DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2021

Food and Drug Administration

Justification of
Estimates for
Appropriations Committees

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FDA U.S. FOOD & DRUG ADMINISTRATION

LETTER FROM THE COMMISSIONER

I am pleased to present the FY 2021 Food and Drug Administration (FDA) Budget. FDA holds critical responsibility for ensuring the safety, effectiveness, and security of human and animal drugs, biological products, medical devices as well as ensuring the safety of our nation's food supply, cosmetics and products that emit radiation. FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by minors.

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

- Combating the Opioid Crisis – FDA is committed to protecting Americans from illegal and potentially dangerous opioids that might otherwise end up on the streets, at stores, and in homes across the country. As part of this effort, in 2019 FDA increased the number of special agents and import investigators responsive to illicit activity involving FDA-regulated products arriving through International Mail Facilities (IMF) and Ports of Entry. In FY 2019, more than 17,000 violative drug products were destroyed across all nine IMFs (an increase of 15,522 over FY 2018), with a reported value of more than $1,500,000 (an increase of more than $1,000,000 over FY 2018).
- Tobacco Regulation – Preventing youth access to and use of e-cigarettes remains one of FDA's top priorities. Amid the epidemic levels of youth use of e-cigarettes, FDA issued a policy prioritizing enforcement[1] against certain unauthorized flavored e-cigarette products that appeal to kids, including fruit and mint flavors. Under this policy, companies that do not stop the manufacture, distribution and sale of unauthorized flavored cartridge-based e-cigarettes (other than tobacco or menthol) within 30 days risk FDA enforcement actions. Additionally, on December 20, 2019, the President signed legislation to raise the federal minimum age of sale of tobacco products from 18 to 21 years. It is now illegal for a retailer to sell any tobacco product – including cigarettes, cigars and e-cigarettes – to anyone under 21.

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-delivery-system-ends-and-other-deemed-products-market

- Modernizing Food Safety – In 2019 FDA launched the New Era of Smarter Food Safety which leverages the use of new and emerging technologies focused on traceability, digital technologies and evolving food business models. FDA also made exceptional progress implementing the Nutrition Innovation Strategy that focuses on reducing preventable death and disease related to poor nutrition.
- Advancing Medical Product Safety and Innovation and promoting choice and competition– 2019 continued to be a banner year for FDA in terms of medical product approvals. FDA approved 48 new drugs, 6 new biologics, 935 generic drugs, 10 new biosimilars, and 71 new devices, including four medical countermeasures to support the Strategic National Stockpile.

The FY 2021 Budget will allow FDA to continue to deliver high-impact results that help Americans every day. FDA is requesting a total of $6.2 billion; an overall increase of $265.4 million compared to the FY 2020 Enacted Level (4.5 percent increase). FDA will invest in initiatives focused on the most urgent priorities as well as critically needed infrastructure.

This includes efforts to:

- apply novel approaches to data management including artificial intelligence and other emerging technologies to drive growth of the United States economy, foster development of safe medical devices, and make the food supply safer
- support oversight of increasing numbers of marketed FDA-regulated products containing cannabis-derived substances that require assessment or review by FDA
- make the United States influenza vaccine supply more robust, secure, and nimble to combat seasonal influenza epidemics and potential influenza pandemics
- work closely with stakeholders to ensure that patients receive the highest quality of compounded drugs when they need them.

Investing in a smarter FDA means investing in the latest tools and technology to keep pace with new regulated products, industry advances, foodborne illness outbreaks, and emerging health threats, while maintaining critical mission-enabling infrastructure. FDA's FY 2021 budget request enables the agency to help industry bring safe products to market, protect and promote public health, and meet consumer expectations for assuring the safety of new food products and dietary supplements.

Sincerely,

Hahn

Stephen M. Hahn, M.D.
Commissioner of Food and Drugs

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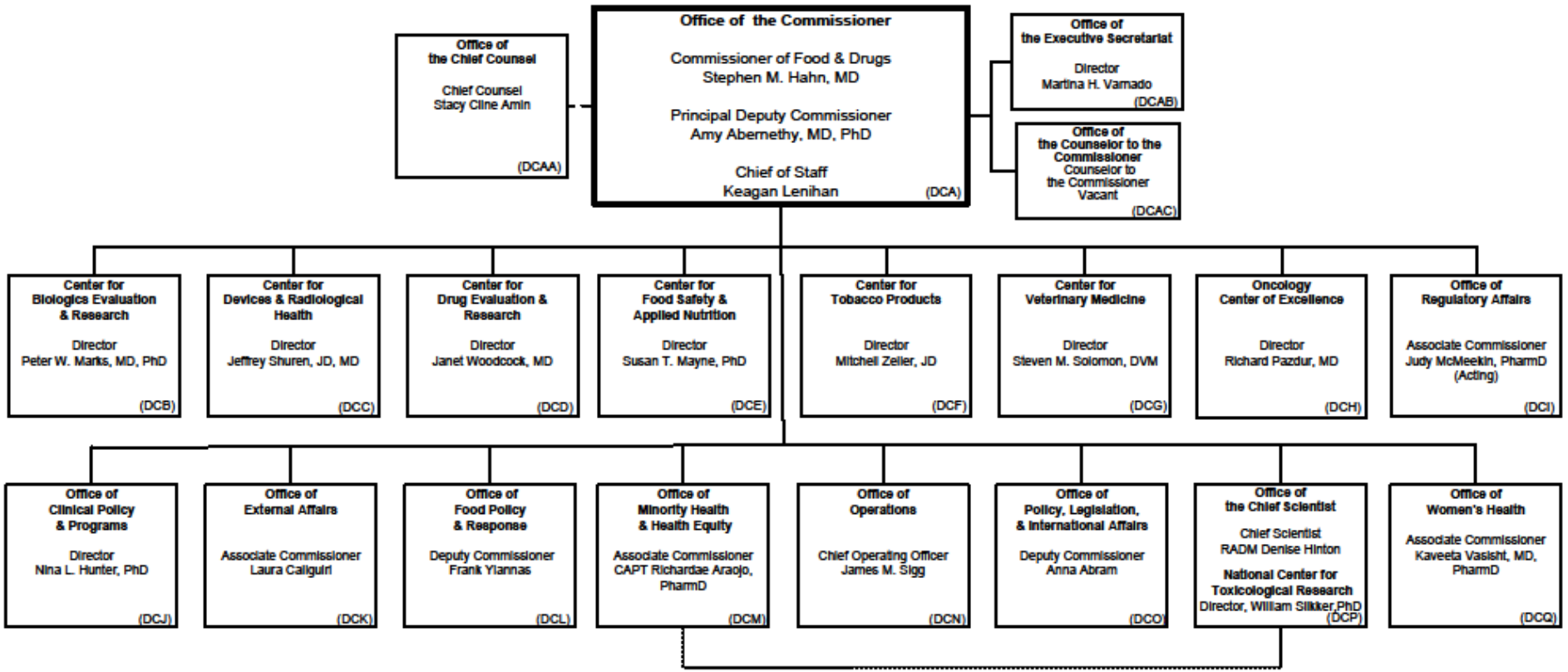
Food and Drug Administration

January 2020



Legend:

- Direct report to DHHS General Counsel
- Direct report to the FDA Commissioner with operational oversight from the Office of the Chief Scientist

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FY 2021 CJ EXECUTIVE SUMMARY

PERFORMANCE BUDGET OVERVIEW

EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2021 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. FDA's customers and key stakeholders include American patients and consumers; healthcare professionals; regulated industry; academia; and, state, local, federal and international governmental agencies.

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

FDA is committed to reducing the burdens of the addiction crisis that are threatening American families by reducing harm from opioids and reducing youth tobacco use.

Combating the Opioid Crisis

FDA is committed to protecting Americans from illegal, and potentially dangerous, opioids that might otherwise end up on the streets, at stores, and in homes across the country. FDA and its partners in government are actively tracking, targeting, and interdicting illicit opioid products arriving through International Mail Facilities (IMF) and other illicit networks to ensure that these products do not continue to fuel the national opioid epidemic.

In FY 2019, FDA increased the number of special agents and import investigators responsive to illicit activities involving FDA-regulated products occurring at IMFs and ports of entry. In FY 2019, the number of criminal investigators assigned to IMFs resulted in 235 cases referred to the OCI field offices and more than 22 special operations conducted at various IMFs and ports of entry.

Additionally, there has been a significant increase in the dollar value of violative drug products destroyed in the IMFs due to the efficiencies gained from the SUPPORT Act, specifically the addition of 801(u) authority. In FY 2019, there were more than 17,000 violative drug products destroyed across all nine IMFs (an increase of 15,522 over FY 2018), with a reported value of more than $1,500,000 (an increase of more than $1,000,000 over FY 2018).

In early FY 2020, the first FDA IMF satellite lab came online. This satellite lab brings screening tools and scientists to selected IMFs, resulting in more entry reviews and associated destructions.

The satellite lab prevents unapproved, adulterated and counterfeit pharmaceuticals, including opioids, from reaching the public.

FDA also is cracking down on cybercrime. FDA took proactive steps to reduce the availability of opioids online by posting warning letters to operators of websites that illegally marketed unapproved opioids and products to treat addiction and chronic pain as well as increasing resources devoted to online pharmacy investigations resulting in the seizure of more than $41M in assets. These warning letters include the first joint FDA and DEA warning letters, issued in September 2019, to four online networks operating a total of 10 websites, illegally marketing unapproved and misbranded opioids.

FDA also is working to better secure the medical product supply chain and to hold distributors responsible for securing their drug supply chain. In February 2019, FDA issued its first warning letter under the Drug Supply Chain Security Act (DSCSA), targeting a violation that resulted from a tampering incident involving opioid medications.

And in FY 2019 FDA also approved the first generic naloxone nasal spray to treat opioid overdose and developed a model Drug Facts Label to support over-the-counter naloxone development programs.

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 goal is to ensure that FDA has the proper scientific and regulatory foundation to efficiently and effectively implement the Family Smoking Prevention and Tobacco Control Act.

The 2019 National Youth Tobacco Survey (NYTS) results on e-cigarette use show that more than 5 million U.S. middle and high school students are current e-cigarette users (having used within the last 30 days) – with a majority reporting cartridge-based products as their usual brand.

FDA remains committed to tackling the troubling epidemic of e-cigarette use among kids. Preventing youth access to and use of ENDS remains one of FDA's top priorities. Our plan combines compliance and enforcement activities with high-profile public education efforts designed to reach nearly 10.7 million youth at risk of starting or continuing to use e-cigarettes.

On January 2, 2020, FDA issued a final guidance for industry titled "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization." Amid the epidemic levels of youth use of e-cigarettes and the popularity of certain products among children, FDA issued a policy prioritizing enforcement against certain unauthorized flavored e-cigarette products that appeal to kids, including fruit and mint flavors. Under this policy, companies that do not cease manufacture, distribution and sale of unauthorized flavored cartridge-based e-cigarettes (other than tobacco or menthol) within 30 days risk FDA enforcement actions.

In addition, on December 20, 2019, the President signed legislation to amend the Federal Food, Drug, and Cosmetic Act, raising the federal minimum age of sale of tobacco products from 18 to

21 years. It is now illegal for a retailer to sell any tobacco product – including cigarettes, cigars and e-cigarettes – to anyone under 21.

Foster Competition and Innovation

FDA is committed to fostering 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.

Drug Competition

FDA plays a pivotal role in fostering competition through the approval of safe, effective, and lower-cost generic drugs and biosimilars. Highlights from 2019 accomplishments in the area of drug competition are shown below.

In 2019, FDA set a record for the greatest number of generic drugs approved in a single fiscal year – 935. These drug approvals help to make treatments more affordable and increase access to medications for millions more patients.

FDA also continued implementation of the Biosimilars Action Plan by publishing guidances that increase the public's access to important biological therapies.

In July 2019, FDA published a Safe Importation Action Plan describing two pathways that manufacturers and other importers may take to provide safe and effective drugs to consumers in the U.S.[1]

FDA also issued a notice of proposed rulemaking in December 2019 that would allow certain prescription drugs to be imported from Canada to the U.S. FDA also issued draft guidance describing procedures drug manufacturers could follow to obtain an additional National Drug Code (NDC) for certain FDA-approved prescription drugs, including biological products, that were originally manufactured and intended to be marketed in a foreign country. The use of an additional NDC would allow greater flexibility for drug companies to offer these products at a lower price than what their current distribution contracts require.

FDA continues to actively identify initiatives to make more safe, effective, and high-quality generic medicines available to the public.

The Administration has and continues to support legislative efforts to make the path to generic and biosimilar development more transparent, efficient, and predictable so that Americans have better access to these medicines that are often more affordable. Overall, addressing regulatory barriers and challenges and closing potential loopholes that hinder development of generics, will promote more competition, and advance patient access to more affordable medicines.

The President's 2021 Budget includes an allowance for bipartisan drug pricing proposals. The Administration supports legislative efforts to improve the Medicare Part D benefit by

[1] https://www.hhs.gov/sites/default/files/safe-importation-action-plan.pdf

establishing an out-of-pocket maximum and reducing out-of-pocket costs for seniors. The Administration also supports changes to bring lower cost generic and biosimilar drugs to patients. These efforts would increase competition, reduce drug prices, and lower out of pocket costs for patients at the pharmacy counter.

Advancing Medical Product Safety and Innovation

To support continued innovation in regenerative medicine and to provide clear recommendations to sponsors and researchers of novel therapies, FDA issued two final regenerative medicine therapy guidances in February 2019. These final guidances build on FDA's comprehensive regenerative medicine framework. The first guidance document explains FDA's expedited development and review programs available to regenerative medicine therapies and strategies for clinical development. The second guidance document describes FDA's approach to the evaluation of devices used with regenerative medicine advanced therapies.

As part of FDA's public health mission, FDA also facilitates medical countermeasure (MCM) product development. 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. In July 2018, FDA approved TPOXX (tecovirimat), the first drug with an indication for the treatment of smallpox, and in September 2019, FDA approved Jynneos, a vaccine for the prevention of smallpox and monkeypox disease. Jynneos is the only FDA-approved vaccine for the prevention of monkeypox disease. Both MCMs are included in the Strategic National Stockpile.

FDA also approved the first vaccines to prevent two tropical diseases. Tropical diseases often become emerging infectious disease threats within the U.S. Dengvaxia was approved in May 2019 to prevent dengue disease and Ervebo was approved in December 2019 to prevent Ebola virus disease. FDA used expedited programs to enhance review and the efficiency of the development programs for these products.

For medical devices, FDA continues to take steps to enhance safety while assuring patients have timely access to safe, effective, high-quality devices. In FY 2019, FDA supported the award of seven new Broad Agency Announcement (BAA) contracts and Center of Excellence in Regulatory Science and Innovation (CERSI) grants. These projects ensure collective and innovative efforts to expedite drug development and bring drugs to market sooner. For example, the use of mobile devices, wearables and other biosensors to gather and store huge amounts of health-related data has been rapidly accelerating. The devices potentially will allow for better design and conduct of clinical trials and studies in the health care setting to answer questions previously thought infeasible. With the development of sophisticated, new analytical capabilities, FDA is better able to apply the results of our analyses to medical product development and approval.

In support of use of mobile technology, FDA developed the MyStudies mobile application.[1] This mobile technology platform can be used in research to consent patients for studies and collect patient reported outcomes.

[1] https://www.fda.gov/drugs/science-and-research-drugs/fdas-mystudies-application-app

In February 2019, FDA continued to implement its 2018 Medical Device Safety Action Plan and to strengthen and modernize the 510(k) program by launching the Safety and Performance Based Pathway - a voluntary alternative to the traditional 510(k) pathway that will help drive market competition to develop safer and more effective devices.

FDA continues working to create a Center of Excellence on Digital Health to further modernize regulatory paradigms, policies and processes in a manner that will continue to provide appropriate patient safeguards, reduce the time and cost to market entry for innovative digital health technologies, and facilitate rapid, iterative improvements to marketed products.

FDA has helped bring many new and innovative devices to market on a daily basis, such as the first interoperable, automated insulin dosing controller, the first test to aid in newborn screening for Duchenne Muscular Dystrophy, and the first disposable duodenoscope, which is not susceptible to cross-patient contamination.

FDA authorizes, on average, 12 new or modified devices every business day. In 2019, FDA designated more than 100 technologies as breakthrough devices – doubling the number of designations in 2018. These represent a pipeline of innovations that will improve and extend patient lives in the years to come.

Strengthening Science and Efficient Risk-Based Decision Making

FDA is committed to strengthening science and efficient risk-based decision making by advancing human and animal food safety, transforming medical device safety, ensuring public health through emerging technologies, 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.

New Era of Smarter Food Safety

In April 2019, FDA launched a new approach to food safety to leverage technology and other tools to create a more digital, traceable and safer food system. This approach builds on the progress that continues to be made in FDA's implementation of the Food Safety Modernization Act (FSMA), while advancing the use of current technologies used in society and business sectors all around us, such as blockchain, sensor technology, the Internet of Things, and artificial intelligence. In October 2019, FDA held a public meeting and opened a Federal Register docket to hear from a broad cross-section of stakeholders on what concepts should be incorporated in the new initiative in order to strengthen the safety of the food supply. To foster dialogue, FDA released a "Food for Thought" document in advance of this meeting which outlined initial FDA-developed ideas on how to begin a "New Era of Smarter Food Safety" by addressing issues such as tech-enabled traceability for foodborne outbreak response, smarter tools, evolving food business models, and food safety culture.[2] In early 2020, FDA plans to release a blueprint that will outline critical steps to protect public health and keep pace with the ever-changing global food supply chain.

Modernizing Food Safety

Since FSMA was signed into law in 2011, FDA has proposed and finalized critical regulations that have established science- and risk-based standards for the production and transportation of domestic and imported human and animal food. In 2019, FDA carried out activities to support the compliance dates for these foundational rules, many of which took effect this past year. FDA also leveraged science and technology to rapidly respond to foodborne outbreaks and continue to improve the safety of the food supply.

In spring 2019, FDA and its state regulatory counterparts began conducting routine inspections of large farms for the Produce Safety Rule established by FSMA. Forty-seven states and one territory received funding through cooperative agreements for produce inspections, resulting in the completion of almost 1,000 large farm inspections. FDA remains focused on outreach to farms, which includes about 1,400 On-Farm Readiness Reviews that National Association of State Departments of Agriculture (NASDA) developed in collaboration with FDA and state partners.

FDA is committed to ensuring that foods imported from other countries are held to the same standards as food produced domestically. In February 2019, the agency released the "FDA Strategy for the Safety of Imported Foods," describing our comprehensive approach to imported food safety.[2]

FDA has been collaborating with partners to respond to and prevent future outbreaks related to leafy greens. This work has included efforts to increase traceability, multiple on-farm investigations, a longitudinal study of the Yuma growing region, a focused sampling assignment of romaine lettuce, and advancing rulemaking to update the agricultural water standard for produce. Recognizing that addressing leafy green safety requires a concerted effort by many actors, FDA has engaged with a number of outside stakeholders to further strengthen preventive actions throughout the supply chain.

In FY 2020, FDA concluded a collaborative effort with the U.S. Centers for Disease Control and Prevention and state agencies to investigate a link between pig ear pet treats and 154 human cases of *Salmonella enterica*. *Salmonella* is a bacterium that can cause illness and death in humans and animals, especially those who are very young, very old, or have weak immune systems. After a series of recalls and public health advisories slowed the rate of human illness reports, FDA provided advice to industry on supply chain and hazards control.

In September 2019, FDA launched a Food Safety Dashboard designed to track the impact of the seven foundational FSMA rules, measure their progress, and help FDA continue to refine FSMA implementation. The dashboard is available as part of the FDA-TRACK program, FDA's agency-wide performance management system.[3]

In November 2019, FDA published a rule to propose establishment of a program for the testing of food by accredited laboratories as required by FSMA. When the rule is finalized, the laboratory accreditation program will require that the testing of food in certain circumstances be

[2] https://www.fda.gov/media/120585/download

[3] https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-food-safety-dashboard

conducted by laboratories that voluntarily become accredited under this program. Establishing such a program will help FDA ensure the safety of the U.S. food supply and protect U.S. consumers.

Artificial Intelligence (AI)

AI and machine learning have the potential to fundamentally transform the delivery of health care. As technology and science advance, we can expect to see earlier disease detection, more accurate diagnosis, more targeted therapies and significant improvements in personalized medicine. AI is also being evaluated to improve FDA's targeting capability of products that may be hazardous to public health.

FDA has granted marketing authorization for several artificial intelligence-based devices – including a device for detecting diabetic retinopathy, a device for alerting providers of a potential stroke in patients, a device to help detect wrist fractures, and most recently, a tool that can read radiographic images to identify potential cases of pneumothorax. These new devices are enabling earlier detection of medical conditions and improving accessibility and quality of care, which can lead to more safe, innovative screening options for patients, the ability for earlier interventions to manage and cure diseases, and the potential for patients to have access to screening and diagnosis that they may not have otherwise.

On April 2, 2019, FDA announced steps toward a new regulatory framework specifically tailored to promote the development of safe and effective medical devices that use advanced artificial intelligence algorithms. The ability of artificial intelligence and machine learning software to learn from real-world feedback and improve its performance is spurring innovation and leading to the development of novel medical devices.

The goal of the framework is to assure that ongoing algorithm changes follow pre-specified performance objectives and change control plans, use a validation process that ensures improvements to the performance, safety, and effectiveness of the artificial intelligence software, and includes real-world monitoring of performance once the device is on the market to ensure safety and effectiveness are maintained.

In 2019, FDA conducted an evaluation of AI/ML to strengthen FDA's capability to predict which shipments of imported goods, specifically seafood for this evaluation, pose the greatest risk of violation and, thus, increase the effectiveness and efficiency of import review resources. This proof of concept evaluated the performance and effectiveness of AI/ML and big data techniques for improving imports screening/targeting, beyond a traditional rule-based model, and developed recommendations for the future use of AI/ML and rules for screening/targeting. In summary, the evaluation revealed the efficiency of selection of violative seafood products may be improved significantly using AI/ML for screening/targeting entries/lines based on the data on which the model was trained. Additionally, FDA can immediately improve the likelihood of targeting violative seafood products by increasing the risk threshold set in the PREDICT tool. It is important to note that any implementation of AI/ML needs to consider current policy/program rule requirements and would constitute significant operational change and require the necessary approval, documentation, and training time.

Empowering and Protecting Consumers and Patients

FDA is committed to empowering and protecting consumers and patients' safety to promote better and more informed decisions-making about their diets and health, modernize regulation and oversight of dietary supplements, and to expanding the opportunities to use nutrition to reduce morbidity and mortality from disease.

Nutrition Innovation Strategy

In 2019 FDA made exceptional progress implementing the comprehensive multi-year Nutrition Innovation Strategy that focuses on reducing preventable death and disease related to poor nutrition. FDA launched this strategy in 2018 and issued guidance to assist with changes to the new Nutrition Facts label on food packages. FDA also provided extensive outreach to establishments subject to menu labeling requirements including resources to help them comply, thereby ensuring consumers have the information they need to make better informed decisions and making the overall food supply healthier.

FDA is committed to facilitating innovation while protecting public health through food standards of identity. As part of the Nutrition Innovation Strategy, FDA issued a request for feedback on the labeling of plant-based products using dairy terms in labeling to help guide FDA's approach to these areas. Standards of identity are mandatory requirements related to the content and production of certain food products such as bread, jam, juices, and chocolate. The goal of modernizing standards of identity is to maintain the basic nature and nutritional integrity of products while allowing industry flexibility for innovation to produce more healthful foods.

Dietary Supplements

In February 2019, FDA announced a new plan for policy advancements with the goal of implementing one of the most significant modernizations of dietary supplement regulation and oversight in more than 25 years. This plan included a number of elements, such as the Dietary Supplement Ingredient Advisory List, a rapid-response tool to communicate more quickly when there are concerns about unlawful ingredients; a flexible regulatory framework and exploring means to partner in protecting public health. One example of this partnership is the creation of the Botanical Safety Consortium (BSC), a public-private enterprise that allows scientists from industry, academia, and government to explore and promote scientific advances in evaluating the safety of botanical ingredients and mixtures in dietary supplements.

INFRASTRUCTURE AND BUILDINGS AND FACILITIES

Funding for Infrastructure – GSA Rent, Other Rent and Rent-Related (OR&RR), and White Oak Consolidation – and Buildings and Facilities (B&F) provides the facilities, infrastructure, and utilities required by 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.

FDA facilities directly support its strategic priorities by ensuring FDA staff have the modern infrastructure and labs across the country to execute the agency's vital public health mission. It

is important that these facilities provide safe, suitable and reliable work environments and to support changing scientific and regulatory requirements and technology.

In September 2019, FDA completed relocation of its ORA lab near San Francisco, California. FDA transformed this aged lab into a new leased facility that improves lab operations for food sensory and microbiological, elemental, chemistry, and product sterility analysis.

In October 2019, FDA completed the renovation of and occupied a critical toxicology lab at its Jefferson Laboratories Complex, an FDA-owned facility in Jefferson, Arkansas. This lab allows NCTR scientists to protect the public health by pursuing cutting-edge research related to the rapid detection of contaminants in FDA-regulated products, researching toxicities and carcinogenic risk of certain chemicals, and evaluating the toxicity and inflammation produced by cigarette smoke.

In 2019 FDA also:

- initiated the construction of a new lab building at the Winchester Engineering and Analytical Center, an FDA-owned facility in Winchester, Massachusetts
- continued coordinating the construction for the relocation of the ORA lab near Kansas City from an aging leased facility to a new leased facility that will improve lab operations for analyzing food items, including infant and toddler foods
- initiated design activities for relocating the ORA Southeast Food and Feed Lab near Atlanta, from an aging leased facility to a new leased facility that will improve lab operations in its areas of expertise, including pesticide residues, chemotherapeutics, metals, entomology, nutrient analyses, colors, food additives, filth and decomposition, pathogens, molecular biology, and bacterial toxins; this project will also relocate the Southeast Tobacco Laboratory (this lab is responsible for supporting CTP efforts to uphold the mandates of the Tobacco Control Act through analytical support and tobacco-related research)
- completed the Program of Requirements, selected a leased location, and initiated design activities for a new CDER headquarters lab that will support research associated with drug manufacturing
- coordinated the expansion of and initiated design efforts for CDER's laboratory in St. Louis, that houses the Division of Pharmaceutical Analysis.

OVERVIEW OF THE BUDGET REQUEST

The FY 2021 Budget Request is $6.2 billion, an overall increase of 4.5 percent or $265.4 million compared to the FY 2020 Enacted Level. The request includes $3.3 billion for budget authority – an increase of $25.4 million compared to the FY 2020 Enacted Level – and $2.9 billion for user fees – an increase of $240 million compared to the FY 2020 Enacted Level.

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 human and animal food 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 people in the U.S., including medical countermeasures - the drugs, vaccines, and medical devices 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 the modern infrastructure and labs across the country to execute the agency's vital public health mission.

The Budget focuses on five strategic priorities:

- *Reduce the burdens of addiction crises* that are threatening American families
- *Leverage innovation and competition* to improve health care, broaden access, enhance value, and advance public health goals for patients and consumers
- *Empower and protect consumers and patient's safety* to promote better and more informed decisions-making about their diets and health; and expand the opportunities to use nutrition to reduce morbidity and mortality from disease
- Assure public health through emerging technologies, strengthening science and efficient risk-based decision making
- *Invest in FDA's next generation expert workforce* and the improvement of infrastructure, including enterprise IT and facilities.

FY 2021 REQUEST

The FY 2021 budget will invest in new initiatives focused on FDA's most urgent priorities as well as critically needed infrastructure. The BA Crosswalk in the suite of numbers tables provides full details. New initiatives are summarized in the following sections by major activity with funding levels identified in parentheses.

Cross-cutting (Food Safety and Medical Product Safety Activities)

Artificial Intelligence and Other Emerging Technologies (+$10.2M)

Artificial Intelligence (AI) and other emerging technologies hold tremendous potential to "drive growth of the U.S. economy, enhance our economic and national security, and improve our quality of life," per the Executive Order on Maintaining American Leadership in Artificial Intelligence. To achieve progress across multiple programs in support of FDA, HHS, and White House priorities, FDA requests a total of $10.2 million across CDRH ($5M), ORA ($2.1M), CFSAN ($1.6M), and FDA HQ ($1.5M) for AI and other emerging technologies.

FDA is specifically requesting $8.2 million to continue to capitalize on the anticipated promise of AI, which effectively benefits U.S. patients, industry, researchers, and our health care system as a whole. New resources will also increase FDA's ability to leverage new technologies, such as blockchain, that make it easier to track and trace products through the supply chain – from the time that they are grown or manufactured, until purchased by a consumer, and back through the supply chain – in the event of an outbreak or recall, such as the recent romaine lettuce outbreaks. This proposal builds specific expertise and capabilities across FDA, while also taking an overall view of FDA and how the elements come together to advance FDA's priorities.

AI in medical devices promises to drive growth of the U.S. economy and improve patient safety and quality of life. For FDA to continue to lead the world in its approach for the smart regulation of these bold, new medical devices, it is imperative that FDA take steps to ensure products are designed to be customer-friendly and able to be used and understood – particularly outside the traditional health care settings – and that FDA leads the development of appropriate, consensus-based international standards to bring safe products to market in a predictable, efficient, transparent, and consistent manner. These efforts will reduce barriers to the safe testing, development, and deployment of AI Devices, make health care interventions more precise and personalized to meet patient needs and preferences, and foster moving technologies out of the hospitals and clinics and into the home environment thereby benefitting patients and modernizing health care delivery while creating enormous savings to the health care system.

This initiative also holds the potential to advance food safety activities in multiple areas ranging from enhancing imports screening to outbreak signal detection and accelerating outbreak response. For ORA, the tremendous shift to a more global market for food has introduced important new challenges. In addition to growth in the sheer volume of imports and the number of foreign facilities, the variety and complexity of imported products has increased, and the number of countries involved in producing these products has expanded to include many with less sophisticated regulatory systems than our own. The implementation of AI is expected to improve FDA's and industry's capabilities to respond to these complexities while also ensuring trade is not adversely impacted.

The use of AI in post-market surveillance and signal detection will enhance CFSAN's ability to detect potential problems associated with foods, dietary supplements, and cosmetics, including leveraging data to investigate outbreaks and potential issues with chronic, long-term consumption of food constituents and contaminants or long-term use of cosmetics. FDA will ultimately utilize this information to enhance the science that supports our guidance to industry for protecting public health. As a specific example, use of this technology in the post-market space will streamline the review of adverse event reports associated with foods, dietary supplements, and cosmetics, so that FDA can act more quickly to intervene earlier, including by removing unsafe products from the marketplace.

This initiative includes $2 million in investments in other emerging technologies that are closely linked to our AI work. In particular, investments will be made in tech-enabled outbreak response and modernized track and trace capabilities for foods. The recent outbreaks related to romaine lettuce underline the urgent need for rapid tracing technologies. By improving traceback, we improve the likelihood of determining the root cause of an outbreak. In turn, FDA can continue

to build the data on contributing factors and incorporate AI and other advanced analytical tools to predict future outbreaks.

Many in the food industry are actively exploring and adopting new technologies that can help to speed our ability to trace outbreaks back to source. And FDA is receiving requests from industry to provide direction on issues like interoperability and common data elements. Harmonization of these elements could greatly improve the effectiveness of these new tools.

The FY 2021 Budget Request represents a meaningful investment to expand FDA's engagement with stakeholders on these new technologies and to begin proof-of-concept testing to ensure that FDA can receive and efficiently process new data streams, particularly in urgent outbreak scenarios. This investment will enable FDA to support the goals of the Executive Order by driving "development of appropriate technical standards and reduce barriers to the safe testing and deployment" of new "technologies in order to enable the creation of new AI-related industries and the adoption of AI" and other emerging technologies "by today's industries." While small, this investment will have a large impact on public health, reduce greater long-term costs, and help ensure American leadership for the application of AI and other emerging technologies.

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FOOD SAFETY

As part of FDA's FY 2021 Budget request, the Agency is focusing on key areas where resources have been historically underfunded and for which there are rising public health needs as growing markets outpace increases to Agency resources. These areas include: outbreak response, oversight of innovative food products, and better regulation of cannabis derivatives.

Strengthening Response Capabilities for Foodborne Outbreaks: (+$1.2 million / 4 FTE)
Center: +$1.2 million/ 4 FTE

Additional funding will expand the Center for Food Safety and Applied Nutrition's (CFSAN) ability 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. In the three 2-year periods beginning in 2014 and ending in 2019, the number of outbreaks has increased steadily by 36%. In 2014-2015, FDA coordinated 38 outbreaks investigations. In 2016-2017, FDA coordinated 43 outbreak

investigations, and in 2018-2019, FDA coordinated 52 outbreak investigations. We expect this trend to continue.

By leveraging new technology, FDA can work with producers and other federal, state, and local health officials to unravel what went wrong more quickly, allowing FDA scientists to identify the outbreak and the food that may have caused it. Through additional resources, FDA is building capacity to investigate the root cause of outbreaks and feed information back to industry producers to prevent future contamination, which ultimately reduces costs to industry in the future and protects public health. These costs can be considerable and lasting to an entire industry and its reputation, even if caused by only one producer.

Proposed User Fee Program: Innovative Food Products User Fee: ($26.1 million / 52 FTE)
Center: $26.1 million/ 52 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. A proposed user fee program will provide the additional resources needed to support increased expertise and scientific review capacity for novel emerging products. Examples include new proteins, new ingredients, and synthetic foods, many produced through biotechnology, all of which can help foster new products and ingredients coming to the market in a timely manner.

Cannabis and Cannabis Derivatives (+$5.0 million)
The Agriculture Improvement Act of 2018 (Farm Bill) helped preserve FDA's authorities under the FD&C Act and section 351 of the Public Health Service Act, such that products derived from hemp as defined in the Farm Bill, while not controlled under the Controlled Substances Act (CSA), are subject to the same authorities and requirements as FDA-regulated products containing any other added substance. This allows FDA to continue enforcing the law to protect patients and the public while also providing potential regulatory pathways, to the extent permitted by law, for products containing cannabis and cannabis-derived compounds. FDA is seeing a significant increase in activity relating to the marketing of unlawful cannabis-derived products, especially those containing cannabidiol (CBD), since the Farm Bill passed. In many cases, product developers make unproven claims to treat serious or life-threatening diseases, and patients may be misled to forgo otherwise effective, available therapy and opt instead for a product that has no proven value or may cause them serious harm.

