased office locations near the White Oak Campus to ensure housing for FDA's growing workforce resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- coordinated leasing a training center and office space in an existing leased location in Rockville, Maryland, to support FDA's workforce in keeping with FDA's strategic priority to strengthen science and efficient risk-based decision making
- coordinated submitting a prospectus lease request for new office space near the White Oak Campus to house FDA's growing workforce resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- relocated one ORA resident post and leased one new OCI field office to facilitate inspection and criminal investigation activities that protect public health
- vacated two office locations in Rockville, Maryland, as part of a headquarters lease consolidation, to minimize real estate costs and consolidate activities to promote operational excellence.

In FY 2019, FDA plans to:

- continue coordinating the construction for the relocation of two ORA laboratories to replace aging facilities and improve operations that protect the American food supply: one near Kansas City, Kansas, responsible for planning processing, and analyzing food items including infant and toddler foods; and one near San Francisco, California, responsible for sensory and microbiological analysis of foods, elemental analysis, food chemistry, and product sterility
- initiate design and construction activities to replace an aging facility and improve the operations of the ORA laboratory near Atlanta, Georgia, that houses the Southeast Food and Feed Lab, with expertise in pesticide residues, chemotherapeutics, metals, entomology, nutrient analyses, colors, food additives, filth and decomposition, pathogens, molecular biology, and bacterial toxins; this location also houses the Southeast Tobacco Laboratory
- occupy two new leased office locations near the White Oak Campus to ensure housing for FDA's growing workforce resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- begin operations in a training center and office space in an existing leased location in Rockville, Maryland, to support FDA's workforce in keeping with FDA's strategic priority to strengthen science and efficient risk-based decision making
- gain Congressional approval for a prospectus lease for new office space near the White Oak Campus to ensure housing for FDA's growing workforce resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- coordinate leasing a new under-prospectus office space near the White Oak Campus to ensure housing for FDA's growing workforce resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- coordinate leasing four new locations for ORA resident posts and border stations to expand inspection operations that protect public health
- coordinate relocating seven ORA resident posts to facilitate inspection operations that protect public health
- coordinate increasing ORA's presence in nine IMFs to expand opioid interdiction efforts and combat the addiction crisis threatening American families
- expand CDER's laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis to increase its operations
- coordinate leasing a new CDER laboratory near the White Oak Campus to house a pilot plant for simulating the processing of drug substances and drug product manufacturing
- coordinate renovating existing buildings to provide additional storage and a security center on the White Oak Campus to support and protect FDA's expanding operations and growing workforce.

Other Rent and Rent-Related Activities

The Other Rent and Rent-Related Activities account includes 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:

- 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 that operate continuously and beyond the GSA standard 10-hour day
- other above-standard level services required to operate FDA facilities 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. Without the services and repairs funded by this account, critical FDA operations, including research and regulatory work, would cease.

Additionally, FDA is implementing energy efficiencies that, over time, will result in significant utility cost savings in the Other Rent and Rent-Related Activities account. These projects support:

- Executive Order 13834, Efficient Federal Operations
- 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 their utility costs would be otherwise due to the energy saving features provided by the ESPC.

Benefits of the ESPC, in addition to annual energy cost savings, include improving Campus electrical power reliability, which safe-guards ongoing medical product research, and reducing recurring maintenance costs. In addition to monetary benefits to the taxpayer, the CUP provides electric power through efficient cogeneration and photovoltaic equipment, funded by the ESPC, to reduce the environmental impact (pollution) of the Campus compared to supporting the Campus by more traditional power sources.

When each ESPC phase begins to provide benefits to the Campus, including utilities to FDA-occupied buildings, FDA is required to pay its 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, utility cost savings of

approximately $300 thousand annually, and 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. This project included the installation of solar panels, which will result in taxpayer energy cost savings and reduced environmental pollution compared to more traditional forms of electric power generation.

FDA implemented the design and construction of ECMs under a UESC for Dauphin Island, Alabama. 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. The contract was awarded, and construction has been completed.

FDA has completed an investment-grade audit for our facilities at the Muirkirk Road Campus to identify facilities projects. We awarded an approximately $900 thousand contract to address urgent projects for replacement of air handling units supporting FDA laboratories. The remainder of the projects identified by the audit, totaling approximately $5 million, are awaiting availability of funds. These projects will improve reliability of failing infrastructure systems and allow the Centers for Food Safety and Applied Nutrition (CFSAN) and Center for Veterinary Medicine (CVM) to continue their testing and oversight programs without disruption. These programs are responsible for promoting and protecting the public's health by ensuring that the nation's food supply is safe, sanitary, wholesome, and honestly labeled; cosmetic products are safe and properly labeled; and food and drugs for animals are safe.

CFSAN's Office of Applied Research Assessment (OARSA) is located at the Muirkirk Road Complex. A key part of OARSA's regulatory research focuses on developing and validating methods to detect foodborne hazards in the nation's food supply. This effort is continuous.

OARSA also is involved in conducting a multi-laboratory validation for detecting Cyclospora in water to be used during the potential outbreak season, or early spring. Multi-laboratory validation is a long (six-month) process involving OARSA labs, the FDA/ORA laboratories, as well as the CDC and USDA laboratories. This research would be negatively impacted if the OARSA laboratory was not operational. If shut down, OARSA would have to stop its part of the validation, the validation would be incomplete, and the process would have to be restarted. Restarting the process would require additional resources from three federal agencies. Ultimately, not having a validated detection method during the next outbreak season would delay response and negatively impact public health and food safety.

GSA is planning to perform 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 13834 Efficient Federal Operations. FDA's activities related to UESCs and renewable energy will mitigate the effect of FDA's operations on the environment.

White Oak

Congressional intent for geographically consolidating most 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 in one location. By consolidating much of its headquarters workforce, FDA increased opportunities for staff to collaborate face-to-face, while reducing overall facility operating costs. In-person collaboration fast-tracks advances and innovation in science, policy, and regulation that protect public health and accelerate access to lifesaving and life-improving products. Additionally, the consolidation centralized headquarters decision-making. During public health crises and emergencies, FDA's emergency operations center on Campus coordinates communications and actions across FDA programs, ORA, and federal, state, local, tribal territorial, and foreign regulatory public health counterparts.

Figure 25 State-of-the-Art Laboratories at White Oak

Figure 26 State-of-the-Art Laboratories at White Oak

Figure 27 Anecohic Chambers Laboratory

Figure 28 Nuclear Magnetic Resonance Laboratory Supporting CBER and CDER

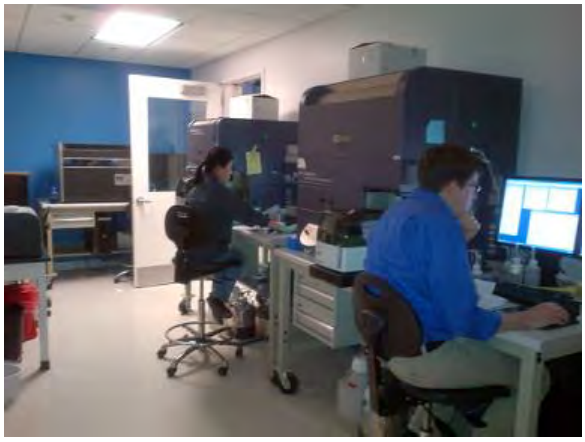

Figure 29 Flow Cytometry Core Facility: Highly Specialized and Expensive Equipment for Vaccine and Cell Therapy Studies

Figure 30 State-of-the-Art White Oak Infrastructure: Advanced Air Terminal Units Supporting Laboratories

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 above-standard infrastructure, building fit-out, specialized equipment, move costs, and operations and logistics.

White Oak funding supports Campus operations and requirements including:

- space alteration activities to meet the needs of rapidly changing laboratory research and medical product review programs
- above-standard Campus and building infrastructure design and construction required by laboratory functions, without which Campus operations would be limited and/or disrupted
- FDA information technology and security infrastructure, equipment, cabling and audiovisual, without which Campus activities would come to a halt
- commissioning and certification of the specialized laboratories required for scientific evaluation and research necessary for medical product approvals and regulations
- support services, including conference center management, labor and loading dock services, and operations and maintenance services, including maintenance of vital specialized laboratory equipment, without which the Campus could not reliably function
- transportation services, including parking management and a campus shuttle and circulator bus program critical to support the growing Campus staff and operations
- a centralized safety program to support expanded lab operations and Campus occupancy and protect the health and well-being of the federal workforce.

FDA initiated relocation activities to White Oak in FY 2002. The total number of employees currently assigned to the White Oak Campus is almost 11,000 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, continued through FY 2018, and is anticipated to be completed in FY 2019.

In FY 2019, in addition to funding Campus operations, FDA will initiate above-GSA-standard repair and improvement projects required to support FDA's specialized functions in support of program requirements.

FUNDING HISTORY – GSA RENTAL PAYMENTS

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$220,122,000	$161,683,000	$58,439,000
FY 2017 Actual	$220,653,000	$170,208,000	$50,445,000
FY 2018 Actual	$219,283,000	$170,208,000	$49,075,000
FY 2019 Annualized CR	$241,024,000	$170,208,000	$70,816,000
FY 2020 President's Budget	$240,928,000	$171,570,000	$69,358,000

FUNDING HISTORY - OTHER RENT AND RENT-RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$119,059,000	$73,484,000	$45,575,000
FY 2017 Actual	$116,653,000	$71,943,000	$44,710,000
FY 2018 Actual	$121,530,000	$71,943,000	$49,587,000
FY 2019 Annualized CR	$123,881,000	$71,943,000	$51,938,000
FY 2020 President's Budget	$146,251,000	$93,444,000	$52,807,000

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$48,944,000	$48,044,000	$900,000
FY 2017 Actual	$46,856,000	$43,044,000	$3,812,000
FY 2018 Actual	$49,453,000	$43,044,000	$6,409,000
FY 2019 Annualized CR	$50,772,000	$43,044,000	$7,728,000
FY 2020 President's Budget	$58,926,000	$50,927,000	$7,999,000

BUDGET REQUEST

The FY 2020 Total Budget Request is $446,105,000, of which $315,941,000 is budget authority and $130,164,000 is user fees. This level provides a net increase of $30,428,000 compared to the amount in the FY 2019 Annualized Continuing Resolution. Budget authority increases by $30,746,000 and user fees decrease by -$318,000.

The request will cover rent increases the agency anticipates in FY 2020 that are related to market changes, including new Occupancy Agreements replacing those expiring in FY 2019 and FY 2020 for approximately 64 GSA Occupancy Agreements that will cause rental rates to reset to market rates. In addition, FDA will also occupy expansion space in one existing and two new GSA-leased buildings, which will house user-fee growth. The increase in OR&RR is needed to meet cost escalations associated with operations and maintenance contracts, utilities, security, and Energy Savings Performance Contract payments for its owned and leased buildings nationwide. In addition, the OR&RR increase is also needed to address more demands for repairs and non-standard maintenance requests as FDA's owned buildings continue to age and equipment and systems failures occur. Operating costs at the White Oak Campus continue to increase with inflation and because several of the buildings on Campus are 10 or more years old. Accordingly, the FY 2020 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 supports FDA's offices and labs across the country and its headquarters White Oak Campus in Silver Spring, Maryland. The program provides the infrastructure and scientific facilities necessary for FDA's workforce to effectively protect and

promote the safety and health of families. Therefore, the program directly affects the productivity and efficacy of the workforce, its ability to grow and strengthen, and its ability to empower consumers and patients to make informed health choices. Without adequate investment, FDA would be unable to respond to food safety, medical product, and public health emergencies, such as opioid addiction and abuse, tobacco use by American youth, and antimicrobial resistance.

GSA Rental Payments

The FY 2020 Budget request for GSA Rental Payments is $240,928,000, of which $171,570,000 is budget authority and $69,358,000 is user fees. The budget authority increases by $1,362,000 compared to the amount requested in the FY 2019 Annualized Continuing Resolution, and user fees decrease by -$1,458,000. The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2020 Budget Request for GSA Rental Payments covers the cost of rental payments to GSA for FDA's almost 6.6 million square feet of GSA-managed space. Increased funding will also address the following critical needs:

- Increased rent and utility costs due to the renewal of a large number of leases expiring in FY 2019 and FY 2020, due to current higher market rates for rent and utilities at leased locations
- Planned lease costs for increasing facilities needs in the National Capital Region and FDA field locations
- Continued rent for existing labs in San Francisco and Kansas City while decommissioning is completed
- Real estate taxes increases.

Other Rent and Rent-Related

The FY 2020 Budget request for Other Rent and Rent Related is $146,251,000, of which $93,444,000 is budget authority and $52,807,000 is user fees. The budget authority increases by $21,501,000 compared to the amount requested in the FY 2019 Annualized Continuing Resolution and user fees increase by $869,000. The FY 2020 Budget will allow FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support more than 17,000 staff members. It will also provide adequate funding to address increased utility and maintenance costs associated with FDA's aging owned buildings.