FDA requests a total of $5 million across ORA ($2.0M), CFSAN ($2.0M), FDA HQ ($0.5M), and CVM ($0.5M). This new funding will enable FDA to continue regulating the usage of cannabis-derived substances, such as cannabidiol (CBD), in FDA-regulated products such as dietary supplements and when used as unapproved food and feed additives. The initiative will support regulatory activities, including developing policy, and continue to perform its existing regulatory responsibilities including review of product applications, inspections, enforcement, and targeted research. FDA must support oversight of increasing numbers of marketed FDA-regulated products containing cannabis-derived substances that may put the public at risk.

Additional resources will directly support regulation of cannabis-derived substances and will indirectly increase capacity of FDA's dietary supplement and food ingredient review programs.

Advancing Safe and Effective Medical Products

Modernizing Influenza Vaccines (+$5.0 million)
This initiative supports the implementation of Executive Order 13877, "Modernizing Influenza Vaccines in the U.S. to Promote National Security and Public Health," to help make the U.S. influenza vaccine supply more robust, secure, and nimble to combat seasonal influenza epidemics and potential influenza pandemics. FDA requests a total of $5 million across CDER ($0.5M), CBER ($2.0M), CDRH ($0.5M), Headquarters ($2.0M).

Key FDA activities will include providing scientific and technical support to U.S. government partners and industry and supporting regulatory science to advance new influenza vaccine manufacturing technologies. The implementation of new manufacturing technologies may expand the domestic manufacturing capacity with alternative methods that could allow for more agile and efficient vaccine production that could adapt to emerging influenza strains. This funding also will support the development and availability of other medical countermeasures (MCMs) – including antiviral drugs, therapeutics, and diagnostic tests – necessary to respond to seasonal and pandemic influenza strains.

Transform Medical Device Safety, Cybersecurity, Review, and Innovation (+$18.0 million)
The FY 2020 budget includes $18 million to build an integrated knowledge management system and portal for medical devices using modern, agile information technology systems with secure data storage. This system and portal 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.

Improved 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. Device reviews, postmarket surveillance, and cybersecurity efforts will become more efficient and informative, which could shorten review cycles, speed up identification and ability to address safety signals and cyber vulnerabilities, and spur development of innovative, safer, and more effective devices. These platforms also will foster interactions between FDA and its customers, provide industry with the ability to track premarket submissions, and give patients clearer information about the benefits and risks of medical devices.

Compounding (+$4.5 million)
The FY 2021 Budget request aligns with the overall Secretarial public health priority to improve the health and well-being of the American people by improving the quality of compounded drugs available to the public. The FY 2021 Budget request will allow FDA to continue oversight of human drug compounding by strengthening the scientific framework, bolstering existing and new regulatory compliance initiatives, and expanding policy development to support the needs of the compounding program.

While compounded drugs have a role in patient care, they are not FDA-approved and are not subject to pre-market review for safety, effectiveness, and quality. FDA's robust implementation of the Drug Quality and Security Act (DQSA), Title I, the Compounding Quality Act (CQA) is essential to help ensure that patients receive the highest-quality compounded drugs when needed.

In November 2013, after a fungal meningitis outbreak linked to contaminated compounded drugs caused more than 60 deaths and 750 cases of illness, the DQSA was enacted, providing FDA with additional responsibilities to oversee compounding.

Since enactment of the DQSA, FDA has worked to build capacity to improve risk-based oversight programs through inspections and enforcement, policy development and implementation, state collaboration and coordination and stakeholder outreach. FDA efforts have made clearer the resources needed to implement key statutory provisions, such as the statutory mandate that FDA establish the list of bulk drug substances that may be used in compounding by outsourcing facilities. To achieve sustainable success in the regulation and oversight of drug compounding, FDA must establish a robust programmatic group with increased capacity to further develop the human drug compounding program to protect public health.

21st Century Cures (-$5.0 million)
The 21st Century Cures Act (Cures Act) enacted into law on December 13, 2016, established an "FDA Innovation Account" for FY 2017 – FY 2025 and authorizes funding, subject to the annual appropriation process, to carry out designated provisions of Title III, which focus on medical product development activities regulated by FDA.[4]

For FY 2021, the Cures Act authorized $70.0 million for the FDA Innovation Account. This amount is $5 million less than the amount authorized for FY 2020. The authorized funding level 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 and Buildings & Facilities (+$6.3 million)
At the FY 2021 President's Budget Level, FDA finds program and GSA rent savings to support $6.3 million in inflationary increases within the Other Rent and Rent Related (ORRR) and White Oak budgets to support repairs, improvements, operations, maintenance, and utilities at FDA owned sites and White Oak, including infrastructure improvements at White Oak to improve capacity and reliability. FDA facilities directly support FDA's strategic priorities by ensuring FDA staff have the modern infrastructure and labs across the country to execute the agency's vital public health mission. It is important that these facilities provide safe, suitable, and reliable

[4] 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.

work environments and support changing scientific and regulatory requirements and technology. This funding is required to meet these facilities-related needs.

OR&RR and B&F resources are critical for operations, maintenance, repairs and improvements at FDA owned sites to prevent the further deterioration of FDA's aged assets creating a higher risk of failure, decreased reliability, and increased frequency of operational shut downs, all of which have a significant negative impact on the FDA mission. Additionally, resources are needed to support program mission needs when facility changes are needed to meet program requirements and to keep pace with the latest advances in technology and science. Adequate funding also is needed to support operations on the White Oak Campus, including infrastructure modifications to improve capacity and reliability to protect critical lab activities.

Reductions to Outreach, Training, and Organizational Excellence (-$19.6M)

The FY 2021 budget reflects a reduction of $19.6 million to Outreach, Training, and Organizational Excellence activities from the FY 2020 budget. FDA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. FDA will preserve its most critical public health and safety activities under these reductions –including engagement with its stakeholders, training and development programs to keep pace with cutting-edge science – and efforts to modernize and improve business processes and streamline regulatory processes.

Supporting the Administration's Drug Pricing Initiative with Increased Competition

The President's 2021 Budget includes an allowance for bipartisan drug pricing proposals. The Administration supports legislative efforts to improve the Medicare Part D benefit by establishing an out-of-pocket maximum and reducing out-of-pocket costs for seniors. The Administration also supports changes to bring lower cost generic and biosimilar drugs to patients. These efforts would increase competition, reduce drug prices, and lower out of pocket costs for patients at the pharmacy counter.

The Administration has and continues to support legislative efforts to make the path to generic and biosimilar development more transparent, efficient, and predictable so that Americans have better access to these medicines that are often more affordable. Overall, addressing regulatory barriers and challenges and closing potential loopholes that hinder development of generics, will promote more competition, and advance patient access to more affordable medicines.

Transforming Tobacco Regulation

Reforms Oversight of Tobacco Products. The Budget proposes to move the Center for Tobacco Products out of the Food and Drug Administration (FDA) and create a new agency within HHS to focus on tobacco regulation. A new agency with a mission focused on tobacco and its impact on public health would have greater capacity to respond rapidly to the growing complexity of new tobacco products. In addition, this reorganization would allow the FDA Commissioner to focus on its traditional mission of ensuring the safety of the Nation's drug, food, and medical products supply.

The Budget also includes a new user fee on e-cigarettes and other ENDS products to support the new agency's regulatory oversight of new tobacco and tobacco related products in the future as appropriate. The current annual user fee cap of $712 million would be increased by $100 million and future collections of all tobacco related products would be indexed to inflation. This proposal would ensure that the new agency has the resources to address today's alarming rise in youth e-cigarette use as well as new public health threats of tomorrow. New tobacco or tobacco related products should also pay, just like the other tobacco related products that are subject to user fees under current law.

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 2019 Enacted		FY 2019 Actuals		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 President's Budget +/- FY 2020 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Foods	**3,758**	**1,077,612**	**3,758**	**1,059,926**	**3,863**	**1,099,970**	**3,934**	**1,127,941**	**71**	**27,971**
Budget Authority	***3,758***	***1,066,741***	***3,758***	***1,059,926***	***3,819***	***1,088,881***	***3,838***	***1,090,530***	***19***	***1,649***
User Fees	---	***10,871***	---	---	***44***	***11,089***	***96***	***37,411***	***52***	***26,322***
Center	1,097	335,244	1,097	327,462	1,144	342,815	1,209	371,490	65	28,675
Budget Authority	1,097	334,412	1,097	327,462	1,141	341,966	1,154	344,524	13	2,558
User Fees	---	832	---	---	3	849	55	26,966	52	26,117
Food and Feed Recall	---	243	---	---	1	248	1	253	---	5
Voluntary Qualified Importer Program	---	243	---	---	1	248	1	253	---	5
Third Party Auditor Program	---	346	---	---	1	353	1	360	---	7
Innovative Food Products (Proposed)	---	---	---	---	---	---	52	26,100	52	26,100
Field	2,661	742,368	2,661	732,464	2,719	757,155	2,725	756,451	6	-704
Budget Authority	2,661	732,329	2,661	732,464	2,678	746,915	2,684	746,006	6	-909
User Fees	---	10,039	---	---	41	10,240	41	10,445	---	205
Food and Feed Recall	---	1,000	---	---	4	1,020	4	1,040	---	20
Food Reinspection	---	4,575	---	---	19	4,667	19	4,760	---	93
Voluntary Qualified Importer Program	---	4,320	---	---	18	4,406	18	4,495	---	89
Third Party Auditor Program	---	144	---	---	---	147	---	150	---	3
Human Drugs	**6,381**	**1,881,529**	**6,381**	**1,851,609**	**6,649**	**1,973,122**	**6,746**	**2,022,348**	**97**	**49,226**
Budget Authority	***2,038***	***663,295***	***2,038***	***662,892***	***2,075***	***683,195***	***2,092***	***683,411***	***17***	***216***
User Fees	***4,343***	***1,218,234***	***4,343***	***1,188,717***	***4,574***	***1,289,927***	***4,654***	***1,338,937***	***80***	***49,010***
Center	5,362	1,676,069	5,362	1,659,208	5,612	1,734,133	5,709	1,782,797	97	48,664
Budget Authority	1,287	525,126	1,287	524,738	1,316	507,726	1,333	509,033	17	1,307
User Fees	4,075	1,150,943	4,075	1,134,470	4,296	1,226,407	4,376	1,273,764	80	47,357
Prescription Drug (PDUFA)	2,649	732,096	2,649	733,999	2,774	788,576	2,854	824,647	80	36,071
Generic Drug (GDUFA)	1,310	382,803	1,310	361,416	1,410	400,252	1,410	410,556	---	10,304
Biosimilars (BsUFA)	110	35,416	110	37,994	110	36,938	110	37,908	---	970
Outsourcing Facility	6	628	6	1,060	2	641	2	653	---	12
Field	1,019	205,460	1,019	192,401	1,037	238,989	1,037	239,551	---	562
Budget Authority	751	138,169	751	138,154	759	175,469	759	174,378	---	-1,091
User Fees	268	67,291	268	54,247	278	63,520	278	65,173	---	1,653
Prescription Drug (PDUFA)	43	9,003	43	7,401	43	8,536	43	8,776	---	240
Generic Drug (GDUFA)	218	56,808	218	45,778	226	53,124	226	54,492	---	1,368
Biosimilars (BsUFA)	4	1,100	4	677	7	1,472	7	1,510	---	38
Outsourcing Facility	3	380	3	391	2	388	2	395	---	7
Biologics	**1,418**	**402,144**	**1,415**	**408,610**	**1,407**	**419,302**	**1,416**	**425,486**	**9**	**6,184**
Budget Authority	***791***	***240,138***	***791***	***240,133***	***803***	***252,138***	***811***	***252,381***	***8***	***243***
User Fees	***627***	***162,006***	***624***	***168,477***	***604***	***167,164***	***605***	***173,105***	***1***	***5,941***
Center	1,189	358,355	1,189	365,148	1,179	375,583	1,188	382,003	9	6,420
Budget Authority	570	198,132	570	198,132	582	210,132	590	210,657	8	525
User Fees	619	160,223	619	167,016	597	165,451	598	171,346	1	5,895
Prescription Drug (PDUFA)	555	144,529	555	153,761	535	149,267	536	154,845	1	5,578
Medical Device (MDUFA)	64	14,444	64	13,232	55	14,578	55	14,850	---	272
Generic Drug (GDUFA)	---	1,072		24	4	960	4	987	---	27
Biosimilars (BsUFA)	---	178	---	---	3	646	3	664	---	18
Field	229	43,789	226	43,462	228	43,719	228	43,483	---	-236
Budget Authority	221	42,006	221	42,001	221	42,006	221	41,724	---	-282
User Fees	8	1,783	5	1,461	7	1,713	7	1,759	---	46
Prescription Drug (PDUFA)	7	1,566	5	1,286	6	1,485	6	1,527	---	42
Medical Device (MDUFA)	1	217	---	174	1	228	1	232	---	4
Animal Drugs and Feed	**1,004**	**224,805**	**1,004**	**216,949**	**1,041**	**238,678**	**1,042**	**238,926**	**1**	**248**
Budget Authority	***801***	***179,209***	***801***	***178,928***	***824***	***190,869***	***825***	***190,081***	***1***	***-788***
User Fees	***203***	***45,596***	***203***	***38,021***	***217***	***47,809***	***217***	***48,845***	---	***1,036***
Center	692	157,717	692	151,056	725	168,474	726	169,145	1	671
Budget Authority	491	113,694	491	113,419	514	122,099	515	121,787	1	-312
User Fees	201	44,023	201	37,637	211	46,375	211	47,358	---	983
Animal Drug (ADUFA)	128	27,267	128	23,896	138	27,670	138	28,315	---	645
Animal Generic Drug (AGDUFA)	73	16,644	73	13,741	73	18,591	73	18,926	---	335
Third Party Auditor Program	---	112	---	---	---	114	---	117	---	3
Field	312	67,088	312	65,893	316	70,204	316	69,781	---	-423
Budget Authority	310	65,515	310	65,509	310	68,770	310	68,294	---	-476
User Fees	2	1,573	2	384	6	1,434	6	1,487	---	53
Animal Drug (ADUFA)	2	431	2	384	2	383	2	392	---	9
Animal Generic Drug (AGDUFA)	---	335	---	---	1	228	1	255	---	27
Food Reinspection	---	807	---	---	3	823	3	840	---	17
Third Party Auditor Program	---	---	---	---	---	---	---	---	---	---

(Dollars in Thousands)	FY 2019 Enacted		FY 2019 Actuals		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 President's Budget +/- FY 2020 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Devices and Radiological Health	**2,120**	**577,113**	**2,120**	**521,951**	**2,302**	**599,940**	**2,345**	**638,529**	**43**	**38,589**
Budget Authority	***1,486***	***387,168***	***1,486***	***386,733***	***1,493***	***395,168***	***1,508***	***415,828***	***15***	***20,660***
User Fees	***634***	***189,945***	***634***	***135,218***	***809***	***204,772***	***837***	***222,701***	***28***	***17,929***
Center	1,614	475,873	1,614	423,376	1,796	501,296	1,839	540,190	43	38,894
Budget Authority	1,000	302,163	1,000	301,738	1,007	310,163	1,022	331,393	15	21,230
User Fees	614	173,710	614	121,638	789	191,133	817	208,797	28	17,664
Prescription Drug (PDUFA)	10	1,460	10	1,834	15	4,162	15	4,302	---	140
Medical Device (MDUFA)	577	165,815	577	113,370	746	180,073	774	197,459	28	17,386
Mammography Quality Standards Act (MQSA)	27	6,435	27	6,434	28	6,898	28	7,036	---	138
Field	506	101,240	506	98,575	506	98,644	506	98,339	---	-305
Budget Authority	486	85,005	486	84,995	486	85,005	486	84,435	---	-570
User Fees	20	16,235	20	13,580	20	13,639	20	13,904	---	265
Medical Device (MDUFA)	11	2,240	11	1,800	11	2,358	11	2,398	---	40
Mammography Quality Standards Act (MQSA)	9	13,995	9	11,780	9	11,281	9	11,506	---	225
National Center for Toxicological Research (BA Only)	**276**	**66,712**	**276**	**66,712**	**276**	**66,712**	**276**	**66,266**	---	-446
Tobacco	**942**	**666,832**	**942**	**686,991**	**1,016**	**661,739**	**1,068**	**762,612**	**52**	**100,873**
Center	**894**	**652,065**	**894**	**676,457**	**947**	**647,055**	**999**	**747,765**	**52**	**100,710**
Family Smoking Prevention and Tobacco Control Act	894	652,065	894	676,457	947	647,055	999	647,765	52	710
Expand tobacco products (Proposed)	---	---	---	---	---	---	---	100,000	---	100,000
Field	**48**	**14,767**	**48**	**10,534**	**69**	**14,684**	**69**	**14,847**	**---**	**163**
Family Smoking Prevention and Tobacco Control Act	48	14,767	48	10,534	69	14,684	69	14,847	---	163
FDA Headquarters	**961**	**311,133**	**961**	**307,092**	**927**	**319,487**	**930**	**326,070**	**3**	**6,583**
Budget Authority	546	180,220	546	187,776	513	185,420	514	186,713	1	1,293
User Fees	***415***	***130,913***	***415***	***119,316***	***414***	***134,067***	***416***	***139,357***	***2***	***5,290***
Prescription Drug (PDUFA)	223	56,391	223	66,425	215	56,756	215	58,501	---	1,745
Medical Device (MDUFA)	36	8,463	36	8,411	36	9,219	36	9,833	---	614
Generic Drug (GDUFA)	98	35,243	98	31,790	100	32,834	100	33,691	---	857
Biosimilars (BsUFA)	8	632	8	2,004	8	1,331	8	1,364	---	33
Animal Drug (ADUFA)	5	1,004	5	948	4	914	4	938	---	24
Animal Generic Drug (AGDUFA)	3	785	3	708	3	756	3	845	---	89
Family Smoking Prevention and Tobacco Control Act	42	27,012	42	9,030	44	30,867	46	30,867	2	---
Mammography Quality Standards Act (MQSA)	---	92	---	---	---	74	---	76	---	2
Food and Feed Recall	---	75	---	---	---	77	---	78	---	1
Food Reinspection	---	480	---	---	2	489	2	499	---	10
Voluntary Qualified Importer Program	---	277	---	---	1	283	1	287	---	4
Third Party Auditor Program	---	39	---	---	---	40	---	40	---	---
Outsourcing Facility	---	420	---	---	1	427	1	438	---	11
Innovative Food Products (Proposed)	---	---	---	---	---	---	---	1,900	---	1,900
FDA White Oak Consolidation	**---**	**50,587**	**---**	**49,255**	**---**	**53,913**	**---**	**63,411**	**---**	**9,498**
Budget Authority	---	43,044	---	43,044	---	45,914	---	55,717	---	9,803
User Fees	**---**	***7,543***	**---**	***6,211***	**---**	***7,999***	**---**	***7,694***	**---**	***-305***
Prescription Drug (PDUFA)	---	3,810	---	3,810	---	3,848	---	3,886	---	38
Medical Device (MDUFA)	---	---	---	---	---	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	---	3,733	---	2,401	---	4,151	---	3,808	---	-343
Other Rent and Rent Related	**---**	**123,735**	**---**	**120,201**	**---**	**132,970**	**---**	**151,359**	**---**	**18,389**
Budget Authority	---	71,943	---	71,943	---	80,173	---	98,518	---	18,345
User Fees	**---**	***51,792***	**---**	***48,258***	**---**	***52,797***	**---**	***52,841***	**---**	***44***
Prescription Drug (PDUFA)	---	26,127	---	25,912	---	26,389	---	26,652	---	263
Medical Device (MDUFA)	---	5,239	---	5,239	---	5,291	---	5,344	---	53
Generic Drug (GDUFA)	---	13,075	---	12,243	---	13,206	---	13,338	---	132
Biosimilars (BsUFA)	---	1,070	---	932	---	1,081	---	1,092	---	11
Animal Drug (ADUFA)	---	790	---	624	---	797	---	805	---	8
Animal Generic Drug (AGDUFA)	---	264	---	132	---	266	---	269	---	3
Family Smoking Prevention and Tobacco Control Act	---	4,752	---	3,137	---	5,283	---	4,847	---	-436
Food and Feed Recall	---	43	---	---	---	44	---	45	---	1
Food Reinspection	---	204	---	---	---	208	---	212	---	4
Voluntary Qualified Importer Program	---	170	---	---	---	173	---	177	---	4
Third Party Auditor Program	---	24	---	5	---	24	---	25	---	1
Outsourcing Facility	---	34	---	34	---	35	---	35	---	---
GSA Rental Payments	**---**	**238,665**	**---**	**218,907**	**---**	**240,549**	**---**	**236,970**	**---**	**-3,579**
Budget Authority	---	170,208	---	170,208	---	171,208	---	167,119	---	-4,089
User Fees	**---**	***68,457***	**---**	***48,699***	**---**	***69,341***	**---**	***69,851***	**---**	***510***
Prescription Drug (PDUFA)	---	35,341	---	22,716	---	35,695	---	36,052	---	357
Medical Device (MDUFA)	---	8,312	---	4,812	---	8,395	---	8,479	---	84
Generic Drug (GDUFA)	---	12,720	---	12,720	---	12,847	---	12,975	---	128
Biosimilars (BsUFA)	---	451	---	451	---	455	---	460	---	5
Animal Drug (ADUFA)	---	839	---	839	---	847	---	856	---	9
Animal Generic Drug (AGDUFA)	---	307	---	307	---	310	---	314	---	4
Family Smoking Prevention and Tobacco Control Act	---	9,671	---	6,845	---	9,960	---	9,866	---	-94
Food and Feed Recall	---	73	---	---	---	74	---	76	---	2
Food Reinspection	---	348	---	---	---	355	---	362	---	7
Voluntary Qualified Importer Program	---	290	---	---	---	296	---	302	---	6
Third Party Auditor Program	---	47	---	9	---	48	---	49	---	1
Outsourcing Facility	---	58	---	---	---	59	---	60	---	1

(Dollars in Thousands)	FY 2019 Enacted		FY 2019 Actuals		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 President's Budget +/- FY 2020 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Color Certification	33	9,892	33	8,734	37	10,263	37	10,469	---	206
Export Certification	23	4,696	23	4,305	26	4,790	26	4,886	---	96
Export Certification (Proposed)	---	---	---	---	---	---	---	4,366	---	4,366
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	2,506	---	2,556	---	50
Priority Review Vouchers (PRV) Pediatric Disease	11	7,686	11	2,423	11	7,840	11	7,997	---	157
Priority Review Vouchers (PRV) Medical Countermeasures	---					2,506	---	2,556	---	50
Over the Counter Monograph (Proposed)	---	---	---	---	---	---	---	28,400	---	28,400
Food and Drug Safety -- No Year (P.L. 113-6)	---	---	---	14	---	---	---	---	---	---
21st Century Cures (BA Only)	136	70,000	136	58,225	136	75,000	136	70,000	---	-5,000
MCMi -- No Year	---	---	10	4,601	---	---	---	---	---	---
Opioids -- No Year	---	---	73	65,408	---	---	---	---	---	---
Subtotal, Salaries and Expenses	**17,063**	**5,713,141**	**17,144**	**5,651,912**	**17,691**	**5,909,287**	**17,967**	**6,191,148**	**276**	**281,861**
Buildings and Facilities (Budget Authority)	---	**11,788**	---	**11,477**	---	**31,788**	---	**13,788**	---	**-18,000**
Total Program Level	**17,063**	**5,724,929**	**17,144**	**5,663,389**	**17,691**	**5,941,075**	**17,967**	**6,204,936**	**276**	**263,861**
Non-Field Activities	*12,152*	*4,055,442*	*12,152*	*3,991,973*	*12,680*	*4,183,460*	*12,950*	*4,446,956*	*270*	*263,496*
Field Activities	*4,775*	*1,174,712*	*4,772*	*1,143,329*	*4,875*	*1,223,395*	*4,881*	*1,222,452*	*6*	*-943*
White Oak, Rent Activities, and B&F	---	*424,775*	---	*399,839*	---	*459,220*	---	*465,528*	---	*6,308*
Food and Drug Safety -- No Year	---	---	---	*14.16*	---	---	---	---	---	---
Opioids -- No Year	---	---	*73*	*65,408*	---	---	---	---	---	---
21st Century Cures	*136*	*70,000*	*136*	*58,225*	*136*	*75,000*	*136*	*70,000*	---	*-5,000*
MCMi -- No Year	---	---	*10*	*4,601*	---	---	---	---	---	---
User Fees:										
Current Law										
Prescription Drug (PDUFA)	*3,487*	*1,010,323*	*3,485*	*1,017,144*	*3,588*	*1,074,714*	*3,669*	*1,119,188*	81	44,474
Medical Device (MDUFA)	*689*	*204,730*	*689*	*147,036*	*849*	*220,142*	*877*	*238,595*	28	18,453
Generic Drug (GDUFA)	*1,626*	*501,721*	*1,626*	*463,972*	*1,740*	*513,223*	*1,740*	*526,039*	---	12,816
Biosimilars (BsUFA)	*122*	*38,847*	*122*	*42,058*	*128*	*41,923*	*128*	*42,998*	---	1,075
Animal Drug (ADUFA)	*135*	*30,331*	*135*	*26,691*	*144*	*30,611*	*144*	*31,306*	---	695
Animal Generic Drug (AGDUFA)	*76*	*18,335*	*76*	*14,889*	*77*	*20,151*	*77*	*20,609*	---	458
Family Smoking Prevention and Tobacco Control Act	*984*	*712,000*	*984*	*708,404*	*1,060*	*712,000*	*1,114*	*712,000*	54	---
Subtotal, Current Law	**7,119**	**2,516,287**	**7,117**	**2,420,194**	**7,586**	**2,612,764**	**7,749**	**2,690,735**	**163**	**77,971**
Indefinite										
Mammography Quality Standards Act (MQSA)	*36*	*20,522*	*36*	*18,215*	*37*	*18,253*	*37*	*18,618*	---	365
Color Certification	*33*	*9,892*	*33*	*8,734*	*37*	*10,263*	*37*	*10,469*	---	206
Export Certification	*23*	*4,696*	*23*	*4,305*	*26*	*4,790*	*26*	*4,886*	---	96
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	*2,506*	---	*2,556*	---	50
Priority Review Vouchers (PRV) Pediatric Disease	*11*	*7,686*	*11*	*2,423*	*11*	*7,840*	*11*	*7,997*	---	157
Priority Review Vouchers (PRV) Medical Countermeasures	---	---	---	---	---	*2,506*	---	*2,556*	---	50
Food and Feed Recall	---	*1,434*	---	---	*5*	*1,463*	*5*	*1,492*	---	29
Food Reinspection	---	*6,414*	---	---	*24*	*6,542*	*24*	*6,673*	---	131
Voluntary Qualified Importer Program	---	*5,300*	---	---	*20*	*5,406*	*20*	*5,514*	---	108
Third Party Auditor Program	---	*712*	---	*13*	*1*	*726*	*1*	*741*	---	15
Outsourcing Facility	*9*	*1,520*	*9*	*1,485*	*5*	*1,550*	*5*	*1,581*	---	31
Subtotal, Indefinite	**112**	**58,176**	**112**	**35,175**	**166**	**61,845**	**166**	**63,083**	---	**1,238**
Proposed										
Export Certification (Proposed)	---	---	---	---	---	---	---	*4,366*	---	*4,366*
Over the Counter Monograph (Proposed)	---	---	---	---	---	---	---	*28,400*	---	*28,400*
Expand tobacco products (Proposed)	---	---	---	---	---	---	---	*100,000*	---	*100,000*
Innovative Food Products (Proposed)	---	---	---	---	---	---	*52*	*28,000*	*52*	*28,000*
Subtotal, Proposed	---	---	---	---	---	---	***52***	***160,766***	***52***	***160,766***
Total User Fees	**7,231**	**2,574,463**	**7,229**	**2,455,368**	**7,752**	**2,674,609**	**7,967**	**2,914,584**	**215**	**239,975**
Total Budget Authority, Pre-Transfer	**9,832**	**3,150,466**	**9,915**	**3,208,021**	**9,939**	**3,266,466**	**10,000**	**3,290,352**	**61**	**23,886**
BA, S&E	*9,696*	*3,068,678*	*9,696*	*3,068,295*	*9,803*	*3,159,678*	*9,864*	*3,206,564*	*61*	*46,886*
BA, B&F	---	*11,788*	---	*11,477*	---	*31,788*	---	*13,788*	---	**-18,000**
Food and Drug Safety -- No Year			---	*14*						
21st Century Cures	*136*	*70,000*	*136*	*58,225*	*136*	*75,000*	*136*	*70,000*	---	*-5,000*
MCMi -- No Year	---	---	*10*	*4,601*	---	---	---	---	---	---
Opioids -- No Year			*73*	*65,408*						
Total Program Level, Pre-Transfer	**17,063**	**5,724,929**	**17,144**	**5,663,389**	**17,691**	**5,941,075**	**17,967**	**6,204,936**	**276**	**263,861**
HHS OIG transfer (BA Only)	---	**-1,500**	---	**-1,500**	---	**-1,500**	---	---	---	**1,500**
Total Budget Authority, Post-Transfer	**9,832**	**3,148,966**	**9,915**	**3,206,521**	**9,939**	**3,264,966**	**10,000**	**3,290,352**	**61**	**25,386**
Total User Fees	***7,231***	***2,574,463***	***7,229***	***2,455,368***	***7,752***	***2,674,609***	***7,967***	***2,914,584***	***215***	***239,975***
Total Program Level, Post-Transfer	**17,063**	**5,723,429**	**17,144**	**5,661,889**	**17,691**	**5,939,575**	**17,967**	**6,204,936**	**276**	**265,361**

*FTE figures do not include an estimated 70 reimbursable and 26 PEPFAR. The table also excludes Opioids FTE supported with one-time funding provided via the FY 2018 Omnibus. Table includes additional base funding as part of the Opioids 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 2019 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.

*****Funding and FTE levels for FY 2019 have been comparably adjusted to reflect the updated realignment of the FDA HQ organizations

******Tropical Disease Priority Review Vouchers collection estimates for FY 2020 and FY 2021 are displayed as a projection of actual FY 2019 collections.

*******Does not reflect the Budget proposal to move CTP from FDA to establish a new agency within HHS.

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

BUDGET AUTHORITY CROSSWALK

(Dollars in Thousands)	FY 2020 Enacted		Budget Authority																						FY 2021 President's Budget	
			Crosscutting						Food Safety						Medical Product Safety											
			Infrastructure	Artificial Intelligence and Other Emerging Technologies**		Outreach, Training, and Organization Excellence	Total Crosscutting		Cannabis and Cannabis Derivatives		Strengthening Response Capabilities For Foodborne Outbreaks		Total Food Safety		Transform Medical Device Safety, Cybersecurity, Review, and Innovation		Modernizing Influenza Vaccines		Compounding		21st Century Cures	Total Medical Product Safety		Total Changes			
	FTE	$000	$000	FTE	$000	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:																											
Foods	**3,819**	**1,088,881**	---	**4**	**3,676**	**-7,267**	**4**	**-3,591**	**11**	**4,000**	**4**	**1,240**	**15**	**5,240**	---	---	---	---	---	---	---	---	---	**19**	**1,649**	**3,838**	**1,090,530**
Center	1,141	341,966	---	3	1,560	-2,242	3	-682	6	2,000	4	1,240	10	3,240	---	---	---	---	---	---	---	---	---	13	2,558	1,154	344,524
Field	2,678	746,915	---	1	2,116	-5,025	1	-2,909	5	2,000	---	---	5	2,000	---	---	---	---	---	---	---	---	---	6	-909	2,684	746,006
Human Drugs	**2,075**	**683,195**	---	---	---	**-4,784**	---	**-4,784**	---	---	---	---	---	---	---	---	**1**	**500**	**16**	**4,500**	---	**17**	**5,000**	**17**	**216**	**2,092**	**683,411**
Center	1,316	507,726	---	---	---	-3,693	---	-3,693	---	---	---	---	---	---	---	---	1	500	16	4,500	---	17	5,000	17	1,307	1,333	509,033
Field	759	175,469	---	---	---	-1,091	---	-1,091	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-1,091	759	174,378
Biologics	**803**	**252,138**	---	---	---	**-1,757**	---	**-1,757**	---	---	---	---	---	---	---	---	**8**	**2,000**	---	---	---	**8**	**2,000**	**8**	**243**	**811**	**252,381**
Center	582	210,132	---	---	---	-1,475	---	-1,475	---	---	---	---	---	---	---	---	8	2,000	---	---	---	8	2,000	8	525	590	210,657
Field	221	42,006	---	---	---	-282	---	-282	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-282	221	41,724
Animal Drugs and Feeds	**824**	**190,869**	---	---	---	**-1,288**	---	**-1,288**	**1**	**500**	---	---	**1**	**500**	---	---	---	---	---	---	---	---	---	**1**	**-788**	**825**	**190,081**
Center	514	122,099	---	---	---	-812	---	-812	1	500	---	---	1	500	---	---	---	---	---	---	---	---	---	1	-312	515	121,787
Field	310	68,770	---	---	---	-476	---	-476	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-476	310	68,294
Devices and Radiological Health	**1,493**	**395,168**	---	**10**	**5,000**	**-2,840**	**10**	**2,160**	---	---	---	---	---	---	**4**	**18,000**	**1**	**500**	---	---	---	**5**	**18,500**	**15**	**20,660**	**1,508**	**415,828**
Center	1,007	310,163	---	10	5,000	-2,270	10	2,730	---	---	---	---	---	---	4	18,000	1	500	---	---	---	5	18,500	15	21,230	1,022	331,393
Field	486	85,005	---	---	---	-570	---	-570	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-570	486	84,435
National Center for Toxicological Research	276	66,712	---	---	---	**-446**	---	-446	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-446**	**276**	**66,266**
FDA Headquarters	513	183,920	---	---	**1,500**	**-1,207**	---	293	**1**	**500**	---	---	1	500	---	---	---	**2,000**	---	---	---	---	**2,000**	1	**2,793**	**514**	**186,713**
FDA White Oak Consolidation	---	45,914	**9,803**	---	---		---	9,803	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**9,803**	---	**55,717**
Other Rent and Rent Related	---	80,173	**18,345**	---	---		---	18,345	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**18,345**	---	**98,518**
GSA Rental Payments	---	171,208	**-4,089**	---	---		---	-4,089	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-4,089**	---	**167,119**
Subtotal, Salaries and Expenses Account	**9,803**	**3,158,178**	**24,059**	**14**	**10,176**	**-19,589**	**14**	**14,646**	**13**	**5,000**	**4**	**1,240**	**17**	**6,240**	**4**	**18,000**	**10**	**5,000**	**16**	**4,500**	---	**30**	**27,500**	**61**	**48,386**	**9,864**	**3,206,564**
Buildings and Facilities Account	---	**31,788**	**-18,000**	---	---	---	---	-18,000				---	---	---						---	---	---	---	---	**-18,000**	---	**13,788**
Total Budget Authority, Pre-Transfer	**9,803**	**3,189,966**	**6,059**	**14**	**10,176**	**-19,589**	**14**	**-3,354**	**13**	**5,000**	**4**	**1,240**	**17**	**6,240**	**4**	**18,000**	**10**	**5,000**	**16**	**4,500**	---	**30**	**27,500**	**61**	**30,386**	**9,864**	**3,220,352**
Non-Field Activities	**5,349**	**1,742,718**	---	**13**	**8,060**	**-12,145**	**13**	**-4,085**	**8**	**3,000**	**4**	**1,240**	**12**	**4,240**	**4**	**18,000**	**10**	**5,000**	**16**	**4,500**	---	**30**	**27,500**	**55**	**27,655**	**5,404**	**1,770,373**
Field Activities	**4,454**	**1,118,165**	---	**1**	**2,116**	**-7,444**	**1**	**-5,328**	**5**	**2,000**	---	---	**5**	**2,000**	---	---	---	---	---	---	---	---	---	**6**	**-3,328**	**4,460**	**1,114,837**
Rent Activities, B&F, and White Oak	---	**329,083**	**6,059**	---	---	---	---	**6,059**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**6,059**	---	**335,142**
21st Century Cures	**136**	**75,000**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-5,000**	---	**-5,000**	---	**-5,000**	**136**	**70,000**
Total Budget Authority with 21st Century Cures	**9,939**	**3,264,966**	**6,059**	**14**	**10,176**	**-19,589**	**14**	**-3,354**	**13**	**5,000**	**4**	**1,240**	**17**	**6,240**	**4**	**18,000**	**10**	**5,000**	**16**	**4,500**	**-5,000**	**30**	**22,500**	**61**	**25,386**	**10,000**	**3,290,352**
HHS OIG transfer	---	---				---		---																---	---	---	---
Total Budget Authority, Post-Transfer	**9,939**	**3,264,966**	**6,059**	**14**	**10,176**	**-19,589**	**14**	**-3,354**	**13**	**5,000**	**4**	**1,240**	**17**	**6,240**	**4**	**18,000**	**10**	**5,000**	**16**	**4,500**	**-5,000**	**30**	**22,500**	**61**	**25,386**	**10,000**	**3,290,352**

*FDA Headquarters reflects the total post OIG Transfer

**Includes $0.5 million for CFSAN and $1.5 million for FDA Headquarters for Track and Trace Activities.

MAJOR ACTIVITIES TABLE

(Dollars in Thousands)	FY 2019 Enacted						FY 2020 Enacted						FY 2021 President's Budget						FY 2021 President's Budget +/- FY 2020 Enacted					
	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	**3,758**	**1,059,980**	---	---	**3,758**	**1,059,980**	**3,819**	**1,088,881**	---	---	**3,819**	**1,088,881**	**3,838**	**1,090,530**	---	---	**3,838**	**1,090,530**	**19**	**1,649**	---	---	**19**	**1,649**
Center	1,097	327,962	---	---	1,097	327,962	1,141	341,966	---	---	1,141	341,966	1,154	344,524	---	---	1,154	344,524	13	2,558	---	---	13	2,558
Field	2,661	732,018	---	---	2,661	732,018	2,678	746,915	---	---	2,678	746,915	2,684	746,006	---	---	2,684	746,006	6	-909	---	---	6	-909
Human Drugs	---	---	**2,038**	**662,907**	**2,038**	**662,907**	---	---	**2,075**	**683,195**	**2,075**	**683,195**	---	---	**2,092**	**683,411**	**2,092**	**683,411**	---	---	**17**	**216**	**17**	**216**
Center	---	---	1,287	524,738	1,287	524,738	---	---	1,316	507,726	1,316	507,726	---	---	1,333	509,033	1,333	509,033	---	---	17	1,307	17	1,307
Field	---	---	751	138,169	751	138,169	---	---	759	175,469	759	175,469	---	---	759	174,378	759	174,378	---	---	---	-1,091	---	-1,091
Biologics	---	---	**791**	**240,138**	**791**	**240,138**	---	---	**803**	**252,138**	**803**	**252,138**	---	---	**811**	**252,381**	**811**	**252,381**	---	---	**8**	**243**	**8**	**243**
Center	---	---	570	198,132	570	198,132	---	---	582	210,132	582	210,132	---	---	590	210,657	590	210,657	---	---	8	525	8	525
Field	---	---	221	42,006	221	42,006	---	---	221	42,006	221	42,006	---	---	221	41,724	221	41,724	---	---	---	-282	---	-282
Animal Drugs and Feeds	**594**	**127,681**	**207**	**51,253**	**801**	**178,934**	**617**	**139,616**	**207**	**51,253**	**824**	**190,869**	**618**	**139,169**	**207**	**50,912**	**825**	**190,081**	**1**	**-447**	---	**-341**	**1**	**-788**
Center	298	65,079	193	48,340	491	113,419	321	73,759	193	48,340	514	122,099	322	73,768	193	48,019	515	121,787	1	9	---	-321	1	-312
Field	296	62,602	14	2,913	310	65,515	296	65,857	14	2,913	310	68,770	296	65,401	14	2,893	310	68,294	---	-456	---	-20	---	-476
Devices and Radiological Health	---	---	**1,486**	**386,743**	**1,486**	**386,743**	---	---	**1,493**	**395,168**	**1,493**	**395,168**	---	---	**1,508**	**415,828**	**1,508**	**415,828**	---	---	**15**	**20,660**	**15**	**20,660**
Center	---	---	1,000	301,738	1,000	301,738	---	---	1,007	310,163	1,007	310,163	---	---	1,022	331,393	1,022	331,393	---	---	15	21,230	15	21,230
Field	---	---	486	85,005	486	85,005	---	---	486	85,005	486	85,005	---	---	486	84,435	486	84,435	---	---	---	-570	---	-570
National Center for Toxicological Research	**45**	**10,317**	**231**	**56,395**	**276**	**66,712**	**45**	**10,317**	**231**	**56,395**	**276**	**66,712**	**21**	**5,087**	**255**	**61,179**	**276**	**66,266**	**-24**	**-5,230**	**24**	**4,784**	---	**-446**
FDA Headquarters	**207**	**64,075**	**339**	**104,994**	**546**	**188,069**	**178**	**53,239**	**335**	**113,181**	**513**	**183,920**	**179**	**54,675**	**335**	**114,538**	**514**	**186,713**	**1**	**1,436**	---	**1,357**	**1**	**1,293**
FDA White Oak Consolidation	---	---	---	---	---	**43,044**	---	---	---	---	---	**45,914**	---	---	---	---	---	**55,717**	---	---	---	---	---	**9,803**
Other Rent and Rent Related	---	**36,300**	---	**35,643**	---	**71,943**	---	**40,450**	---	**39,723**	---	**80,173**	---	**49,706**	---	**48,812**	---	**98,518**	---	**9,256**	---	**9,089**	---	**18,345**
GSA Rental Payments	---	**79,477**	---	**90,731**	---	**170,208**	---	**79,947**	---	**91,261**	---	**171,208**	---	**78,038**	---	**89,081**	---	**167,119**	---	**-1,909**	---	**-2,180**	---	**-4,089**
SUBTOTAL, BA Salaries and Expenses	---	**1,377,830**	**5,092**	**1,628,804**	**9,696**	**3,068,678**	**4,659**	**1,412,450**	**5,144**	**1,682,314**	**9,803**	**3,158,178**	**4,656**	**1,417,205**	**5,208**	**1,716,142**	**9,864**	**3,206,564**	**-3**	**4,755**	**64**	**33,828**	**61**	**46,886**
Building and Facilities	---	---	---	---	---	**11,788**	---	---	---	---	---	**31,788**	---	---	---	---	---	**13,788**	---	---	---	---	---	**-18,000**
Non-Field Activities	**1,647**	**467,433**	**3,620**	**1,234,337**	**5,267**	**1,720,770**	**1,685**	**479,281**	**3,664**	**1,245,937**	**5,349**	**1,742,718**	**1,676**	**478,054**	**3,728**	**1,274,819**	**5,404**	**1,770,373**	**-9**	**-1,227**	**64**	**28,882**	**55**	**26,155**
Field Activities	**2,957**	**794,620**	**1,472**	**268,093**	**4,429**	**1,062,713**	**2,974**	**812,772**	**1,480**	**305,393**	**4,454**	**1,118,165**	**2,980**	**811,407**	**1,480**	**303,430**	**4,460**	**1,114,837**	**6**	**-1,365**	---	**-1,963**	**6**	**-3,328**
White Oak, Rent Activities, and B&F	---	**115,777**	---	**126,374**	---	**296,983**	---	**120,397**	---	**130,984**	---	**329,083**	---	**127,744**	---	**137,893**	---	**335,142**	---	**7,347**	---	**6,909**	---	**6,059**
21st Century Cures	---	---	**136**	**70,000**	**136**	**70,000**	---	---	**136**	**75,000**	**136**	**75,000**	---	---	**136**	**70,000**	**136**	**70,000**	---	---	---	**-5,000**	---	**-5,000**
Total BA	**4,604**	**1,377,830**	**5,228**	**1,698,804**	**9,832**	**3,150,466**	**4,659**	**1,412,450**	**5,280**	**1,757,314**	**9,939**	**3,264,966**	**4,656**	**1,417,205**	**5,344**	**1,786,142**	**10,000**	**3,290,352**	**-3**	**4,755**	**64**	**28,828**	**61**	**23,886**
Total BA, Pre-Transfer	**4,604**	**1,377,830**	**5,228**	**1,698,804**	**9,832**	**3,150,466**	**4,659**	**1,412,450**	**5,280**	**1,757,314**	**9,939**	**3,264,966**	**4,656**	**1,417,205**	**5,344**	**1,786,142**	**10,000**	**3,290,352**	**-3**	**4,755**	**64**	**28,828**	**61**	**23,886**
Total User Fees	---	**15,863**	**6,214**	**1,836,708**	**7,231**	**2,574,463**	**50**	**16,140**	**6,605**	**1,936,206**	**7,752**	**2,674,609**	**102**	**44,423**	**6,714**	**2,047,692**	**7,967**	**2,914,584**	---	**28,283**	**109**	**111,486**	**215**	**239,975**
Current Law																								
Prescription Drug (PDUFA)	---	---	3,487	1,010,323	3,487	1,010,323	---	---	3,588	1,074,714	3,588	1,074,714	---	---	3,669	1,119,188	3,669	1,119,188	---	---	81	44,474	**81**	**44,474**
Medical Device (MDUFA)	---	---	689	204,730	689	204,730	---	---	849	220,142	849	220,142	---	---	877	238,595	877	238,595	---	---	28	18,453	**28**	**18,453**
Generic Drug (GDUFA)	---	---	1,626	501,721	1,626	501,721	---	---	1,740	513,223	1,740	513,223	---	---	1,740	526,039	1,740	526,039	---	---	---	12,816	---	**12,816**
Biosimilars (BsUFA)	---	---	122	38,847	122	38,847	---	---	128	41,923	128	41,923	---	---	128	42,998	128	42,998	---	---	---	1,075	---	**1,075**
Animal Drug (ADUFA)	---	---	135	30,331	135	30,331	---	---	144	30,611	144	30,611	---	---	144	31,306	144	31,306	---	---	---	695	---	**695**
Animal Generic Drug (AGDUFA)	---	---	76	18,335	76	18,335	---	---	77	20,151	77	20,151	---	---	77	20,609	77	20,609	---	---	---	458	---	**458**
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	984	712,000	---	---	---	---	1,060	712,000	---	---	---	---	1,114	712,000	---	---	---	---	**54**	---
Mammography Quality Standards Act (MQSA)	---	---	36	20,522	36	20,522	---	---	37	18,253	37	18,253	---	---	37	18,618	37	18,618	---	---	---	365	---	**365**
Color Certification	---	---	---	---	33	9,892	---	---	---	---	37	10,263	---	---	---	---	37	10,469	---	---	---	---	---	**206**
Export Certification	---	2,003	23	2,693	23	4,696	---	2,003	26	2,787	26	4,790	---	2,003	26	2,883	26	4,886	---	---	---	96	---	**96**
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	---	---	---	---	2,506	---	2,506	---	---	---	2,556	---	2,556	---	---	---	50	---	**50**
Priority Review Vouchers (PRV) Pediatric Disease	---	---	11	7,686	11	7,686	---	---	11	7,840	11	7,840	---	---	11	7,997	11	7,997	---	---	---	157	---	**157**
Priority Review Vouchers (PRV) Medical Countermeasures					---	---				2,506	---	2,506			---	2,556	---	2,556			---	50	---	**50**
Food and Feed Recall	---	1,434	---	---	---	1,434	5	1,463	---	---	5	1,463	5	1,492	---	---	5	1,492	---	29	---	---	---	**29**
Food Reinspection	---	6,414	---	---	---	6,414	24	6,542	---	---	24	6,542	24	6,673	---	---	24	6,673	---	131	---	---	---	**131**
Voluntary Qualified Importer Program	---	5,300	---	---	---	5,300	20	5,406	---	---	20	5,406	20	5,514	---	---	20	5,514	---	108	---	---	---	**108**
Third Party Auditor Program	---	712	---	---	---	712	1	726	---	---	1	726	1	741	---	---	1	741	---	15	---	---	---	**15**
Outsourcing Facility	---	---	9	1,520	9	1,520	---	---	5	1,550	5	1,550	---	---	5	1,581	5	1,581	---	---	---	31	---	**31**
Proposed																								
Export Certification (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	4,366	---	4,366	---	---	---	4,366	---	**4,366**
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	---	---	---	---	---	**100,000**
Food and Feed additive user fee (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	52	28,000	---	---	52	28,000	---	28,000	---	---	52	**28,000**
Total Program Level, Pre-Transfer	**4,604**	**1,393,693**	**11,442**	**3,535,512**	**17,063**	**5,724,929**	---	**1,428,590**	---	**3,693,520**	**17,691**	**5,939,575**	---	**1,461,628**	---	**3,833,834**	**17,967**	**6,204,936**	---	**33,038**	---	**140,314**	**276**	**263,861**
HHS OIG transfer	---	---	---	---	---	**-1,500**	---	---	---	---	---	**-1,500**	---	---	---	---	---	---	---	---	---	---	---	**1,500**
Total BA, Post-Transfer	**4,604**	**1,377,830**	**5,228**	**1,698,804**	**9,832**	**3,148,966**	---	**1,412,450**	---	**1,757,314**	**9,939**	**3,263,466**	---	**1,417,205**	---	**1,786,142**	**10,000**	**3,290,352**	---	**4,755**	---	**28,828**	**61**	**25,386**
Total Program Level, Post-Transfer	**4,604**	**1,393,693**	**11,442**	**3,535,512**	**17,063**	**5,723,429**	---	**1,428,590**	---	**3,693,520**	**17,691**	**5,938,075**	---	**1,461,628**	---	**3,833,834**	**17,967**	**6,204,936**	---	**33,038**	---	**140,314**	**276**	**265,361**

*Total Budget Authority includes $10 million for the China Initiative and $7.5 million 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 Medical Product Safety and Availability activities. Medical Countermeasures are included in Medical Product Safety and Availability activities.

** For FY 2019 and FY 2020, 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.

***Funding and FTE levels for FY 2019 are shown without comparably adjustment to reflect the updated realignment of the FDA HQ organizations

****NCTR is reallocating $5.23 million and 24 FTE from Food Safety project to Medical Product Safety in FY 2021

TECHNICAL NOTES

FY 2019 Comparability Adjustment

(Dollars in Thousands)	HQ Reorganization	
	FTE	$000
Salaries and Expenses Account:		
Foods	**29**	**6,761**
Center	27	6,450
Field	2	311
Human Drugs	**2**	**388**
Center	2	388
Field	---	---
Biologics	---	---
Center	---	---
Field	---	---
Animal Drugs and Feeds	**1**	**275**
Center	1	275
Field	---	---
Devices and Radiological Health	**2**	**425**
Center	2	425
Field	---	---
National Center for Toxicological Research	---	---
FDA Headquarters	**-34**	**-7,849**
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	**-2**	**-311**
Field Activities	**2**	**311**
Rent Activities, B&F, and White Oak	---	---

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; in addition to amounts appropriated to the FDA Innovation Account, for carrying out the activities described in section 1002(b)(4) of the 21st Century Cures Act (Public Law 114-255); 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; [$5,772,442,000] *$5,897,299,000*: Provided, That of the amount provided under this heading, [$1,074,714,000] *$1,119,188,000* 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; [$220,142,000] *$238,595,000* 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; [$513,223,000] *$526,039,000* 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; [$41,923,000] *$42,998,000* 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; [$30,611,000] *$31,306,000* 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; [$20,151,000] *$20,609,000* 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 new animal drug user fees that exceed the respective fiscal year [2020] *2021* 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 new animal drug assessments for fiscal year [2020] *2021*, including any such fees collected prior to fiscal year [2020] *2021* but credited for fiscal year [2020] *2021*, shall be subject to the fiscal year [2020] *2021* limitations: Provided further, That the Secretary may accept payment during fiscal year [2020] *2021* of user fees specified under this heading and authorized for fiscal year [2021] *2022*, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year [2021] *2022* for which the Secretary accepts payment in fiscal year [2020] *2021* shall not be included in amounts under this heading: Provided further, That none of these funds shall be used to develop, establish, or operate any program of user fees authorized by 31 U.S.C. 9701: [Provided further, That of the total amount appropriated: (1) $1,088,881,000 shall be for the Center for Food Safety and Applied Nutrition and related field activities in the Office of Regulatory Affairs, of which no less than $15,000,000 shall be used for inspections of foreign seafood manufacturers and field

examinations of imported seafood; (2) $1,972,093,000 shall be for the Center for Drug Evaluation and Research and related field activities in the Office of Regulatory Affairs; (3) $419,302,000 shall be for the Center for Biologics Evaluation and Research and for related field activities in the Office of Regulatory Affairs; (4) $237,741,000 shall be for the Center for Veterinary Medicine and for related field activities in the Office of Regulatory Affairs; (5) $581,761,000 shall be for the Center for Devices and Radiological Health and for related field activities in the Office of Regulatory Affairs; (6) $66,712,000 shall be for the National Center for Toxicological Research; (7) $661,739,000 shall be for the Center for Tobacco Products and for related field activities in the Office of Regulatory Affairs; (8) $186,399,000 shall be for Rent and Related activities, of which $53,913,000 is for White Oak Consolidation, other than the amounts paid to the General Services Administration for rent; (9) $239,717,000 shall be for payments to the General Services Administration for rent; and (10) $318,097,000 shall be for other activities, including the Office of the Commissioner of Food and Drugs, the Office of Foods and Veterinary Medicine, the Office of Medical and Tobacco Products, the Office of Global and Regulatory Policy, the Office of Operations, the Office of the Chief Scientist, and central services for these offices:] Provided further, That not to exceed $25,000 of this amount shall be for official reception and representation expenses, not otherwise provided for, as determined by the Commissioner: Provided further, That any transfer of funds pursuant to section 770(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379dd(n)) shall only be from amounts made available under this heading for other activities: [Provided further, That of the amounts that are made available under this heading for ``other activities'', and that are not derived from user fees, $1,500,000 shall be transferred to and merged with the appropriation for ``Department of Health and Human Services--Office of Inspector General'' for oversight of the programs and operations of the Food and Drug Administration and shall be in addition to funds otherwise made available for oversight of the Food and Drug Administration:] Provided further, That funds may be transferred from one specified activity to another with the prior approval 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, and, contingent upon the enactment of the Over-the-Counter Monograph User Fee Act of [2019] *2020*, fees relating to over-the-counter monograph drugs authorized by part 10 of subchapter C of Chapter VII of the Federal Food, Drug and Cosmetic Act 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] *$13,788,000*, 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 2021 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 2021 received during fiscal year 2021, including any such fees assessed prior to fiscal year 2021 but credited for fiscal year 2021, shall be subject to the fiscal year 2021 limitations: Provided further, That the Secretary may accept payment during fiscal year 2021 of user fees specified in this paragraph and authorized for fiscal year 2022, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2022 for which the Secretary accepts payment in fiscal year 2021 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.

FY 2021 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] *2021*; and (ii) for each subsequent fiscal year, the prior fiscal year maximum amount multiplied by the inflation adjustment under section 738(c)(2)(C), applied without regard to the limitation in clause (ii)(II) of such 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
OIG Transfer	The Administration proposes elimination of the transfer to OIG and making the funding to OIG via direct appropriation.
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 modernize FDA's regulatory oversight of innovative biotechnology products and emerging food production technologies
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.
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 $9,252,000. This proposal, and the increased certification fee ceiling it promotes, is necessary to ensure that FDA can efficiently implement the export certification program.

AMOUNTS AVAILABLE FOR OBLIGATION

(dollars in thousands)	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
General Fund Discretionary Appropriation:			
Appropriation	3,206,521	3,264,966	3,290,352
Total Discretionary Appropriation	**3,206,521**	**3,264,966**	**3,290,352**
Mandatory Appropriation:			
CRADA	2,000	2,000	2,000
Total Mandatory Appropriation	**2,000**	**2,000**	**2,000**
Offsetting Collections:			
Non-Federal Sources:	2,455,368	2,674,609	2,914,584
Total Offsetting Collections	**2,455,368**	**2,674,609**	**2,914,584**
Total Obligations	**5,663,889**	**5,941,575**	**6,206,936**

*For FY 2019 and FY 2020 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 2021, FDA proposes to discontinue the transfer.

SUMMARY OF CHANGES

Food and Drug Administration
Summary of Changes
(Dollars in Thousands)

(dollars in thousands)	Budget Authority	User Fees	Program Level	*FTE
FY 2020 Omnibus	**3,264,966**	**2,674,609**	**5,939,575**	**17,691**
FY 2021 Program Changes				
Budget Authority Changes				
Infrastructure and B&F	6,059	---	6,059	---
Artificial Intelligence	8,176	---	8,176	14
Outreach, Training, and Organization Excellence	-19,589	---	-19,589	---
Cannabis Derivatives	5,000	---	5,000	13
Strengthening Response Capabilities For Foodborne Outbreaks	1,240	---	1,240	4
Track and Trace	2,000	---	2,000	---
Transform Medical Device Safety, Cybersecurity, Review, and Innovation	18,000	---	18,000	4
Modernizing Influenza Vaccines	5,000	---	5,000	10
Compounding	4,500	---	4,500	16
21st Century Cures	-5,000	---	-5,000	---
Total Budget Authority Changes	**25,386**	**---**	**25,386**	**61**
User Fee Changes				
Current Law				
Prescription Drug (PDUFA)	---	44,474	44,474	81
Medical Device (MDUFA)	---	18,453	18,453	28
Generic Drug (GDUFA)	---	12,816	12,816	---
Biosimilars (BsUFA)	---	1,075	1,075	---
Animal Drug (ADUFA)	---	695	695	---
Animal Generic Drug (AGDUFA)	---	458	458	---
Family Smoking Prevention and Tobacco Control Act	---	---	---	54
Indefinite				
Mammography Quality Standards Act (MQSA)	---	365	365	---
Color Certification	---	206	206	---
Export Certification	---	96	96	---
Priority Review Vouchers (PRV) Tropical Disease	---	50	50	---
Priority Review Vouchers (PRV) Pediatric Disease	---	157	157	---
Priority Review Vouchers (PRV) Medical Countermeasures	---	50	50	---
Food and Feed Recall	---	29	29	---
Food Reinspection	---	131	131	---
Voluntary Qualified Importer Program	---	108	108	---
Third Party Auditor Program	---	15	15	---
Outsourcing Facility	---	31	31	---
Export Certification (Proposed)	---	4,366	4,366	---
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	**---**	**239,975**	**239,975**	**215**
Net Program Changes	**25,386**	**239,975**	**265,361**	**276**
Total FDA Request for FY 2021	**3,290,352**	**2,914,584**	**6,204,936**	**17,967**

* FTE figures do not include an estimated 70 reimbursable and 26 PEPFAR.

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2019 Actual	FY 2020 Enacted	FY 2021 President's Budget
Salaries and Expenses Account:			
Foods	**1,059,926**	**1,088,881**	**1,090,530**
Center	327,462	341,966	344,524
Field	732,464	746,915	746,006
Human Drugs	**662,892**	**683,195**	**683,411**
Center	524,738	507,726	509,033
Field	138,154	175,469	174,378
Biologics	**240,133**	**252,138**	**252,381**
Center	198,132	210,132	210,657
Field	42,001	42,006	41,724
Animal Drugs and Feeds	**178,928**	**190,869**	**190,081**
Center	113,419	122,099	121,787
Field	65,509	68,770	68,294
Devices and Radiological Health	**386,733**	**395,168**	**415,828**
Center	301,738	310,163	331,393
Field	84,995	85,005	84,435
National Center for Toxicological Research	**66,712**	**66,712**	**66,266**
FDA Headquarters	**187,776**	**185,420**	**186,713**
FDA White Oak Consolidation	**43,044**	**45,914**	**55,717**
Other Rent and Rent Related	**71,943**	**80,173**	**98,518**
GSA Rental Payments	**170,208**	**171,208**	**167,119**
Subtotal, Salaries and Expenses Account	**3,068,295**	**3,159,678**	**3,206,564**
Food and Drug Safety -- No Year (P.L. 113-6)	**14**	---	---
Food Safety	14	---	---
Drug Safety	---	---	---
21st Century Cures	**58,225**	**75,000**	**70,000**
MCMi - No Year	**4,601**	---	---
Opioids - No Year	**65,408**	---	---
Buildings and Facilities Account	**11,477**	**31,788**	**13,788**
Total Budget Authority	**3,208,021**	**3,266,466**	**3,290,352**
HHS OIG Transfer	**-1,500**	**-1,500**	---
Total Budget Authority, Post-Transfer	**3,206,521**	**3,264,966**	**3,290,352**
FTE	**9,915**	**9,939**	**10,000**

*For FY 2019 and FY 2020 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 2021, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 70 reimbursable and 26 PEPFAR.

APPROPRIATIONS HISTORY

Salaries and Expenses

(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	5,584,965,000
FY 2020	5,990,342,000	5,866,703,000	5,781,442,000	5,772,442,000
FY 2021	6,058,585,000			

* 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 2017, $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	11,788,000
FY 2020	11,788,000	11,788,000	11,788,000	11,788,000
FY 2021	13,788,000			

*FY 2020 Appropriation excludes $20 million for one time general provision.

OVERVIEW OF LEGISLATIVE PROPOSALS

The FY 2021 Budget Request includes legislative proposals to address drug pricing, medical product shortages, and other priority areas.

Increased Competition

The President's 2021 Budget includes an allowance for bipartisan drug pricing proposals. The Administration supports legislative efforts to improve the Medicare Part D benefit by establishing an out-of-pocket maximum and reducing out-of-pocket costs for seniors. The Administration also supports changes to bring lower cost generic and biosimilar drugs to patients. These efforts would increase competition, reduce drug prices, and lower out of pocket costs for patients at the pharmacy counter.

The Administration has and continues to support legislative efforts to make the path to generic and biosimilar development more transparent, efficient, and predictable so that Americans have better access to these medicines that are often more affordable. Overall, addressing regulatory barriers and challenges and closing potential loopholes that hinder development of generics, will promote more competition, and advance patient access to more affordable medicines.

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 Proposals

Clarify Standard for Biologics Novelty for Priority Review Vouchers

The FD&C Act includes three priority review voucher (PRV) programs where sponsors of drugs, including biologic products, that are approved and meet certain criteria are awarded a PRV. That PRV can be redeemed to obtain priority review for a subsequent NDA or BLA that would not otherwise qualify for priority review. Each PRV program has criteria that are directed towards those specific product types, but, as general matter, all require that the product for which a sponsor receives a PRV be a drug, eligible for priority review on its own merits, and novel. The current statutory standard of drug novelty (i.e., no active ingredient of which has been approved in any other application) is potentially problematic in the context of biological products, which are often more complex than small molecule drugs and may be challenging to characterize. Due to their complexity, these products' "active ingredients" may not be precisely identifiable or may only be known to a limited extent. Clarification of the novelty standard for a biological product, based on its containing key structural features not contained in a previously licensed biological product, would help provide a more predictable standard for sponsors seeking PRVs and would help the PRV programs achieve their intended goal of incentivizing the development of innovative products.

Identifying Drug Supply Chain Security Act (DSCSA) Covered Products

In September 2017, the HHS Office of the Inspector General (OIG) completed a study that examined how wholesale distributors were exchanging product tracing information to comply

with drug supply chain security provisions of the Drug Supply Chain Security Act (DSCSA). OIG found that there was significant confusion and, in some cases, disagreements between trading partners about which drugs meet the definition of a "product" under the DSCSA and are subject to the DSCSA's product tracing and other provisions. Currently, there is no requirement in the DSCSA for manufacturers and repackagers to provide information to FDA on whether a particular drug is a "product" for DSCSA purposes. FDA proposes requiring manufacturers and repackagers to indicate whether a drug meets the definition of a "product" under the DSCSA when they list the drug in FDA's electronic drug registration and listing system. FDA could incorporate this information into the National Drug Code (NDC) directory or another public resource. This would mitigate confusion in the marketplace as to whether a particular prescription drug is a "product" subject to traceability, serialization, verification, and other requirements of the DSCSA.

Establishing a Regulatory Framework for Digital Health Medical Devices

Regulatory pathways under current authority do not promote flexibility for FDA to optimally regulate emerging technologies. This is exemplified in the digital health space, where the current statutory framework for regulation of medical devices is not well suited to the faster cycle of innovation, iterative design and development, and validation approaches used for digital health devices. FDA proposes establishing a framework that would allow FDA to tailor and apply the appropriate requirements for the reasonable assurance of safety and effectiveness for a software as a medical device product based on the risk of the product and throughout the product lifecycle.

Ability for CVM to Require Labeling Changes on Animal Drug Products for Safety-Related Reasons

Currently, CVM has no authority to require application holders of new animal drug products or abbreviated new animal drug products to make safety-related labeling changes based on information that becomes available after approval, such as from adverse event reporting. Often animal drug application holders respond to CVM requests for labeling changes by negotiating appropriate language with CVM staff to address the concerns and then submit a supplemental application to obtain approval of the labeling changes. However, these negotiations are not time limited and the application holder can refuse to make changes. For safety purposes, FDA proposes authorizing CVM to require safety-related labeling changes for drug products with an approved NADA, or an approved ANADA if the NADA RLD is not currently marketed in a manner similar to that provided for human drug products under section 505(o)(4) of the FD&C Act.

Amending the Definition of "Major Species" in 21 U.S.C. §321

The Minor Use & Minor Species Animal Health Act of 2004 (MUMS Act) was passed in part to address the critical shortage of animal drugs available for minor species. The markets for drugs intended to treat these species are so small that there are often insufficient economic incentives to motivate sponsors to develop data to support approvals. The MUMS Act amended section 201 of the FD&C Act (21 U.S.C. §321) by adding definitions for several important terms, including "minor species" and "major species." Section 201(oo) of the FD&C Act defines "minor species"

as animals other than humans that are not major species. "Major species" are defined at section 201(nn) of the FD&C Act as, "cattle, horses, swine, chickens, turkeys, dogs, and cats, except that the Secretary may add species to this definition by regulation." Since the enactment of the MUMS Act, animal populations have shifted. CVM expects that, in the near future, some species that have been classified as major species may no longer have numbers that support that classification. Horses are an example of one such species. FDA proposes amending the definition of "major species" in section 201 of the FD&C Act to grant the Secretary authority to not only add to the list of major species but also to delete species, as necessary, to account for the potential for growing or shrinking populations of animal species.

Expanding Temporary Access to Diagnostic Testing During Certain Emergencies

FDA requests that section 564A of the FD&C Act be amended to allow FDA to issue (and amend or revoke) an order designating that certain approved, cleared or licensed in vitro diagnostic tests (IVDs) can temporarily be used in additional settings, with conditions as deemed warranted, without issuing an Emergency Use Authorization (EUA). The requested authority would be comparable to the other section 564A emergency use authorities that provide streamlined mechanisms to facilitate certain emergency activities without the need to issue an EUA. It would provide FDA the ability to quickly and temporarily enable access to certain approved, cleared or licensed IVDs to facilitate testing in an increased number of patients in additional settings, when necessary to protect public health.

Administrative Detention of Foods and Temporary Holds at a Port of Entry

Current law states that an official may not be designated by the Secretary to approve an order for the administrative detention of food or a temporary hold of an article of food at a port of entry unless the official is an FDA "director of the district" or an official senior to such director. These references are now out of date and FDA is proposing to remove the statutory language specifying the title of the officials who may be designated. FDA's Office of Regulatory Affairs has since reorganized and many of the roles and responsibilities related to these statutory provisions have been transferred to officials now titled "program division directors" and removing the specific designation provides FDA with the same flexibility afforded to the Agency in the similar statutory provision for the administrative detention of devices, drugs, and tobacco products.

Extend the Requirement for Field Alert Reports to Non-Application Distributed Drug Products

FDA is proposing to require Field Alert Reports (FARs) for drug products that are not marketed under an approved application. FARs are part of an early warning system to protect patient health and the quality of therapeutic products. Alerts are currently required for issues concerning any bacteriological contamination, or any significant chemical, physical, or other change or deterioration in a distributed drug product that is marketed under an approved application, or any failure of one or more distributed batches of the approved drug product to meet established specification; or any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article. FDA regulates many drugs that are not marketed under approved applications, such as OTC drugs marketed under the OTC monograph system, homeopathic drugs, drugs compounded at 503B outsourcing facilities, and other marketed unapproved drugs.

While alerts are required by statute and further described by regulation for drugs marketed under an approved application to be submitted by the applicant, there is no similar reporting system for distributed products which are not marketed under an approved application. Further, quality and labeling incidents for such products may go undetected by the Agency if not reported. According to data analysis from the last five years, there were nine class I recalls and approximately 104 Class II recalls that would have potentially required Field Alert Report submission. If non-application drug product manufacturers are required to report these issues to the Agency, FDA can encourage them to investigate the complaints more thoroughly and recall the product sooner, if necessary.