White Oak

The FY 2020 Budget request for White Oak is $58,926,000, of which $50,927,000 is budget authority and $7,999,000 is user fees. The budget authority increases by $7,883,000 compared to the amount requested in the FY 2019 Annualized Continuing Resolution and user fees increase by $271,000. The FY 2020 Budget provides the necessary resources for increased above GSA-standard repairs and improvements, as well as mission support services on a daily basis for the almost 11,000 employees assigned to the White Oak Campus. The FY 2020 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.

Reliability of the utility infrastructure at White Oak is critical to Campus operations, especially laboratory operations. For example, utility outages adversely impact CBER laboratory activities supporting U.S. readiness for seasonal and pandemic influenza. CBER's laboratories play several critical roles in the development and manufacture of influenza vaccines, from participating in global surveillance for circulating influenza strains and developing candidate vaccine strains to deriving and distributing critical reagents for manufacturers to use in their assessment of influenza vaccine quality. If utility outages disrupt any one of these activities, it could delay vaccine availability to the public, thus negatively impacting public health and increasing flu-related deaths.

BUILDINGS AND FACILITIES

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020	
				President's Budget	+/- FY 2019 Annualized CR
Buildings and Facilities (Budget Authority).....	11,788	14,618	11,788	11,788	---

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 directly supports FDA's strategic policy areas. The program is responsible for ensuring that FDA's owned offices and labs across the country function optimally and empower FDA's workforce to carry out its public health mission, respond to food safety and medical product emergencies, and protect and promote the safety and health of American families. Improving the condition of site infrastructure and buildings at FDA's owned locations, most of which are in poor condition, and modernizing them are essential to strengthening FDA's scientific workforce.

B&F objectives are tied to providing FDA's workforce with the work environments necessary to effectively evaluate and regulate medical, food, and tobacco products. The currently poor overall condition of FDA's owned buildings and facilities, especially its labs, directly affects FDA's ability to foster the scientific innovation necessary to improve healthcare, expand access to medical products, and advance public health goals. Investing in FDA's facility objectives will provide the infrastructure and scientific capabilities necessary to ensure FDA can achieve its strategic priorities: protect and promote the safety and health of families, foster competition and innovation, empower consumers and patients to make better choices, and strengthen science and efficient risk-based decision making.

Strengthen Science and Efficient Risk-Based Decision Making

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.

In keeping with the Commissioner's priority to strengthen science and build a strong FDA workforce, FDA strives 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 and repair site infrastructure and buildings – an inventory of 77 existing FDA-owned facilities at six sites in the United States and Puerto Rico.

Figure 31 Newly Renovated Lab Building at the Jefferson Labs Complex

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 positively affects 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.

The current BMAR for the six FDA-owned sites, including renewals, is approximately $192.1 million. Approximately 73 percent of FDA-owned assets have an FCI score below the HHS-established goal of 90 and require significant repairs and improvements.

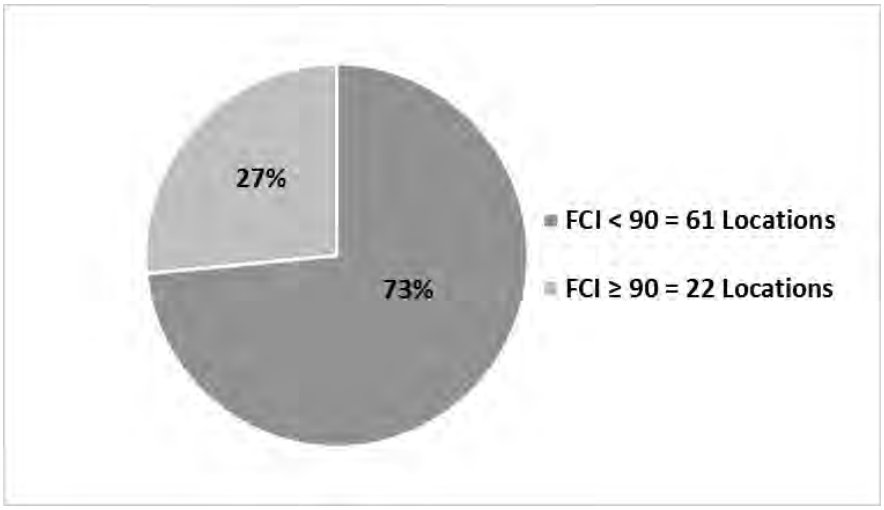

Figure 32 Facility Condition Index FDA-Owned Assets

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, Alabama
- Jefferson Labs Complex (JLC), Jefferson, Arkansas
- Muirkirk Road Complex, Laurel, Maryland
- Pacific Regional Laboratory SW, Irvine, California
- San Juan District Office and Laboratory, San Juan, Puerto Rico
- Winchester Engineering & Analytical Center (WEAC), Winchester, Massachusetts.

Activities in FY 2018 and Planned for FY 2019

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 2018, FDA initiated a project

to replace the roof of and HVAC equipment serving the main lab building and to replace the seawall protecting the site. In FY 2019, FDA will initiate projects to replace asphalt roads and parking lots, repair subfloor and replace floor finishes in the main lab building and provide supplemental funding for the construction of a new office building that will replace aged office trailers.

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 2018, FDA initiated projects to:

- construct a new Data and Disaster Recovery Center
- support the renovation of two lab buildings
- complete modifications to the site master plan
- upgrade HVAC in LAN rooms in support of the installation of new IT switches.

In FY 2019, FDA plans to initiate projects to:

- complete construction of a new Data and Disaster Recovery Center
- create a design for a new cafeteria and conference facility
- replace an air handling unit in a lab building
- renovate Campus dorms used for visiting scientists
- design building envelope repairs for several buildings
- replace the roof of a lab/animal research building
- install a new domestic water well.

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 in the following areas:

- Food and Animal Drug Safety: Isolating, identifying, and characterizing microorganisms potentially harmful to animals and humans, particularly the effects of antimicrobial use in animals on efficacy against pathogens, changes in the environmental microbial ecology, and the development of antimicrobial resistance in pathogenic and commensal microorganisms
- Toxicology: Reproductive toxicology, neurotoxicology, immunotoxicology, molecular toxicology, and in vitro toxicology, with special emphasis on developing higher throughput methods in hepatotoxicity, neurotoxicity, renal toxicity, cardiotoxicity, dermal and nanoparticle toxicity
- Microbiology: Foodborne parasites and viruses and immunobiology
- Molecular Biology: Genetic and biomarkers, microbial genetics, including molecular epidemiology and molecular virology, and foodborne allergens and glutens

In FY 2018, FDA initiated projects to:

- replace two air handling units in a lab building
- renovate the landscaping building to accommodate equipment and supplies
- conduct an investment-grade audit for electric panel boards and four generators
- install emergency eyewash stations in several animal research buildings
- renovate various operations, maintenance, and break rooms in a lab building
- replace flooring in the atrium of the main lab building.

In FY 2019, FDA will initiate a project to upgrade HVAC equipment in four lab/animal research buildings.

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 2018, FDA initiated projects to:

- design renovation of laboratories to support mission needs
- upgrade building HVAC system and upgrade controls
- relocate underground utilities and repair roads to avoid catastrophic failure associated with ground settlement issues.

In FY 2019, FDA will initiate projects to:

- provide supplemental funding for design effort for renovation of laboratories to support mission needs
- provide supplemental funding for Non-Recurring Expenses Fund projects to stabilize the parking lot and roadway, upgrade HVAC equipment, and upgrade controls.

San Juan District Office and the National Drug Servicing Laboratory – San Juan, Puerto Rico

The National Drug Servicing Laboratory specializes in pharmaceutical analysis. Drug analyses include, but are not limited to, method validation, drug surveillance testing, poison screenings, and the Department of Defense (DOD) Shelf-life Extension Program (SLEP). The DOD maintains significant pre-positioned stocks of critical medical material. SLEP defers drug replacement costs for these date-sensitive stocks by extending their useful life. In recent years, the value of the material tested has exceeded $33 million, while the cost of testing is about $350,000 a year. The SLEP assures that only safe and effective drugs are made available to personnel during war and other significant events; in the last few years, this program was extended to include CDC's National Strategic Stockpile samples.

In FY 2018, FDA initiated a project to replace the roof and an air handling unit serving the main lab building as well as multiple projects to respond to damage caused by Hurricane Maria and to improve the condition of the buildings and site infrastructure to better prepare the site for future hurricanes. In FY 2019, a project will be initiated to repave and restripe the parking lot and create a new access road to the site 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 2018, FDA utilized funds to support the laboratory replacement project, including a project to demolish or relocate six (6) small out buildings that are located within the footprint of the replacement building. In FY 2019, funding will continue to support the Non-Recurring Expenses Fund project to construct an addition to the main administration building.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actuals	$7,539,000	$7,539,000	$0
FY 2017 Actual	$9,243,000	$9,243,000	$0
FY 2018 Actual	$14,618,000	$14,618,000	$0
FY 2019 Annualized CR	$11,788,000	$11,788,000	$0
FY 2020 President's Budget	$11,788,000	$11,788,000	$0

BUDGET REQUEST

The FY 2020 Budget Request is $11,788,000, consisting solely of budget authority, which is flat with the FY 2019 Annualized Continuing Resolution. The funding level requested sustains the current condition of FDA's owned buildings and site infrastructure at its six mission-critical sites.

At the Gulf Coast Seafood Laboratory facility, FDA will:

- replace hot water piping in the main lab building
- replace eight R-22 refrigerant air conditioning units.

Figure 33 Gulf Coast Seafood Laboratory - Existing Air Conditioning Unit

At the Jefferson Labs Complex, FDA will:

- design and replace roof for Building 5D – roof failure will significantly impact operations in animal diet processing/storage, pathology, office space and the existing data center
- replace the HVAC system on the 2nd floor of an animal research building to support relocating critical animal research
- replace an air handling unit in a lab building that will ensure the safety of FDA scientists and support critical research
- provide supplemental funding for the Non-Recurring Expenses Fund project to repair road and drainage infrastructure – roads and drainage are in disrepair and will negatively impact traffic in and out of the facility, including future construction traffic, and continue to present safety hazards without upgrades
- design new electrical service and standby generation for a lab building that will ensure reliable power to protect research and scientific equipment
- repair building envelopes for multiple Campus buildings
- install new central steam and air lines to a critical lab building to ensure reliability of these utilities for in support of FDA's scientific mission
- install a new domestic water well to provide a reliable water supply for the site
- install new fire alarm and reporting systems in two buildings – these systems are beyond their useful life and will soon begin to fail, creating life-safety concerns that will negatively impact the ability to safely occupy these buildings.

Figure 34 Jefferson Labs Roof Deck

Figure 35 Jefferson Labs Roof Deck

Figure 36 Jefferson Labs Drainage Infrastructure

Figure 37 Jefferson Labs Road Infrastructure

Figure 38 Jefferson Labs Road Infrastructure

At the Muirkirk Road Complex, FDA will provide supplemental funding for the Non-Recurring Expenses Fund project to replace four generators that are beyond their useful life and undersized, as well as upgrade the electrical distribution system that serves critical lab and animal-research buildings that support of the FDA food-safety program.

Figure 39 Muirkirk Road Complex - Existing Out-Dated Generators

In the Pacific Regional Laboratory Southwest, FDA will:

- install an additional steam boiler to provide required redundancy to support lab operations
- correct various facility condition deficiencies such as replacement of Security Gate Arm Systems, which are safety and security concerns for the site
- provide supplemental funding to support projects to replace HVAC-system components and stabilizing soil settlement issues associated with the site parking area and roadways.

Figure 40 Pacific Regional Laboratory Southwest - Soil Settlement Issues

In the San Juan District Office and Laboratory, FDA will provide supplemental funding for the Non-Recurring Expenses Fund project to construct an addition to the main administration building – this project will allow administrative programs to vacate the lab building and provide needed space for future lab improvements and expansion.

The following table provides an allocation plan by site for use of the FY 2020 funds.

FY 2020 BUILDINGS AND FACILITIES ALLOCATION PLAN

BUILDINGS AND FACILITIES ALLOCATION PLAN
FY 2020
Congressional Justification

Site	Total
CFSAN Gulf Coast Seafood Laboratory	$350,000
Jefferson Laboratories Complex (NCTR & ARL) – Jefferson, AR	$5,894,000
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	$2,844,000
ORA Pacific Regional Laboratory SW – Irvine, CA	$1,500,000
San Juan District Office and Laboratory – San Juan, PR	$1,200,000
Winchester Engineering and Analytical Center – Winchester, MA	$0
B&F Project Total	**$11,788,000**

In FY 2020, 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 Sustainability Implementation Plan. More specifically, projects planned in FY 2020 will help reduce Scope 1, 2, and 3 greenhouse gas emissions by replacing or repairing aged, inefficient HVAC controls and equipment.