Closing the Drug Exclusion Loophole for Dietary Supplements

Under current law, products are excluded from the definition of "dietary supplement" if they contain certain articles that are approved or were studied as new drugs unless the article was first marketed as a dietary supplement or as a food. This is because the definition of dietary supplement does not include an article that "is approved" as a new drug, or an article "authorized for investigation as a new drug…for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public," unless the article was marketed as a dietary supplement or food before such approval or authorization. However, some older drug products that were not first marketed as a dietary supplement or food may fall into a loophole with respect to this exclusion if they were approved as new drugs, but their approvals are later withdrawn, and they are not otherwise excluded by the other part of the provision. This is because when these older drug products are no longer approved, they may fall outside of the statutory exclusion for an article that "is approved" as a new drug.

FDA Import Filer Evaluation Program

When articles regulated by FDA that are offered for import, entry filers are required to submit FDA-specific electronic information for FDA to screen, evaluate risk, and target imported products for examination, as well as determine admissibility into U.S. commerce. FDA has encountered filers who, after repeated attempts to educate and admonish them, continue to commit significant filing errors that are critical to FDA's review, such as incorrect FDA product codes or inaccurate manufacturer and country of origin information. There are cases where FDA has taken the effort to explain and educate entry requirements to filers with filing errors, and in subsequent filings the firms still do not comply. Such filers demonstrate inexcusable negligence and disregard of FDA's import requirements, or even a deliberate attempt to bypass them. As a result, FDA is requesting explicit authority to conduct mandatory inspections of filers of import entry data with respect to their records that are related to the submission of electronic import information to FDA and to issue civil monetary penalties against entry filers who exhibit repeated and egregious errors in their submission of import information to FDA and fail to correct them.

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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FOODS

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Foods	**1,077,612**	**1,059,926**	**1,099,970**	**1,127,941**	**27,971**
Budget Authority	***1,066,741***	***1,059,926***	***1,088,881***	***1,090,530***	***1,649***
User Fees	***10,871***	---	***11,089***	***37,411***	***26,322***
Center	335,244	327,462	342,815	371,490	28,675
Budget Authority	334,412	327,462	341,966	344,524	2,558
User Fees	832	---	849	26,966	26,117
Food and Feed Recall	*243*	---	*248*	*253*	*5*
Voluntary Qualified Importer Program	*243*	---	*248*	*253*	*5*
Third Party Auditor Program	*346*	---	*353*	*360*	*7*
Innovative Food Products (Proposed)	---	---	---	*26,100*	*26,100*
Field	742,368	732,464	757,155	756,451	-704
Budget Authority	732,329	732,464	746,915	746,006	-909
User Fees	10,039	---	10,240	10,445	205
Food and Feed Recall	*1,000*	---	*1,020*	*1,040*	*20*
Food Reinspection	*4,575*	---	*4,667*	*4,760*	*93*
Voluntary Qualified Importer Program	*4,320*	---	*4,406*	*4,495*	*89*
Third Party Auditor Program	*144*	---	*147*	*150*	*3*
FTE	**3,758**	**3,758**	**3,863**	**3,934**	***71***

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[5]
- An estimated 128,000 hospitalizations and 3,000 deaths result
- Foodborne illnesses cost an average of $3,630 per case
- More than $36 billion per year in medical costs, lost productivity, and other burdens to society.[6]

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. Approximately 90 percent of the nation's health care expenditures are for people with one or more chronic medical conditions.[7]

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

[5] https://www.cdc.gov/foodborneburden/2011-foodborne-estimates.html Center of Disease Control and Prevention (CDC) 2011 Estimates and Findings. A comparable analysis cannot be made between CDC's 2011 estimates and findings from earlier years due to a new methodology being used in 2011.

[6] https://www.cdc.gov/chronicdisease/about/costs/index.htm

[7] Centers for Disease Control and Prevention. "Chronic Disease Prevention and Health Promotion: Chronic Disease Overview." https://www.cdc.gov/chronicdisease/about/index.htm,

In addition to the high-priority initiatives listed above, the Foods Program conducts other important activities related to food safety, nutrition, and cosmetics. These include:

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

The FDA Food Safety Modernization Act

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.[8]

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. As of October 2019, FDA has awarded 47 states and 1 territory a total of $112 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. Furthermore, FDA worked with NASDA in 2018 to finalize informational resources and to train states to implement the On-Farm Readiness Review (OFRR) program, which allows farms to request a review of the readiness of their operations for produce safety rule (PSR) implementation by regulators.

8 https://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm

FDA Launches the FDA-TRACK: Food Safety Dashboard to Track FSMA Progress

In September 2019, FDA established a Food Safety Dashboard designed to track the impact of the seven foundational rules of the FDA Food Safety Modernization Act (FSMA), measure their progress, and help us continue to refine our implementation. The dashboard is available as part of the FDA-TRACK program, the FDA's agency-wide performance management system.[9]

As FDA embarks on a New Era of Smarter Food Safety, continuing the successful implementation of FSMA will support FDA's goal of reducing the incidence of illness and death attributable to preventable contamination of FDA-regulated human and animal food products. In September 2019, FDA announced the availability of the initial metrics that will track outcomes for three FSMA rules in the areas of inspections and recalls:

- "Current Good Manufacturing Practice, Hazard Analysis and Risk-Based Preventive Controls" rules for both human food and food for animals (preventive controls rules)
- Imported food safety, including data relevant to the "Foreign Supplier Verification Program" (FSVP) rule.

Over time, the Food Safety Dashboard will be populated with additional data to show more FSMA outcomes. Additional performance measures and data will be released for other FSMA rules in the future.

FDA Begins Produce Safety Rule Inspections

In 2019, FDA and its state regulatory counterparts began conducting routine inspections of large farms for the Produce Safety Rule established by FSMA. Leading up to 2019, FDA collaborated with the NASDA and state partners to help prepare farmers to comply with the rule. FDA also supported states in the development of their own produce safety programs. FDA remains committed to doing everything it can to prevent produce outbreaks, working with fellow regulators and the food industry to identify and address causes and keep consumers aware of potential risks.

Under cooperative agreements with FDA and state regulatory partners, almost 1,000 large farm inspections have been completed. The first routine inspections of small farms are set to begin in January 2020. FDA also remains focused on education, training and outreach to farms. This outreach includes about 1,400 On-Farm Readiness Reviews that NASDA developed in collaboration with the FDA and state partners to help farmers assess their readiness to comply with the rule.

FDA is committed to ensuring that foods imported from other countries are held to the same standards as food produced domestically. In February 2019, the agency released the "FDA Strategy for the Safety of Imported Foods," describing our comprehensive approach to imported food safety. Part of our strategy is to ensure that farmers in other countries who export to the U.S. have access to resources that include training and On-Farm Readiness Reviews.

[9] https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-food-safety-dashboard

Surveillance sampling is an important part of FDA's public health mission. FDA has two ongoing microbiological surveillance sampling assignments in fresh herbs and frozen berries, types of produce that have been associated with past outbreaks of foodborne illness.

FDA is also conducting a focused assignment to test samples of romaine lettuce grown in the Central Coast, Central Valley, and Imperial Valley in California and in Yuma, Arizona for pathogenic E.coli and Salmonella. This assignment follows multiple outbreaks of foodborne illness associated with romaine lettuce over the past two years. This also follows testing that the FDA conducted last summer in which samples of romaine lettuce grown in the Yuma region were collected from commercial coolers and cold storage facilities. No pathogenic bacteria were found in the testing. Across all of these assignments, thousands of samples have and will be tested for pathogens. FDA will continue to work closely with state regulatory partners to help ensure that farmers understand the requirements for produce safety.[10]

FDA Finalizes New Compliance Dates for Agricultural Water Requirements

In 2019, FDA issued a rule that finalizes the new compliance dates for the agricultural water requirements in the FSMA Produce Safety Rule. Larger farms are now required to comply with the agricultural water requirements by January 26, 2022, while small farms have until January 26, 2023 and very small farms until January 26, 2024. The rule did not change the compliance dates for sprout operations.[11]

The compliance dates have been extended while FDA considers how best to protect public health while addressing widespread concerns about the complexity of the agricultural water requirements and the practicality of implementing them across a wide variety of farms, water sources, and uses. FDA intends to use this time to work with stakeholders to address these concerns. While this rule extends the compliance dates for the agricultural water provisions, produce remains subject to the other provisions of the Produce Safety Rule and the adulteration provisions of the Federal Food, Drug, and Cosmetic Act.

FDA Announces Produce Safety Rule Enforcement Discretion Policy for Certain Commodities

In 2019, FDA announced that it intends to exercise enforcement discretion for the requirements of the FSMA Produce Safety Rule as they apply to entities growing, harvesting, packing, and holding wine grapes, hops, pulse crops, and almonds. FDA is doing this because after the Produce Safety Rule was finalized, it received feedback from stakeholders that wine grapes, hops, pulses, and almonds should be exempt. After conducting an initial review of the production and use of these commodities, FDA has decided to exercise enforcement discretion with respect to these commodities, while it considers pursuing rulemaking to address the unique

[10] https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/outbreaks-emphasize-importance-implementing-produce-safety-standards

[11] https://www.fda.gov/food/cfsan-constituent-updates/fda-finalizes-new-compliance-dates-agricultural-water-requirements

circumstances they each present. FDA will continue to enforce the statutory prohibition against introduction or delivery for introduction of adulterated food into interstate commerce.

Selected Guidances Issued in 2019

Below are selected guidances issued by the Foods Program this calendar year. This list does not represent degree of importance or priority ranking among the published guidances.[12]

Date	#	Title	Description
Mar 2019	FDA-2019-D-1266	Guidance for Industry: Enforcement Policy for Entities Growing, Harvesting, Packing, or Holding Hops, Wine Grapes, Pulse Crops, and Almonds	Provides FDA's intent not to enforce requirements of the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption regulation (21 CFR Part 112) for certain commodities.
Mar 2019	FDA-2011-N-0144	Guidance for Industry: FDA's Voluntary Qualified Importer Program (VQIP)	Describes FDA's policy on participation in VQIP by importers of food for humans or animals. Provides guidance on the benefits of VQIP participation, eligibility criteria, application instructions, and conditions.
Feb 2019	FDA-2018-D-1398	Draft Guidance for Industry: Mitigation Strategies to Protect Food Against Intentional Adulteration	Provides the food industry with information needed to employ mitigation strategies in their facilities to help ensure food's protection from intentional adulteration to comply with the Intentional Adulteration Rule (21 CFR 121).

Improved Outbreak Response

The Foods Program and the Coordinated Outbreak Response and Evaluation (CORE) Network rapidly detect and respond to outbreaks of illness related to food, cosmetics, and dietary supplements. This group coordinates activities across FDA field and compliance offices, state investigative and laboratory resources, and local city and county resources. CORE works with other federal agencies, such as the Centers for Disease Control and Prevention (CDC) and U.S. Department of Agriculture (USDA), to ensure timely and effective resolution of foodborne illness outbreaks. FDA continues to improve its current response and evaluation process. In 2019, FDA has invested in improving certain areas such as root-cause investigation procedures and regulations for enhanced record keeping.

In August 2019, FDA issued a letter calling on all sectors of the papaya industry (growers, packers, shippers and retailers) to review their operations and make all necessary changes to strengthen public health safeguards. Since 2011, American consumers have been exposed to eight

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

outbreaks caused by *Salmonella* serotypes linked to imported, fresh papaya. The first seven outbreaks accounted for almost 500 reported cases of illness, more than 100 hospitalizations, and two deaths. The most recent, in June 2018, resulted in 81 illnesses and 27 hospitalizations. In addition to the papaya industry letter, FDA issued a warning letter to the distributor of the papayas implicated in the outbreak.

FDA scientists also develop methods to assist in outbreak response. The incidence of infections from *Cyclospora* at 10 U.S. sites increased by 399 percent in 2018, compared with 2015-17, in part due to large outbreaks associated with produce.[13] As a result of information learned from past *Cyclospora cayetanensis* outbreaks, including one linked to imported basil and one associated with vegetable trays, FDA developed a sampling method for *Cyclospora*. This sampling method will improve the ability to detect this parasite in produce, thus helping in the prevention of some of these illnesses in the future.

Additionally, a newly developed and validated sample preparation method and Real-Time Polymerase Chain Reaction (PCR) Assay for Detection of *Cyclospora* was approved and implemented. FDA staff have been trained in this new method for use in all future domestic and imported food sampling.

FDA's investigations and public communications create awareness among consumers of food safety risks that are not regularly considered, and FDA works with industry to improve that awareness. For example:

- Ice cream, frozen food, and caramel apples were found to be contaminated with Listeria. These prompted public warnings, and improved public awareness;
- Salmonella has been found in kratom. This prompted warnings to firms and identified a new risk to the public from kratom;
- In response to an E. coli outbreak associated with flour, FDA expanded messaging for the safe handling of dry flour and suggested more effective labeling;
- Recent work on E. coli outbreaks associated with romaine lettuce resulted in improving public warnings,and assisting industry in implementing a voluntary labeling system.

FDA investigations of food and dietary supplements have led to the use of FDA's mandatory recall authority. FDA's process includes a team devoted to evaluating potential foodborne illness incidents to find those possibly linked to FDA products. Through coordination with CDC, this work allows FDA to start a response earlier, focus limited resources, and try to bring the investigation to quick resolution to minimize the number of people who become sick.

[13] https://www.cdc.gov/mmwr/volumes/68/wr/mm6816a2.htm

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 seventh year and has collected more than 388,000 whole bacterial genome sequences (including more than 240,000 Salmonella) 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
- identifying emerging antimicrobial resistance threats in the food supply
- supporting research to improve preventive controls and good agricultural practices.

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 Shiga toxin-producing *E. coli* (STEC), *Salmonella* and *Listeria monocytogenes*. By generating about two whole genomes per hour, GenomeTrakr is rapidly increasing the number of STEC, *Salmonella* and *Listeria monocytogenes* genomes in the database. The network includes more than 60 state, international, FDA, and federal partner (CDC and USDA-Food Safety and Inspection Service [FSIS]) laboratories.

In 2019, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions. To date, WGS has supported more than 500 cases of product adulteration and contaminated conditions investigated by the FDA. For example, in 2018 a well-known variety of children’s puffed rice cereal contaminated with *Salmonella* Mbandaka was implicated in an outbreak that affected 73 people in 31 states. Whole genome sequencing provided a strong linkage between the production facility and clinical cases, and helped identify specific areas

within the production facility that lacked preventive controls, leading to the recall of all of the product in question and adjudication through an official warning letter.

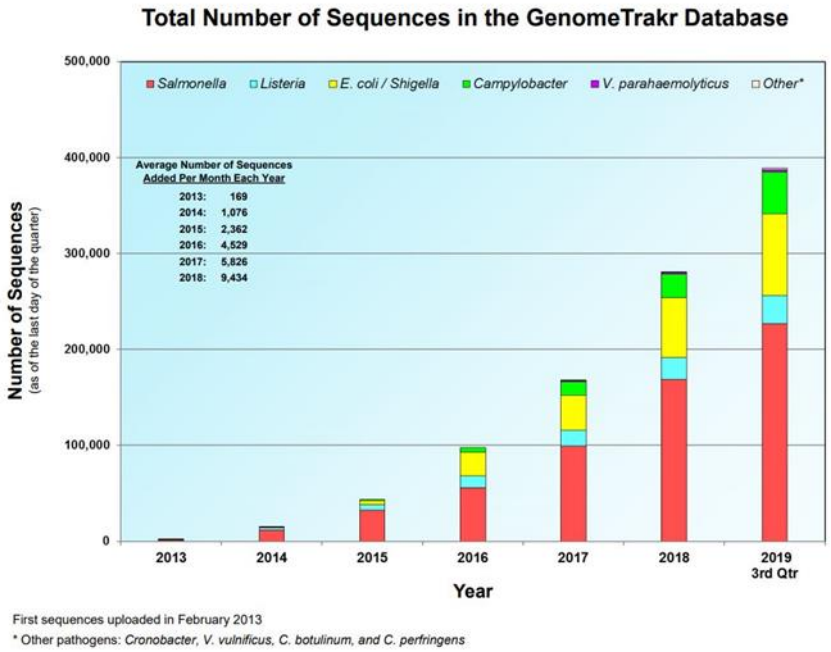

Figure 2 The Total Number of Sequences in the GenomeTrakr Database

Release of a New Report on the Sources of Foodborne Illnesses for 2017 from the Interagency Food Safety Analytics Collaboration

In 2019, the Interagency Food Safety Analytics Collaboration (IFSAC) released a report titled "Foodborne illness source attribution estimates for 2017 for *Salmonella*, *Escherichia coli* O157, *Listeria monocytogenes*, and *Campylobacter* using multi-year outbreak surveillance data, United States."[14] The authors used the most recently available national foodborne disease outbreak data to produce new estimates for foods responsible for foodborne illnesses caused by four pathogens in 2017. CDC estimates that, together, these four pathogens cause 1.9 million foodborne illnesses in the United States each year.

The updated estimates, combined with other data, may help shape agency priorities and inform the creation of targeted interventions that can help to reduce foodborne illnesses caused by these pathogens. As more data become available and methods evolve, attribution estimates may improve. These estimates are intended to inform and engage stakeholders and to improve federal agencies' abilities to assess whether prevention measures are working.

14 https://www.cdc.gov/foodsafety/ifsac/annual-reports.html

Three participating federal agencies—CDC, FDA, and USDA's FSIS— created IFSAC in 2011 to improve coordination of federal food safety analytic efforts and address cross-cutting priorities for food safety data collection, analysis, and use.

In the report, IFSAC analyzed data from just over 1,329 foodborne disease outbreaks that occurred from 1998 through 2017 to assess which categories of foods were most responsible for *Salmonella*, *E. coli* O157, *Listeria monocytogenes*, and *Campylobacter* infections. The pathogens were chosen because of the frequency or severity of the illnesses they cause, and because targeted interventions can have a major impact in reducing them. The implicated foods were divided into 17 categories for the analysis, and the method gives the greatest weight to the most recent five years of outbreak data (2013–2017). Of note in the 2017 report:

- *Salmonella* illnesses came from a wide variety of foods, with 75% of illnesses linked to seeded vegetables, chicken, fruits, pork, eggs, produce, and beef.
- *E. coli* O157 illnesses were most often linked to vegetable row crops (such as leafy greens) and beef
- *Listeria monocytogenes* illnesses were most often linked to dairy products and fruits.
- *Campylobacter* illnesses were most often linked to chicken with a statistically significantly higher estimate than any other categories.

Resources for Food Producers in Areas Flooded Due to Tropical Storm Barry and Hurricane Dorian

In July 2019, FDA provided resources to help growers in the Gulf Coast region impacted by Tropical Storm Barry. FDA's Guidance for Industry: Evaluating the Safety of Flood-affected Food Crops for Human Consumption provides information that producers can use as they assess potential damage to their food crops. This guidance is an important resource for the growers who produce and market these crops, as they are responsible for assuring the safety of flood-affected food crops for human consumption.[15]

In August 2019, FDA provided guidance and resources for growers and food producers in Puerto Rico, the U.S. Virgin Islands, and Florida impacted by the devastation of Hurricane Dorian. In this guidance, FDA reminds harvesters that if the edible portion of a crop is exposed to 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.[16]

FDA encourages growers to work with state regulators and local FDA offices to assess their unique situations and to take into consideration all possible types and routes of contamination from flood waters in determining whether a particular crop is adulterated.

[15] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-evaluating-safety-flood-affected-food-crops-human-consumption

[16] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-evaluating-safety-flood-affected-food-crops-human-consumption

FDA reminded 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 (e.g., peanuts, potatoes). For crops (e.g., 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. Sometimes, crops that have been harvested and then subsequently deemed unsuitable for human use can be salvaged for animal food. For more information please see CVM Update: Resources for Animal Food Producers in Flooded Areas.[17]

FDA Outlines Multi-Layer Approach to Ensure Food Imports Are Safe

In 2019, FDA released its "Strategy for the Safety of Imported Food" which outlines the agency's comprehensive approach to helping ensure the safety of food imported into the United States.[18]

The strategy is guided by four goals:

- Goal 1: Food Offered for Import Meets U.S. Food Safety Requirements
- Goal 2: FDA Border Surveillance Prevents Entry of Unsafe Foods
- Goal 3: Rapid and Effective Response to Unsafe Imported Food
- Goal 4: Effective and Efficient Food Import Program.

The U.S. imports about 15 percent of its overall food supply from more than 200 countries or territories, with 13.8 million food shipments in 2018, with the number of food shipments expected to rise in future years. Other countries supply approximately 55 percent of fresh fruit, 32 percent of vegetables, and 94 percent of seafood consumed in this country.

While the U.S. food supply is among the safest in the world and significant food safety advances are being made, a preventable level of foodborne illness continues to occur – arising from both domestically produced and imported food. For imported food, the volume and variety of imports and the complexity of global supply chains make food safety a challenging issue to address. Further complicating the issue, some exporting countries may have food safety systems different from ours and differing levels of regulatory capacity.

Fortunately, FDA has been provided with a range of tools and authorities to address the situation both domestically and in the foreign arena. The strategy document released on February 25, 2019 describes how FDA is integrating new import oversight tools with existing tools to help ensure that imported food is safe for consumers in the United States.

[17] https://www.fda.gov/animal-veterinary/cvm-updates/resources-animal-food-producers-flooded-central-southern-plains-us

[18] https://www.fda.gov/food/importing-food-products-united-states/fda-strategy-safety-imported-food

New Certification Bodies Accredited Under FDA's Third-Party Program

FDA's Accredited Third-Party Certification Program is a voluntary program in which FDA recognizes accreditation bodies (ABs) that will have the responsibility of accrediting third-party certification bodies (CBs). The certification bodies will conduct food safety audits and issue certifications of foreign food facilities.

Currently, the Third-Party Program (TPP) has eight CBs that have been accredited by three of the four recognized ABs in the program. In 2019, nine certifications were issued under the TPP.

This accreditation means that CBs have been given the authority to conduct food safety audits and issue food and facility certifications for their relevant program scopes. Certifications issued by a CB accredited through FDA's TPP can be used by importers to establish eligibility for participation in the Voluntary Qualified Importer Program (VQIP), and in certain circumstances FDA can require that imported products be certified before entering the United States.

FDA Makes Available Testing Method for PFAS and Results from Surveys

In 2019, FDA made available a scientifically validated method for testing for 16 types of per-and polyfluoroalkyl substances (PFAS) in a variety of food groups.[19] PFAS are a family of human-made chemicals that are found in a wide range of products used by consumers and industry. There are nearly 5,000 types of PFAS, some of which have been more widely used and studied than others. Many PFAS are resistant to grease, oil, water and heat. Beginning in the 1940's, PFAS have been used in a variety of applications including in stain- and water-resistant fabrics and carpeting, cleaning products, paints, and fire-fighting foams. In addition, certain PFAS are authorized by the FDA for limited use in cookware, food packaging and processing. FDA continues to lead national efforts to estimate overall dietary exposure to PFAS. FDA also shared final results from its limited food sample testing in three surveys released in June, based on the application of the validated method, which established a method detection limit (MDL) for each food group tested. These three surveys included a general sampling of foods collected as part of FDA's Total Diet Study (TDS), as well as a survey of produce and a survey of dairy products, both from specific areas affected by PFAS environmental contamination. [20]

The final results show reductions in the number of positive samples compared to initial results. These reductions stem in part from the application of the newly established MDL, the level at which PFAS can be reliably measured over repeated testing. In initial testing, very low levels of certain PFAS chemicals in certain foods were reported. After validating the method and finalizing the results, some of those concentrations are below the MDL and therefore are no longer reported as having detectable levels of PFAS.

[19] https://www.fda.gov/food/cfsan-constituent-updates/fda-makes-available-testing-method-pfas-foods-and-final-results-recent-surveys

[20] https://www.fda.gov/food/chemicals/and-polyfluoroalkyl-substances-pfas

FDA is currently analyzing additional TDS samples to increase baseline knowledge of PFAS occurrence in foods and expects to release those results later this year. As new information becomes available, FDA will continue to share updates on fda.gov.

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 2019, FDA issued four injunctions and one seizure 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. FDA works with Federal, state, and local partners to identify the products causing problems and take efficient and effective compliance actions.

FDA also issues import controls when non-compliant food products are discovered or when food companies manufacture or ship non-compliant products. In FY 2019, FDA issued 712 import alert notices (of which 210 were reviewed by CFSAN) for human food, cosmetic, and dietary supplement products. Additionally, CFSAN worked with the FDA field offices to assist in 779 cases where the district needed CFSAN's technical expertise to determine import admissibility. In FY2019, FDA issued Import Alert # 99-41, "Detention Without Physical Examination of Human and Animal Foods Imported from Foreign Suppliers by Importers Who Are Not in Compliance with the Requirements of the Foreign Supplier Verification Program (FSVP) Regulation." The Import Alert for FSVP noncompliance is applicable to any human and animal food subject to the FSVP regulation and allows FDA to detain imported foods at the port of entry under the protocol for Detention Without Physical Examination (DWPE). As part of this, FDA also issued the first warning letter to the importer of tahini implicated in a recent Salmonella outbreak under the Foreign Supplier Verification Programs and added that firm to the new Import Alert #99-41.

FDA monitors the recalls of human food, cosmetic, and dietary supplement products and ensures the removal of violative products from commerce. In FY 2019, FDA classified 167 Class I (most serious), 318 Class II, and 41 Class III recall events for human food, cosmetic, and dietary supplement products. FDA also used its authority to post retail consignees lists to assist the general public in identifying melon potentially contaminated with Salmonella in April 2019.

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 and fall within the FDA goal of improving and safeguarding access:

- review and approval of all petitions for direct food additives or for color 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 2019, FDA ensured safe access to the food supply by reviewing 5 Food Additive or Color Additive Petitions, 64 GRAS notifications, and 86 premarket notifications for Food Contact Substances.

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 2019, 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:

- 57 warning letters
- 46 detentions
- 1 injunction (filed)
- 2 seizures.

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 Alzheimer's disease

and other serious conditions, as well as products containing the ingredients tianeptine, Dimethylhexylamine (DMHA), and phenibut.[21]

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 2019, FDA responded to 40 NDI notifications. FDA acknowledged 19 of the notifications submitted with no objection. Of the remaining 21 notifications, 17 were deemed incomplete or determined to not pertain to an ingredient intended to be used in a dietary supplement, while FDA raised safety or identity concerns with four.

In FY 2019, FDA received more than 2,559 adverse event reports (AERs) related to dietary supplements. The reports are evaluated by clinical reviewers in CFSAN to monitor the safety of consumer products.

In February 2019, FDA announced a new plan for policy advancements with the goal of implementing one of the most significant modernizations of dietary supplement regulation and oversight in more than 25 years. This plan includes a number of elements, including the Dietary Supplement Ingredient Advisory List, a rapid-response tool to communicate more quickly when there are concerns about unlawful ingredients; a flexible regulatory framework, and exploring means to partner in protecting public health. One example of this partnership is the creation of the Botanical Safety Consortium (BSC), a public-private enterprise that allows scientists from industry, academia, and government to explore and promote scientific advances in evaluating the safety of botanical ingredients and mixtures in dietary supplements.

Nutrition Innovation Strategy

In September 2019, FDA held a public meeting to give interested parties an opportunity to discuss FDA's effort to modernize food standards of identity and to provide information about changes FDA could make to existing standards of identity. FDA is particularly interested in changes that could be made across categories of standardized foods, often referred to as horizontal changes, to provide flexibility for manufacturers to develop healthier foods. Material and comments from this meeting can be found through FDA.gov.[22]

This public outreach initiative is part of the agency's comprehensive, multi-year Nutrition Innovation Strategy (NIS), which is designed to encourage industry innovation to improve the nutrition and healthfulness of food. As part of the NIS, FDA is seeking to modernize food standards of identity in a manner that will: (1) protect consumers against economic adulteration; (2) maintain the basic nature, essential characteristics, and nutritional integrity of food; and (3) promote industry innovation and provide flexibility to encourage manufacturers to produce healthier foods.[23]

[21] https://www.fda.gov/food/dietary-supplement-products-ingredients/dmha-dietary-supplements

[22] https://www.fda.gov/food/workshops-meetings-webinars-food-and-dietary-supplements/public-meeting-horizontal-approaches-food-standards-identity-modernization-09272019-09272019

[23] https://www.fda.gov/food/food-labeling-nutrition/fda-nutrition-innovation-strategy

The NIS's overall focus is 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
- modernizing standards of identity
- implementing the nutrition facts label and menu labeling
- reducing sodium

FDA Announces Available Resources for Consumers on Menu Labeling

In August 2019, FDA issued a fact sheet to inform stakeholders about the agency's continued efforts to implement menu labeling in chain restaurants and similar retail food establishments. FDA will continue to support industry to implement the menu labeling requirements, assess implementation progress to further inform education and outreach as well as engage with state, local, tribal and territorial regulatory partners to ensure consistent implementation of the menu labeling requirements.[24] Chain restaurants and similar retail food establishments were required to comply with the menu labeling requirements on May 7, 2018. The requirements are meant to provide consumers with consistent nutrition information, including calories, for standard menu items (including food on display and self-service foods) in certain establishments with 20 or more locations. This enables consumers to make informed and healthy dietary choices for themselves and their families when eating foods away from home. FDA is also developing a document presenting the agency's menu labeling regulations in model ordinance form for states and localities that may find such a tool helpful in adopting menu labeling requirements identical to FDA's.

[24] https://www.fda.gov/food/food-labeling-nutrition/nutrition-education-resources-materials

FDA Provides Uniform Compliance Date and Resources for Nutrition Facts Labeling Rules

FDA announced that January 1, 2022, will be the uniform compliance date for final food labeling regulations that are issued in calendar years 2019 and 2020. All food products subject to the January 1, 2022, uniform compliance date must comply with the appropriate labeling regulations when initially introduced into interstate commerce on or after January 1, 2022. This action does not change existing requirements for compliance dates contained in final rules published before January 1, 2019.

Figure 3 Nutrition Facts Label

FDA is making available a nutrition toolkit for use by organizations and health education professionals to help them educate their audiences on the new Nutrition Facts label.[25] The toolkit provides resources that can help consumers understand the new Nutrition Facts label and how to use the information it provides to make informed food choices. The toolkit resources also provide realistic tips on how to shop, prepare, and order food when eating out to build a healthy diet. Next year, FDA will launch a major educational campaign for consumers on the new Nutrition Facts label.[26]

FDA Advises and Informs Industry and Consumers on 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 alerts consumers, tattoo artists, and retailers of the potential for serious injury from use of tattoo inks that are contaminated with bacteria. Tattoo inks contaminated with microorganisms can cause infections and lead to serious health injuries when injected into the skin during a tattooing procedure, since there is an increased risk of infection any time the skin barrier is broken.

[25] https://www.fda.gov/food/nutrition-education-resources-materials/health-educators-nutrition-toolkit-setting-table-healthy-eating

[26] https://www.fda.gov/food/food-labeling-nutrition/nutrition-facts-label-programs-and-materials

In September 2019, FDA completed its sample analyses and follow-up for its FY 2018 inspections of tattoo ink manufacturers and distributors with the goal of reducing the incidence of microbial contamination of tattoo inks. FDA identified six tattoo inks contaminated with bacteria harmful to human health and is working with the manufacturers/distributors to remove all contaminated product from the market. The tattoo inks were manufactured or distributed by four firms inspected under an ongoing assignment. Tattoo inks were analyzed using methods described in the Bacteriological Analytical Manual Chapter 23: Microbiological Methods for Cosmetics, which is the general method used to determine bacterial contamination of cosmetics.27 FDA will continue to inform consumers and industry of any future contamination threats, and work with manufacturers and retailers to remove contaminated products from the market.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2017 Actual	$1,025,503,000	$1,025,503,000	---
FY 2018 Actual	$1,059,291,000	$1,059,291,000	---
FY 2019 Actual	$1,059,926,000	$1,059,926,000	---
FY 2020 Enacted	$1,099,970,000	$1,088,881,000	$11,089,000
FY 2021 President's Budget	$1,127,941,000	$1,090,530,000	$37,411,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Foods Program is $1,127,941 of which $1,090,530 is budget authority and $37,411,000 is user fees. The budget authority increases by $1,649,000 compared to the FY 2020 Enacted level. User Fees increase by $26,322,000. The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is $371,490,000. The Office of Regulatory Affairs amount is $756,451,000.

In FY 2021, 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: (Budget Authority: +$ 5.7 million / 15 FTE/ User Fee: $26.3 million/ 52 FTE)

Strengthening Response Capabilities for Foodborne Outbreaks: (+$1.2 million / 4 FTE)

[27] https://www.fda.gov/cosmetics/cosmetics-recalls-alerts/fda-advises-consumers-tattoo-artists-and-retailers-avoid-using-or-selling-certain-tattoo-inks

Center: +$1.2 million/ 4 FTE

Additional funding will expand the Center's ability 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. In the three 2-year periods beginning in 2014 and ending in 2019, the number of outbreaks has increased steadily by 36%. In 2014-2015, FDA coordinated 38 outbreaks investigations. In 2016-2017, FDA coordinated 43 outbreak investigations, and in 2018-2019, FDA coordinated 52 outbreak investigations. FDA expects this trend to continue.

By leveraging new technology, FDA can work with producers and other Federal, state, and local health officials to unravel what went wrong more quickly, allowing FDA scientists to more rapidly identify the outbreak and the food that may have caused it. Through additional resources, FDA is building capacity to investigate the root cause of outbreaks and feed information back to industry producers to prevent future contamination, which ultimately reduces costs to industry in the future and protects public health. These costs can be considerable and lasting to an entire industry and its reputation, even if caused by only one producer.

Cannabis and Cannabis Derivatives: (+$4 million / 11 FTE)
Center: +$2 million / 6 FTE

Field: +$2 million / 5 FTE

The Agriculture Improvement Act of 2018 (Farm Bill) helped preserve FDA's authorities under the FD&C Act and section 351 of the Public Health Service Act, such that products derived from hemp as defined in the Farm Bill, while not controlled under the Controlled Substance Act (CSA), are subject to the same authorities and requirements as FDA-regulated products containing any other added substance. This allows the FDA to continue enforcing the law to protect patients and the public while also providing potential regulatory pathways, to the extent permitted by law, for products containing cannabis and cannabis-derived compounds. FDA is seeing a significant increase in activity relating to the marketing of unlawful cannabis-derived products, especially those containing cannabidiol (CBD), since the Farm Bill passed. In many cases, product developers make unproven claims to treat serious or life-threatening diseases, and patients may be misled to forgo otherwise effective, available therapy and opt instead for a product that has no proven value or may cause them serious harm.