Program Activity Data[1]

Facility	Average FCI Score		
	FY 2018 Actual	FY 2019 President's Budget	FY 2020 Request
CFSAN Gulf Coast Seafood Laboratory	87	88	88
Jefferson Laboratories Complex	65	67	68
Muirkirk Road Complex	56	56	56
ORA Pacific Regional Laboratory Southwest	95	95	95
San Juan District Office and Laboratory	74	74	74
Winchester Engineering And Analytic Center	69	69	69

[1] The Backlog of Maintenance and Repairs (BMAR) at each site is significant. Funding is allocated to projects at sites in an effort to reduce the BMAR and sustain or improve the average Facility Condition Index (FCI) for the site. Based on funding levels in FY 2019 and FY 2020, FDA's remaining total BMAR is estimated to be $183.1 million, without escalation.

WORKING CAPITAL FUND

INTRODUCTION

In FY 2014, FDA launched a multi-year initiative to define and evaluate the cost of centrally administered services provided internally to Centers and Offices. The aim of this initiative was to create a structure to be managed under a Working Capital Fund (WCF) that provides FDA with greater visibility into budget and management decisions for these services.

As an intra-governmental revolving fund, the WCF allows FDA to operate in a more efficient business environment by relying on the collection of funds through customer billings. The fund helps FDA achieve the following:

- Enhance budget justifications and user fee negotiations with additional cost information on centrally administered services
- Streamline budget decisions under an integrated governance and financial infrastructure
- Create a customer-focused and service-oriented mechanism by improving customer investment and management decisions.

STRUCTURE

Program Management

To directly support the operation of the WCF, FDA has established a WCF program management team to be responsible for the fund's management and execution, communications, financial and performance reports, policy and documentation management, and change management activities. The Cost Allocation and Recovery Services group serves as the WCF program management team. The group is in the Office of Finance, Budget and Acquisitions within the Office of Operations.

Governance

In FY 2017, FDA established a governance structure to support the WCF. This governance structure, referred to as The Working Capital Fund Council (WCFC), consists of:

- FDA's Chief Operating Officer (COO)
- Chief Financial Officer (CFO)
- Center Directors (customers)
- Service Provider Directors (providers).

This group serves as a steering committee for the WCF Program at large and represents the decision-making body for topics such as budget, cost recovery methodology, and policy direction.

A Working Group made up of Executive Officers from each of FDA's Centers supports the WCFC by reviewing Program operations and making recommendations to the WCFC. Additionally, the Working Group includes representatives from service providers, customers, and the Office of Finance, Budget and Acquisitions (OFBA). This Working Group reviews service catalogs, consumption metrics, and proposed budgets for the annual Cost Allocation assessments associated with the WCF.

While the scope of these governance bodies is expected to evolve as the Program matures, its roles and responsibilities will, at a minimum, include the following:

- Provide direction and oversight to activities and policies of the Cost Allocation Program
- Review activities and services to be included or excluded in the WCF
- Coordinate with councils to review and approve cost allocation frameworks, resulting service rates, efficiency and performance targets, and approval parameters to manage risk
- Provide support for any needed reviews of WCF financial and operational processes and present findings to FDA leadership.

PROGRAM DESCRIPTION

The WCF provides funding for a wide array of services across FDA's programs, managed by Offices housed in FDA Office of Operations. Each of the services fall under categories described in more detail in this section. Each service was identified as an ideal candidate for a WCF based on the following criteria:

- Services are centrally managed and provided for internal customers across FDA, appropriate for a charge-back structure
- Data regarding consumption-based activities and services with appropriate and suitable cost data is available to assess and approximate the full costs to FDA
- Services provided at the Agency level reduce or eliminate redundancy and achieve economies of scale.

Information Technology

Information Technology (IT) services provide FDA customers with information, communication, knowledge infrastructure and quality customer service delivery to enhance and sustain systems and IT operations. These services support:

- personal and mobile computing
- enterprise applications
- professional IT services
- related training and support resources.

Informatics and technology-based innovation needs are addressed through the study, development, and testing of prototypes to make recommendations addressing:

- key mission activities related to big data and analytics
- cloud and high performance scientific computing
- mobility
- digitization
- open data.

IT support further ensures the appropriate security controls are applied to FDA systems to protect privacy and ensuring confidentiality, integrity, and availability of FDA information in accordance with Federal, Department and Agency regulations. The IT function manages technology strategies to reduce costs through the elimination of duplication efforts and adopting new technology to improve services, and leverage knowledge and resources to reduce security and system failures.

Human Resources

Human Resources (HR) services support FDA's workforce through the provision of labor support services. These support services include:

- benefits and retirement
- worker's compensation
- HR policy development and accountability
- staffing services
- FDA University employee development programs and training opportunities.

HR support allows FDA to work with labor unions and address labor practices through the employee and labor relations programs, as well as the ability to address the Commissioned Corps' unique needs. Additional information systems support, workforce and demographic data reporting, and information dissemination strategies are managed Agency-wide to support enterprise human resources system needs.

Facilities and Environmental Management

Facilities and Environmental Management services incorporate a broad range of vital needs to support a safe and sustainable working environment. These services include:

- lease and facilities project management
- maintenance and logistics support
- strategy and performance management.

To maintain a safe working environment, FDA centrally manages occupational safety and health programs, special security operations, and physical and personnel security. These services require collaboration and communication with the Department's other HHS Operating Divisions to meet a wide range of policy requirements.

Finance and Procurement

Finance and Procurement services enable FDA to perform budgetary, financial, acquisition, and grants functions. The support includes:

- contracts, grant awards and administration
- the implementation of all FDA policies and procedures governing acquisitions
- inter-agency agreements
- grants management.

In addition, financial, accounting, managerial and reporting services are provided to stakeholders, along with policy guidance and travel support in accordance with standards and requirements. Budget execution, control and compliance services further enable FDA to provide guidance, high-level analysis, and reliable data to ensure dollars are utilized in accordance with the Congressional intent and FDA's mission.

Administrative

Administrative operations provide FDA employees and stakeholders with additional services to further support day-to-day functions and needs. These services include:

- equal employment opportunities

- a work environment that values and supports diversity
- ethics and integrity assistance to help current and former employees avoid conflicts of interest and follow laws and regulations in their business activities.

The Paperwork Reduction Act (PRA) Team also is made available to FDA customers requiring information collection guidance, and related compliance reporting and rulemakings.

NONRECURRING EXPENSES FUND

Program Description and Accomplishments

The Nonrecurring Expenses Fund (NEF) permits HHS to transfer unobligated balances of expired discretionary funds from FY 2008 and subsequent years into the NEF account. Congress authorized use of the funds for capital acquisitions necessary for the operation of the Department, specifically information technology (IT) and facilities infrastructure acquisitions. FDA depends upon the NEF to fund its lab revitalization initiatives;

From FY 2015 through FY 2017, FDA has received a total of $155.2 million from the NEF to replace one owned laboratory, significantly renovate two owned laboratories, address urgent owned facilities and infrastructure needs, and relocate two aged and deteriorated leased labs. NEF resources have allowed FDA to expend $94 million to replace the Office of Regulatory Affairs' (ORA) functionally obsolete owned laboratory at FDA's Winchester Engineering and Analytical Center in Winchester, Massachusetts, with an efficient, modern laboratory. NEF resources were also used to renovate laboratory Buildings 14 and 53A as well as an animal research processing area in Building 53B for the National Center for Toxicological Research (NCTR) located at FDA's owned Jefferson Laboratories Complex (JLC), in Jefferson, Arkansas. These resources have also allowed FDA to expend $61.2 million to relocate ORA's aged, leased laboratories in Kansas City, Kansas, and Atlanta, Georgia, into new, modern, and efficient laboratories designed to meet ORA's mission.

In FY 2019, HHS notified Congress of the planned use of $89 million in NEF resources to advance the ongoing laboratory relocation project at the Southeast Regional Laboratory. Funding will also support construction and facilities needs at the Denver Laboratory, the San Juan Complex, and infrastructure projects at the Pacific Regional Laboratory SW. Funds will also be used for facility and site infrastructure upgrades at FDA-owned locations that also support the reliability and safety of lab operations.

FY 2019 FDA Notification ($89M)

- **Irvine, California, $3.300M**, to design and construct a retaining wall, or an alternative, due to the continuing decompositin and settlement of the landfill that the facility is partially built upon, which is posing a significant safety hazard at the site.
- **Denver District Laboratory, $36.000M**, for replacement or relocation of the ORA Denver laboratory. GSA intends to initiate a capital project to construct a new federal building for the laboratory in FY 2019. If the capital construction project cannot move forward in FY 2019, GSA will acquire leased space and relocate the lab instead. GSA and FDA will not postpone the relocation if the federal construction project– which is included in GSA's Capital Plan in the FY 2019 President's Budget – cannot move forward because the existing condition of the laboratory is untenable.
- **Southeast Regional Laboratory, Atlanta, Georgia, $17.300M**, for the relocation of the GSA leased laboratory within the same geographic location. This funding complements NEF funding received in FY 2016 and is based on updated construction requirements for laboratory environmental systems.
- **San Juan Complex, (Puerto Rico) $8.000M**, for the construction of an addition to the Toro Building to consolidate all District Office staff and functions currently housed in multiple buildings across the site.
- **New Chiller Plant Design (Jefferson Labs Complex), $1.185M**, for the construction of a new chiller plant in Building 2, which will be strategically located on campus and sized to replace the chiller plants located in Buildings 26 and 05B. This funding is for the design phase.
- **Gulf Coast Seafood Lab Construction, Dauphin Island, Alabama, $2.400M**, for the demolition of two aged modular trailers that are beyond their useful life and construction of a one-story 3,840 GSF building on an elevated concrete slab to house 25 people (employees and contractors).
- **Muirkirk Road Complex, Laurel, Maryland, $5.000M**, for replacing six air handling units in MOD 1. Replacing these units is necessary to ensure building operational reliability and continuity of mission critical work.
- **Jefferson Labs Complex Infrastructure Renovations, $4.600M**, for repairs to Site Infrastructure (Roads, Sidewalks, Drainage)
- **Pacific Regional Laboratory SW, Irvine, California, $5.000M**, for repairs of Surface Parking Areas.
- **Pacific Regional Laboratory SW, Irvine, California, $6.000M**, for repairs to HVAC and Controls in Building IRV-1.

SUPPLEMENTARY TABLES

OBJECT CLASSIFICATION TABLES

BUDGET AUTHORITY

(Dollars in Thousands)	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 Request
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	939,813	940,104	964,225
Other than full-time permanent (11.3)	86,304	86,331	88,546
Other personnel compensation (11.5)	43,670	43,684	44,804
Military personnel (11.7)	58,906	60,438	62,009
Special personnel services payments (11.8)	814	814	835
Subtotal, Personnel Compensation	**1,129,507**	**1,131,371**	**1,160,419**
Benefits:			
Civilian benefits (12.1)	354,153	354,263	363,352
Military benefits (12.2)	31,630	32,452	33,296
Benefits to former personnel (13.0)	400	400	400
Subtotal, Benefits	**386,183**	**387,115**	**397,048**
Total Personnel Compensation and Benefits	**1,515,690**	**1,518,486**	**1,557,467**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	55,793	60,023	75,155
Transportation of things (22.0)	3,567	3,837	4,805
Rental payments to GSA (23.1)	170,208	170,208	171,570
Rent payments to others (23.2)	2,639	2,839	3,555
Communication, utilities, and misc. charges (23.3)	21,116	22,717	28,444
Printing and reproduction (24.0)	2,508	2,698	3,378
Subtotal, Contractual Services	**255,831**	**262,322**	**286,907**
Other Contractual Services:			
Consulting services (25.1)	53,641	57,708	72,257
Other services (25.2)	419,757	451,584	565,429
Purchase of goods and svcs from Govt Acts. (25.3)	157,915	169,888	212,718
Operation and maintenance of facilities (25.4)	94,969	102,170	127,927
Research and Development Contracts (25.5)	27,542	29,630	37,100
Operation and maintenance of equipment (25.7)	62,999	67,776	84,862
Subsistence and support of persons (25.8)	---	---	---
Subtotal, Other Contractual Services	**816,823**	**878,756**	**1,100,293**
Supplies and Materials:			
Supplies and materials (26.0)	46,926	50,484	63,211
Equipment (31.0)	48,054	51,697	64,731
Land and Structures (32.0)	3,293	3,543	4,436
Grants, subsidies, and contributions (41.0)	183,637	197,560	247,366
Insurance claims and indemnities (42.0)	1,293	1,391	1,742
Interest and dividends , Refunds (43.0, 44.0)	118	127	159
Subtotal, Supplies and Materials	**283,321**	**304,802**	**381,645**
Total Contractual Services and Supplies	**1,355,975**	**1,445,880**	**1,768,845**
Total Budget Authority by Object Class	**2,871,665**	**2,964,366**	**3,326,312**
Average Cost per FTE			
Civilian FTE	9,320	9,315	9,554
Civilian Average Salary	$153	$153	$153
Percent Change	0.0%	0.0%	0.0%
Military FTE	668	668	668
Military Average Salary	$136	$139	$143
Percent change		2.6%	2.6%
Total FDA FTE	9,988	9,983	10,222
Total FDA Average Salary	$152	$152	$152
Percent change		0.0%	0.0%

*For FY 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 and FY 2020, FDA proposes to discontinue the transfer.

USER FEE

(Dollars in Thousands)	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 Request
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	661,867	721,330	743,137
Other than full-time permanent (11.3)	94,175	102,636	105,739
Other personnel compensation (11.5)	74,816	81,538	84,003
Military personnel (11.7)	51,064	52,392	53,754
Special personnel services payments (11.8)	258	281	290
Subtotal, Personnel Compensation	**882,180**	**958,177**	**986,923**
Benefits:			
Civilian benefits (12.1)	263,083	286,719	295,387
Military benefits (12.2)	29,725	30,498	31,291
Benefits to former personnel (13.0)	---	---	---
Subtotal, Benefits	**292,808**	**317,217**	**326,678**
Total Personnel Compensation and Benefits	**1,174,988**	**1,275,394**	**1,313,601**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	24,086	22,482	27,106
Transportation of things (22.0)	1,016	948	1,143
Rental payments to GSA (23.1)	49,785	70,816	69,358
Rent payments to others (23.2)	916	855	1,031
Communication, utilities, and misc. charges (23.3)	7,003	6,537	7,881
Printing and reproduction (24.0)	1,057	987	1,190
Subtotal, Contractual Services	**83,863**	**102,625**	**107,709**
Other Contractual Services:			
Consulting services (25.1)	60,534	56,504	68,124
Other services (25.2)	655,515	611,875	737,703
Purchase of goods and svcs from Govt Acts. (25.3)	247,784	231,288	278,851
Operation and maintenance of facilities (25.4)	28,176	26,300	31,709
Research and Development Contracts (25.5)	34,173	31,898	38,458
Operation and maintenance of equipment (25.7)	74,614	69,647	83,969
Subsistence and support of persons (25.8)	9	9	9
Subtotal, Other Contractual Services	**1,100,805**	**1,027,521**	**1,238,823**
Supplies and Materials:			
Supplies and materials (26.0)	14,868	13,878	16,732
Equipment (31.0)	16,965	15,836	19,092
Land and Structures (32.0)	---	---	---
Grants, subsidies, and contributions (41.0)	106,428	99,343	119,772
Insurance claims and indemnities (42.0)	40	37	45
Interest and dividends , Refunds (43.0, 44.0)	---	---	---
Subtotal, Supplies and Materials	**138,301**	**129,094**	**155,641**
Total Contractual Services and Supplies	**1,322,969**	**1,259,240**	**1,502,173**
Total Reimbursable by Object Class	**2,497,957**	**2,534,634**	**2,815,774**
Average Cost per FTE			
Civilian FTE	6,556	7,145	7,361
Civilian Average Salary	$167	$167	$167
Percent Change		0.0%	0.0%
Military FTE	479	479	479
Military Average Salary	$168.7	$173.0	$177.5
Percent change		2.6%	2.6%
Total FDA FTE	7,035	7,624	7,840
Total FDA Average Salary	$167	$167	$168
Percent change		0.2%	0.2%

TOTAL PROGRAM

(Dollars in Thousands)	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 Request
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	1,601,680	1,661,434	1,707,362
Other than full-time permanent (11.3)	180,479	188,967	194,285
Other personnel compensation (11.5)	118,486	125,222	128,807
Military personnel (11.7)	109,970	112,830	115,763
Special personnel services payments (11.8)	1,072	1,095	1,125
Subtotal, Personnel Compensation	**2,011,687**	**2,089,548**	**2,147,342**
Benefits:			
Civilian benefits (12.1)	617,236	640,982	658,739
Military benefits (12.2)	61,355	62,950	64,587
Benefits to former personnel (13.0)	400	400	400
Subtotal, Benefits	**678,991**	**704,332**	**723,726**
Total Personnel Compensation and Benefits	**2,690,678**	**2,793,880**	**2,871,068**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	79,879	82,505	102,261
Transportation of things (22.0)	4,583	4,785	5,948
Rental payments to GSA (23.1)	219,993	241,024	240,928
Rent payments to others (23.2)	3,555	3,694	4,586
Communication, utilities, and misc. charges (23.3)	28,119	29,254	36,325
Printing and reproduction (24.0)	3,565	3,685	4,568
Subtotal, Contractual Services	**339,694**	**364,947**	**394,616**
Other Contractual Services:			
Consulting services (25.1)	114,175	114,212	140,381
Other services (25.2)	1,075,272	1,063,459	1,303,132
Purchase of goods and svcs from Govt Acts. (25.3)	405,699	401,176	491,569
Operation and maintenance of facilities (25.4)	123,145	128,470	159,636
Research and Development Contracts (25.5)	61,715	61,528	75,558
Operation and maintenance of equipment (25.7)	137,613	137,423	168,831
Subsistence and support of persons (25.8)	9	9	9
Subtotal, Other Contractual Services	**1,917,628**	**1,906,277**	**2,339,116**
Supplies and Materials:			
Supplies and materials (26.0)	61,794	64,362	79,943
Equipment (31.0)	65,019	67,533	83,823
Land and Structures (32.0)	3,293	3,543	4,436
Grants, subsidies, and contributions (41.0)	290,065	296,903	367,138
Insurance claims and indemnities (42.0)	1,333	1,428	1,787
Interest and dividends , Refunds (43.0, 44.0)	118	127	159
Subtotal, Supplies and Materials	**421,622**	**433,896**	**537,286**
Total Contractual Services and Supplies	**2,678,944**	**2,705,120**	**3,271,018**
Total Program Level by Object Class	**5,369,622**	**5,499,000**	**6,142,086**
Average Cost per FTE			
Civilian FTE	15,876	16,460	16,915
Civilian Average Salary	$159	$159	$159
Percent Change	0.0%	0.2%	0.0%
Military FTE	1,147	1,147	1,147
Military Average Salary	$149.4	$153.3	$157.2
Percent Change	0.0%	2.6%	2.6%
Total FDA FTE	17,023	17,607	18,062
Total FDA Average Salary	$158	$159	$159
Percent change	0.0%	0.4%	0.2%

*For FY 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 and FY 2020, FDA proposes to discontinue the transfer.

SALARY AND EXPENSES

(Dollars in Thousands)	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 Request
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	939,813	940,104	964,225
Other than full-time permanent (11.3)	86,304	86,331	88,546
Other personnel compensation (11.5)	43,670	43,684	44,804
Military personnel (11.7)	58,906	60,438	62,009
Special personnel services payments (11.8)	814	814	835
Subtotal, Personnel Compensation	**1,129,507**	**1,131,371**	**1,160,419**
Benefits:			
Civilian benefits (12.1)	354,153	354,263	363,352
Military benefits (12.2)	31,630	32,452	33,296
Benefits to former personnel (13.0)	400	400	400
Subtotal, Benefits	**386,183**	**387,115**	**397,048**
Total Personnel Compensation and Benefits	**1,515,690**	**1,518,486**	**1,557,467**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	55,793	60,023	75,155
Transportation of things (22.0)	3,567	3,837	4,805
Rent payments to others (23.2)	2,639	2,839	3,555
Communication, utilities, and misc. charges (23.3)	21,116	22,717	28,444
Printing and reproduction (24.0)	2,508	2,698	3,378
Subtotal, Contractual Services	**85,623**	**92,114**	**115,337**
Other Contractual Services:			
Consulting services (25.1)	53,641	57,708	72,257
Other services (25.2)	419,757	451,584	565,429
Purchase of goods and svcs from Govt Acts. (25.3)	157,915	169,888	212,718
Operation and maintenance of facilities (25.4)	94,969	102,170	127,927
Research and Development Contracts (25.5)	27,542	29,630	37,100
Operation and maintenance of equipment (25.7)	62,999	67,776	84,862
Supplies and materials (26.0)	46,926	50,484	63,211
Total Contractual Services and Supplies	**949,372**	**1,021,354**	**1,278,841**
Rental payments to GSA (23.1)	**170,208**	**170,208**	**171,570**
Grand Total, Salaries and Expense and Rent	**2,635,270**	**2,710,048**	**3,007,878**
Direct FTE	**9,988**	**9,983**	**10,222**

*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 2018 Actuals			FY 2019 Estimate			FY 2020 Estimate		
	Civilian	**Military**	**Total**	**Civilian**	**Military**	**Total**	**Civilian**	**Military**	**Total**
Center for Food Safety and Applied Nutrition	1,069	36	1,105	1,114	36	1,150	1,194	36	1,230
Center for Drug Evaluation and Research	4,697	506	5,203	4,996	506	5,502	5,118	506	5,624
Center for Biologics Evaluation and Research	1,142	60	1,202	1,103	60	1,163	1,131	60	1,191
Center for Veterinary Medicine	608	12	620	620	12	632	647	12	659
Center for Devices and Radiological Health	1,652	85	1,737	1,731	85	1,816	1,802	85	1,887
National Center for Toxicological Research	307	---	307	301	---	301	301	---	301
Office of Regulatory Affairs	4,449	338	4,787	4,601	338	4,939	4,659	338	4,997
Headquarters and Office of the Commissioner	1,094	75	1,169	926	75	1,001	943	75	1,018
Export Certification	22	---	22	26	---	26	26	---	26
Color Certification	36	---	36	37	---	37	37	---	37
Family Smoking Prevention and Tobacco Control Act	773	36	809	896	36	932	956	36	992
Priority Review Vouchers (PRV) Pediatric Disease	---	---	---	---	---	---	---	---	---
MCMi - No Year	---	---	---	---	---	---	---	---	---
Opiods - No Year	---	---	---	8	---	8	---	---	---
21st Century Cures (BA Only)	26	---	26	100	---	100	100	---	100
Total	**15,875**	**1,148**	**17,023**	**16,459**	**1,148**	**17,607**	**16,914**	**1,148**	**18,062**

Five Year History of GS/GM Average Grade

Year	Grade
FY 2016	13
FY 2017	13
FY 2018	13
FY 2019	13
FY 2020	13

* FTE figures do not include an estimated 87 reimbursable, 2 CRADA, 2 FOIA, and 36 PEPFAR.

DETAIL OF POSITIONS

	FY 2018 Actuals	FY 2019 Annualized CR	FY 2020 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	**$158,532**	**$161,544**	**$161,544**
Executive Service (ES)			
Executive Service	58	60	62
Total Executive Service	**58**	**60**	**62**
Total - ES Salary	**$10,656,456**	**$11,233,374**	**$11,607,820**
General Schedule (GS)			
GS-15	1,397	1,449	1,489
GS-14	3,726	3,863	3,969
GS-13	4,845	5,023	5,166
GS-12	2,153	2,232	2,294
GS-11	729	755	776
GS-10	12	12	12
GS-9	450	467	480
GS-8	74	77	79
GS-7	305	317	325
GS-6	36	37	38
GS-5	58	60	61
GS-4	30	32	32
GS-3	11	11	11
GS-2	8	8	8
GS-1	2	2	2
Total General Schedule	**13,836**	**14,345**	**14,742**
Total - GS Salary	**$1,543,654,848**	**$1,630,851,376**	**$1,675,985,430**
Administrative Law Judges (AL)	---	---	---
Scientific/Senior Level (ST/SL)	4	4	4
Senior Biomedical Research Service (RS)	47	49	50
Scientific Staff Fellows (RG) (Title 42)	947	982	1,009
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	170	176	181
Former Performance Mgmt Recognition System Employees (GM)	1	1	1
Physicians and Dentists - (GP) (Title 38)	772	800	823
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06	287	287	287
Commissioned Corps - Other	861	861	861
Total Commissioned Corps	**1,148**	**1,148**	**1,148**
Administratively Determined (AD) (includes Title 42)[2]	5	5	5
Wage Grade	14	15	15
Consultants[2]	20	21	21
Total FTE (End of Year)[1]	**17,023**	**17,607**	**18,062**
Average ES Level	3	3	3
Average ES Salary	$183,732	187,223	187,223
Average GS grade	13	13	13
Average GS Salary	$111,568	113,688	113,688
Average GM Salary	$148,967	151,797	151,797
Average GP Salary	$216,270	220,379	220,379

[1] Does not include an estimated 87 reimbursable, 2 CRADA, 2 FOIA, and 26 PEPFAR 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.