New funding will enable FDA to better regulate the usage of cannabis-derived substances, such as cannabidiol (CBD), in FDA-regulated products such as dietary supplements and when used as unapproved food additives. The initiative will support regulatory activities, including developing policies and continue to perform its existing regulatory responsibilities including review of product applications, inspections, enforcement, and targeted research. FDA must support oversight of increasing numbers of marketed FDA-regulated products containing cannabis-derived substances that may put the public at risk.

Crosscutting Initiatives: -$4.1 million/ 4 FTE

Artificial Intelligence and Other Emerging Technologies: (+$3.2 million/ +4 FTE)
Center: + $1.1 million/ 3 FTE

The use of AI in post-market surveillance and signal detection will enhance CFSAN's ability to detect potential problems associated with CFSAN commodities, including leveraging data to investigate outbreaks and potential issues with chronic, long-term consumption of food constituents and contaminants or long-term use of cosmetics. FDA will ultimately utilize this information to enhance the science that supports our guidance to industry for protecting public health. As a specific example, use of this technology in the post-market space will streamline the review of adverse event reports for foods, dietary supplements, and cosmetics so that FDA can act more quickly to intervene earlier, including by removing unsafe products from the marketplace. Removing problematic products from the marketplace will protect consumer confidence in the industry and ultimately protect manufacturers by limiting consumer exposure to problematic products and limiting the scope of product recalls. This initiative also includes $500 thousand in investments in tech-enabled outbreak response and modernized track and trace capabilities to expand FDA's engagement with stakeholders on these new technologies and to ensure that FDA can receive and efficiently process new data streams, particularly in urgent outbreak scenarios.

Field: + $2.1 million/ 1 FTE

The tremendous shift to a more global market for food and medical products has introduced important new challenges. In addition to growth in the sheer volume of imports and foreign facilities, the variety and complexity of imported products has increased, and the number of countries involved in producing these products has expanded to include many with less sophisticated regulatory systems than our own. Simultaneously, the supply chain from manufacturer to consumer has become increasingly complex — with an expanding web of consolidators and redistributors — making oversight significantly more difficult by both FDA as well as industry managing its own supply chain. The implementation of AI is expected to improve FDA and industry's capabilities to respond to these complexities while also ensuring trade isn't adversely impacted.

With this funding ORA will focus on incorporating AI modeling (machine learning) into the import screening process for commodities in several regulatory program areas. Full incorporation of AI into ORA's import screening tools is dependent upon both a modernized screening system as well as development of machine learning models across all commodities. FDA also will evaluate the predictive power of the ML model by comparing the model recommendations to recorded outcomes of FDA's current import screening tool, Predictive Risk-Based Evaluation for Dynamic Import Compliance Targeting (PREDICT). This modernization is intended to incorporate AI as well as update the rules engine and code supporting entry screening functionality. FDA will develop and evaluate a machine (ML) model to target import shipments that have a higher likelihood of violation. It is important to note that any implementation of AI/ML needs to consider current policy/program rule requirements and would constitute a significant operational change and require the necessary approval, documentation, and training time.

Outreach, Training and Organizational Excellence (-$7.3 million)
Center: -$2.3 million

CFSAN will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. CFSAN will preserve its most critical public health and safety activities under this reduction, including: responding to outbreaks, working with industry to implement FSMA regulations, reviewing infant formula notifications, ensuring the safety of dietary supplements, conducting reviews of food ingredients and packaging, and ensuring that foods are safe and properly labeled.

Field: -$5.0 million

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

Proposed User Fee Program: Innovative Food Products User Fee ($26.3 million / 52 FTE)
Center: $26.1 million User Fee Program/ 52 FTE

Field: $0.2 million

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. A 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, many produced through biotechnology, 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
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 2019: 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 2019: 852 enrolled Target: 853 enrolled (Target Not Met)	867	882	+15
212404: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: Campylobacter species. *(Outcome)*	CY 2018: 19.6 cases/100,000 Target: 9.7 cases/100,000 (Target Not Met)	8.6 cases/ 100,000	Not available[28]	Not available
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[29]: 0.95 cases/100,000 Target: 0.95 cases/100,000 (Target Met)	0.60 cases/ 100,000	Not available[30]	Not available
212407: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: *Salmonella species*. *(Outcome)*	CY 2018: 18.3 cases/100,000 Target: 12.4 cases/100,000 (Target Not Met)	11.4 cases/ 100,000	Not available[31]	Not available
214306: The average number of working days to serotype priority pathogens in food (Screening Only) *(Output)*	FY 2019: 3 working days Target: 3 working days (Target Met)	3 working days	3 working days	Maintain
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 95.9% Target: 80% (Target Exceeded)	80%	80%	Maintain
214222: Percentage of Human and Animal[32] Food follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2019: 80.6% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2019: 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 2019: 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 2018 performance of 100% completed within the same timeframe.

Voluntary National Retail Food Regulatory Program Standards

Strong and effective regulatory programs at the state, local, and tribal level are needed to prevent foodborne illness and reduce the occurrence of foodborne illness risk factors in retail and food service 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 foodborne illness. The FY 2019 actual enrollment number of state, local and tribal agencies in the Retail Program Standards reflects an annual increase of 14 enrollments from the year-end FY2018 total enrollments (838). The FY 2019 enrollment was one enrollment less than the target due to a variety of unusual factors. This goal has a steady record of success and progress over the past few years and FDA expects to meet the target in 2020 and future fiscal years. Awareness of the value of 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

[28] FY 2021 targets for measures 212404, 212405 and 212407 are not available because HHS agencies, including FDA and CDC and USDA, are working to finalize the Healthy People 2030 goals as of January 2020. FDA will update the new targets when they are published.

[29] For STEC, all serogroups were combined and individual CY 2018 data are not available for this measure in the CDC Morbidity and Mortality Weekly Report (MMWR).
https://www.cdc.gov/mmwr/volumes/68/wr/mm6816a2.htm

[30] FY 2021 targets for measures 212404, 212405 and 212407 are not available because HHS agencies, including FDA and CDC and USDA, are working to finalize the Healthy People 2030 goals as of January 2020. FDA will update the new targets when they are published.

[31] FY 2021 targets for measures 212404, 212405 and 212407 are not available because HHS agencies, including FDA and CDC and USDA, are working to finalize the Healthy People 2030 goals as of January 2020. FDA will update the new targets when they are published.

[32] 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.

achieving key milestones. The FY 2020 and FY 2021 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, have dramatically improved FDA's foodborne response and traceback capabilities. Technologies such as next-generation whole-genome sequencing (WGS) and others have reduced the time required to conduct these analyses from 14 days to just three days over the past few years. 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 2019, FDA met the target of reducing the average number of days to serotype priority pathogens in foods in three days. The proposed targets for FY 2020 and FY 2021 are three days, maintaining the critically important progress in analytical return times achieved in prior years.

New ORA Field Performance Measures

ORA's new performance goals 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

CFSAN Workload and Outputs	FY 2019 Enacted[8]	FY 2020 Estimate	FY 2021 Estimate
Food and Color Additive Petitions			
Petitions Filed [1]	5	10	10
Petitions Reviewed [2]	5	10	10
Premarket Notifications for Food Contact Substances			
Notifications Received	86	94	94
Notifications Reviewed [3]	86	94	94
Infant Formula Notifications			
Notifications Received [4]	24	31	31
Notifications Reviewed [5]	16	22	22
FDA Review Time	90 days	90 days	90 days
New Dietary Ingredient Notifications			
Notifications Received [6]	40	40	40
Notifications Reviewed [7]	36	36	36
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.

[8] During the government shutdown (furlough) from December 22, 2018 through January 25, 2019, the majority of CFSAN employees were on furlough status, which directly impacted the FY 2019 Q2 data for various food safety programs. The furlough precluded CFSAN program offices from accepting new industry notifications or applications, which impacted CFSANs ability to accomplish performance targets, including conducting timely reviews of industry submissions.

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY2019 Actuals	FY2020 Estimate	FY2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***7,254***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	4,961	**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	114		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	207		
Domestic Fish & Fishery Products (HACCP) Inspections	740		
Import (Seafood Program Including HACCP) Inspections	187		
Juice HACCP Inspection Program (HACCP)	164		
Interstate Travel Sanitation (ITS) Inspections	803		
Domestic Field Exams/Tests	1,986	2,500	2,500
Domestic Laboratory Samples Analyzed	16,419	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,747***	***1,400***	***1,400***
All Foreign Inspections	1,747	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***9,001***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	141,905	168,200	168,200
Import Laboratory Samples Analyzed	17,770	35,300	35,300
Import Physical Exam Subtotal	**159,675**	**203,500**	**203,500**
Import Line Decisions	17,722,742	17,702,780	18,587,918
Percent of Import Lines Physically Examined	0.90%	1.15%	1.09%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	80,013	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***7,485***	***9,062***	***9,062***
State Contract Food Safety (Non HACCP) Inspections	6,627	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	757	1,000	1,000
State Contract Juice HACCP	50	100	100
State Contract LACF	101	100	100
State Contract Foods Funding	$13,359,092	$13,756,200	$13,893,762
Number of FERN State Laboratories	33	33	33
Annual FERN State Cooperative Agreements/Operations Funding	$8,894,886	$15,865,891	$15,865,891
Total State & Annual FERN Funding	**$22,253,978**	**$29,622,091**	**$29,759,653**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***16,486***	***18,462***	***18,462***

[1] The FY 2019 actual unique count of foreign inspections includes 133 OIP inspections (67 for China, 59 for India, & 7 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 Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***73***	***100***	***100***
Domestic Inspections	73	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***2***	***0***	***0***
Foreign Inspections	2	0	0
IMPORTS			
Import Field Exams/Tests	4,586	1,600	1,600
Import Laboratory Samples Analyzed	249	400	400
Import Physical Exam Subtotal	**4,835**	**2,000**	**2,000**
Import Line Decisions	2,762,411	2,866,063	3,009,366
Percent of Import Lines Physically Examined	0.18%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***75***	***100***	***100***

1 ORA is currently evaluating the calculations for future estimates.

HUMAN DRUGS

(Dollars in Thousands)	FY 2019 Final	2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Human Drugs	**1,881,529**	**1,851,609**	**1,973,122**	**2,022,348**	**49,226**
Budget Authority	***663,295***	***662,892***	***683,195***	***683,411***	***216***
User Fees	***1,218,234***	***1,188,717***	***1,289,927***	***1,338,937***	***49,010***
Center	1,676,069	1,659,208	1,734,133	1,782,797	48,664
Budget Authority	525,126	524,738	507,726	509,033	1,307
User Fees	1,150,943	1,134,470	1,226,407	1,273,764	47,357
Prescription Drug (PDUFA)	*732,096*	*733,999*	*788,576*	*824,647*	*36,071*
Generic Drug (GDUFA)	*382,803*	*361,416*	*400,252*	*410,556*	*10,304*
Biosimilars (BsUFA)	*35,416*	*37,994*	*36,938*	*37,908*	*970*
Outsourcing Facility	*628*	*1,060*	*641*	*653*	*12*
Field	205,460	192,401	238,989	239,551	562
Budget Authority	138,169	138,154	175,469	174,378	-1,091
User Fees	67,291	54,247	63,520	65,173	1,653
Prescription Drug (PDUFA)	*9,003*	*7,401*	*8,536*	*8,776*	*240*
Generic Drug (GDUFA)	*56,808*	*45,778*	*53,124*	*54,492*	*1,368*
Biosimilars (BsUFA)	*1,100*	*677*	*1,472*	*1,510*	*38*
Outsourcing Facility	*380*	*391*	*388*	*395*	*7*
FTE	**6,381**	**6,381**	**6,649**	**6,746**	***97***

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Public Health Service Act of 1944 (42 U.S.C. 201); Federal Advisory Committee Act (FACA) of 1972 as amended; Orphan Drug Act of 1983 (21 U.S.C. 360ee); Drug Price Competition and Patent Term Restoration Act of 1984 (Section 505(j) 21 U.S.C. 355(j)) (a.k.a. "Hatch Waxman Act"); Prescription Drug Marketing Act (PDMA) of 1987 (21 U.S.C. 353); Anti-Drug Abuse Act of 1988; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Orphan Drug Amendments of 1988; Generic Drug Enforcement Act of 1992; Prescription Drug User Fee Act (PDUFA) of 1992; FDA Export Reform and Enhancement Act of 1996; Food and Drug Administration Modernization Act (FDAMA) of 1997; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Best Pharmaceuticals for Children Act (BPCA) of 2002; Freedom of Information Act (FOIA) as amended in 2002 (5 U.S.C. § 552); Pediatric Research Equity Act (PREA) of 2003; Project Bioshield Act of 2004 (21 U.S.C. 360bbb-3); Food and Drug Administration Amendments Act (FDAAA) of 2007; Public Health Service Act of 2010 (42 U.S.C. 262); Protecting Patients and Affordable Care Act of 2010; Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA); Drug Quality and Security Act (2013); Sunscreen Innovation Act (2014); Adding Ebola to the FDA Priority Review Voucher Program Act (2014); 21st Century Cures Act (Cures Act) (2016); Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52); and 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.

Figure 3 Medicine for a Patient

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.

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 regulates the drugs and devices used in the treatment of pain, as well as opioid addiction and overdose, to ensure that the actions taken are in the best interest of public health.

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.

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. FDA continues to accomplish goals laid out under the HHS Opioid Strategy — the comprehensive, evidence-based plan that provides the overarching framework to strategically leverage HHS resources and expertise. 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 U.S. FDA has identified four priority areas to address the epidemic. Some of FDA's recent actions are described below:

Decreasing Exposure and Preventing New Addiction:

- Awarded a contract to the National Academies of Sciences, Engineering, and Medicine to help advance the development of evidence-based guidelines for appropriate opioid analgesic prescribing
- Approved the Opioids Analgesic REMS, providing additional training resources to health care providers involved in the pain-management process
- Launched the "Remove the Risk" campaign to help educate the public on the importance of safe removal of unused opioid pain medicines from homes.

Supporting the Treatment of Those with Opioid Use Disorder:

- Convened a public workshop titled "Expanding Access to Effective Treatment for Opioid Use Disorder: Provider Perspectives on Reducing Barriers to Evidence-Based Care" to explore expanding access to effective treatment for opioids use disorder
- Held a public advisory committee meeting, soliciting advice on strategies to increase the availability of naloxone — a medication that rapidly reverses the effects of opioid overdose
- Approved the first generic naloxone nasal spray to treat opioid overdose.

Fostering the Development of Novel Pain Treatment Therapies:

- Hosted a two-day public meeting, "Opioid and Nicotine Use, Dependence, and Recovery: Influences of Sex and Gender" to discuss how differences in sex may influence susceptibility to substance abuse, and the potential implications for prevention and treatment
- Convened a meeting of the Anesthetic and Analgesic Drug Products Advisory Committee to discuss the assessment of opioid analgesic sparing outcomes in clinical trials of acute pain, trial design and endpoints, and how to determine the clinical relevance of the results.
- Improving Enforcement and Assessing Benefit-Risk.
- Announced ongoing efforts to stop the spread of illicit opioids, further secure the U.S. drug supply chain and forcefully confront opioid epidemic
- Announced new steps to strengthen FDA's safety requirements aimed at mitigating risks associated with transmucosal immediate-release fentanyl products
- Hosted stakeholders, including thought leaders, government entities, academic researchers, and advocacy groups at the second Online Opioid Summit to combat illegal online opioid sales.

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. The issue of 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 significantly help to advance patient treatment and public health. In calendar year 2018, CDER approved 59 novel drugs. From 2009 through 2018, CDER has averaged about 36 novel drug approvals per calendar year. More than 71% of CDER's 2018 novel drug approvals 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 breakthrough therapy designations. Early and repeated communications between FDA and sponsors have also helped expedite development and review, which can lead to getting products to market more quickly.

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 second-line 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. The FD&C Act (as amended by FDASIA) requires 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 have helped ensure that FDA is able to 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. Unfortunately, this downward trend did not continue into 2017 and 2018. A major drug manufacturer closed a manufacturing facility for remediation purposes in 2017, and this closure resulted in the loss of manufacturing capacity needed for the supplies of numerous drug products. In 2017, there were a total of 39 new drug and biological product shortages identified and 54 for 2018.

FDA has been working with manufacturers to resume production and has expedited review of new submissions, helping to increase supplies. FDA helped to prevent 145 additional drug and biological shortages in 2017 and 160 during 2018 and continued these important prevention efforts int 2019.

To continue transparency on FDA's 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.[33] To further understand and address shortages, in July 2018, FDA created a Task Force, comprising of senior leaders from FDA, the Centers for Medicare and Medicaid and Medicaid Services, and the Department of Veterans Affairs to identify the root causes and holistic solutions for this critical public health problem. The task force intends to submit a report on this issue to Congress by the end of 2019.

On November 27, 2018, the FDA 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 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.

33 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[34] (BAP) to provide information about the key actions FDA is taking to encourage innovation and competition among biological products and the development of biosimilar products. 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 biosimilar products 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 July 1, 2019, 80 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 36 different reference products. As of July 23, 2019, FDA has licensed 23 biosimilar products. These accomplishments represent the next step to increasing treatment options for patients.

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.

Additionally, in December 2018 FDA issued two draft guidances and two final guidances for industry. The final guidance entitled "Questions and Answers on Biosimilar Development and the BPCI Act" 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, are intended to inform prospective applicants and facilitate the development of proposed *biosimilars* and *interchangeable products*, 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 '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,

34 For additional information visit https://www.fda.gov/media/114574/download

will be deemed to be a license for the biological product under the Public Health Service Act (PHS Act) on March 23, 2020.

In March 2019, FDA issued a draft guidance for industry, "Nonproprietary Naming of Biological Products – Update." This draft guidance describes FDA's current thinking that the nonproprietary names of biological products licensed under section 351 of the PHS Act without an FDA-designated suffix do not need to be revised to add a suffix to accomplish the objectives of the naming convention described in the final guidance for industry, issued in January 2017. The draft guidance also describes FDA's current thinking on the appropriate suffix format for the proper name of an interchangeable biological product licensed under section 351(k) of the PHS Act. For each interchangeable product, FDA intends to designate a proper name that is a combination of the core name and a distinguishing suffix that is devoid of meaning and composed of four lowercase letters.

In May 2019, FDA held a public hearing to discuss access to affordable insulin products and issues related to the development and approval of biosimilar and interchangeable insulin products. In addition, FDA issued two guidance documents for industry. FDA issued a final guidance, "Considerations in Demonstrating Interchangeability with a Reference Product." This guidance on interchangeable products reflects FDA's current thinking on important scientific considerations in demonstrating that a proposed product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under section 351(k) of the PHS Act. FDA also issued a draft guidance for industry, "Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations." This guidance describes FDA's recommendations on the design and evaluation of comparative analytical studies intended to support a demonstration that a proposed product is biosimilar to a reference product licensed under section 351(a) of the PHS Act. Additionally, this guidance is intended to provide recommendations to sponsors on the scientific and technical information for the chemistry, manufacturing, and controls (CMC) portion of a marketing application for a proposed product submitted under section 351(k) of the PHS Act.

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

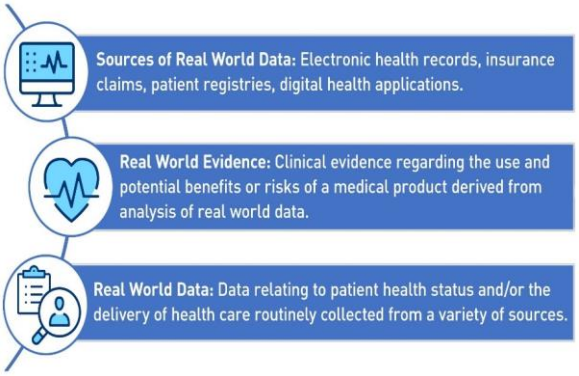

Figure 4 Data used to support postmarket safety activities

FDA's Sentinel System started as a congressional mandate in the FDA Amendments Act of 2007 and has given rise to one of the world's premier real-world evidence generation platforms. From 2000-2019 the distributed database has collected information on more than 300 million patients, including 70 million patients who are accruing new data, and beneficiaries of both federal and private insurance. The Sentinel System operates on a distributed database design that enables Sentinel to be one of the world's largest multi-site, privacy-preserving, medical product safety surveillance systems with highly-curated data.

The year 2019 marks three years of the Sentinel System serving as a fully-functional and integrated part of FDA's regulatory process. Sentinel has proven to be a vital source of safety information that can inform regulatory decision-making and expand our knowledge of how medical products perform once they are widely used in medical practice. Using the Sentinel System, FDA has found it feasible to study more than 18 different safety issues that would have otherwise resulted in industry-required postmarket safety studies.

On March 11, 2019, FDA hosted a public, pre-bid forum largely attended by community, academic and industry stakeholders to officially introduce the third, five-year Sentinel contract recompete released in advance of the event. The new Sentinel contract is set to be awarded in October 2019 to enhance the systemic benefits and impact across FDA.

In April 2019, FDA held the Eleventh Annual Sentinel Initiative Public Workshop. Day three of this event served as the first International Forum for Regulators, *by regulators*—highlighting the conceptual, analytic and regulatory pathways utilized by the FDA through use of the Sentinel System to conduct analyses.

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 to the rising healthcare costs fueled largely by 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. To encourage generic drug development and approval FDA has:

- issued multiple industry guidances to bring greater transparency to the generic drug review and approval process and to support prospective generic drug developers
- updated FDA's list of off-patent, off-exclusivity branded drugs without unapproved generic to encourage generic drug development with limited competition
- enhanced FDA's review process efficiency to improve the speed and predictability of generic drug review process
- issued guidances for industry, launched informational web pages, and held workshops to maximize scientific and regulatory clarity with respect to complex generic drugs to help reduce the time, uncertainty, and cost of drug development
- updated FDA's list identifying all drug products about which FDA has received a request for assistance in obtaining samples of the branded drug for generic drug development.

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 products that are on FDA's drug shortage list. Our GDUFA II commitment also includes a pre-Abbreviated New Drug Application (pre-ANDA) program designed to support development of complex generic drug products. 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.

FDA has also taken several actions under the FDA 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.

In FY 2019, FDA established policies and took actions under the DCAP to promote generic drug development in areas where there is inadequate competition. As of July 23, 2019, FDA published 199 new and revised drug development guidance documents. Of these, 125 address the development of generic versions of complex, difficult-to-copy, drugs. Furthermore, FDA

launched a new website35 with information about FDA's plans for issuing these new or revised product-specific guidances in the coming year for complex products as defined in the GDUFA II Commitment Letter. The information on this web page is anticipated to help generic drug companies better plan their development of complex generic drug products.

In FY 2019, FDA also published two updates to the List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic. This list is comprised of approved new drug application (NDA) drug products that are no longer protected by patents or exclusivities, and for which the FDA has not approved an ANDA referencing that NDA product. FDA maintains this list to improve transparency and encourage the development and submission of generic drug applications for products in markets with little competition.

In February 2019, FDA took another step to encourage generic entry for drugs that face inadequate competition by publishing a draft guidance36entitled Competitive Generic Therapies (CGTs). This guidance lays out new, efficient guidelines for the use of a novel pathway that provides incentives for developing generic versions of drugs that currently face little or no competition. As of July 23, 2019, FDA has approved 11 ANDAs for generic drugs designated as CGTs.

In July 2019, FDA issued a draft guidance37 explaining the FDA-related aspects of a process where drug applicants and drug master file holders can propose the development of a new monograph or suggest revisions to an existing United States Pharmacopeia (USP) monograph during the FDA's evaluation of a product application or drug master file in order to help prevent potential generic drug approval delays due to USP monograph noncompliance.

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.[38]

[35] Visit https://www.fda.gov/drugs/guidances-drugs/upcoming-product-specific-guidances-complex-generic-drug-product-development for additional information

[36] Guidance posted at https://www.fda.gov/media/125134/download.

[37] Guidance posted at https://www.fda.gov/media/128689/download.

[38] 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
Opioid Dependence	Apr 2019	Naloxone Hydrochloride Nasal Spray (generic of Narcan)	For the emergency treatment of known or suspected opioid overdose
Infections	Aug 2018	Cefepime Hydrochloride for Injection (generic of Maxipime)	For the treatment of infections caused by susceptible strains of microorganisms
	Oct 2018	Cefixime Capsules, 400 mg (generic of Suprax)	For the treatment of adults and children six months and older with urinary tract infections, pharyngitis, tonsillitis, acute exacerbations of chronic bronchitis, and uncomplicated gonorrhea (cervical/urethral)
Cancer	Oct 2018	Abiraterone Acetate Tablets (generic of Zytiga)	For the treatment of patients with metastatic castration-resistant prostate cancer
	Dec 2018	Toremifene Citrate Tablets (generic of Fareston)	For the treatment of metastatic breast cancer in postmenopausal women with estrogen-receptor positive or unknown tumors
	Mar 2019	Fulvestrant Injection (generic of Faslodex)	For the treatment of: • HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy • HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib, in women with disease progression after endocrine therapy
Other	Jan 2019	Lurasidone Hydrochloride Tablets (generic of Latuda)	For the treatment of schizophrenia and depressive episodes associated with Bipolar I Disorder (bipolar depression) in adults
	Feb 2019	Sevelamer Hydrochloride Tablets (generic of Renagel)	For the control of serum phosphorus in patients with chronic kidney disease on dialysis
	Apr 2019	Bosentan Tablets (generic of Tracleer)	For the treatment for pulmonary arterial hypertension

New Drug Review

With PDUFA V, FDA created a new review program (the Program) for Enhanced Review Transparency and Communication 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 were 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 provided 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 Program. As of September 2018, FDA has received 355 applications through this Program since its October 1, 2012 inception, with more communication and transparency between the applicant and the FDA review team during review of marketing applications.

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-one percent of the novel drugs approved in 2018 were approved in United States before any other country. Thirty-two 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, 73% of 2018 novel drugs approvals were designated in one or more expedited categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval.

During FY 2018, CDER's, Office of New Drugs (OND) published 59 guidance documents. Thirty-five of these guidance documents were considered clinical/medical in nature and included guidance on notable topics such as the submission procedures for human factors protocols for new drug applications and biologics license applications, as well as guidance on adaptive design for clinical trials. OND also conducted nine public meetings related to the process for the review of human drugs, including biological products.

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 in regulatory decision making
- Additional postmarket funding for FDA's Sentinel system
- Process improvement work related to combination product review.

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.[39]

Product Category	Approved	Product Name	FDA-Approved Use on Approval Date
	May 2019	Mayzent	To treat adults with relapsing forms of multiple sclerosis

[39] 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
Autoimmune Disease	Apr 2019	Skyrizi	To treat moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy
Cancer	Apr 2019	Balversa	To treat adult patients with locally advanced or metastatic bladder cancer
	May 2019	Piqray	To treat breast cancer
	Jun 2019	Polivy	To treat adult patients with relapsed or refractory diffuse large B-cell lymphoma
	Jul 2019	Xpovio	To treat adult patients with relapsed or refractory multiple myeloma (RRMM)
Heart Disease	May 2019	Vyndaqel	To treat heart disease (cardiomyopathy) caused by transthyretin mediated amyloidosis (ATTR-CM) in adults
Hematology	Feb 2019	Cablivi	To treat adult patients with acquired thrombotic thrombocytopenic purpura (aTTP)
Infectious Diseases	Feb 2019	Egaten	To treat fascioliasis, a parasitic infestation caused by two species of flatworms or trematodes that mainly the affect the liver, sometimes referred to as “liver flukes”
	Jul 2019	Recarbrio	To treat complicated urinary tract and complicated intra-abdominal infections
Other	Feb 2019	Jeuveau	For the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients
	Mar 2019	Zulresso	To treat postpartum depression (PPD) in adult women
	Mar 2019	Sunosi	To treat excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea
	Apr 2019	Evenity	To treat osteoporosis in postmenopausal women at high risk of fracture
	Jun 2019	Vyleesi	To treat hypoactive sexual desire disorder in premenopausal women

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 includes provisions regarding FDA’s ongoing activities to:

- Facilitate greater patient engagement in drug development
- Advance innovative clinical trials through adaptive designs and novel statistical modeling
- Evaluate the potential use of real-world evidence derived from real-world experience in regulatory decision-making
- 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 the 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 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.

Under the Cures Act, FDA launched the susceptibility test interpretive criteria (STIC or "breakpoints") web pages. This new approach allows the FDA to simultaneously update the breakpoints for multiple antimicrobial drugs that have the same active ingredient and share that information transparently via a dedicated FDA web page that will list FDA-recognized breakpoints. This system provides up-to-date information to the healthcare community in a more streamlined manner. 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 established 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 (SE)
- Facilitating a public process to support biomarker qualification as a DDT

In 2018, FDA published a list of SEs which were the basis of approval or licensure (as applicable) of a drug or biological product for both accelerated and traditional approval. The information is intended to provide greater clarity for drug developers on SEs that may be considered and discussed with FDA for individual development programs. It will also help facilitate discussions of potential SEs with FDA review divisions. The SE table will be updated every six months. In addition, FDA actively works with NIH and other stakeholders in the development of evidentiary criteria to support qualification tools. The Cures Act requires FDA to publish a guidance describing the standards, process, and timeframes for DDT qualification. In November 2018, FDA developed and presented a draft taxonomy for public comment in a federal register notice, and discussed it at a public workshop in December. In 2019, FDA launched a new grant program to fund significant research conducted under the qualified DDT program topics. FDA anticipates that up to 30 awards will be made to further the development of tools that, once qualified, will be made publicly available to fill unmet needs in drug development.

The Cures Act authorized 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 three-year grants to Rutgers, Georgia Tech and MIT to study and recommend improvements to the process of continuous manufacturing of drugs and biological products, and similar innovative monitoring and control techniques. In 2019, FDA continued support for these ongoing grants. 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 requires FDA to evaluate the potential use 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 evaluating how real-world data sources such as electronic health records, registries, and claims and billing data may potentially be useful in regulatory decision making. In December 2018 FDA published a framework to evaluate the use of RWE to support regulatory decisions, which was informed by feedback gathered from industry, academia and patient advocacy stakeholders. Additionally, in January 2019 FDA, through its cooperative agreement with Duke Margolis, met with specific data curators to gather organizational perspectives and explore potential best practices for data curation steps or techniques. In July 2019, FDA held a public workshop to bring the stakeholder community together to explore key considerations for utilizing real-world data to generate RWD in randomized designs, such as large simple trials or those that incorporate pragmatic elements.

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.

To advance this initiative, FDA facilitated ICH's review and approval of an FDA-proposed "reflection paper" outlining a new strategic approach for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for generic drugs. Following ICH's approval of this paper, ICH established an FDA-led discussion group to discuss regional requirements for bioequivalence study design and to identify opportunities for harmonization. Harmonization of these requirements could allow manufacturers to use the data submitted in support of a generic drug marketing application to meet other regions' regulatory requirements for approval thereby resulting in more efficient development and increased patient access.

In addition, FDA has advanced several new harmonization projects under ICH. This includes two recent FDA proposals to revise the ICH E6(R3) Guideline on *Good Clinical Practices* to address the increasing diversity of study types and data sources that are being employed to support regulatory and other health policy decisions; and revision of ICH Q5A *Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin* to provide updated guidance on technologies for virus detection and quantification, and validation approaches for virus clearance, and expand the scope of the Guideline to include new

biotechnology products such as viral-like particles and viral-vectored particles. Further, FDA will be actively participating in several other harmonization projects that are currently initiating.

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; and to develop guidelines to improve the quality and efficiency of drug development, manufacturing, and post-market safety oversight across multiple regulatory regions. FDA participates in each of ICH's 26 working groups and plays a leading role in half of them. These working groups achieve significant progress in the development of new guidelines, revision of existing guidelines, and the development of question and answer documents and training materials to facilitate consistency in the global implementation of ICH guidelines.

FDA believes that harmonizing scientific and technical standards for human drugs will help advance markets that drive 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 patients' needs. Patients and clinicians are increasingly confronting infections caused by pathogens resistant to many 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 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, there are significant economic challenges in the field of antibacterial therapeutics.

Despite these considerable challenges in developing an antibacterial drug, FDA approved thirteen new antibacterial drugs over the past five 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 the development and informed use of antibacterial drugs.

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

- 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.

In addition, CDER awarded Interagency Agreements to work with other federal agencies to fund:

- CDC studies to understand the microbiome disruption potential for antibacterial drugs and the generation of data to assess antibacterial drug susceptibility
- Assistant Secretary for Planning and Evaluation (ASPE) studies to understand the market for antibacterial drugs, as well as the incentives for, and social value of developing new antibacterial drugs
- NIH study to identify patients from electronic health records treated with new antibiotics active against resistant gram-negative infections to help complement the ASPE study above to understand the market.

CDER also funded research fellowships through the OAK Ridge Institute for Science and Education (ORISE) to:

- Perform research analysis in conducting comparative epidemiologic studies of the causes of serious bacterial infections and resistance phenotypes in different geographical regions
- Establish a database of antimicrobial drugs in development with elements such as the class of drug, mechanism of action, ability to maintain activity in the presence of various resistance mechanisms, and stage of development
- Evaluate the current state of animal models of serious bacterial infection by cataloguing previously-used models, conducting an assessment focused on the ability of various models to predict human response, and hypothesizing explanations for model failures
- Study the impact of ethnic factors to the Pharmacokinetics and Pharmacodynamics of anti-infective products
- Conduct a scientific assessment of data from FDA-funded external research projects focused on antibacterial drug resistance.

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 over 750 cases of illness, the Drug Quality and Security Act (DQSA) was enacted, providing FDA with additional responsibilities to oversee compounding. DQSA added a new section 503B to the 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. 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 DQSA, FDA has acted quickly to increase its drug compounding oversight through inspections and enforcement, developing policies regarding the compounding provisions of Federal law, convening and obtaining input from an advisory committee, collaborating and coordinating with state regulators, and conducting stakeholder outreach.

Since enactment of DQSA, FDA has continued to receive reports of serious adverse events associated with compounded drugs and to identify poor drug production practices, and has completed the following actions to mitigate the risk of patient harm:

- Conducted over 700 inspections of compounders, including over 180 inspections of compounders registered as outsourcing facilities
- Issued over 230 warning letters to compounders, including one warning letter that addressed violations identified at four facilities
- Issued over 120 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
- Oversaw over 240 recall events regarding compounded drug products.

FDA has issued 24 draft and revised draft guidance documents regarding compounding and related activities, 18 of which have been finalized. FDA has also issued four proposed rules, three 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 two draft memoranda 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 continues to convene 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 held two meetings of the PCAC in FY 2015, three meetings in FY 2016, two meetings in FY 2017, and one meeting in FY 2018.