SIGNIFICANT ITEMS

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (115-706)

1. Food Safety and the Food Safety Modernization Act Funding

The Committee directs FDA to provide information to the public via reports and on its website as it relates to the link between FSMA activities and performance measures, especially as outcome measures support reductions in foodborne illnesses, hospitalizations, and deaths.

Also, the Committee directs FDA to continue their outreach and education efforts to inform the regulated industries how they come into compliance with the FSMA foundational regulations. As previously noted, it is the intent of Congress for FDA to ensure an even playing field in the application of FSMA regulations as it relates to both domestic and imported producers, processors, and manufacturers of food and animal feed. Lastly, the Committee believes that FSMA implementation places additional requirements on state governments and private stakeholders, and therefore urges the FDA to provide sufficient resources to state education and inspection programs to address these needs.

FDA Response:

FDA is developing measures to monitor compliance and industry's implementation of the FDA Food Safety Modernization Act (FSMA) rules. The measures will be categorized by rule and are at various stages of review, prioritization, approval, and implementation. The first set of measures tracks the implementation of the Preventive Controls for Human Food (PCHF) and Preventive Controls for Animal Food (PCAF) rules. A set of PCHF and PCAF measures will be published in early 2019 via FDA's Agency-wide performance management system, FDA-TRACK. The second set of measures to be published on the FDA-TRACK website will cover the Foreign Supplier Verification Programs (FSVP) for Importers of Food for Humans and Animals rule. This set of measures is slated to be released in Spring 2019.

Regarding the reduction in foodborne illness, hospitalizations, and deaths, FDA will evaluate the number of reported outbreaks and estimated illnesses in the U.S. population as measures of the effectiveness of the rules in collaboration with the Centers for Disease Control and Prevention (CDC). The development of additional public health outcome measures related to FSMA activities will be subject to the availability of sufficient data.

FDA is committed to continuing outreach and education efforts to assist regulated industries' compliance with the FSMA rules. Training the food industry is critical to the success of FSMA. To help facilitate training, FDA, together with United States Department of Agriculture (USDA), has funded a network of public and private partners in state, federal, tribal, and international governments, industry, and academia for the development and delivery of training.

The vision of FSMA training began in 2010-2012 with the creation of public-private Alliances funded primarily by FDA as a resource for industry and to facilitate widespread understanding of the new standards to support compliance. The Produce Safety Alliance (PSA), Food Safety Preventive Controls Alliance (FSPCA), and Sprout Safety Alliance (SSA) have developed training programs to help domestic and foreign food businesses—including small and very small farms and facilities—understand the requirements of the preventive controls regulations, FSVP, the Intentional Adulteration rule, and the Produce Safety rule. The Alliances are composed of representatives from the government, including FDA, USDA, and state regulatory agencies, the food industry, and academia.

The Alliances are working to ensure that training opportunities available to international food businesses are consistent with those being provided domestically. FSPCA—working with PSA, as well as representatives of importers and foreign governments, and others—has established an International Subcommittee to address the training, education, and technical assistance needs of global stakeholders.

To further address the training needs of the global food industry, FDA and the University of Maryland established through a cooperative agreement the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) to support FDA's mission through the delivery of food safety training programs throughout the world. Among other things, JIFSAN oversees the implementation of international education, outreach, and training, delivers international trainings, and establishes relationships with organizations that may provide technical assistance to the foreign farming community. JIFSAN is currently engaged in training efforts on FSMA to international audiences.

To meet the specific training and technical assistance needs of local food and tribal producers, FDA established relationships with and provided financial support to groups that can best meet the training and technical assistance needs of these populations. One such group is tasked with bringing training to tribal producers and food businesses to fulfill the requirements of FSMA, while another group is tasked with providing training, education, and outreach to local producers and processors to enhance the fundamental knowledge of food safety and to help these local producers and processors comply with applicable FSMA regulations.

FDA recognizes the importance of engaging with our state partners on FSMA implementation, especially in the implementation of the Produce Safety rule. One of the resources now available to farmers is the On-Farm Readiness Review (OFRR) program. The National Association of State Departments of Agriculture (NASDA) created this program in collaboration with FDA. On-Farm Readiness Reviews are voluntary and provide farmers real-time feedback on their current operations and facilities before inspections begin in 2019. Working together, the aim is to improve the safety of the food supply.

Additionally, FDA provides funding to states, through a series of state produce cooperative agreements, to establish produce regulatory programs that include inspections, training, outreach, and technical assistance elements. FDA is also providing training to state regulators on produce

safety and preventive controls inspections and works with our state partners to roll out inspection programs for the preventive controls rules.

2. Cancer Immunotherapy Clinical Trials

The Committee is aware of the remarkable promise of cancer immunotherapy and encouraged by the FDA's recent approval of new treatments that harness this approach to fighting cancer. More than 1,500 immuno-oncology clinical trials are in some stage of development. As more patients turn to immune-based treatments, and more clinical trials are conducted to evaluate them, understanding how to recognize and manage the side effects of cancer immunotherapies will become increasingly important. Currently, however, standard parameters for reporting cancer immunotherapy-related adverse events in clinical trials are lacking, and this makes comparisons and management across studies challenging. The Committee, therefore, urges the FDA to work with the research community and the pharmaceutical industry to develop standardized templates for reporting toxicities in cancer immunotherapy clinical trials.

FDA Response:
The Oncology Center of Excellence (OCE), along with FDA's Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research, is currently engaged in developing standardized templates for reporting toxicities in cancer immunotherapy trials, as noted below.

- OCE is leveraging the experience within FDA in review of cancer immunotherapeutics, including immune checkpoint inhibitors (ICI) with over 2,000 clinical trials evaluating ICIs and nearly 50 new or supplemental FDA approvals in oncology across seven approved ICIs, to provide recommendations for standardizing templates for the identification and reporting of toxicities in cancer immunotherapy trials.
- OCE has an immune-mediated toxicity working group that is addressing key concerns for standardization of identification and management of immune-mediated adverse reactions (imAR) with immuno-oncology products.
- OCE is engaging with multiple stakeholders including the research community, professional societies, patient advocacy organizations, and the pharmaceutical industry on identification, management, and reporting of cancer immunotherapy-related adverse events in clinical trials and in the postmarketing setting.

3. Comprehensive Tobacco Framework

The Committee commends the FDA for its 2017 comprehensive plan for tobacco and nicotine regulation to protect public health and create more predictability in tobacco regulation via the consideration of reduced-risk products. FDA must balance the needs of current adult smokers with the risks of attracting new youth to the marketplace. As FDA moves forward, the Committee directs the agency to consider foundational regulations and guidance for its new rulemakings, including for the Substantial Equivalence (SE) and Pre-market Tobacco Application (PMTA) pathways. These rulemakings should reflect a minimum of 24 months for compliance and additional flexibility and assistance for small tobacco product manufacturers. Clear definitions of terms and requirements for submission to FDA, including those for same characteristics and questions related to public health, will help to provide certainty and limit excessive speculation in

the process. A foundational approach to rulemaking and guidance should also rely on product standards, reference products for the SE pathway, performance standards for FDA in certifying reports and applications, and the acceptance of identical specifications in SE reports. In providing transparency, FDA should consider the quarterly release of Center for Tobacco Products reviewer guides. Finally, FDA should consider the expedited or privileged review of quantity and packaging changes that do not affect the core characteristics of products in the PMTA process.

FDA Response:
FDA's comprehensive plan for tobacco and nicotine regulation will serve as a multi-year roadmap to better protect kids and significantly reduce tobacco-related disease and death. As part of this comprehensive plan, FDA announced that it will issue foundational rules to make the product review process more efficient, predictable, and transparent for manufacturers, while also advancing the agency's public health mission. Among other things, FDA intends to issue proposed regulations outlining what information the agency expects to be included in Premarket Tobacco Product Applications (PMTAs) and Substantial Equivalence Reports (SE Reports). The first of these foundational rules for SE Reports is currently in the interdepartmental review process at the Office of Management and Budget. FDA also intends to issue product standards on electronic nicotine delivery systems (ENDS) and testing standards for batteries and battery management systems in ENDS. Additional information about FDA's regulatory activities under development can be found in the latest edition of the Unified Agenda, which is published twice a year in the spring and fall. When each proposed rule is issued, the Agency will solicit comments from the public on all aspects of the rule and will take all of the comments into consideration before issuing a final rule. In addition, FDA intends to provide further information on its thinking with respect to premarket review through guidance documents, as appropriate, such as on considerations relevant to ENDS and the PMTA pathway.

On October 22 and 23, 2018, FDA held a public meeting to improve public understanding and seek feedback on the policies and processes for the submission and review of tobacco product marketing applications, including the general scientific principles relevant to various application pathways, in order to assist applicants considering submitting marketing applications for tobacco products.

Additionally, FDA intends to continue providing web updates with information around decisions and the basis for those decisions. These updates are intended to provide transparency around the timing and review of submissions, including submissions that may only need a limited amount of information (e.g., changes to quantity or packaging). The web updates also provide information on certain deficient applications and how those deficiencies could be addressed to obtain a marketing order. On August 14, 2018, FDA announced that it will proactively provide applicants certain reviews to facilitate understanding of a provisional Not Substantially Equivalent (NSE) decision. Applicants are no longer required to file a Freedom of Information Act request to obtain these documents following a decision.

4. 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:
FDA takes seriously its responsibilities under federal law to protect consumers from misbranded food and understands the Committee's concern regarding plant-based products marketed with names that include the names of standardized dairy foods, e.g., "milk."

Under FDA's Nutrition Innovation Strategy, the Agency is undertaking efforts to modernize the framework for standards of identity. In addition to these efforts, the agency is considering the labeling of plant-based dairy alternatives.

To help the FDA examine the labeling of plant-based dairy alternatives, on September 27, 2018, FDA issued a request for comments and data from stakeholders about consumer awareness, understanding, and perceptions, including nutritional considerations, of these products when labeled with names that include the names of dairy foods. The docket closed on January 28, 2019, and the comments we receive will help inform the development of draft guidance to provide greater clarity on labeling of plant-based dairy alternatives.

5. Food Date Labeling

The Committee recognizes that the lack of food date labeling standardization has resulted in significant consumer confusion. Because food manufacturers use a variety of food date labeling phrases, such as ''freshest by'' or ''use by,'' consumers frequently throw out food that is wholesome and safe, which contributes to the country's food waste problem. The Committee encourages FDA and USDA to provide outreach and guidance to food manufacturers and retailers on food date labeling.

FDA Response:
FDA is committed to improving consumer knowledge about the safety and quality of the food they purchase, including how to understand the handling information and date labels that appear on packaged food.

FDA is responsible for promoting and protecting the public's health by ensuring that the nation's food supply is safe, sanitary, wholesome, and honestly labeled. No federal law or regulation requires date labels, such as expiration dates and use-by dates, on food products, except for infant formula. Any date labels that are used, however, must be truthful and not misleading.

FDA is aware of ongoing efforts by government agencies, industry groups, non-governmental organizations, academia, and others to promote standardized date label phrases and to educate consumers about the meaning of quality-based dates. FDA has engaged in these discussions and continues to enhance its consumer messages related to the meaning of voluntary date labels.

FDA is also working to address the broader problem of food waste through the *Winning on Reducing Food Waste Initiative*, which was recently established through an intergovernmental agreement signed between FDA, the Environmental Protection Agency (EPA), and the U.S. Department of Agriculture (USDA). The agreement is aimed at improving coordination and communication across federal agencies attempting to better educate Americans on the impacts

and importance of reducing food loss and waste. In August 2018, FDA appointed a representative to an interagency discussion group on food waste that is coordinated by USDA and includes representatives from EPA and the National Oceanic and Atmospheric Administration. The group meets every three weeks to consider ways the agencies can work together on food loss and waste initiatives.

As these efforts continue, FDA will consider whether guidance on food date labeling might be appropriate for food manufacturers.

6. Naloxone to Treat Over-usage of Opioids

United States public health agencies have appropriately highlighted the risk of overdose from doses of opioids greater than 90 morphine milligram equivalents (MME) per day. Also concerning are the hundreds of millions of prescriptions each year of immediate release (IR) lower MME opioids such as hydrocodone and oxycodone. These opioids are commonly associated with abuse and are a common pathway to addiction and also present a risk of overdose. Some states have begun to limit the prescribing of these IR opioids. An additional consideration might be to assess the benefit of co-prescribing naloxone with IR and extended release (ER) opioids. Prescribers including dentists and other primary care providers have an opportunity to become more attuned to the risks of all opioids through the consideration of co-prescribing naloxone with each opioid prescription. The Committee requests the FDA develop a strategy to test this hypothesis and assess the benefit for enacting such a policy as a national strategy.