Further, FDA continues 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 seven 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, with an eighth to occur in October 2019. FDA also held a public meeting titled "Proposed Current Good Manufacturing Practice Policies for Outsourcing Facilities: Considerations Regarding Access to Office Stock" in FY 2019, and a meeting with its federal partners on drug compounding in FY 2018.

In addition, FDA responds to numerous inquiries from stakeholders, including consumers, about compounding. In response to stakeholder feedback, FDA recently began to offer pre-operational meetings and site visits to compounders that have newly registered as an outsourcing facility or that are considering registering, and we have met with companies that are developing automated equipment technology aimed at improving the quality of compounded drugs.

FDA is working to establish the Center of Excellence on Compounding for Outsourcing Facilities. Among other activities, FDA is implementing a series of in-person and web-based trainings for outsourcing facilities on current Good Manufacturing Practices and other FDA policies.

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. FDA plans to continue these critical efforts to protect 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 dispensers (primarily pharmacies) to develop the new system for enhanced drug distribution security by 2023. The 2023 system is expected to enable:

- Electronic exchange of information by trading partners at the package level
- Verification of product identifiers at the package level
- Prompt response to suspect and illegitimate products at the time they are found
- Improved efficiency of recalls
- Transparency and accountability in the pharmaceutical distribution supply chain

As of November 27, 2018, manufacturers are required to include unique product identifiers on prescription drug packages and homogenous cases. FDA created a decision tree graphic to help supply chain stakeholders determine whether the medicine they have can continue to move through the supply chain with or without a product identifier.

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.[40] FDA has issued ten draft guidance documents and six final guidances, including two final guidances that were issued in September 2018 to assist stakeholders in understanding when a product without a product identifier is grandfathered and when certain product identifier requirements will be enforced. FDA continues its stakeholder outreach and communications through activities such as public meetings, continuing education courses and listening sessions to increase awareness of the DSCSA.

FDA's DSCSA pilot project program began on February 8, 2019. Under this program, FDA is working with the participants of 20 different pilot projects to explore and evaluate methods to enhance the safety and security of the drug supply chain. The program is a means for FDA and stakeholders to share learnings and information obtained from the pilots in an open way to further inform the enhanced system that goes into effect in 2023. When the program concludes, FDA will make a final program report available to the public so that all supply chain stakeholders can benefit from the information gathered and learned from FDA's DSCSA pilot project program.

FDA continues to refine its long-term schedule for implementing the DSCSA's various statutory requirements. Several new DSCSA requirements will go into effect over the next four years. FDA will continue to engage supply chain stakeholders during this time to facilitate the successful and efficient implementation of these requirements. We will also continue working with stakeholders to plan for implementation of the enhanced drug distribution security requirements that go into effect in 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.[41]

Date	Docket #	Title	Description
Jan 2019	FDA-2014-D-0250	Labeling for Human Prescription Drug and Biological Products Approved Under the Accelerated Approval Regulatory Pathway	Discusses FDA's recommendations for developing the indication and usage statements in the prescribing information for drugs approved under the accelerated approval regulatory pathway.
Feb 2019	FDA-2018-D-1334	Opioid Use Disorder: Developing Depot Buprenorphine Products for Treatment	Reflects the FDA's current thinking regarding drug product development and trial design issues relevant to the study of depot buprenorphine products for the treatment of opioid use disorder.

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

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

Date	Docket #	Title	Description
Mar 2019	FDA-2018-D-1540	Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials	Provides the pharmaceutical industry, clinical investigators, and review boards with information to facilitate the inclusion of adolescent patients in relevant adult oncology clinical trials.
Apr 2019	FDA-2016-D-2730	REMS: FDA's Application of Statutory Factors in Determining When a REMS Is Necessary	Applies the factors set forth in the FD&C Act in determining whether a risk evaluation and mitigation strategy (REMS) is necessary to ensure that the benefits of a drug outweigh its risks.
May 2019	FDA-2017-D-0154	Considerations in Demonstrating Interchangeability with a Reference Product	Assists sponsors in demonstrating that a proposed therapeutic protein product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under the PHS Act.
Jul 2019	FDA-2018-D-1562	Uncomplicated Urinary Tract Infections: Developing Drugs for Treatment Guidance for Industry	Addresses FDA's current thinking regarding the overall development program and clinical trial designs for drugs to support an indication for the treatment of uncomplicated urinary tract infections.
Aug 2019	FDA-2018-D-1772	Oncology Therapeutic Radiopharmaceuticals: Nonclinical Studies and Labeling Recommendations	Provides information to assist sponsors in the design of an appropriate nonclinical program for the development of radiopharmaceuticals to treat cancer, and recommendations for certain aspects of product labeling.

Rules

Below are some rules recently published by CDER. This list does not represent any degree of importance or priority ranking among the published rules.[42]

Date	Docket #	Purpose or Benefit
Dec 2018	FDA-2016-N-2462	List of Drug Products That Have Been Withdrawn or Removed from the Market for Reasons of Safety or Effectiveness
Dec 2018	FDA-2018-N-2732	Definition of the Term "Biological Product"
Dec 2018	FDA-2013-N-0500	Withdrawal of Proposed Rule on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products
Feb 2019	FDA-1978-N-0018 (formerly Docket # FDA-1978-N-0038)	Sunscreen Drug Products for Over-the-Counter Human Use
Apr 2019	FDA-2016-N-0124 (formerly part of Docket # FDA-1975-N-0012)	Safety and Effectiveness of Consumer Antiseptic Rubs; Topical Antimicrobial Drug Products for Over-the-Counter Human Use

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

Date	Docket #	Purpose or Benefit
Apr 2019	FDA-2016-N-3464	List of Bulk Drug Substances That Can Be Used to Compound Drug Producers in Accordance with Section 503A of the Federal Food, Drug, and Cosmetic Act

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:

- 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 this data by including "Patient Experience Data" in drug review documents and requiring that reviewers include the statement in keeping with statutory requirements.

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.[43] 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

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

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
- Select, develop or modify Fit-for-Purpose Clinical Outcome Assessments (COA) to measure the patent experience in clinical trials.

The public workshop and the comments received through the public docket informed the development of the second in a series of four methodological PFDD guidance documents. The draft guidance will be issued for public comment by the end of FY 2019. In FY 2020, FDA will begin addressing comments received through the public docket and finalizing the guidance. The public workshop and the comments received through the public docket are also informing the development of the third guidance in the series.

FDA is planning a public workshop to convene a discussion on methodologies, standards, and technologies to collect and analyze COAs for purposes of regulatory decision making. FDA will host a public workshop in early FY 2020 (December 2019) to inform the development of this draft guidance. This public workshop will inform the development of the fourth, and final, PFDD methodological guidance.

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.[44] 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, FDA conducted a public workshop in March 2018 to obtain input from external stakeholders. The final guidance will be issued in FY 2020.

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. Under this program, CDER issued a request for applications, soliciting applications for grants to support the development of publicly available standard core set(s) of COAs and their related endpoints for specific disease indications. Developing a standard core set of COAs will support long-term sustainability of more comprehensive incorporation of patients' experience. CDER intends to award multiple grants to support the development of standard core sets for specific disease indications. The application deadline was May 31, 2019. CDER is currently reviewing all applications and anticipates announcing the awards around August 2019.

[44] Additional information available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/developing-and-submitting-proposed-draft-guidance-relating-patient-experience-data

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, including biologics. Modeling and simulation play a critical role in integrating 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 (e.g., guiding enrichment of the study population and selection of appropriate endpoints)
- Support evidence of effectiveness
- Optimize dosing
- Predict product safety and evaluate potential adverse event mechanisms
- Optimize clinical development programs (e.g., support efficacy extrapolation in pediatric patients or rare disease)
- Develop new policies.

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 same strategies in the review of Investigational New Drug 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 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 are 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.

The modeling and simulation results for various diseases are published or presented at public meetings. All the knowledge generated from these disease models enhances our capability to design an efficient clinical trial. For example, Parkinson's disease modeling and simulation was used to assess alternative endpoints and trial designs for products intended to alter the underlying disease progression. The findings based on our Alzheimer's disease model laid a solid foundation to determine that the Alzheimer's disease model prepared by the Critical Path Institute is fit for purpose in the context for new clinical trial design. The result of our Non-Small Cell Lung Cancer disease model was applied by various pharmaceutical companies to optimize the dose and trial design for the registration trials. Our disease model for Bipolar Disorder paved the way for extrapolating efficacy from adult patients to pediatric patients to improve the drug development efficiency for pediatric Bipolar treatments. The finding of our Pulmonary Arterial Hypertension model changed the primary efficacy endpoint in an ongoing pediatric trial to a more efficient endpoint. The Idiopathic Pulmonary Fibrosis (IPF) disease model verified a decline in Forced Vital Capacity as an appropriate efficacy endpoint in IPF drug development. The Huntington's disease model supports the enrichment strategy to increase the chance of success for a trial targeting disease-modifying drugs. The research on Muscular Dystrophy improves our understanding for disease progression among different patient subgroups.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$1,851,609,000	$662,892,000	$1,188,717,000
FY 2020 Enacted	$1,973,122,000	$683,195,000	$1,289,927,000
FY 2021 President's Budget	$2,022,348,000	$683,411,000	$1,338,937,000

BUDGET REQUEST

The FY 2021 Budget Request for the Human Drugs Program is $2,022,348,000, of which $683,411,000 is budget authority and $1,338,937,000 is user fees. The budget authority increases by $216,000 compared to the FY 2020 President's Budget. User fees increase by $49,010,000. The Center for Drug Evaluation and Research (CDER) amount in this request is $1,782,797,000. The Office of Regulatory Affairs amount is $239,551,000.

The Human Drugs Program will continue activities to uphold its public health mission of ensuring that new, generic, biosimilar, and OTC drugs are safe and effective.

The FY 2021 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 to support the development of abuse-deterrent formulations as one of many strategies intended to mitigate the harms associated with prescription opioid analgesic abuse while maintaining legitimate access to opioid analgesics for patients who need them.

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 2021 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 2021 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.

Medical Product Safety (+$5.0 million / 17 FTE)

Establish a Robust Human Drug Compounding Program (+$4.5 million / 16 FTE)
Center: +$4.5 million / 16 FTE

The FY 2021 Budget request will help FDA to begin establishing a dedicated, program to optimize processes and address the ongoing needs and initiatives of the Human Drug Compounding program. Additional funds will allow FDA to strengthen the scientific framework, support activities to promote development of the 503B bulks list, bolster existing and new regulatory compliance initiatives, and expand policy development - activities that cannot be supported with the current base funding.

While compounded drugs have a role in patient care, they are not FDA-approved and are not subject to pre-market review for safety, effectiveness, and quality. Robust implementation of federal compounding law is essential to help ensure that patients receive the highest-quality compounded drugs when needed. It is also essential to ensure that compounded drugs are only used when approved drugs are not appropriate for patient care, and that inappropriate use of compounded drugs does not undermine incentives to bring new innovative therapies to market.

In the wake of significant outbreaks linked to compounded drugs and the passage of the Compounding Quality Act (CQA) of 2013, FDA has worked diligently to build capacity across existing functional areas to improve risk-based oversight programs and implement federal law. These efforts have garnered important successes but have also revealed new needs, such as needs for new types of engagement with regulated industry and additional guidance. Our efforts have also made clearer the resources needed to implement key statutory provisions, such as the

statutory mandate that FDA establish the list of bulk drug substances that may be used in compounding by outsourcing facilities. To achieve sustainable success in the regulation and oversight of drug compounding, FDA must establish a dedicated, robust programmatic group with increased capacity to address these ongoing needs. The activities described below will allow the FDA to continue to further build up the human drug compounding program to promote public health.

Promote Development of the 503B Bulks List

Outsourcing facilities were created by the CQA to uniquely supply healthcare providers with compounded drugs for "office stock" to hold in their offices or healthcare facilities in advance of patient need. Therefore, under section 503B, drugs produced by outsourcing facilities are subject to stricter standards such as current good manufacturing practice (CGMP) requirements and other conditions, such as the condition relating to the use of bulk drug substances. Stakeholders are awaiting establishment of a list of bulk drug substances that can be used in compounding by outsourcing facilities. While development of this list is a top priority for FDA, it is also a complex, resource-intensive endeavor that may involve, among other things, research and review of safety, effectiveness, and chemistry information; consultation with entities such as the Pharmacy Compounding Advisory Committee; and issuance of Federal Register notices. FDA has received more than 700 nominations for over 300 unique bulk drug substances nominated with sufficient supporting information for FDA to evaluate them. These additional funds will enable FDA to hire additional staff to continue to evaluate the current set of bulk drug substances nominated for review, as well as to begin addressing future substances nominated to the FDA. This will also support development of an overarching program structure to begin to optimize FDA's process to assess nominated substances.

Regulatory Compliance and Center of Excellence (New Domestic Drug Industry)

The outsourcing facility sector is not yet fulfilling its potential. The sector continues to experience challenges, and FDA continues to find quality and safety problems during inspections. FDA seeks additional funds to fully support new initiatives related to engagement with outsourcing facilities, including continuing efforts to build a Center of Excellence and develop new programs to provide increased feedback on scientific and regulatory matters to the sector. FDA is actively implementing the actions needed for the Center of Excellence and other engagement work. However, these activities will incur significant ongoing operating costs, and additional funding is needed to support FTEs to work towards full implementation of the initiatives proposed. Support of these initiatives will help outsourcing facilities meet provider needs for higher quality compounded drugs by furthering FDA's work to reduce future compliance failures, support technical advancements and encourage market entry and growth.

Policy Development, Rulemaking and Stakeholder Engagement

Implementing the compounding provisions of the law, sections 503A and 503B, has been a significant priority for the FDA, and FDA has made substantial progress since the Drug Quality and Security Act was enacted in 2013 (e.g. publishing nearly twenty final guidance documents after a public comment process). However, FDA needs to develop policies, in collaboration with stakeholders, to address remaining provisions of the law as well as provide guidance concerning

other activities in which compounders engage. In addition, FDA intends to promulgate regulations implementing sections 503A and 503B, taking into account FDA's experience and stakeholder input received during its prior policy initiatives. These regulations, which will be resource-intensive to develop and issue, will provide the compounding community with increased certainty concerning compliance with the law and, as a result, promote the public health. Ongoing stakeholder engagement initiatives will also ensure regulated stakeholders and the public have meaningful opportunities to share feedback and information with FDA to inform policy development work.

Modernizing Influenza Vaccines (+$0.5 million / 1 FTE)

Center: +$0.5 million / 1 FTE

The FY 2021 Budget Request includes $0.5 million towards activities related to Modernizing Influenza Vaccines. This includes increased review capacity to facilitate the development and availability of medical products to support modernizing influenza vaccines.

Crosscutting Initiatives: -$4.8 million

Outreach, Training and Organizational Excellence (-$4.8 million)

Center: -$3.7 million

CDER will reduce Outreach, Training and Organizational Excellence activities while maintaining the most critical programmatic activities. CDER will preserve its most critical public health and safety activities under this reduction, including providing the essential training and development needed for drug application reviewers to maintain knowledge of the latest science to uphold FDA's public health mission.

Field: -$1.1 million

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
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 2018: 88% Target: 90% (Target Not Met)	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 2018: 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 2018: 97% 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 2018: 94% 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 2018: 96%[45] 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)*	FY 2018: 100%[45] Target: 90% (Target Exceeded)	90%	90%	Maintain
224221: Percentage of Human and Animal[46] Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (*Output*)	Baseline: 86% (New Measure)	80%	80%	Maintain
224222: Percentage of Human and Animal[47] Drug follow-up inspections conducted due to regulatory action on	Baseline: 67% (New Measure)	55%	55%	Maintain

[45] In accordance with the GDUFA II Commitment Letter, FDA may continue to work through the goal date if, in FDA's judgement continued work would likely result in an imminent tentative approval (TA) that could prevent forfeiture of 180-day exclusivity or in an imminent approval. FDA considers an action to be an imminent approval action if an approval or TA occurs within 60 days of the goal date. When applying the GDUFA II Commitment Letter's imminent approval program enhancement to the metrics noted in this table, FDA is exceeding the 10-month goal at 98% (2% more than just applying the 10-month metric). This imminent approval performance number reflects FDA's decision to achieve an approval or TA within 60 days of the goal date rather than act on the goal date, e.g., issue a complete response letter.

[46] 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.

[47] 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
significant inspection violations that moved toward compliance. (*Outcome*)				
292203: Number of medical product analyses conducted through FDA's Sentinel Active Risk Identification and Analysis (ARIA) System. *(Output) (New Measure)*	FY 2019: 68 (Historical Actual)	55	60	+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. Two FY 2018 standard NME applications are still being reviewed after their PDUFA date. Due to the relatively small number of applications in this review category, when the review goal was missed for two applications due to complex issues, the standard NME performance goal was missed. 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 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. 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 were presented at FDA Advisory Committee Meetings and 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 55 and 60 analyses for FY 2020 and 2021 respectively and will be reassessed periodically. These targets reflect the trend toward more complex analyses that employ more sophisticated analytical methods and yield more meaningful inputs to public health and regulatory decision making.

ORA Field Performance Measures

ORA's performance goals 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 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	159	159	159
Efficacy Supplements	258	258	258
Manufacturing Supplements	1,901	1,901	1,901
Commercial INDs (Drugs and Biologics) with Activity	7,490	7,490	7,490
Sponsor Requests: IND-Phase Formal Meetings	3,167	3,167	3,167
Sponsor Requests: Review of Special Study Protocols	155	155	155
Submissions of Promotional Materials	111,637	115,000	120,000
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	60	60	60
Reviews: Standard NDA/BLA	123	123	123
Approvals: Priority NDA/BLA	49	49	49
Approvals: Standard NDA/BLA	71	71	71
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	8.2	8.2	8.2
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	20.1	20.1	20.1
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	8.0	8.0	8.0
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	10.1	10.1	10.1
Reviews: NDA Supplementals	3,161	3,161	3,161
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	6,540	6,998	7,488
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	230	230	230
Receipts: IND/IDE Amendments (Biologics Only)	25,906	25,906	25,906
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	13	13	13
Approvals: PLA/BLA	12	12	12
Reviews: License Supplement (PLA/ELA/BLA)	401	401	401
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	909	1,000	1,000
Outputs – Reviews/Approvals			
Actions – ANDA	3,869	3,700	3,500
Approval Actions - ANDA (both Tentative and Full Approvals)	1,171	900	850
Median Review Time from ANDA Receipt to Approval (months)	24.03	24	24
Actions - ANDA Supplementals (Labeling and Manufacturing)	7,955	8,250	8,500
Over-the-Counter Drug Review			
OTC Monographs Under Development*	25	25	25
OTC Monographs Published*	3	3	4
OTC Monographs published in FY 2019: Sunscreen Proposed Rule (82 FR 6204; 26 February 2019); Consumer Antiseptic Rub Final Rule (84 FR 14847; 12 April 2019); Food Handlers Antiseptics Request for Information (83 FR 63168; 7 December 2018)			

CDER Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information **	21	23	25
New Written Requests Issued**	20	21	21
Pediatric Exclusivity Determinations made**	17	20	22
Post Exclusivity Safety Report **	6	8	7
**Category includes Proposed Rules and Final Rules			
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	2,167,449	2,256,510	2,349,230
Electronic Submissions: % of Total Adverse Drug Reaction Reports	100%	100%	100%
Electronic Submissions: % of Serious/Unexpected Adverse Drug Reaction Repor	100%	100%	100%
Submissions: Drug Quality Reports	23,468	26,000	29,000
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,349	7,700	8,000
Number of drugs with Risk Communications	365	215	235
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	29	33	33
Number of FOI Requests	3,006	3,300	3,300
Number of FOI Requests Processed	2,991	3,325	3,325
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	97	106	106
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	186	194	194
Number of Citizen Petitions Completed [1] (excluding suitability petitions and OTC monograph-related petitions)	115	106	106

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

Field Human Drugs Program Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,569***	***1,695***	***1,695***
Pre-Approval Inspections (NDA)	62	100	100
Pre-Approval Inspections (ANDA)	89	90	90
Bioresearch Monitoring Program Inspections	625	600	600
Drug Processing (GMP) Program Inspections	589	650	650
Compressed Medical Gas Manufacturers Inspections	35	50	50
Adverse Drug Events Project Inspections	73	88	88
OTC Monograph Project and Health Fraud Project Inspections	17	70	70
Compounding Inspections[1]	127	127	127
Domestic Laboratory Samples Analyzed	936	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1265***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	99	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	220	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	284	255	255
Foreign Drug Processing (GMP) Program Inspections	722	900	900
Foreign Adverse Drug Events Project Inspections	6	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,834***	***3,055***	***3,055***
IMPORTS			
Import Field Exams/Tests	7,617	10,000	10,000
Import Laboratory Samples Analyzed	843	620	620
Import Physical Exam Subtotal	**8,460**	**10,620**	**10,620**
Import Line Decisions	838,267	845,143	904,303
Percent of Import Lines Physically Examined	1.01%	1.26%	1.17%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,834***	***3,055***	***3,055***

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

[2] The FY 2019 actual unique count of foreign inspections includes 141 OIP inspections (69 for China, 70 for India, and 2 for Latin America).

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Office of Orphan Products Development (Budget Authority).....	29,099	29,099	29,099	29,099	---
User Fees.....	4,158	4,158	4,158	4,158	---
FTE.....	39	39	39	39	---

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.

Orphan Product Grants Activity[48]

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.

Clinical Trials Grants Program

[48] FY 2018 and FY 2019 each includes $1.2 million of OOPD program funds to support Orphan Product Grants

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 70 orphan products for serious or life-threatening orphan indications. In FY 2019, OOPD received 89 clinical trial applications and funded 12 new grants from those applications, including studies to treat sickle-cell respiratory complications and acute myeloid leukemia. In addition, in FY 2019, 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 31 applications in the second cycle of this new program, which were reviewed in 13 disease specialty primary panels. OOPD published a new RFA for FY 2019 and funded two new grants from those applications including studies to follow medullary thyroid cancer patientsand cardiac disease in Duchenne muscular dystrophy patients. These studies will add valued data to help develop targeted therapies and lead to more efficient and better designed clinical trials.

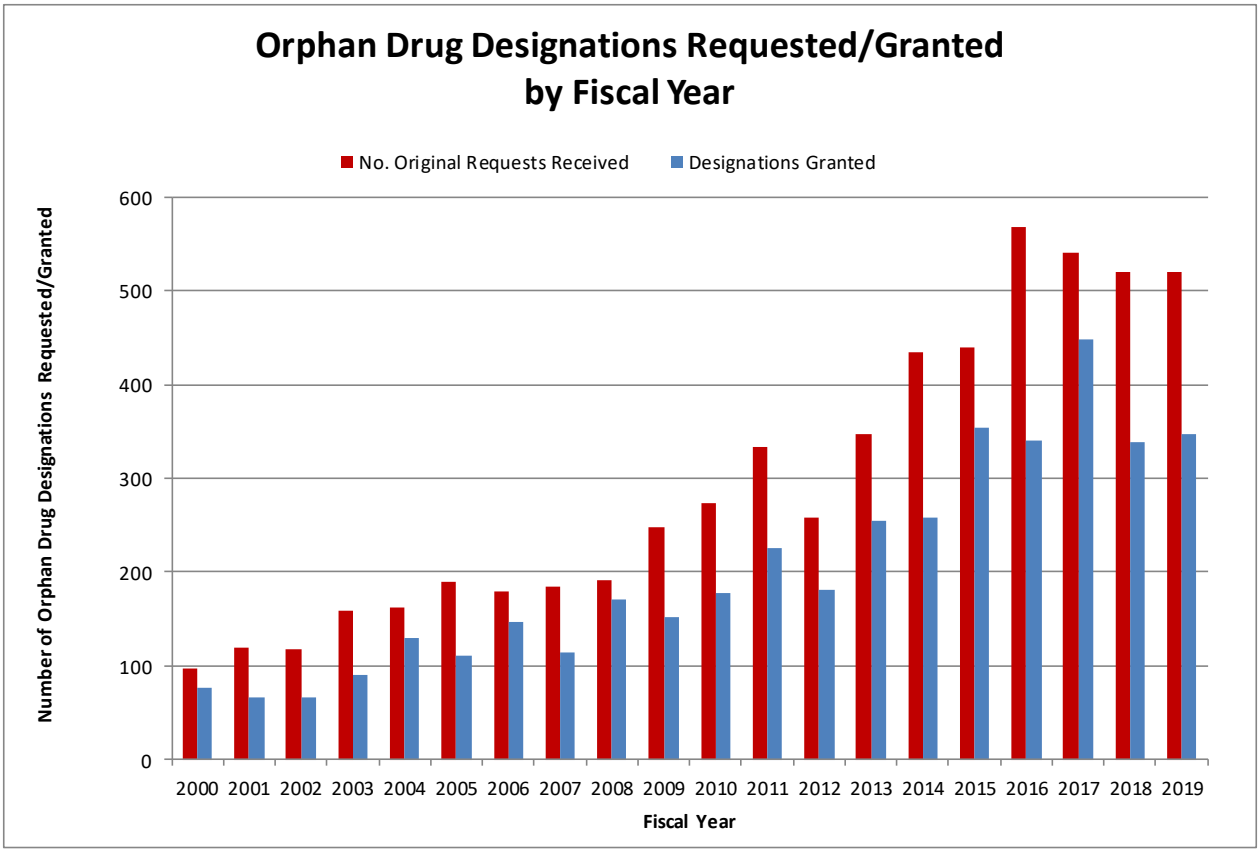

Figure 5 Orphan Drug Designations Requested/Granted by Fiscal Year

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 5,000 orphan drug designations OOPD issued since 1983 have resulted in over 840 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 2019, OOPD received 520 new applications and designated 348 orphan drugs. These included potential treatments for many kinds of rare cancers, sickle cell disease, and cystic fibrosis. FDA approved 83 orphan designated drugs for marketing indications in FY 2019.

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

Product Designations

Below are examples of Orphan Product designations that occurred in 2019.[49]

Date	Product	Purpose or Benefit
January 2019	Odevixibat	Biliary Atresia
August 2019	Leriglitazone	Friedreich's ataxia

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 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 2019, OOPD received 54 new rare pediatric disease designation requests. OOPD determined that 44 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 2019, a total of two 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, 75 HUD devices have been approved for marketing through the HDE pathway.

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

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 FY 2019, 20 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 2019 to date, OOPD received 26 new HUD applications and designated 10 devices. In FY 2019, three devices received HDE approval from CDRH.

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, 19 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, more than $43 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 25 new devices are now available for use in pediatric patients as a result of advisory assistance received from the consortia, including PolyVascular, a polymeric transcatheter synthetic valve that incorporates thinner yet durable polymeric leaflets allowing for percutaneous placement of smaller diameter

valves in much younger children than currently available valves; BabySteps Platform Software, a platform device which incorporates 3D scanning, computer modeling and 3D printing to improve assessment and treatment of the clubfoot deformity; Palmm, a bioelectronic device system that applies a mild electrical current to the skin through wearable garments and provides a convenient at-home treatment for excessive sweating that stops sweat production on targeted body parts, such as the hands. The consortia collectively have also raised more than $300 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 2019, OOPD participated in 35 individual industry outreach and 15 patient-oriented meetings. In addition, OOPD received 45 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 26 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 2019 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. In FY 2020, OOPD will continue the mission critical outreach efforts to enhance all stages of the development and approval process for products to treat rare disease patients.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2017 Actual	$33,257,000	$29,099,000	$4,158,000
FY 2018 Actual	$33,257,000	$29,099,000	$4,158,000
FY 2019 Actual	$33,257,000	$29,099,000	$4,158,000
FY 2020 Enacted	$33,257,000	$29,099,000	$4,158,000
FY 2021 President's Budget	$33,257,000	$29,099,000	$4,158,000

BUDGET REQUEST

The FY 2021 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 two 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 2019 Actuals	FY 2020 Estimate	FY 2021 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)	8	12	12
Orphan Drug Designation Requests/Designations Granted/Orphan Drug Approvals			
New Orphan Drug Designation Requests	520	550	550
Drug Designations Granted	348	370	370
FDA Orphan Drug Marketing Approvals	83	90	90
HUD Requests and Designations			
New HUD Designation Requests	26	30	30
HUD Designations	10	20	20
Rare Pediatric Disease Priority Review Voucher Requests and Designations			
New RPD Requests	54	65	65
RPD Designations	44	55	55

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BIOLOGICS

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Biologics	**402,144**	**408,610**	**419,302**	**425,486**	**6,184**
Budget Authority	***240,138***	***240,133***	***252,138***	***252,381***	***243***
User Fees	***162,006***	***168,477***	***167,164***	***173,105***	***5,941***
Center	358,355	365,148	375,583	382,003	6,420
Budget Authority	198,132	198,132	210,132	210,657	525
User Fees	160,223	167,016	165,451	171,346	5,895
Prescription Drug (PDUFA)	*144,529*	*153,761*	*149,267*	*154,845*	*5,578*
Medical Device (MDUFA)	*14,444*	*13,232*	*14,578*	*14,850*	*272*
Generic Drug (GDUFA)	*1,072*	*24*	*960*	*987*	*27*
Biosimilars (BsUFA)	*178*	---	*646*	*664*	*18*
Field	43,789	43,462	43,719	43,483	-236
Budget Authority	42,006	42,001	42,006	41,724	-282
User Fees	1,783	1,461	1,713	1,759	46
Prescription Drug (PDUFA)	*1,566*	*1,286*	*1,485*	*1,527*	*42*
Medical Device (MDUFA)	*217*	*174*	*228*	*232*	*4*
FTE	**1,418**	**1,415**	**1,407**	**1,416**	**9**

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); Pandemic and All-Hazards Preparedness and Advancing Innovation Act (PAHPAIA) of 2019.
Allocation Methods: Direct Federal; Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Biologics Control Act of 1902 established the Biologics Program in the Department of Treasury's Hygienic Laboratory, which 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 by which CBER can most effectively allocate its fiscal and human resources to successfully navigate the challenges and opportunities of the 21st century. The CBER goals are to:

- Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology;
- Conduct research to address challenges in the development and regulatory evaluation of medical products;
- Increase preparedness for emerging threats and promote global public health; and
- Manage for strategic excellence and organizational accountability.

The following selected accomplishments demonstrate the Biologics Program's delivery of its regulatory and public health responsibilities within the context of current priorities.[50] They align with the Department of Health and Human Services' strategic plan, FDA's strategic priorities, and CBER's strategic plan, and reflect implementation of legislative mandates.

FOSTER COMPETITION AND INNOVATION

Science and technology are advancing at an unprecedented rate. FDA's Biologics Program is committed to helping to set the stage for the continued advancement of novel products and, when appropriate, expediting the development and review of new biological products for a broad range of complex and life-threatening diseases. This includes ground-breaking treatments and those that provide new treatment options where few exist. CBER also works to promote innovation in manufacturing to create a more robust manufacturing process with fewer interruptions in production, fewer product failures, and greater assurance that the biologic products manufactured will provide the expected clinical performance.

FDA's strategic priority to foster competition and innovation aligns with the HHS Strategic Plan FY 2018-2022 goals to "Foster Sound, Sustained Advances in the Sciences" and "Protect the Health of Americans Where They Live, Learn, Work, and Play," and CBER's strategic goals to "Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology" and "Conduct research to address challenges in the development and regulatory evaluation of medical products."

Modernizing the Regulatory Process to Improve Innovation

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

To ensure that the regulatory process is predictable, transparent, scientifically modern, and facilitates innovation through a risk-based regulatory approach, FDA develops and updates policies and guidance for product regulation. The goal is to create clear recommendations, frameworks, and pathways that allow beneficial novel technologies to efficiently reach patients while maintaining standards for product safety and effectiveness.

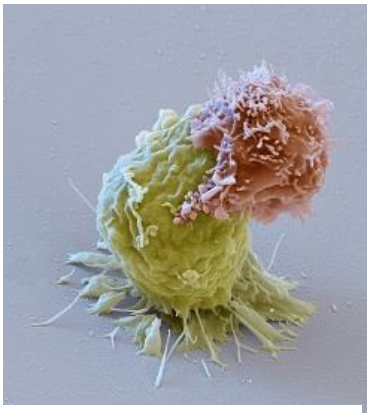


Figure 6 Gene Therapy: CAR-T Cell Attacking Cancer Cell

Once just a theory, gene therapies are now a therapeutic reality for some patients. Gene therapies have the potential to treat a broad spectrum of conditions, from rare genetic disorders, including those affecting one or several individuals, to more common diseases such as some cancers. In May 2019, FDA approved Zolgensma for the treatment of children at least 6 months of age with spinal muscular atrophy type 1 (SMA1), the first directly administered gene therapy given by the intravenous route. It has had a remarkable effect in transforming the course of disease in those children to whom it has been administered.

CBER now has over 900 active Investigational New Drug (IND) applications for gene therapies. FDA continued to develop guidances to advance gene therapies. FDA also launched a new webpage in May 2019 called "Resources Related to Regenerative Medicine Therapies" to provide information more effectively to stakeholders. Guidances issued over the last year in this area include information on:

- Expedited regulatory programs, strategies for clinical development, such as limited study population size, potential feasibility and safety issues (February 2019); and
- Evaluation of devices used with regenerative medicine advanced therapies (February 2019).

To facilitate more efficient development programs for rare diseases that can ultimately support approval, FDA revised its 2015 guidance about drug and biological product development issues for rare diseases (February 2019). The revised 2019 guidance helps sponsors address challenges encountered in drug development due to limited medical and scientific knowledge, natural history data, and drug development experience.

FDA finalized the guidance for 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 (November 2019). FDA also published a guidance to describe an optional streamlined submission process for determining whether use of an investigational in vitro diagnostic in a clinical trial for an oncology therapeutic to help reduce administrative burden for FDA and sponsors (October 2019).

FDA recognizes the value of standards and encourages their appropriate use to facilitate product development and provide more efficient evaluation of regulatory submissions. To provide recommendations to industry on the use of standards in both product development and control and the managed review process, a final guidance was issued for use of standards in regulatory submissions by CBER (March 2019).

Facilitating the development of standards and consensus definitions of terms specifically for regenerative medicine therapies with stakeholders is a priority for FDA. In March 2019, FDA collaborated with NIST and the Standards Coordinating Body[51] to leverage their respective expertise in hosting a workshop to identify opportunities to accelerate medical product development. FDA also launched a new webpage in May of 2019 to provide information on "Standards Development for Regenerative Medicine Therapies," to consolidate information for stakeholders.

To help streamline drug and biological product development, FDA provides scientific and regulatory advice to sponsors early in product development to address issues such as assessment of safety, complex manufacturing technologies, incorporation of innovative devices, and the use of cutting-edge testing methodologies. These early pre-IND interactions are helpful for small- and medium-sized enterprises and academic researchers who often have limited knowledge and experience with new technologies.

Two recently launched programs help facilitate this communication: 1) the CBER Advanced Technologies Team (CATT) was established in July 2019 to promote dialogue, education, and input from prospective innovators and developers of advanced manufacturing technologies; and 2) the Initial Targeted Engagement for Regulatory Advice on CBER products (INTERACT) program, which was launched in June 2018, provides opportunities for potential sponsors to obtain advice early in the development process. Both programs have been well-received and have seen a steady increase in requests for early consultation prior to pre-IND meetings.

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 48 Breakthrough Therapy designations, with 30 of the products being for rare diseases (Orphan designated). The Agency has also granted 45 RMAT Designations since program inception in December 2016 with 27 being for rare diseases.[52]

Advancing Science to Facilitate Access

To modernize its regulatory toolbox, FDA incorporates scientific advancements into its regulatory and scientific work and implements policies to expedite availability of beneficial innovations to consumers. By adopting the most advanced science and risk management tools to inform policy, FDA helps to advance science and technology to design better ways of predicting and evaluating the safety, purity, potency, and effectiveness of biological products early in their lifecycle. The Biologics Program has a cadre of scientific experts who are proficient in the regulatory process and conduct research to address scientific gaps. In addition, the applied research program supports development of new tools, models, standards, and methods,

[51] https://www.standardscoordinatingbody.org/

[52] As of September 30, 2019

harnessing new technologies to expedite product development and provide effective scientific regulatory responses to public health emergencies.

In November 2019, FDA convened a public hearing entitled, “Use of Fecal Microbiota for Transplantation (FMT) to Treat Clostridium difficile Infection Not Responsive to Standard Therapies” to obtain public input on the state of the science regarding FMT to treat *C. difficile* infection not responsive to standard therapies, including the available clinical evidence for safety and effectiveness of FMT for this use and to better understand the impact of FDA’s enforcement policy on product development.

In September 2019, FDA, in collaboration with NIH and Coalition for Epidemic Preparedness Innovations, convened a public workshop entitled "Identification and Use of Biomarkers to Advance Development of Preventive Vaccines." The workshop brought together government agencies, academia, industry, and other stakeholders to discuss the scientific, clinical, and regulatory challenges encountered in the identification, characterization, and qualification of biomarkers for preventive vaccines for infectious diseases indications. The workshop included discussions on exploring the use of biomarkers to inform the clinical development of preventive vaccines and in regulatory decision making. The use of biomarkers, and their qualification under the process established by the 21st Century Cures Act, can help to accelerate the development and availability of safe and effective products.

To support the application of novel technologies for advanced manufacturing, FDA enhanced its work on advanced manufacturing in its intramural regulatory science program and made several awards to support new efforts to foster innovation in the development and creation of more modern, domestically-based manufacturing. Modernization of manufacturing processes improves the agility, flexibility, cost, and reliability of manufacturing of products such as vaccines and cell- and gene-based therapies to improve the health of patients. With these awards, FDA supported projects to evaluate the safety and quality of a 3D printed bioreactor for beads-free CART T-cell manufacturing, continuous acoustic separation for cell therapeutic cell manufacturing, and nondestructive analytics for vaccines. Additionally, as part of its continued implementation of the 21st Century Cures Act, FDA continued to make grants to study and recommend improvements for emerging manufacturing and testing technologies and to support the development and adoption of these technologies.

FDA’s Blood Products Advisory Committee (BPAC) reviews and evaluates available data concerning the safety, effectiveness, and appropriate use of blood and blood products and provides advice on their findings. In March 2019, the BPAC discussion included blood donation policies regarding men who have sex with men (MSM), the current scientific data on HIV and MSM, and identification of additional information that could support alternative procedures to FDA’s current MSM time-based donor deferral policy using pathogen reduction technology. The BPAC also discussed recommendations on strategies to reduce the risk of Zika virus. In November 2019, the advisory committee discussed scientific considerations for cold stored platelet products intended for transfusion, including product characterization, duration of storage and clinical indications for use, and the potential role of cold stored platelets in clinical care, which have the potential to benefit military and civilian patient populations in remote or rural U.S. locations.

FDA scientists continue working to improve vaccine production. To produce enough vaccine quickly in case of a pandemic, scientists must develop candidate vaccine viruses (CVVs) that grow well in both eggs and animal cells, while ensuring they retain their low pathogenicity in animals and the ability to stimulate the immune system effectively. Avian CVVs do not always grow well in mammalian cells or chicken eggs, making it difficult to produce enough vaccine during an emergency or in the event of a pandemic. FDA developed two CVVs that may be used as the starting material to produce inactivated influenza vaccines that protected laboratory animals against a highly pathogenic strain of Influenza A (H7N9). Use of these CVVs could facilitate large-scale production of these viruses in chicken eggs and animal cells.

Immune responses against protein drugs, such as Factor VIII (FVIII), is a major safety and efficacy concern during both clinical trials and in the postmarket setting. FDA developed a technique for determining whether immune system cells (dendritic cells) appear primed to trigger the production of antibodies against FVIII products used to treat hemophilia A. The presence of such primed dendritic cells may be used as biomarkers for potential immune reactions that would block the therapeutic effects of FVIII and would increase the ability to identify individuals and groups of individuals at risk for producing antibodies against FVIII drugs.

Certain growth factors stimulate mesenchymal stromal cells (MSCs) so they can help the body control inflammation by suppressing immune cell functions. FDA developed a strategy that may improve identification of batches of MSCs that can suppress certain immune system activity. This method may be useful to sponsors developing MSCs for the treatment of certain diseases, such as Crohn's disease and multiple sclerosis. The new technique, called functionally-relevant morphological profiling, predicts how much a population of stimulated MSCs would be able to suppress key types of immune cells. It can help refine manufacturing methods to make MSCs more consistent and reliable and determine how other types of cells respond to a variety of different growth factors.

FDA developed a poliovirus assay that is faster and more versatile than those now used. The assay is the first to measure the amount of several different strains simultaneously in a mixture of polioviruses. The assay identifies and quantifies several different viruses simultaneously, enabling the assay to rapidly process the large number of fecal samples collected from subjects during clinical trials and facilitating public health surveillance of vaccine virus in the environment. The assay thus offers a better way to track poliovirus by simplifying and speeding high-throughput processing of sample, which will be useful for achieving the Global Polio Eradication Initiative goal of eradicating polio worldwide.

Since the beginning of the Zika virus (ZIKV) epidemic, FDA has worked with device manufacturers to facilitate the development of ZIKV blood donor screening and diagnostic tests. FDA laboratories developed ZIKV reference reagents for nucleic acid tests (NAT) for use by blood donor screening test developers and have collaborated with CDRH to facilitate ZIKV diagnostic test development.

Real-World Evidence to Evaluate Effectiveness and Safety

Real-world evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of Real-World Data (RWD). RWE can be

generated by different study designs or analyses, including but not limited to, randomized trials, including large simple trials, pragmatic trials, and observational studies (prospective and/or retrospective).

FDA uses RWD and RWE to monitor postmarket safety and adverse events and to help make regulatory decisions. To encourage sponsors and applicants who are using RWD to use a simple, uniform format to report their use of RWE in regulatory submissions FDA issued the draft guidance, "Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics Guidance" (May 2019).

RWD can come from a variety of sources, such as electronic health records (EHRs), claims and billing activities, product and disease registries, patient-generated data including in home-use settings, and data gathered from other sources that can inform on health status, such as mobile devices. CBER's Biologics Effectiveness and Safety (BEST) Program, expanded and enhanced access to new and better data sources, methods, tools, expertise, and infrastructure to conduct surveillance and epidemiologic studies of biological products. BEST is a part of the FDA Sentinel Initiative and provides access to 80 million EHRs with 270 million claims to conduct robust, rapid safety and effectiveness studies of blood, advanced therapeutics and vaccines. Through the BEST System, CBER built a network of EHR and claims databases, gained better access to medical charts, and reduced the data lag to three to four months compared to nine to twelve months using previously available databases.

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. It has also enabled innovative approaches such as machine learning, artificial intelligence, and natural language processing (NLP) to conduct queries and medical chart reviews of EHR records. This has improved FDA's ability to identify cases of the serious, life-threatening adverse effects, Transfusion-Associated Circulatory Overload and Post-transfusion Sepsis.

RWD is being used to inform FDA policies, such as blood donor eligibility. The Transfusion Transmissible Infections Monitoring System (TTIMS), a collaborative effort with the National Heart, Lung, and Blood Institute and the HHS Office of the Assistant Secretary of Health, is gathering and using RWD to help ensure 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 and developed methods to calculate the incidence and prevalence of HIV, hepatitis B virus, and hepatitis C virus pre- and post-implementation of the MSM one-year donor deferral policy based on RWD collected.

STRENGTHEN SCIENCE AND EFFICIENT RISK-BASED DECISION MAKING

FDA provides risk-based oversight of product compliance in keeping with regulatory policy to ensure that approved products are safe, effective, and available, and that unapproved treatments are not on the market. 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.

FDA collaborates with other agencies, both domestic and international, to promote international harmonization to help facilitate development and availability of safe and effective medical products and improve preparedness for public heath emergencies. This network contributes to FDA success during public health emergencies by enabling a rapid and effective response using established communication channels, relationships, and partnerships. The following accomplishments related to strengthening science and efficient risk-based decision making support the HHS strategic plan goals to "Protect the Health of Americans Where They Live, Learn, Work, and Play" and "Foster Sound, Sustained Advances in the Sciences," FDA's strategic priorities and CBER's strategic goals to "Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology" and "Increase preparedness for emerging threats and promote global public health."

Protect Public Health from Infectious Diseases

The spread of infectious diseases and the emergence of new ones is a global public health issue. Infectious diseases can spread through contact with infected individuals, travel by individuals to endemic areas, arthropod vectors, risk behaviors, and other mechanisms. Protecting and enhancing public health by ensuring the availability of safe and effective vaccines to prevent infectious diseases is a priority for FDA.

Vaccines have contributed to a significant reduction in many childhood infectious diseases, and some diseases, such as polio and smallpox, have been eliminated in the United States due to the use of effective vaccines. With high vaccination rates, it is now rare for children in the United States to experience the devastating and often deadly effects of diseases that were once common in the United States and other countries. However, hesitancy to vaccine children in the U.S. has led to recent outbreaks, such as the measles. The World Health Organization recently named vaccine hesitancy one of the top 10 threats to global health. FDA joined colleagues at HHS, CDC, NIH and state and local health departments across the country to continue to promote vaccinations against these preventable diseases during the 2019 US measles outbreak.

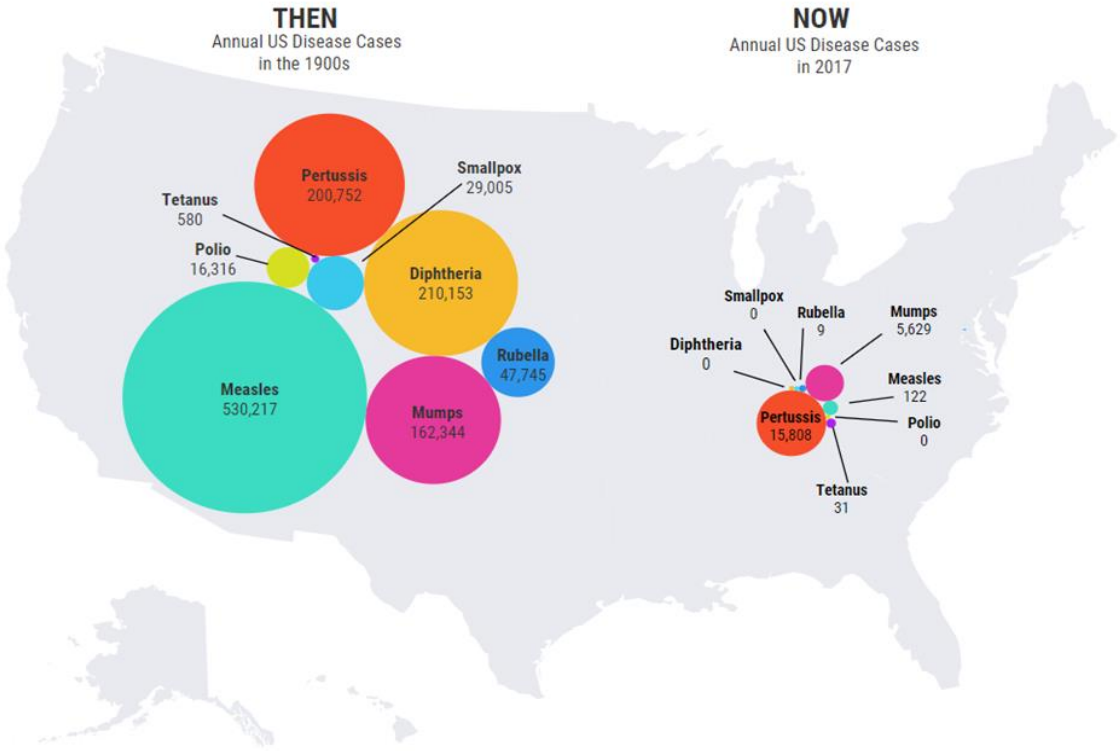


Figure 7 US Disease Cases Now vs the 1900's

FDA approved the first live, non-replicating vaccine for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk (September 2019). This is the only FDA-approved vaccine for monkeypox and provides an important countermeasure in the event of the intentional release of smallpox, it will be included in the Strategic National Stockpile.

Under a priority review, FDA approved the first vaccine for the prevention of dengue disease caused by all dengue virus serotypes (1, 2, 3 and 4) in people ages 9 through 16 who have laboratory-confirmed previous dengue infection and who live in endemic areas. Dengue disease is the most common mosquito-borne viral disease in the world and global incidence has increased in recent decades.

The first FDA-approved vaccine for the prevention of Ebola virus disease was approved in December 2019. FDA leveraged expertise to facilitate the development of the vaccine, which will help to protect against the Zaire ebolavirus and prepare and respond to biological threats. The research approach used to study the effectiveness and safety of this vaccine was precedent-setting during a public health emergency and may help create a model for future studies under similar circumstances.

To help protect patients from seasonal influenza, as it does for every influenza season, FDA selected the strains for inclusion in the influenza vaccines for the 2019-2020 U.S. influenza season. The selection of influenza virus strains is based on the review by FDA, WHO, CDC and other public health experts, of influenza disease surveillance and laboratory data collected from

around the world and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee made in March 2019.

Ensuring the safety of blood and blood products is one of FDA's highest priorities because of the important role that they play in medical care and the unique risks they pose. Blood products can be susceptible to contamination by both existing and emerging pathogens. There is a risk that recipients of blood products could be exposed to an emerging pathogen before it is identified. FDA is working to advance improved pathogen reduction technologies to proactively address public health challenges and emerging infectious diseases.

FDA issued recommendations to control the risk of bacterial contamination of room temperature stored platelets intended for transfusion in the final guidance "Bacterial Risk Control Strategies for Blood Collections Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion" (September 2019).

To further enhance the safety of the blood supply, FDA finalized guidances for industry on further testing of donations that are reactive on a licensed donor screening test for antibodies to hepatitis C virus (October 2019). FDA also approved assays for qualitative detection of antibodies to human T-lymphotropic virus Type I and/or human T-lymphotropic virus Type II (June 2019) and antibodies to hepatitis C virus (July 2019).

Figure 8 Blood Donation

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). FDA finalized guidance providing recommendations for donor screening, donation testing, donor deferral and product management to reduce the risk of transfusion-transmitted Babesiosis (May 2019) and approved two assays for the qualitative detection of Babesia in living donors of whole blood and blood components and for screening organ and tissue donors (January and August 2019).

FDA licensed screening assays for the detection of other infectious diseases, including T. cruzi, the causative agent of Chagas disease (August 2019), hepatitis B virus core antigen (August 2019), and hepatitis B surface antigen (June 2019) to help protect the safety of the blood supply. Supplemental tests were licensed for human serum and plasma samples with repeatedly reactive results by an FDA licensed donor screening test for antibodies to HIV (August 2019).

FDA also approved the first next-generation sequencing test for detecting HIV-1 drug resistance mutations to select an effective combination of drugs for treating patients taking or about to start antiviral therapy (November 2019).

FDA continues to work with the U.S. Department of Defense (DoD) to ensure 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, in a manner similar to breakthrough designated therapies, through ongoing implementation of a Memorandum of Understanding (MOU) signed in 2018. The MOU enhances collaboration and coordination between DoD and FDA, placing

particular priority on products regulated by CBER to help ensure safe and effective products are available to those protecting our nation.

To further advance the development and availability of dried plasma, FDA finalized the guidance "Considerations for the Development of Dried Plasma Products Intended for Transfusion" (December 2019). Also, in 2019, FDA granted a variance to the Department of the Army that allows storage of cold stored platelets for up to 14 days for the treatment of active bleeding when conventional platelets are unavailable or their use not practical.

Improve Global Public Health Through International Collaboration

A critical component of how FDA carries out its regulatory responsibilities is through international engagements that support both national and global public health. These engagements are important because many of the products FDA regulates directly address infectious disease threats that are not unique to the U.S. That means the discovery, development, production and distribution of its regulated products is now a globalized enterprise. International collaborations enable a rapid and 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 or from endemic areas.

Over the past year, FDA has participated in several meetings of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). ICH is a unique harmonization project by which regulator and industry representatives work to improve the efficiency of the new drug development and registration process, promote public health, prevent duplication of clinical trials in humans, and minimize the use of animal testing without compromising safety and effectiveness.

ICH harmonizes technical guidance that FDA adopts upon finalization. In 2019 the following draft ICH guidelines were adopted for public consultation: Optimization of Safety Data Collection (April); Bioanalytical Method Validation (February); Revision on General Considerations for Clinical Trials (May). Four topics have been initiated for harmonization: updating Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin; revising Guideline for Good Clinical Practice, to address the increasing diversity of study types and data sources; updating Post Approval Safety Data Management: Definition and Standards for Expedited Reporting, to incorporate risk-based approaches to the management of information from existing and any new data sources, and enable a greater focus on the data sources that will optimize signal detection activities and public health; and initiating a new Guideline on Non-clinical Biodistribution Studies for Gene Therapy Products.

To help accelerate Ebola virus vaccine development programs, FDA collaborated with CDC and WHO to enable the availability of an investigational Ebola vaccine provided to individuals in the Democratic Republic of the Congo, which is currently suffering from an outbreak of this disease. The FDA focused on advancing the availability of an Ebola vaccine to help advance the ongoing public health response, since prevention is one of the most effective ways to curb the spread of emerging infectious diseases.

In June and December 2019, FDA participated in meetings of 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 that could affect short or long-term national immunization programs. FDA representatives also serve as members of the WHO Blood Regulators Network, a forum for international blood regulatory authorities to share insights and address threats and opportunities to promote global blood product safety, efficacy and availability.

FDA hosted the 22nd U.S. Japan Cellular and Gene Therapy Conference (March 7, 2019), in conjunction with Japan's Ministry of Education, Culture, Sports, Science and Technology, under the U.S.-Japan Cooperative Research Program. The conference focused on adeno-associated virus (AAV)-mediated gene therapy which is a promising approach to treat a variety of human diseases. The speakers from Japan and the U.S. discussed the most recent advances, key achievements and emerging issues in the AAV-mediated gene therapy. The FDA presented U.S. regulatory considerations for clinical development of AAV-based vectors.

To yield greater efficiencies, FDA actively participates in a Mutual Recognition Agreement with the European Union. The MRA allows FDA to avoid duplication of inspections and enables reallocation of resources to inspection of manufacturing facilities with potentially higher global public health risks. This agreement has enabled assessments that resulted in twenty-eight-member states achieving positive capability assessments for their inspectorates; FDA has begun reviewing their recent inspection reports and related information for firms under its auspices.

Compliance and Oversight

FDA conducts a wide range of compliance and surveillance activities to ensure the quality of products through their entire lifecycle. These activities include: 1) conducting pre-license and pre-approval inspections of manufacturing facilities and clinical studies; 2) monitoring the safety, purity and potency of biological products through review of Biological Product Deviation Reports and Human Cell and Tissue and Cellular and Tissue-Based Product (HCT/P) Deviation Reports, investigations into transfusion and donation related fatalities and other adverse events, and product recalls; 3) reviewing notifications of a permanent discontinuance or an interruption in manufacturing or shortage of CBER-regulated products; 4) initiating regulatory action to address non-compliance with FDA laws and regulations; 5) monitoring research on biological products and assessing the protection of the rights, safety, and welfare of human research subjects and the quality and integrity of research data; 6) monitoring import and export activities; and reviewing product advertising and promotional labeling.

To ensure marketed products are meeting quality standards, to maintain safety and effectiveness of products, the Biologics Program monitors the quality of the marketed biological products through surveillance, inspections, and compliance programs. These inspections are performed to ensure that products are manufactured in compliance with Current Good Manufacturing Practice (CGMP) and other applicable FDA regulations. Inspections are conducted at domestic and foreign manufacturing facilities and clinical study sites, including blood and tissue establishments, vaccine facilities, allergenic facilities, device manufacturers, gene and cell therapy facilities, and plasma fractionators.

Though cell-based regenerative medicine holds significant medical promise, the marketing of unapproved treatments potentially puts patient health at risk. In November 2017, FDA announced its comprehensive regenerative medicine framework, which provides that until November 2020 the agency generally intends to exercise enforcement discretion for certain HCT/Ps with respect to FDA's investigational new drug application (IND) and premarket approval requirements, if the use of the product does not raise reported safety concerns or potential significant safety concerns.

Since the framework was announced, FDA has seen only modest progress by regulated industry in coming into compliance. To help improve compliance, FDA established the Tissue Reference Group Rapid Inquiry Program (TRIP) to help manufacturers of HCT/Ps, including those stakeholders that market HCT/Ps to physicians or patients (hereafter referred to collectively as regulated industry), obtain a rapid, preliminary, informal, non-binding assessment of how specific HCT/Ps are regulated. The TRIP is a temporary program of the TRG, effective June 12, 2019 to December 31, 2019. It is intended to help product developers come into compliance with premarket approval requirements, advance an efficient path for the safe and effective regenerative medicine products, and help foster beneficial new innovations. FDA has also provided many different avenues for developers of these products to obtain regulatory advice on their development programs, starting in the pre-clinical stage through clinical development and regulatory submissions.

Innovative products that are reliably and carefully developed will be harder to advance if bad actors are able to make hollow claims and market unsafe science. As a part of the regenerative medicine framework, FDA took regulatory and compliance action against a number of companies and individuals over the last year for marketing products without FDA approval and for significant deviations from current good manufacturing practice requirements, both of which put patients at risk. These included:

- In June 2019, a U.S. District Judge issued an order that stops a Florida-based clinic from, among other things, manufacturing or distributing, any and all stromal vascular fraction (SVF) products, which are adipose (fat) tissue derived cellular products, until they come into compliance with the law.
- On FDA's behalf, the Department of Justice is actively litigating another action in California for permanent injunction against multiple entities and individuals involving their unapproved SVF products.
- FDA sent eight Warning Letters and Untitled Letters since October 2018 to those manufacturing or marketing unapproved HCT/Ps that require premarket approval and create potential significant safety concerns that put patients at risk.
- Since December 2018, FDA issued over 80 letters to manufacturers and health care providers who may be offering unapproved stem cell treatments, reiterating FDA's compliance and enforcement policy. In addition, FDA separately contacted 50 stem cell clinics affiliated with the recipient of one of the above-mentioned untitled letters.
- FDA also issued a warning letter to a hospital Institutional Review Board (IRB) in June 2019 due to significant deviations from the regulations governing IRBs including: 1) Failure to review proposed research at convened meetings at which a majority of members of the IRB are present and 2) failure to prepare and maintain adequate documentation of IRB activities.

FDA issued two communications to provide important information about the safety of biological products. The first communication (April 2019), informed blood establishments and transfusion services about recent cases of contamination of platelets with Acinetobacter sp. and encouraged reporting to FDA of new cases of such contamination, which can cause septic transfusion reactions. The second communication (June 2019), informed health care providers and patients of the potential risk of serious or life-threatening infections following the use of fecal microbiota transplantation (FMT), after two patients developed antibiotic-resistant infections and one of the patients died. FDA noted additional safety protections were needed for any investigational use of FMT and communicated this information to all holders of Investigational New Drug (IND) applications for FMT.

FDA works to ensure the domestic supply of CBER-regulated products. For FY 2019, the Biologics Program has documented seven new product shortages, 19 prevented shortages, five ongoing shortages, and 44 notifications from 25 different manufacturers. CBER has used regulatory flexibility and expedited reviews to prevent or mitigate shortages. In addition, to help mitigate an Immune Globulin (IG) product shortage, FDA worked closely with industry to explore ways to improve the manufacturing yield of IG products, which are derived from donor plasma.

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 and are primarily for industry, but also for other stakeholders and internal staff. FDA uses guidances 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. Since guidances are not legally binding, stakeholders are free to use other approaches that satisfy the relevant law and regulations, though they help to guide stakeholders in reaching their regulatory goal. Below are other selected guidance documents recently issued by CBER, not discussed elsewhere in the Biologics Program Description and Accomplishments.[53]

Date	#	Title	Description
DEC 2019	FDA-2018-D-1216	Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review	Recommends the submission of standardized datasets to facilitate review and analyses of the data and allows for pooling of data, when appropriate.
JUN 2019	FDA-2019-D-1876	Testing for Biotin Interference in In Vitro Diagnostic Devices; Draft Guidance	Provides recommendations on the testing for interference by biotin on the performance of in vitro diagnostic devices (IVDs).

[53] 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
FEB 2019	FDA - 1998D-0315	Providing Lot Release Protocol Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format; Final Guidance	Assists manufacturers of biological products in submitting lot release protocols in electronic format to CBER's Product Release Branch, within the Office of Compliance and Biologics Quality
FEB 2019	FDA-2019-D-0078	Principles of Premarket Pathways for Combination Products – Draft Guidance	Presents current thinking FDA on principles for premarket review of combination products. Intended to enhance clarity, predictability, efficiency, and consistency of premarket regulatory expectations for combination products.

Selected Biologics Product Approvals

New biological drugs such as vaccines, blood products, biotechnology products, and gene therapy and biological medical devices must be demonstrated to be safe and effective before companies can market them in the United States. FDA evaluates the results of studies conducted in the laboratory, animals, and humans to determine if the product is safe and effective for use in the United States. FDA's Biologics Program has reviewed and approved an array of biological products to treat and prevent diseases. Below are selected recent Biological product approvals not discussed elsewhere in the Biologics Program Description and Accomplishments.

Disease	Approved	Trade Name	Proper Name	Purpose or Benefit
Humoral Immunodeficiency	APR 2019	ASCENIV	Immune Globulin Intravenous, Human-slra, 10% Liquid	Indicated for the treatment of primary humoral immunodeficiency for adults and adolescents (12 to 17 years of age).
Hemophilia A	FEB 2019	ESPEROCT	Antihemophilic Factor (Recombinant), GlycoPEGylated-exei	For adults and children with hemophilia A: (1) on-demand treatment and control of bleeding episodes, (2) perioperative management of bleeding, and (3) routine prophylaxis to reduce frequency of bleeding episodes.

Influenza	NOV 2019	Fluzone High Dose Quadrivalent	Influenza vaccine	For the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine in persons 65 years of age and older
Primary Humoral Immunodeficiency	JUL 2019	XEMBIFY	Immune Globulin Subcutaneous, Human-klhw, 20%; Grifols Therapeutics LLC	Indicated for the treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$408,610,000	$240,133,000	$168,477,000
FY 2020 Enacted	$419,302,000	$252,138,000	$167,164,000
FY 2021 President's Budget	$425,486,000	$252,381,000	$173,105,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Biologics Program is $425,486,000, of which $252,381,000 is budget authority and $173,105,000 is user fees. The budget authority increases by $243,000 compared to the FY 2020 Enacted Budget. User Fees increase by $5,941,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is $382,003,000. The Office of Regulatory Affairs amount is $43,483,000.

The FY 2021 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.

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 Regenerative Medicine Advanced Therapy 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.

FDA will advance the use of real-world evidence including through use of new tools and 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.

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 helps CBER keep pace with the tremendous scientific advancements being made in the field.

The Agency will continue to protect the public against the threats of emerging infectious diseases and bioterrorism. The spread of infectious diseases and the emergence of new ones is a global public health issue. FDA will protect and enhance public health by facilitating the availability of safe and effective vaccines and by working to reduce the risk of transmission through donated blood or tissues.

FDA collaborates and establishes relationships with other regulators and health agencies in the U.S. and throughout the world to support public health in the US and globally. Many of the products FDA regulates address infectious disease threats which are not isolated to the U.S. and the discovery, development, production and distribution of its regulated products is a globalized enterprise. FDA also strategizes to harmonize existing regulatory standards and works with international scientific efforts to establish and maintain reference materials and standards for biologics.

In addition to work on gene therapies to address conditions that affect may individuals, the Agency also will address the need for gene therapies addressing conditions that affect one or a small number of individuals (less than about 100), and manufacturing challenges are particularly relevant in this space. The manufacturing of vectors to enable research and development of gene therapies for these very rare conditions can be cost prohibitive and, at this time, not commercially viable. FDA will work with stakeholders to facilitate end-to-end solutions for key issues limiting the development and application of gene therapy for conditions affecting one or a small number of individuals.

BUDGET AUTHORITY

Medical Product Safety (+$2.0 million/ +8 FTE)

Modernizing Influenza Vaccines (+$2.0 million/ 8 FTE)
Center: +$2.0 million/ 8 FTE

Seasonal influenza vaccines prevent millions of cases of disease and thousands of deaths in the United States. This initiative supports the Executive Order on "Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health" to help make the United States influenza vaccine supply more robust, secure, and nimble to combat seasonal influenza epidemics and potential influenza pandemics. FDA will work with industry to implement new manufacturing technologies to potentially expand the domestic capacity of alternative methods

that could allow for vaccines to have reduced production times and account for emerging influenza strains.

Crosscutting Initiatives (-$1.8 million)

Outreach, Training and Organizational Excellence -$1.8 million
Center: -$1.5 million

The Center for Biologics Evaluation and Research (CBER) will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. CBER will preserve its most critical public health and safety activities under this reduction, including activities that support pandemic preparedness, programs facilitating efficient product review and innovation in the drug development process, and work that advances the application of real-world evidence.

Field: -$0.3 million

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

USER FEES

Current Law User Fees: +$5.9 million

Center: +$5.9 million / Field: $0.046 million

The Biologics Program request includes an increase of $5,941,000 for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health, treating and curing diseases, and accelerating innovation in the industry.

PERFORMANCE

The Biologics Program's performance measures focus on biological product review, manufacturing diversity and capacity for influenza vaccine production, strengthening detection and surveillance of FDA-regulated products and postmarket inspections 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
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 2018: 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 2018:100% 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 2018: N/A Target 90% (No applications received)	90%	90%	Maintain
233206: Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. *(Output)*	FY 2018: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
233211: Review and act on new non-user fee, non-blood product applications within 12 months of receipt. *(Output)*	FY 2018: 100% Target: 60% (Target Exceeded)	60%	60%	Maintain
234101: Increase manufacturing diversity and capacity for influenza vaccine production. *(Output)*	FY 2019: Continued evaluation of new methods to produce high-yield influenza vaccine reference strains. (Target Met)	Continue evaluation of new methods to produce more stable high-yield influenza vaccine reference strains and improve current manufacturing processes	Continue evaluation of new methods to produce more stable high-yield influenza vaccine reference strains and improve current manufacturing processes	Maintain
231301: Percentage of Lot Distribution Reports that were entered into the Regulatory Management System - Biologics License Applications (RMS-BLA) within 7 Days.	FY 2019: 99% Target 85% (Target Exceeded)	85%	85%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 90.0% Target: 70% (Target Exceeded)	70%	70%	Maintain
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2019: 85.7% Target: 65% (Target Exceeded)	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 2019, 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 new international collaborative study comparing several alternative potency methods and alternative reference reagents was designed and initiated in FY 2019. This study will assess whether reference standard in the same HA conformation as a vaccine sample can more accurately assess potency in alternative potency assays than whole inactivated virus (SRID) reference standard and may simplify the current process that entails production of many different reference antigens. Additional follow-up studies are being planned for FY 2020 that will continue to evaluate and compare alternative potency methods.

FDA developed two candidate vaccine viruses (CVVs) that may be used as the starting material to produce inactivated influenza vaccines. FDA scientists developed – CBER-RG7C and CBER-RG7D from the highly pathogenic H7N9 strain of influenza A (A/Guangdong/17SF003/2016), by genetically modifying hemagglutinin, a viral protein the influenza virus uses to bind to cells that it infects. Specifically, the amino acid glycine is substituted with a glutamic acid at position G218E in the HA. This change affected the balance of both HA and NA functions during virus amplification in cells and the targeted amino acid substitution significantly enhanced virus growth in both MDCK cells (68.3% increase) and eggs (170% increase) without affecting its antigenicity and its ability to provide protection from wildtype H7N9 virus challenge in an animal model. Use of these CVVs could facilitate large-scale production of these viruses in chicken eggs and animal cells.