FDA Response:
FDA remains committed to fighting the opioid crisis and will continue to advance using a multipronged strategy. FDA is focusing on four broad areas to help address the opioid crisis: 1) decreasing exposure and preventing new addiction; 2) supporting the treatment of those with opioid use disorder; 3) fostering the development of novel pain treatment therapies; and 4) improving enforcement and assessing benefit-risk. 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. Naloxone is currently a prescription drug nationwide. FDA has reached out to, and met with, sponsors of 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. The study has concluded and an independent FDA review team is currently analyzing the data. Once analysis is 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.

In addition, on December 17-18, FDA held a two-day advisory committee meeting to solicit input and advice on strategies to increase the availability of naloxone products intended for use in the community. FDA asked our external advisors from the Anesthetic and Analgesic Drug Products and the Drug Safety and Risk Management Advisory Committees to consider various options for increasing access to naloxone. This information will help us weigh logistical, economic, and harm reduction aspects of different strategies, and FDA will consider whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death.

7. Olive Oil Standards of Identity

Because of the substantial interest in and consumption of olive oil throughout the United States, driven in part by the significant scientifically-confirmed health benefits of these oils, and the fact that the United States has become a globally-important producer of olive oils, especially extra virgin olive oil, the Committee directs the FDA to establish a separate U.S. Standard of Identity for different grades of olive oil (e.g. refined, virgin and extra virgin) and pomace oils.

The Committee is particularly concerned with the number of different oil state standards for olive oils in the U.S. Because the health benefits of olive oil vary by grade, it is important to establish a uniform set of the standards to better inform and protect consumers. Extra virgin olive oil is the highest quality of olive oil and provides the greatest health benefits for consumers. The FDA is directed to consult and meet with domestic extra virgin olive oil representatives and olive oil representatives in developing a science-based Standard of Identity for extra virgin olive oil and olive oil, respectively, best suited to ensure the integrity of these products for U.S. consumers.

FDA Response:
Under FDA's Nutrition Innovation Strategy, the Agency is working to modernize the framework for standards of identity with the goal of maintaining the basic nature, essential characteristics, and nutritional integrity of food products while allowing industry flexibility for innovation to produce more healthful foods. To support this effort, FDA has indicated its intention to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity. While FDA is working hard on this comprehensive effort to modernize food standards, the Agency is proceeding with ongoing work on standards and labeling consistent with our priorities and resources.

FDA is currently reviewing a citizen petition related to olive oil. The petition was submitted in 2012 by the North American Olive Oil Association (Docket No. FDA-2012-P-0754) and requests FDA to develop a standard of identity for olive oil and olive pomace oil that includes compositional standards and analytical testing. No final decision has been made on this petition. In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA would be happy to have further dialogue with the North American Olive Oil Association and other industry representatives to discuss this matter.

8. 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.

9. Sunscreen Ingredients

The Committee remains significantly concerned that the FDA has not approved a new over-the-counter (OTC) sunscreen ingredient since the 1990s despite increased skin cancer rates 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 having a number of ingredients pending approval for more than 15 years. The Committee directs the FDA to continue to work with sponsors to reach a path forward on a testing regimen for sunscreen ingredients that is consistent with current scientific standards, has a proven track record with sunscreen ingredients, and appropriately balances the benefit of additional skin cancer prevention tools.

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*, FDA relies on industry to submit the data needed to make the required safety and effectiveness determinations for each pending sunscreen active ingredient being evaluated under the SIA framework and in every case FDA has determined that the evidence supplied to date is insufficient to support a determination that the sunscreen containing the active ingredient would be Generally Recognized as Safe and Effective (GRASE).[121] The Agency has also 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. Although not required to do so by the SIA,

[121] US Government Accountability Office (November 15, 2017). Retrieved November 15, 2017, from www.gao.gov/products/GAO-18-61.

FDA continues to meet with sponsors upon request to discuss data development.[122] In May 2018, FDA published a draft guidance that, when finalized, will provide manufacturers with recommendations for how to conduct a MUsT (maximal usage trial) for topically applied active ingredients being considered for inclusion in an OTC drug monograph, including sunscreen active ingredients.[123] 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.

To date, FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future. The FDA is working to finalize OTC monograph regulations for sunscreens by November 26, 2019, as required by the SIA.

[122] Regulations.gov (November 15, 2017). Retrieved November 15, 2017, from www.regulations.gov/document?D=FDA-2005-N-0453-0051.

[123] Guidance for Industry. Maximal Usage Trials for Topical Active Ingredients Being Considered for Inclusion in an Over-The-Counter Monograph: Study Elements and Considerations.
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM608356.pdf

SENATE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

SENATE COMMITTEE REPORT (115-259)

5. 1. Animal Feed Ingredients

The Committee is concerned with the slow pace of review and approval of ingredients for feed for animals. The Committee urges FDA to dedicate additional personnel to speed the review and approval process.

FDA Response:
FDA's budget authority currently allocates 12 full-time equivalents (FTE) to work on animal food ingredient review. These positions work across the vital review areas of target animal safety (i.e., safety of the animals eating the food ingredient), safety of the human food derived from food-producing animals, manufacturing of the animal food ingredient, functionality of the ingredient, and communication with the ingredient manufacturers during the review process. FDA has done considerable work to enhance the efficiency of the review process, but the number and complexity of submissions have increased dramatically. Submissions of Food Additive Petitions (FAPs) have gone up by 150 percent in the last four years and submissions of Generally Recognized As Safe (GRAS) notices have gone up by 200 percent in the last year. FDA analyzed the resources needed to meet performance goals and statutory requirements and is requesting funding to hire more personnel to speed up the review process and stay current with the science.

2. Breast Density

The Committee recognizes the importance of patients receiving their own personal medical information and directs the Food and Drug Administration to ensure that mammography reports and summaries received by patients and their providers include appropriate information about breast density specified by the Secretary, including, at a minimum, the effect of breast density in masking the presence of breast cancer on a mammogram, the qualitative assessment of the provider who interpreted the mammogram, and a reminder to patients that individuals with dense breast tissue should talk with their providers if they have any questions or concerns about their summary.

FDA Response:
The Agency agrees with this Committee. FDA is committed to ensuring that mammogram lay summaries and medical reports provided to patients and their healthcare providers contain the information they need to make informed health care decisions. To further this goal, FDA has drafted proposed amendments to the implementing regulations of the Mammography Quality Standards Act of 1992 that, among other updates, address breast density reporting, and plans to publish the proposed rule in early 2019.

3. Cancer Immunotherapy Clinical Trials

The Committee is aware of the remarkable promise of cancer immunotherapy and encouraged by the FDA's recent approval of new treatments that harness this approach to fighting cancer. More than 1,500 immuno-oncology clinical trials are in some stage of development. As more patients turn to immune-based treatments, and more clinical trials are conducted to evaluate them, understanding how to recognize and manage the side effects of cancer immunotherapies will become increasingly important. Currently, however, standard parameters for reporting cancer immunotherapy-related adverse events in clinical trials are lacking, and this makes comparisons and management across studies challenging. The Committee, therefore, urges the FDA to work with the research community and the pharmaceutical industry to develop standardized templates for reporting toxicities in cancer immunotherapy clinical trials.

FDA Response:
The Oncology Center of Excellence (OCE), along with FDA's Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research, is currently engaged in developing standardized templates for reporting toxicities in cancer immunotherapy trials, as noted below.

- OCE is leveraging the experience within FDA in review of cancer immunotherapeutics, including immune checkpoint inhibitors (ICI) with over 2000 clinical trials evaluating ICIs and nearly 50 new or supplemental FDA approvals in oncology across seven approved ICIs, to provide recommendations for standardizing templates for the identification and reporting of toxicities in cancer immunotherapy trials.
- OCE has an immune-mediated toxicity working group that is addressing key concerns for standardization of identification and management of immune-mediated adverse reactions (imAR) with immuno-oncology products.
- OCE is engaging with multiple stakeholders including the research community, professional societies, patient advocacy organizations, and the pharmaceutical industry on identification, management, and reporting of cancer immunotherapy-related adverse events in clinical trials and in the post marketing setting.

4. Computational Medicine

The Committee appreciates FDA's continued support for and use of modeling and simulation in clinical trials, as well as its work toward the establishment of an affiliation agreement with an academic institution with expertise in this field. This partnership will allow for the development of personalized medical interventions, optimizes the regulatory process with in silico clinical trials and bridges gaps in the current regulatory infrastructure. The Committee directs FDA to formalize this important function in improving outcomes and reducing costs inherent to drug and device discovery.

FDA Response:
Modeling and simulation can be valuable tools deployed throughout medical product development and review, for example, to estimate and evaluate appropriate doses, to help design efficient clinical trials, and to predict and assess product safety. They can also help to explain

variable patient response and provide an alternate path forward in challenging areas where there may be an unmet need or small patient population. FDA is committed to advancing both important methods.

Application of clinical trial simulations and predictive or mechanistic safety evaluation for advancing drug development have been identified as priority areas under the model informed drug development (MIDD) Pilot Program. FDA committed to develop the MIDD Pilot Program as part of the performance goals associated with the Prescription Drug User Fee Act (PDUFA VI), included as part of the FDA Reauthorization Act of 2017. FDA announced the Pilot Program on April 16, 2018. This program provides an opportunity for drug developers and FDA to discuss the application of MIDD approaches to the development and regulatory evaluation of medical products and to provide advice on the use of particular MIDD approaches in a drug development program. Under this pilot, FDA will accept 2-4 paired-meeting requests quarterly each year throughout the PDUFA VI period where selection will prioritize requests that focus on dose selection or estimation, clinical trial simulation, and predictive or mechanistic safety evaluations. So far, FDA has granted paired-meeting requests to 6 sponsors that are applying modeling and simulation approaches to inform the ongoing drug development. Additionally, FDA co-sponsored a public workshop with the International Society of Pharmacometrics on Model-Informed Drug Development for Oncology Products in February 2018. Meeting participants discussed best practices in integrating data of all kinds (pharmacokinetics, pharmacodynamics, efficacy, safety) into models, novel imaging techniques and biomarkers, and potential regulatory implications of model-informed decisions in drug development. This is the first of four workshops FDA plans to hold to help identify best practices for MIDD. FDA will also develop and revise relevant existing guidance on MIDD.

In addition, FDA is committed to advancing the use of complex innovative trial designs and has launched several efforts to fulfill commitments outlined in PDUFA VI. The scope of the efforts includes, but is not limited to, complex adaptive, Bayesian, and other novel clinical trial designs, with a focus on designs for which simulations are necessary to evaluate properties of the trial. Such designs hold the promise of increasing trial efficiency and providing an alternate path forward in challenging areas where there may be an unmet need or small patient population. In March 2018, FDA convened a public workshop on complex innovative trial designs that included a panel of expert academicians. Moreover, FDA launched the CID Pilot Meetings Program on August 29, 2018. Under this program, FDA will grant sponsors of proposals accepted into the Pilot Meetings Program two meetings with the FDA to discuss the planned clinical trial design and analysis including simulations. To further promote innovation, FDA may present the trial designs developed under the pilot program as case studies, including trial designs for drugs that have not yet been approved. In September 2018, the FDA also published a draft guidance on adaptive designs to better guide pharmaceutical companies on the use of such designs.

For medical devices, FDA continues advancing these methodologies and techniques to best take advantage of the benefits for continued product innovation and more rapid introduction of life saving technology to U.S. patients. For instance, FDA has demonstrated that the Virtual Patient Model can serve as one framework for in silico clinical trials and created a virtual population to enable computer-based simulations for medical devices. This allows CDRH to harness data from computer-based simulations to augment clinical trials, i.e., an in silico clinical trial. As an

example, CDRH has completed a fully in silico replication of a pivotal trial submitted as part of the PMA for a novel breast cancer imaging system (for new digital breast tomosynthesis systems). The successful completion of this pivotal in silico trial is now publicly available through a recent publication in JAMA[124] and will provide industry and others with the tools for performing fully in silico clinical trials for imaging systems, which will greatly minimize cost and radiation exposure for patients and help to assure devices meet our gold standard to come to market.

CDRH also currently partners with the University of Mississippi Medical Center (UMMC), using its sophisticated in silico models to predict how interventions, such as renal denervation, can affect certain patient populations. This partnership will build upon UMMC's robust model to evaluate the impacts of drugs and devices across the entire body, to project the long-term effects of particular treatments and interventions and study the ways in which drugs and devices might impact populations differently.

Regulatory evaluation of modeling and simulation is advancing alongside the power and sophistication of the tools. Therefore, FDA formed an Agency-wide working group on modeling and simulation with objectives that include aligning regulatory decision-making with modeling and simulation, and, where appropriate, employing in silico clinical trials. Completing these objectives will advance the in silico clinical trial framework for the medical product Centers and help clarify appropriate methods and guidelines for in silico clinical trials.

As noted, FDA employs a broad range of modeling disciplines, including mechanistic-based, chemistry-based, physics-based, exposure-based, biological, and statistical models. These techniques can also enhance the mechanistic understanding of disease progression and the complex interplay between genetics and predictive biomarkers with response to therapy. FDA will develop guidance and standards related to use of modeling and simulation in device and drug development and evaluation to continue such advancement, which is critical to enabling safe and effective medical products to continue coming to market.

5. 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

[124] JAMA Network Open. 2018;1(7):e185474. doi:10.1001/jamanetworkopen.2018.5474

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." In January 2018, FDA announced its intent to pursue rulemaking related to the farm definition and will consider the concerns of the cotton ginning industry in that evaluation. The Agency also announced its intent to exercise enforcement discretion with respect to application of the ''Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals'' (PCAF) regulation to facilities that would be considered secondary activities farms except for the ownership of the facility, which would include certain cotton ginning entities. The Agency intends to continue the exercise of enforcement discretion until it is able to address cotton industry concerns through additional rulemaking or by other means. See Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs: Guidance for Industry at https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM590661.pdf.

FDA has had multiple meetings with the cotton ginning industry on this topic. In October 2017, FDA staff 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.[125] During the meetings with the industry and the educational tour, FDA reiterated its commitment to resolving the industry's concerns about the applicability of the PCAF rule to ginning operations. Since that time, FDA formalized its commitment by releasing the January 2018 enforcement discretion guidance for industry ("Policy Regarding Certain Entities Subject to the Current Good Manufacturing Practice and Preventive Controls, Produce Safety, and/or Foreign Supplier Verification Programs"). Since the issuance of the guidance document, FDA has responded to requests for status updates from the cotton industry and remains committed to providing additional information on the status when more information becomes publicly available.

6. 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:

[125] https://blogs.fda.gov/fdavoice/index.php/2017/11/talking-fsma-in-the-land-of-cotton-and-looking-for-middle-ground/

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. 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. In October 2018, FDA issued a draft compliance and implementation guidance to assist farmers in meeting Produce Safety Rule requirements. To further assist farmers and other stakeholders, we published "At-A-Glance" overviews that highlight the key points in each chapter in the draft guidance. The draft guidance document is open for public comment for 180 days. FDA also held four public meetings around the country at which the Agency had an opportunity to engage with stakeholders on the Produce Safety Rule draft guidance. In addition, 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.

7. FSMA Cooperative Agreements

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 have or 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:
The funding opportunity announcement (FOA) for the cooperative agreement "State and Territory Cooperative Agreement to Enhance Produce Safety in Preparation of Implementation of FDA's Rule: Standards for the Growing, Harvesting, Packing, & Holding of Produce for Human Consumption" (PAR 16-137) includes language allowing funding to be provided to the agency

with state legislative and/or regulatory authority to implement the Produce Safety Rule adopted in accordance with the FDA Food Safety Modernization Act and to provide education, outreach, and technical assistance for the rule.

If another agency is granted said authority, it is permissible under applicable regulations covering federal grant funding and under the HHS Grants Policy Statement to change the implementing agency awarded the funds upon the submission of a change request and subsequent review and approval by the grant funding agency. Doing so, per established regulations and the HHS Grants Policy Statement, results in the state or territory continuing to receive funding without delay or loss of funding.

8. Human Drug Review Committee

The Committee strongly encourages the FDA to fully utilize its authorities under 18 U.S.C. 208(b)(3) to include no less than two members with an expertise in the indication for which the drug is meant to treat on each Advisory Committee when that Committee is reviewing a drug that has been designated an Orphan Drug.

FDA Response:
Advisory committees play an important role in FDA activities to protect and promote public health, and provide FDA with independent advice on scientific, technical, and policy matters related to the development and evaluation of FDA-regulated products.

FDA agrees with the intent suggested by the Committee and is diligent in trying to get experts in the relevant disease to participate in each advisory committee meeting. It is valuable to have several such experts at the meeting, as each may bring a different perspective on important scientific, technical and policy matters.

On the other hand, FDA is committed to adhering to the laws and regulations governing the process for selecting advisory committee members, which are intended to help minimize bias and potential conflicts of interest. FDA for many years has screened, prior to each advisory committee meeting, all potential participants who are Special Government Employees (SGEs) or regular Government employees, to determine whether the potential for a financial conflict of interest exists. Where such a conflict exists, the agency may grant a waiver allowing participation in an advisory committee meeting when statutory criteria are met; for example, when the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved (18 U.S.C. 208(b)(3)).[126] FDA works diligently to have two or more individuals with an expertise in the indication for which the drug is meant to treat on each advisory committee; however, in some cases it is not feasible given the statutory constraints. FDA will continue to work on this matter and consider the committee's suggestion within the statutory framework.

[126] Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees. https://www.fda.gov/oc/advisory/waiver/coiguidedft.html

9. 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 the Committee's concern for the truthful labeling of products and the importance of having consumers be able to make informed choices about their foods. Current regulations allow use of terms like "maple," "maple-flavored," or "artificially maple-flavored" on the food label without having any maple syrup in the product if it contains maple flavoring. The Agency's website includes information to help educate consumers about these regulations and the differences in the ways that ingredients and flavors are declared on product labels, including use of the terms "maple" and "maple syrup." That consumer update is available at www.fda.gov/ForConsumers/ConsumerUpdates/ucm521518.htm.

FDA has conducted a preliminary review of potential consumer perception issues and has met with representatives of the maple syrup industry regarding the applicable labeling regulations. The Agency is happy to continue meeting with industry representatives to discuss available data and other industry information on consumer perceptions regarding maple and maple syrup that may complement our own monitoring of the issue. FDA will consider taking action against products that are misbranded, as appropriate, consistent with our food safety priorities and resources.

10. Olive Oil

Because of the substantial interest in and consumption of olive oil throughout the United States, driven in part by the significant scientifically-confirmed health benefits of these oils and the fact that the United States has become a globally-important producer of olive oils, especially extra virgin olive oil, the Committee directs the FDA to establish a separate U.S. Standard of Identity for different grades of olive oil (e.g. refined, virgin and extra virgin) and olive-pomace oils. The Committee is particularly concerned with the number of different state standards for olive oils in the U.S. Because the health benefits of olive oil vary by grade, it is important to establish a uniform set of the standards to better inform and protect consumers. Extra virgin olive oil is the highest quality of olive oil and provides the greatest health benefits for consumers. The FDA is directed to consult and meet with domestic producers and importers of olive oil to develop a science-based Standard of Identity for extra virgin olive oil and olive oil best suited to ensure the integrity of these products for U.S. consumers.

FDA Response:

Under FDA's Nutrition Innovation Strategy, the Agency is working to modernize the framework for standards of identity with the goal of maintaining the basic nature, essential characteristics, and nutritional integrity of food products while allowing industry flexibility for innovation to produce more healthful foods. To support this effort, FDA has indicated its intention to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity. While FDA is working hard on this comprehensive effort to modernize food standards, the Agency is proceeding with ongoing work on standards and labeling consistent with our priorities and resources.

FDA is currently reviewing a citizen petition related to olive oil. The petition was submitted in 2012 by the North American Olive Oil Association (Docket No. FDA-2012-P-0754) and requests FDA to develop a standard of identity for olive oil and olive pomace oil that includes compositional standards and analytical testing. No final decision has been made on this petition. In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA would be happy to have further dialogue with the North American Olive Oil Association and other industry representatives to discuss this matter.

11. Opioids

The Committee continues its directive for FDA to refer any drug application for an opioid 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 public health.

The Committee directs the Commissioner to seek recommendations from the Drug Safety and Risk Management Advisory Committee regarding a framework for the inclusion of information in the labeling and/or REMS of drugs that are opioids or used in Medically-Assisted Treatment relating to the co-prescription of opioid overdose reversal drugs along with opioids prescribed to patients that meet CDC guidelines as at risk for overdose.

FDA Response:
FDA will continue to follow section 106 of the Comprehensive Addiction and Recovery Act (CARA) concerning advisory committees. 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 held 11 opioid-related advisory committee meetings in 2018.

FDA recognizes that emergency treatment of known or suspected opioid overdose is an urgent public health priority, and to advance these efforts, there is still a need to improve access to naloxone. On December 17-18, 2018, FDA held a two-day advisory committee meeting to solicit input and advice on strategies to increase the availability of naloxone products intended for use in the community. FDA asked our external advisors from the Anesthetic and Analgesic Drug Products and the Drug Safety and Risk Management Advisory Committees to consider various options for increasing access to naloxone. This information will help us weigh logistical, economic, and harm reduction aspects of different strategies, and FDA will consider whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death.

12. Polypharmacy

The routine usage of five or more prescription medications within the same period is becoming increasingly prevalent among older adults, elevating risk factors for drug-drug interactions and adverse events. The Committee directs the FDA to assess potential impacts of polypharmacy, which might help inform the design of clinical studies.

FDA Response:
As a part of new drug evaluation, FDA routinely assesses the potential for drug-drug interactions. This evaluation considers the potential for drug interactions that result from polypharmacy. The results of FDA evaluations can inform prescription drug labeling that is often used by prescribers, drug information specialists, and clinical decision support platform developers to aid in therapeutic decision-making at the patient level. Additionally, FDA is developing guidance for sponsors on how to evaluate drug-drug interactions (DDIs) during drug development. In October 2017, the FDA published a draft guidance entitled *Clinical Drug Interaction Studies - Study Design, Data Analysis, and Clinical Implications*. This guidance, when finalized, is intended to help sponsors of investigational new drug applications and applicants of new drug applications evaluate DDIs during drug development.

13. Ready To Eat Foods

The Committee is aware that FDA is in the process of finalizing guidance regarding Listeria monocytogenes [Lm] in RTE foods. Reducing incidents of listeriosis is an important health goal and the Committee supports efforts to accomplish this objective. The Committee urges FDA to complete a comprehensive risk assessment to ensure any final guidance document is realistic and fully based in science prior to making any changes to the action level of Lm in RTE foods.

FDA Response:

FDA is careful to ensure that its guidances are solidly grounded in current science and offer flexibility to firms in implementing controls as appropriate to their products, processes, and facilities. In 2008, FDA published a draft compliance policy guide (CPG) for *Listeria monocytogenes* (Lm) stating that the Agency would not consider a ready-to-eat (RTE) food that does not support growth to be adulterated if Lm did not exceed 100 cfu/g. This CPG was not finalized. FDA determines the risk associated with Lm in food on a case-by-case basis depending on a number of factors, including whether the food supports the growth of the pathogen.

FDA has significant scientific expertise in Lm and has devoted substantial effort toward advancing the science in this area, including through risk assessment. FDA, the Centers for Disease Control and Prevention, and the USDA's Food Safety and Inspection Service jointly developed a Quantitative Assessment of Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods. The assessment took four

years to complete, beginning with a *Federal Register* notice of intent issued in 1999 and culminating in completion of the final assessment in 2003. FDA continues to gather data and monitor developments in the body of science around the presence of Lm in RTE foods, such as information related to a 2015 outbreak of listeriosis from ice cream that was found to contain very low levels of Lm, and to develop models to characterize the risk of listeriosis in highly susceptible population subgroups.

14. Seafood Advisory

The Committee remains concerned that the FDA published final seafood advice for pregnant and nursing women on January 18, 2017, without going through the 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 reissue the final ''Advice About Eating Fish'' (published in 82 Fed. Reg. 6571 (January 19, 2017)) in a manner that is consistent with the FDA's nutrition science on the net effects of seafood consumption.

FDA Response:
The 2017 final fish advice, entitled "Fish: What Pregnant Women and Parents Should Know,"[127] 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. When updating the fish advice, FDA gave broad consideration to the available research, including FDA's own net effects assessment. This 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.[128]

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 updated draft 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 Agency officials in attendance. Documentation of the public and expert input is available at FDA's website. FDA believes this

[127] https://www.federalregister.gov/documents/2017/01/19/2017-01073/advice-about-eating-fish-from-the-environmental-protection-agency-and-food-and-drug-administration

[128] https://www.fda.gov/Food/ResourcesForYou/Consumers/ucm393070.htm

additional information demonstrates the rigor of our process for reviewing and updating the fish advice.

FDA issued denial letters in response to a citizen petition and then a petition for reconsideration requesting that FDA withdraw and reissue the 2017 seafood advice. FDA's response letters, which include information about FDA's consideration of the FDA Net Effects Assessment, are available in Docket No. FDA-2017-P-3196.[129]

15. Sunscreen Labeling Regulations

The Committee remains significantly concerned that the FDA has not approved a new over-the-counter [OTC] sunscreen ingredient since implementation of the Sunscreen Innovation Act, which improved the process by which the FDA reviews sunscreen ingredients and required the FDA to finalize an effective sunscreen monograph within 5 years. The Committee directs the FDA to meet with sponsors regarding the development of a testing regimen for sunscreen ingredients, consistent with current scientific standards, that appropriately balances the benefit of additional skin cancer prevention tools versus the risk of skin cancer. 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 2018 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 being evaluated under the SIA framework, and in every case FDA has determined that the evidence supplied to date is insufficient to support a determination that a sunscreen containing the active ingredient would be Generally Recognized as Safe and Effective (GRASE).[130]

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

[129] https://www.regulations.gov/docket?D=FDA-2017-P-3196

[130] US Government Accountability Office (November 15, 2017). Retrieved November 15, 2017, from www.gao.gov/products/GAO-18-61.

of the pending sunscreen ingredients that were the subject of SIA-required proposed sunscreen orders issued in 2015.

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 effective 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. In order to finalize such a monograph, FDA intends to first publish a proposed rulemaking on sunscreens in order to provide the opportunity for public comment.

16. 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. In the Committee's report for fiscal year 2016, the Committee requested a feasibility study to update and issue a revised Master Plan for land inside and contiguous to the White Oak Campus in order to address its expanded workforce and the facilities needed to accommodate them. The Committee directs FDA to complete this study as soon as possible. Due to the challenging fiscal environment, the Committee encourages the FDA and GSA to consider innovative financing options and partnership opportunities with non-federal government entities that provide reasonable cost options 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 the Government Services Administration (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 for the White Oak Campus. These documents 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. On December 6, 2018, the National Capital Planning Commission voted to approve the new FRC Master Plan, which will be implemented in phases subject to the availability of funding. The FDA Housing Strategy/Migration Plan is still under development.

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 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 needs 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 satisfying FDA's housing needs required Congressional prospectus lease authority and that, after Congressional approval, the housing needs would 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 submitted to OMB for FY 2019 approval.

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FDA SPECIFIC ITEMS

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES

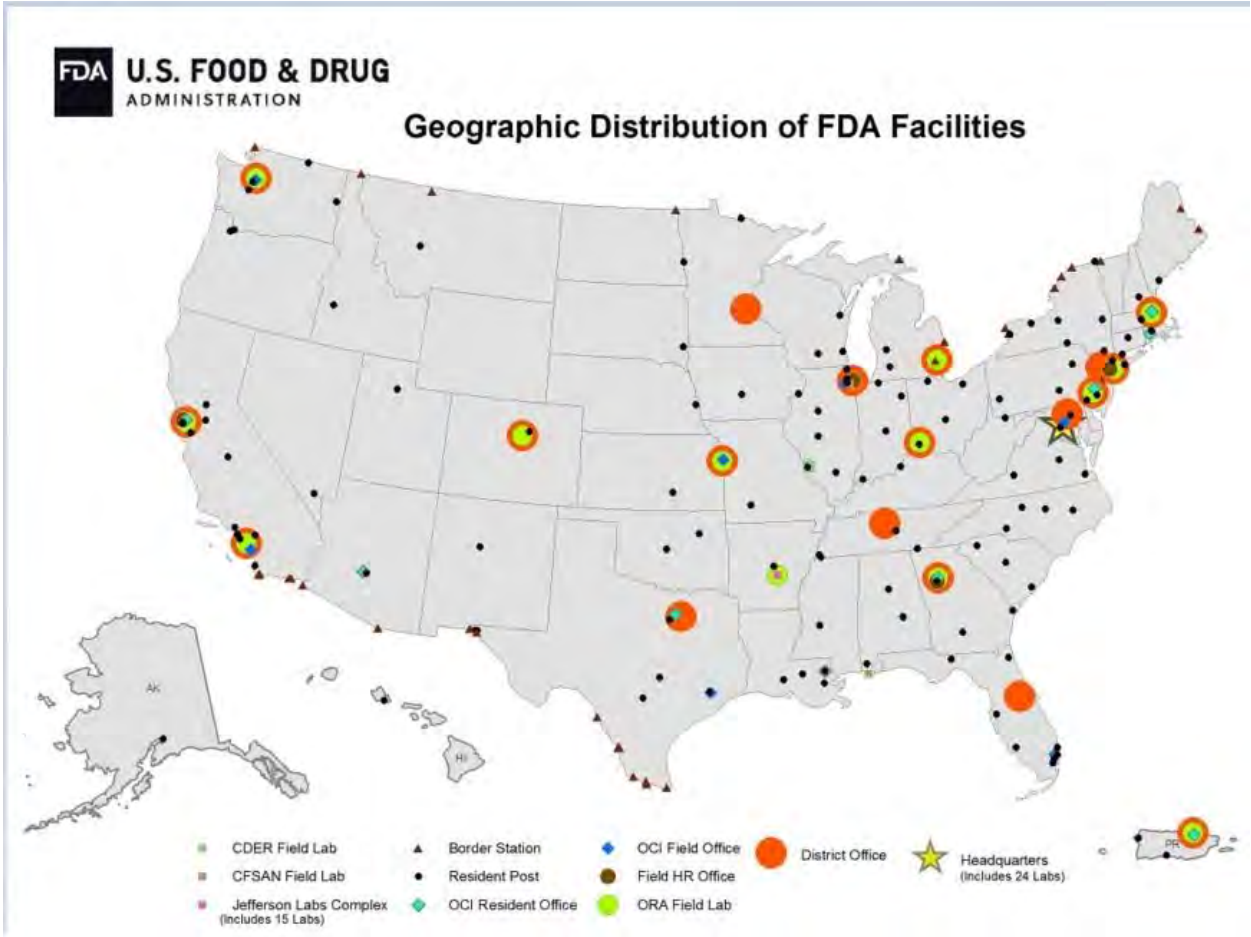

Figure 1 Geographical Distribution of FDA Facilities

HIV/AIDS FUNCTIONAL TABLE

Program	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Human Drugs	$29,869	$29,869	$29,869
Biologics	$29,006	$28,046	$31,665
Medical Devices	$318	$318	$318
Field Activity	$34,980	$35,640	$36,300
Toxicological	$3	---	---
Other Activities	$3,395	$3,395	$3,395
Total HIV/AIDS	**$97,571**	**$97,268**	**$101,547**

CROSSCUTS

(dollars in thousands)	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Alzheimer's Disease	6,326	5,626	5,755
AIDS/HIV	97,571	97,268	101,547
Antimicrobial Resistance	38,557	38,131	40,232
Diabetes	22,306	22,701	23,114
Drug Abuse	13,058	13,061	12,977
Global Health	163,885	161,238	161,281
Immunization	29,065	29,451	30,982
Pandemic Influenza	40,502	41,119	43,678
Patient Safety	31,070	31,044	30,116
Pediatric Drugs	7,094	8,104	8,001
Precision Medicine	4,892	4,892	4,892
Prevention	4,893,054	4,896,590	5,553,286
Mental Health	19,648	19,476	19,449
Opioids	59,054	59,666	114,666
Tobacco	672,000	712,000	812,000
Women's Health	100,345	106,124	104,446

CENTRAL ACCOUNTS

Program (dollars in thousands)	FY 2018 Actuals		FY 2019 Estimates		FY 2020 Estimates	
	BA	UF	BA	UF	BA	UF
Foods	**16,061**	-	**17,772**	-	**18,359**	-
Center	5,246	-	5,245	-	5,350	-
Field	10,815	-	12,526	-	13,009	-
Human Drugs	**15,037**	**58,642**	**20,880**	**51,255**	**21,060**	**51,039**
Center	11,973	55,819	17,278	50,514	17,624	50,514
Field	3,064	2,823	3,602	741	3,436	525
Biologics	**4,906**	**7,574**	**6,399**	**5,575**	**6,528**	**5,711**
Center	4,005	6,709	5,368	5,346	5,475	5,346
Field	901	865	1,032	229	1,052	365
Animal Drugs and Feeds	**3,066**	**1,870**	**4,185**	**910**	**4,275**	**910**
Center	1,804	1,837	2,731	910	2,786	910
Field	1,262	33	1,454	00	1,490	00
Devices and Radiological Health	**7,121**	**8,348**	**11,062**	**4,245**	**11,282**	**4,325**
Center	5,139	8,223	8,781	4,142	8,956	4,142
Field	1,983	125	2,281	103	2,326	183
National Center for Toxicological Research	**807**	-	**766**	-	**781**	-
FDA Headquarters	**10,007**	**5,618**	**11,104**	**5,899**	**11,327**	**5,899**
Total	**57,005**	**82,053**	**72,168**	**67,884**	**73,611**	**67,884**

HHS CHARGES AND ASSESSMENTS

Food and Drug Administration Department of Health and Human Services Charges and Assessments Fiscal Year 2018 Actuals	
Assessments:	**217,850.00**
NIH eRA Grants Management System Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	214,592
Federal Audit Clearinghouse	3,258
Fee For Service:	**69,595,718**
Program Support Center/ Office of the Secretary Provides various services to the FDA, including some Information and Systems Management Services	**18,333,791**
Financial Management Portfolio (FMP)	579,411
Procurement Management Portfolio (PMP)	
Administrative Operations Portfolio (AOP)	8,393,102
Includes costs for digital, forms and travel management, board of corrections, printing, trans-share, mail	
Real Estate and Logistics Portfolio Includes building operations, shredding, storage, property disposal,	2,448,320
Equal Employment Opportunity Compliance and Operations Includes Complaint Investigations, FAD/Counseling, Mediation	278,763
Miscellaneous Services	6,634,195
Includes AIM, Category Mgmt., Commissioned Corps Force Mgmt (CCFM), Departmental Contracts Information System Program (DCIS), Ethics Program, Grants, Broadcast studio, HPO, Medio Monitoring, OGC Claims, Small Business Consolidation, Strategic Planning, TAGGS	
Federal Occupational Health (FOH): FDA agency health units and services	**2,437,579**
Information & System Management Services	**41,184,377**
Freedom of Information (FOIA)	160,000
Unified Financial Management Systems (UFMS) Includes services for Consolidated Financial Reporting System (CFRS), Financial Business Intelligence System (FBIS), Governance and UFMS O&M support	10,195,051
HCAS Operations and Maintenance HCAS O&M services provide support for daily operations of the HCAS application.	2,171,000
Information Technology Infrastruction & Operations (ITIO) Telecommunications team offers expertise on Network / Telecomunnications / Security.	3,341,204
Office of IT Strategy, Policy & Governance	2,255,637
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	6,166,013
Office of Information Security (OIS)	4,215,306
Includes computer security incident reponse center. Trusted Internet Connections and IT Security.	
Office of Security and Strategic Information (OSSI)	6,450,624
HSPD-12 System: FICAM Services, identity & logical access, etc. Badging Operations	
Digital Communications Web Crawler, Web Media	6,229,542
Office of Human Resource Services Includes HR Center services teir I, payroll liaison, systems planning and implemenation	**7,639,971**

Jointly Funded Projects:	**$3,666,133**
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	**2,434,974**
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.	474,696
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	59,649
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	27,000
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.	117,847
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.	79,369
Implementation of the DATA Act (PMO)	162,494
Tick-Borne Disease Working Group The work group will provide expertise and review all efforts within the Department of HHS related to all tick-borne diseases, to help ensure interagency coordination and minimize overlap and to examine research priorities.	150,000
Pain Management Interagency Task Force The task force shall review gaps in or inconsistencies between best practices for pain management (including chronic and acute pain); and propose updates as necessary towards prevention, treatment, recovery, law enforcement reform and overdose reversal.	150,000
National Clinical Care Commission The Commission is required to establish a committee to evaluate and make recommendations regarding improvements to the coordination and leveraging of progams within the Department and other Federal agencies related to awareness and clinical care for at least one, but not more than two, complex metabolic or autoimmune diseases resulting from issues related to insulin that represent a significant disease burden in the US.	90,000

HHS CHARGES AND ASSESSMENTS: FY 2018 - FY 2020

Activity	FY 2018 Actual	FY 2019 Estimate	FY 2020 Estimate
Assessments	**$ 217,850**	**$ 250,234**	**$ 282,629**
Fee for Service	**$ 69,595,718**	**$ 74,266,463**	**$ 79,573,000**
Program Support Center/OS	$ 18,333,791	$ 30,701,040	$ 32,479,000
Federal Occupational Health	$ 2,437,579	$ 3,514,224	$ 3,580,000
Information System Management Service	$ 41,184,377	$ 32,411,227	$ 33,489,000
Human Resource Center – Rockville, Maryland	$ 7,639,971	$ 7,639,972	$ 10,025,000
Jointly Funded Services	**$ 3,666,133**	**$ 3,461,035**	**$ 3,517,580**
International Health - Bilateral Agreement	$ 1,231,159	$ 1,231,159	$ 1,231,159
Other Jointly Funded Projects	$ 2,434,974	$ 2,229,876	$ 2,286,421
Total	**$ 73,479,701**	**$ 77,977,732**	**$ 83,373,210**

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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
OLS	Office of Laboratory 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.