ORA Field Performance Measures

ORA's performance goals 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 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
Original Biologics License Applications (BLA)			
Workload [1]	21	21	21
Total Decisions [2]	37	37	37
Approved	27	27	27
BLA Efficacy Supplements			
Workload [1]	13	13	13
Total Decisions [2]	27	27	27
Approved	18	18	18
BLA Manufacturing Supplements			
Workload [1]	1,177	1,177	1,177
Total Decisions [2]	1,422	1,422	1,422
Approved	1,349	1,349	1,349
BLA Labeling Supplements			
Workload [1]	245	245	245
Total Decisions [2]	276	276	276
Approved	235	235	235
Original New Drug Application (NDA)			
Workload [1]	1	1	1
Total Decisions [2]	1	1	1
Approved	1	1	1
NDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	1	1	1
Approved	1	1	1
NDA Manufacturing Supplements			
Workload [1]	13	13	13
Total Decisions [2]	13	13	13
Approved	12	12	12
NDA Labeling Supplements			
Workload [1]	2	2	2
Total Decisions [2]	0	0	0
Approved	0	0	0
Original Abbreviated New Drug Application (ANDA)			
Workload [1]	2	2	2
Total Decisions [2]	0	0	0
Approved	0	0	0
ANDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0

CBER Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
ANDA Manufacturing Supplements			
Workload [1]	1	1	1
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]	75	75	75
Final Decision - SE	43	43	43
Device Premarket Applications (PMA)[6]			
Workload [1]	5	5	5
Total Decisions [2]	7	7	7
Approved	2	2	2
Device Premarket Applications (PMA) Supplements [7]			
Workload [1]	87	87	87
Total Decisions [2]	106	106	106
Approved	30	30	30
Investigational New Drugs (IND)			
Receipts: IND (new)	617	617	617
Receipts: IND Amendments	13,340	13,340	13,340
Total Active IND [3]	3,250	3,250	3,250
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	11	11	11
Receipts: IDE Amendments	315	315	315
Total Active IDE [3]	165	165	165
Patient Safety			
Adverse Event Reports Received [4]	95,133	105,000	115,000
Biological Deviation Reports Received	49,257	49,000	49,000
Sponsor Assistance Outreach			
Meetings	424	424	424
Final Guidance Documents [5]	46	35	35
Admin/Management Support			
Advisory Committee Meetings Held	6	9	9
FOI Requests Processed	361	370	380

[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 for blood tansfusions or blood collection (under 21CFR606.170) 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.

[6] Includes PMA original, PMA shell, HDE and de novo original applications.

[7] Includes all PMA and HDE supplements, PMA modules, excluding HDE-Other and 513(g) submission types.

Field Biologics Program Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,734***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	93	100	100
Blood Bank Inspections	770	900	900
Source Plasma Inspections	216	190	190
Pre-License, Pre-Market Inspections	93	55	55
GMP Inspections	48	28	28
GMP (Device) Inspections	8	7	7
Human Tissue Inspections	552	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***65***	***47***	***47***
Bioresearch Monitoring Program Inspections	8	11	11
Foreign Human Tissue Inspections	3	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	9	7	7
GMP Inspections (Biologics & Device)	38	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,799***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	107	45	45
Import Line Decisions	181,328	179,104	188,059
Percent of Import Lines Physically Examined	0.06%	0.03%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,799***	***1,939***	***1,939***

ANIMAL DRUGS AND FEEDS

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Animal Drugs and Feed	**224,805**	**216,949**	**238,678**	**238,926**	**248**
Budget Authority	***179,209***	***178,928***	***190,869***	***190,081***	***-788***
User Fees	***45,596***	***38,021***	***47,809***	***48,845***	***1,036***
Center	157,717	151,056	168,474	169,145	671
Budget Authority	113,694	113,419	122,099	121,787	-312
User Fees	44,023	37,637	46,375	47,358	983
Animal Drug (ADUFA)	*27,267*	*23,896*	*27,670*	*28,315*	*645*
Animal Generic Drug (AGDUFA)	*16,644*	*13,741*	*18,591*	*18,926*	*335*
Third Party Auditor Program	*112*	---	*114*	*117*	*3*
Field	*67,088*	*65,893*	*70,204*	*69,781*	*-423*
Budget Authority	65,515	65,509	68,770	68,294	-476
User Fees	1,573	384	1,434	1,487	53
Animal Drug (ADUFA)	431	384	383	392	*9*
Animal Generic Drug (AGDUFA)	*335*	---	*228*	*255*	*27*
Food Reinspection	*807*	---	*823*	*840*	*17*
FTE	**1,004**	**1,004**	**1,041**	**1,042**	**1**

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 more than 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 utilizes budget authority and user fees to help meet its mission of protecting human and animal health. Congress passed and the President signed the Animal Drug User Fee Amendment IV and Animal Generic Drug User Fee Amendment III in FY 2018. ADUFA and AGDUFA supplement the appropriated budget authority 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 animal drugs and food products.

Foster Competition and Innovation

FDA protects and promotes public health by ensuring that animal pharmaceutical products are properly evaluated for safety and efficacy, manufactured under quality standards, and properly labeled. Promoting public health also requires the Agency to take steps that can help facilitate access to safe, effective, and innovative products that can address existing, novel, and emerging animal health challenges.

Fostering Innovation in Plants and Animal Drugs

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

The Plant and Animal Biotechnology Innovation Action Plan was published in October 2018 to provide an overview of priorities FDA will pursue to support innovation in these areas, while advancing the agency's public health mission. This new plan identified priorities in three important areas:

1. advancing human and animal health by promoting product innovation and applying modern, 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.

FDA began implementing the action plan in FY 2019 by hosting a public webinar on genome editing in animals and launching the Veterinary Innovation Program (VIP). The VIP pilot offers technical assistance to developers of innovative veterinary products to

- enhance regulatory predictability
- improve Agency responsiveness
- enable early, sustained interactions with innovators.

As of FY 2020, there are 13 animal drug sponsors participating in the pilot, including 7 sponsors of animal cell or tissue-based products and 6 sponsors of animal biotechnology products. Promising new technologies that can edit animal and plant genomes have the potential to improve human and animal health, animal welfare, and food safety and security.

The safety of human and animal 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. FDA is drafting a new guidance to help innovators understand their responsibilities so as to better navigate the regulatory pathway toward bringing safe, innovative plant biotechnology products to market.

Advancing Plant and Animal Biotechnology Innovation

American agriculture and food technology are in a period of exceptional innovation with the increasing development and use of new technologies. These innovations present FDA with the opportunity to provide sufficient risk-based flexibility in the regulatory process to support the development of significant and beneficial technology, while safeguarding human and animal health.

In FY 2019, FDA published the Plant and Animal Biotechnology Innovation Action Plan[54] to provide an overview of priorities FDA will pursue to support innovation in these areas, while advancing the agency's public health mission. This new plan identified priorities in three important areas:

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

As of FY 2020, there are 13 animal drug sponsors participating in the Veterinary Innovation Program (VIP) pilot, including 7 sponsors of animal cell or tissue-based products and 6 sponsors of animal biotechnology products. The VIP pilot is a key component of the Plant and Animal Biotechnology Innovation Action Plan and offers technical assistance to developers of innovative veterinary products to enhance regulatory predictability, improve FDA's responsiveness and enable early, sustained interactions with innovators. Promising new technologies that can edit

[54] https://www.fda.gov/media/119882/download

animal and plant genomes have the potential to improve human and animal health, animal welfare, and food safety and security. The safety of human and animal food from more than 180 varieties of genetically engineered plants have also been evaluated and many of these products are consumed by Americans every day.

Animal Drug Review

FDA 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 all animals, while ensuring that food from treated food-producing animals is safe for humans to eat. Based on current data, FDA exceeded the Animal Drug User Fee Amendment (ADUFA) and Animal Generic Drug User Fee Amendment (AGDUFA) performance goals and commitments for both pioneer and generic animal drugs in the FY 2018 and FY 2019 reporting period.

As part of the ADUFA reauthorization, Congress expanded FDA's authority to grant conditional approval to include certain animal drugs for use in major species (horses, dogs, cats, cattle, pigs, turkeys and chickens) for some diseases or conditions that were not previously eligible. In September 2019, FDA released draft Guidance for Industry (GFI) #261 entitled "Eligibility Criteria for Expanded Conditional Approval in New Animal Drugs" to assist animal drug sponsors interested in pursuing conditional approval. Expanded conditional approval has the potential to incentivize drug development and provide veterinarians with legally marketed new animal drugs to treat serious or life-threatening diseases or conditions, and to fill treatment gaps where no other therapies are available.

In July 2019, FDA held a public meeting to gather input about alternative approaches in clinical investigations for new animal drugs, as required by the Animal Drug and Animal Generic Drug User Fee Amendments of 2018. The meeting focused on potential alternative approaches in clinical investigations, including incorporating complex adaptive and other novel investigation designs, data from foreign countries, real-world evidence (including ongoing surveillance activities, observational studies, and registry data), biomarkers, and surrogate endpoints into proposed clinical investigation protocols and applications for new animal drugs. With the feedback collected in the public meeting, FDA intends to issue draft guidance on innovative study designs that will enable industry to put these principles into action to further advance approval of animal drugs.

The **conditional approval** pathway allows drug companies to legally sell animal drugs for a limited period of time that have been proven to be safe but have not yet met the standard of effectiveness for full approval.

In August 2019, FDA published medicated feed information on the Animal Drugs @ FDA website making it available for the first time via a searchable database. This one-stop-shop for animal drug information, that was previously only available in PDF format, includes:

- labels of medicated feeds
- lists of licensed medicated feed mills, and
- lists of Veterinary Feed Directive (VFD) distributors.

The Animal Drugs and Feeds Program also continues to enhance international harmonization and collaboration with international organizations, other countries' regulatory agencies and related industry. The Program simultaneously reviewed and approved 11 applications and is currently reviewing 16 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

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

The Mutual Recognition Agreement (MRA) between FDA and European Union allows drug inspectors to rely upon information from drug inspections conducted within each other's borders. Under the Food and Drug Administration Safety and Innovation Act, enacted in 2012, FDA has the authority to enter into agreements to recognize drug inspections conducted by foreign regulatory authorities if the FDA determined those authorities are capable of conducting inspections that met U.S. requirements. FDA and the EU have collaborated since May 2014 to evaluate the way they each inspect drug manufacturers and assess the risk and benefits of mutual recognition of drug inspections. The FDA and the EU have decided to work to include animal drugs under this MRA. In June of 2019, the EU conducted an assessment of FDA animal drug programs using the harmonized EU Joint Audit Programme (JAP) and PIC/S Joint Re-assessment Programme (JRP) template under the MRA. The Animal Drugs and Feeds Program has participated and will continue to participate in MRA assessments of animal drug programs in several EU member countries as we move toward full implementation of the MRA.

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 in treating the wide diversity of animal species.

MUMS drug incentives are needed since the small size of these markets does not provide sufficient return on investment for sponsors seeking approval. FDA granted 149 MUMS drug "designations" over the last 14 years to support drug development for minor uses and minor species, and this has contributed to the approval of drugs ranging from antiparasitic drugs for sheep and goats, to 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.

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, an alternative process known as "the Index of

legally marketed new unapproved animal drugs for minor species" provides a faster and less expensive way to obtain legal marketing status for eligible products. As of November 2019, 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 sponsors 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 have led to the approval of 29 MUMS products.

Selected Product Approvals in 2019

Below are product approvals issued by the Animal Drugs and Feeds Program in the last calendar year. This list does not represent any degree of importance or priority ranking of products. For more information, go to the Approved Animal Drug Products (Green Book) website.

Species	Date	Product Name	Purpose or Benefit
Dogs	Oct. 2019	Clomipramine Hydrochloride Tablets	First generic approval used as part of a comprehensive behavioral management program to treat separation anxiety in dogs greater than 6 months of age.
Dogs	Sep. 2019	Credelio™	Provides for the addition of the following indication: prevention of flea infestations for one month in dogs and puppies 8 weeks of age and older and weighing 4.4 pounds or greater.
Dogs	Jul. 2019	ProHeart12	For prevention of heartworm disease for 12 months and treatment of existing hookworm infections.
Finfish and Salmonid	Jul 2019	35% PEROX-AID™	Provides for the addition of the following indications: for control of mortality or treatment of specific fungi, external parasites, and bacterial species in various finfish and salmonids.
Lactating dairy cows	Jul. 2019	Estrumate™	Provides for the addition of the following indication: For use in Fertagyl™ (gonadorelin) to synchronize estrous cycles to allow for fixed time artificial insemination (FTAI) in lactating dairy cows.

Protect and Promote the Safety and Health of Families

The Animal Drugs and Feeds Program protects and promotes human and animal health by ensuring the safety of the American food supply, the safety of animal food and devices and the safety and effectiveness of animal drugs. The program accomplishes this by leveraging sound scientific data and risk-based decision making at all stages of the products lifecycle, from pre-market review of new animal drugs and animal food ingredients to post-market response to adverse drug events and food safety emergencies.

Animal Food Safety

One of the key responsibilities of the Animal Drugs and Feeds Program is to ensure the safety of 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, animal food ingredients, and animal food labels and labeling
- monitoring and taking appropriate action, when needed, 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.

Animals generally eat a very limited and defined diet as their sole ration for their whole lifetime. Reviewing new animal food ingredients will allow livestock producers to use new scientific discoveries and provide optimal nutrition to help keep animals healthy, while also ensuring that the meat, milk, and eggs from those animals are safe for people to eat. 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. Between FY 2013 and FY 2018, submissions of FAPs have gone up by 150 percent. In FY 2019, these data were made publicly available as part of the Animal Drug and Animal Generic Drug User Fee Amendments of 2018.

The animal food ingredient industry is evolving, and submissions of innovative new animal food ingredients are more complex data in their submissions. For example, FDA recently reviewed and approved the use of marine microalgae in dog food. These single cell algae are farmed to serve as an alternative source of an omega-3 fatty acid, Docosahexaenoic Acid (DHA), most commonly found in fish from the ocean. FDA also reviewed the safety and usefulness of black soldier fly larvae and approved it for use in animal food. These insects are raised on food scraps, which would otherwise have gone to waste. Instead, the insects eat the food scraps and are turned into high-quality food for other animals, like poultry and salmon.

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.

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 requirements for current good manufacturing practice (CGMPs) and hazard analysis and risk-based preventive controls (PCs). As of September 2019, all business

sizes reached their compliance dates for CGMPS, and large, small and very small businesses reached their compliance dates for PCs.

FDA published a proposed rule on laboratory accreditation in November 2019. In this rule, FDA proposes to establish a program for the testing of human and animal food by accredited laboratories as required by the FSMA. As proposed, there are certain circumstances where testing for food for animals would need to be done using an accredited laboratory under this program.

In FY 2019, FDA continued to develop and publish guidance documents and resources to foster a greater understanding and to educate stakeholders on how to comply with FSMA. FDA proactively engages with industry and regulatory partners through:

- the FSMA Technical Assistance Network (TAN), a central source for information and questions related to FSMA rules, programs, and implementation strategies
- webinars, conferences and meetings on FSMA-related regulations and guidance
- delivering CGMP and PC regulator training on the PCAF regulation
- the cooperative agreement FDA has with National Association of State Departments of Agriculture (NASDA) to develop framework for how state programs can update, modernize, or transform their programs to implement a prevention-oriented program, with the PCAF regulation as a foundation.

In September 2019, FDA launched a Food Safety Dashboard designed to track the impact of the seven foundational rules of FSMA, measure their progress, and help the agency continue to refine implementation. Continuing the successful implementation of FSMA will support the FDA's goal of reducing the incidence of illness and death attributable to preventable contamination of FDA-regulated human and animal food products.

In October 2019, the Food Safety Preventive Controls Alliance (FSPCA), in collaboration with FDA, published the CGMP for Animal Food Online Course. This course will focus on the CGMP regulation and introduce the provisions of this regulatory authority to facilities that need to understand and comply with the requirements.

In FY 2020, FDA announced it would continue its enforcement discretion policy for compliance with certain FSMA supply-chain program requirements designed to ensure suppliers are addressing hazards requiring a supply-chain-applied control. To comply with the supply-chain program requirements, co-manufacturers often need detailed information about suppliers that only the brand owner has, and that cannot be shared because of confidentiality clauses in the contracts. The Agency plans to broaden efforts to provide education and outreach to industry on critical traceability attributes, such as data standards, governance, and interoperability to support modernization of food supply chains.

While this announcement was specific to one type of enforcement discretion, FDA continues to provide enforcement discretion from the Preventive Control for Animal Food regulation for certain types of animal food facilities (e.g. cotton ginners, nut hullers and shellers, and silage makers) or certain requirements in the regulation (e.g. written assurance provisions, certain requirements for human food by-products that are further processed at the human food facility).

FDA also continues to conduct outreach to stakeholders to ensure they are aware of the relevant enforcement discretion provisions and to discuss any changes that may be forthcoming, as appropriate.

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 43 state and university veterinary diagnostic laboratories. These laboratories collaborate with FDA on a Veterinary Early Warning Surveillance System, which includes pet food and feed issues in livestock, to help the agency prevent and respond to animal food emergencies by carefully investigating the clinical aspects of reported illnesses. Such partnerships expand FDA's ability to protect animal and human health.

Veterinary diagnostic laboratories often have opportunities for early detection of emerging diseases. In FY 2019, FDA and the Vet-LIRN increased its capacity for conducting state-of-the-art susceptibility testing and genetic analysis. Laboratories conducted dozens of investigations into consumer adverse event complaints of illness or death potentially due to animal food.

In FY 2020, FDA concluded a collaborative effort with the U.S. Centers for Disease Control and Prevention and State agencies to investigate a link between pig ear pet treats and 154 human cases of *Salmonella enterica*, with ill people ranging from one year to 90 years old. *Salmonella* is a bacterium that can cause illness and death in humans and animals, especially those who are very young, very old, or have weak immune systems. Testing also found that some of the strains of *Salmonella* were antibiotic resistant. After a series of recalls and public health advisories slowed the rate of human illness reports, FDA has provided advise to industry on supply chain and hazards control.

In FY 2019, when multiple brands of raw pet food tested positive for *Salmonella* and *Listeria monocytogenes (L. mono)*, FDA worked to recall impacted products and with a state agriculture department to issue a stop sale to prevent further distribution. FDA cautioned pet owners not to feed these raw pet food products to their animals. Pet food and treats contaminated with *Salmonella* and *L. mono* are of particular public health importance because while pets may get sick from these pathogens, they may also become carriers of the bacteria without appearing to be ill and pass it on to their human companions.

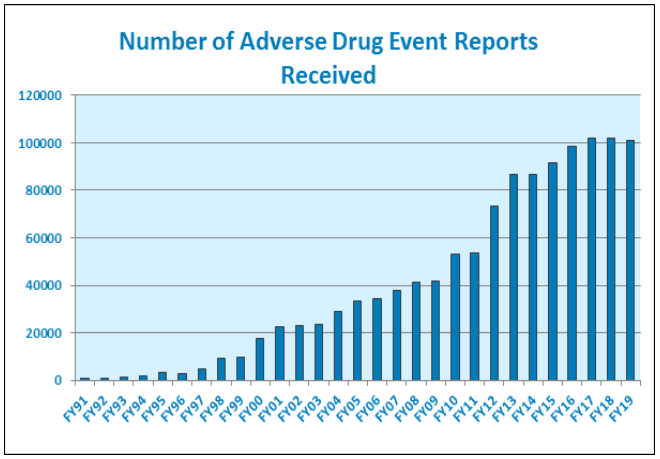
FDA and Vet-LIRN are actively investigating reports of a potential link between a heart condition in dogs known as canine dilated cardiomyopathy (DCM) and diets of certain pet foods. Between January 1, 2014 and April 30, 2019, the FDA received 524 reports of DCM and approximately 42 percent of these were reported between December 1, 2018 and April 30, 2019. Investigators are:

- interviewing pet owners
- collecting and analyzing blood, urine, feces, and DNA
- reviewing echocardiogram results, cardiology/veterinary records, and detailed diet histories

Cases of DCM reported to FDA have involved a wide range of dog breeds, ages and weights, and included breeds of dogs not previously known to have a genetic predisposition to the disease. Based on the data collected and analyzed thus far, the agency believes that the potential association between diet and DCM in dogs is a complex scientific issue that may involve multiple factors.

Leveraging Real-World Adverse Event Data

The Program monitors the safety of animal food and drugs, human user safety, and the effectiveness of approved animal drugs through a comprehensive adverse event reporting system. 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 910,000 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 data includes adverse events reported in more than 89,600,000 food animals, and approximately 800,000 companion animals.



In FY 2019, more than 100,000 adverse event reports were received; one case can include both initial and follow up 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.

In its continuing commitment to increase transparency, the FDA announced in April 2019 the availability of over 30 years' worth of data from adverse event reports associated with approved animal drugs, unapproved or compounded animal drugs and devices used in animals. This detailed data was previously only available via a Freedom of Information Act request and now is available in machine-readable format on openFDA.gov, a platform used by the public, researchers, statisticians and other academics to access large, valuable public health datasets collected by the agency.

Efforts continue to increase the functionality, utilization, and analysis of this pharmacovigilance database to improve animal drug safety. In FY 2019, adverse event signal detection (data mining) and management strategies were developed 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 also modified database functionality and revised Form FDA 1932a to improve identification and detection of safety issues and trends associated with compounded animal drug products.

Compounded Animal Drugs

Animal drugs compounded from bulk drug substances are marketed and used in the United States to treat companion and food-producing animals, even though many of these products have not met FDA's standards for safety and effectiveness and may not be properly manufactured or

labeled. Drug companies that make and sell these compounded animal drugs unfairly compete against drug companies that spend the time and financial resources to prove that new animal drugs are safe and effective.

In FY 2019, FDA led a number of for-cause compliance actions to reduce the risk of harm from these compounded animal drugs, including:

- reviewed 28 inspections of compounders of animal drugs
- oversaw 15 recalls regarding compounded animal drug products
- reviewed 10 voluntary animal drug compounding Adverse Drug Event reports.
- worked on 1 injunction against a human and animal drug compounder, in collaboration with the Human Drugs Program

In November 2019, the FDA published draft GFI #256 and is soliciting public comment on proposed conditions under which the FDA generally would not take action against compounded animal drugs. Although current law does not permit compounding of animal drugs from bulk drug substances, the FDA recognizes that there are circumstances where there is no approved drug that can be used or modified through compounding to treat a particular animal with a particular condition. In those limited situations, veterinarians may prescribe an animal drug compounded from bulk drug substances as an appropriate treatment option. The guidance document is intended to clarify when compounding from bulk drug substances might be acceptable and is seeking public input.[55]

Selected Guidances Published in 2019

Below are notable Animal Drugs and Feeds Program guidances recently issued by FDA. This list does not represent any degree of importance or priority ranking among the guidances.

Issued	**Docket #**	**Title**	**Description**
Sep. 2019	FDA-2019-D-3764	CVM GFI #171: Demonstrating Bioequivalence for Soluble Powder Oral Dosage Form Products or Type A Medicated Articles from Active Pharmaceutical Ingredients Considered to be Soluble in Aqueous Media	Describes how CVM intends to evaluate requests for waiving the requirements for performing in vivo bioequivalence studies (biowavers) for animal drugs administered orally as soluble powders or as Type A medicated articles manufactured from active pharmaceutical ingredients (APIs) considered to be soluble in aqueous media (water soluble APIs)
Aug. 2019	FDA-2018-D-2354	CVM GFI #257 (VICH GL57): Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs	Provides study design recommendations that will facilitate the universal acceptance of the generated residue depletion data to fulfill the national /

[55] https://www.fda.gov/animal-veterinary/cvm-updates/fda-releases-revised-draft-guidance-compounding-animal-drugs-bulk-drug-substances

		in Food-Producing Species: Marker Residue Depletion Studies to Establish Product Withdrawal Periods in Aquatic Species	regional requirements for drugs intended for use in aquatic food-producing species.
Jul. 2019	FDA-2008-D-0165	CVM GFI #181: Blue Bird Medicated Feed Labels	Provide New Animal Drug Application (NADA) sponsors of Type A medicated articles with CVMs current thinking on the recommended content and format for labeling proposed to be used for Type B and Type C medicated feeds; these are referred to as Blue Bird Labels
Jun. 2019	FDA-2018-D-0671	Guidance for Industry: Determining the Number of Employees for the Purposes of the "Small Business" Definitions in Parts 117 and 507	The purpose of this guidance is to help industry subject to 21 CFR part 507 determine the number of employees for the purposes of the "small business" definition under parts 117 and 507.

Combating Antimicrobial Resistance

The Animal Drugs and Feeds Program ensures the safety and effectiveness of animal drugs, including 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.

The Program collaborated with key stakeholders in recent years to make significant public health progress to entirely eliminate production uses of medically important antimicrobial drugs (i.e., antimicrobials important for treating human disease) used in the feed or water of food-producing animals. CVM also worked to change the OTC status of these products to ensure that 95 percent of medically important antimicrobials sold or distributed for use in food-producing animals are under veterinary oversight.

A limited number of other dosage forms of medically important antimicrobials, such as injectables, are currently marketed as OTC products for both food-producing and companion animals. In September 2019, the Program published draft GFI #263 to explain the recommended process for voluntarily bringing the remaining 5% of approved medically important antimicrobial drugs under the oversight of licensed veterinarians by changing the approved marketing status from over-the-counter (OTC) to prescription (Rx).

In October 2019, the Program announced the availability of performance measures to track the progress of its five-year plan: "Supporting Antimicrobial Stewardship in Veterinary Settings: Goals for Fiscal Years 2019 - 2023." This five-year action plan 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.

Antimicrobial Drug Sales

In December 2019, FDA published the sales and distribution summary report that reflects changes in the marketplace since all antimicrobials important for treating disease (specifically, antimicrobials used in feed and water) transitioned from over-the-counter marketing status to veterinary oversight. The report indicated sales:

- increased by 9% from 2017 through 2018
- decreased by 38% from 2015 (the year of peak sales) through 2018
- decreased by 21% from 2009 (the first year of reported sales) through 2018

While some sales increased slightly in 2018, there remains a substantial reduction in the quantity of these drugs sold or distributed in 2018 as compared with peak sales in 2015. This demonstrates that ongoing stewardship efforts, including those initiated by FDA and other key stakeholders, continue to have a measurable impact.

Antimicrobial Drug Use

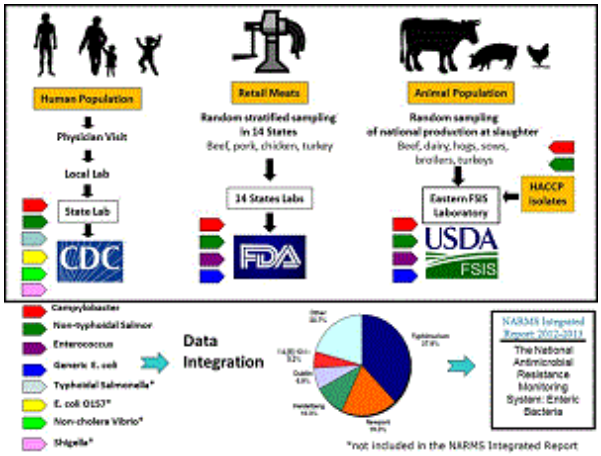
One contributor to the development of antimicrobial resistance could be the administration of medically important antimicrobial drugs for undefined periods of time. The principles of antimicrobial stewardship, including judicious use, emphasize that medically important antimicrobial drugs should only be used to treat, control, or prevent a disease and be administered for an appropriately targeted period of time (that is, have a defined duration of use).

In 2019, FDA awarded grants for studies to help target and define durations of use for certain medically important antimicrobial drugs approved for use in the feed of food-producing animals. Updating the dosage regimens of the affected approved animal drug products is a significant scientific and technical challenge. Changes to the use conditions of these products will be based on science and available evidence, and the FDA believes these grants may help generate such information.

In December 2018, investigators from the University of Minnesota and Kansas State University submitted to FDA interim reports summarizing 2016 and 2017 data collected from pilot studies to characterize the use of antimicrobial drugs in major food-producing animal species (cattle, swine, chickens and turkeys); data collection will continue through FY 2021. An initial report for the poultry pilot project was recently published. The information being collected may help 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.

National Antimicrobial Resistance Monitoring System (NARMS)

The National Antimicrobial Resistance Monitoring System (NARMS) monitors antimicrobial resistance in enteric (intestinal) foodborne bacteria. FDA uses data from NARMS and other sources to estimate the overall risk of antimicrobial resistance when determining whether to approve the new animal antimicrobial drug for a proposed use. A drug's conditions of use may be limited based on this risk estimation to mitigate the risk of antimicrobial resistance development.



In November 2019, NARMS published the 2016-2017 Integrated Summary. This was the first time NARMS included data on animal pathogens in collaboration with FDA's Veterinary Laboratory Investigation and Response Network (Vet-LIRN). These data included *Salmonella* infections from any host, and 2 pathogens (*E. coli* and *S. pseudointermedius*) in dogs. In addition, the summary was the first time that NARMS provided genomic information for *Campylobacter* and *E. coli* retail meat and food animal isolates. Until the recent publication, genomic information was only available for *Salmonella*.

NARMS continues to implement the FDA's Science Board recommendations, including expanding NARMS surveillance to new commodities. In 2019, NARMS launched a pilot study of specific seafood products and in 2018 completed a pilot study of veal. These data may improve understanding about the post-approval impact of antimicrobial use in these animals.

Advances in Whole Genome Sequencing (WGS), a high capacity and low-cost rapid DNA sequencing technology, 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.

Resistome Tracker is a tool launched by NARMS in FY 2017 to examine the distribution of antimicrobial resistance genes in all Salmonella genomes. The tool is being further developed in FY 2019 to include other organisms, such as *Campylobacter*, *E. coli* and *Shigella* within the National Institutes of Health's National Center for Biotechnology Information (NCBI) system. Making these data available to the public allows researchers, academics and public health officials using new genomic technologies to:

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

Veterinary diagnostic laboratories are poised to play an increased role in biosurveillance for antibiotic-resistant bacteria that could affect humans. In FY 2019, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) conducted antimicrobial susceptibility testing

and sequencing of selected veterinary pathogens, including *Salmonella, E. coli* and *Staphylococcus pseudintermedius.* Over 1,500 isolates were tested and over 600 of these pathogens were sequenced during the first two quarters of 2019. Additional pathogens were added to the 2019 program and it is expected that a total of approximately 2,000 isolates will be tested and 1,000 sequenced in FY 2020. All sequences are immediately uploaded to NCBI and are quickly made public for use in facilitating outbreak investigation of animal and zoonotic illnesses.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$216,949,000	$178,928,000	$38,021,000
FY 2020 Enacted	$238,678,000	$190,869,000	$47,809,000
FY 2021 President's Budget	$238,926,000	$190,081,000	$48,845,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Animal Drugs and Feeds Program is $238,926,000, of which $190,081,000 is budget authority and $48,845,000 is user fees. The budget authority decreases by -$788,000 compared to the FY 2020 Enacted. User Fees increase by $983,000. The Center for Veterinary Medicine (CVM) amount in this request is $169,145,000. The Office of Regulatory Affairs amount is $69,781,000.

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 companion animals, including minor species, and enhances the availability and diversity of approved products. The Program'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.

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 stewardship 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 2021 Budget Request support mission critical activities, and Presidential, HHS, and FDA human and animal health priorities.

BUDGET AUTHORITY

Crosscutting Initiatives: -$1.3 million

Outreach, Training and Organizational Excellence: -$1.3 million
Center: -$0.8 million

CVM will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. CVM will preserve its most critical public health and safety activities under this reduction, by prioritizing ensuring the safety of the American food supply, the safety of animal food and devices and the safety and effectiveness of animal drugs.

Field: -$0.5 million

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

Food Safety: +$0.5 million /1 FTE

Cannabis and Cannabis Derivatives: +$0.5 million / 1 FTE

Center: +$0.5 million / 1 FTE

The Animal Drugs and Feeds Program will use this increase to strengthen its capacity to evaluate scientific data related to the safe use of cannabis and cannabis derivatives in animal products. This increase also will enable the Program to continue policy development and respond to the growing volume of requests for information from consumers, partners in federal, state and local government, and other stakeholders.

USER FEES

Current Law User Fees: +$1.0 Million

Center: +$0.983 million / Field: +$0.053 million

The Animal Drugs and Feeds Program request includes an increase of $1,036,000 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
243201: Complete review and action on original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. (Output)	FY 2018[56]: 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 applications received during the fiscal year. (Output)	FY 2018[57]: 100% w/in 270 day Target: 90% w/in 270 days (Target Exceeded)	90% w/in 240 days	90% w/in 240 days	Maintain
244204: Complete review and action on warning letters received to better safeguard our food supply by alerting firms to identified deviations in order to become compliant. (Output)	FY 2019: 38% w/in 25 working days Target: 50% w/in 25 working days (Target Not Met)	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 2019: 100% Target: 90% w/I 30 working days (Target Exceeded)	90% w/in 30 working days	90% w/in 30 working days	Maintain
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 95.9% Target: 80% (Target Exceeded)	80%	80%	Maintain
224221: Percentage of Human and Animal Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 85.5% Target: 80% (Target Exceeded)	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)	FY 2019: 80.6% Target: 65% (Target Exceeded)	65%	65%	Maintain

[56] Represents FDA's preliminary performance for FY 2018 cohort submissions. Final performance will be available via the FY 2019 ADUFA and AGDUFA performance reports

[57] Represents FDA's preliminary performance for FY 2018 cohort submissions. Final performance will be available via the FY 2019 ADUFA and AGDUFA performance reports

224222: Percentage of Human and Animal Drug follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2019: 68.8% Target: 55% (Target Exceeded)	55%	55%	Maintain

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

New Animal Drug Application Review

CVM exceeded all ADUFA performance goals for 15 years, except for two submissions, and all AGDUFA performance goals for 10 years, except for one submission. In FY 2018, CVM completed review and action on 100 percent of original NADAs as well as other ADUFA sentinel submissions within the timeframes specified and completed review and action on 100 percent of original ANADAs as well as other AGDUFA sentinel submissions within the timeframes.

Warning Letters

FDA monitors marketed animal drugs, food additives, and veterinary devices to assure their safety and effectiveness. Warning Letters are issued when firms are found to be in violation of the FD&C Act. Violators are encouraged to take prompt action to correct violations; otherwise FDA may take additional regulatory action without further notice, including seizure of products and/or injunction. The resources required to review each Warning Letter may vary greatly, depending on the subject matter and evidence, and some Warning Letters require additional input, clearance and time to process. In FY 2019, CVM saw an increase in the complexity of novel warning letters that required extensive legal review by CVM staff as well as the Office of Chief Counsel which contributed to missing the target of 50% within 25 days. However, now that the legal groundwork has been completed, and new operating procedures have been established to handle the novel cases, CVM still expects to meet the performance targets for FY 2020 and FY 2021.

ORA Field Performance Measures

ORA's performance goals 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 & Feeds Program Activity Data (PAD)

CVM Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
New Animal Drug Applications (NADAs) [1]			
Received	14	22	23
Completed	15	21	23
Approved	13	17	19
Pending [2]	14	13	13
New Animal Drug Application Supplements [1,3]			
Received	685	750	750
Completed	648	700	740
Approved	569	550	600
Pending [2]	194	273	283
Abbreviated New Animal Drug Applications (ANADAs) [1]			
Received	40	26	27
Completed	36	23	27
Approved	31	18	19
Pending [2]	15	22	22
Abbreviated New Animal Drug Application Supplements [1,3]			
Received	257	300	315
Completed	288	290	300
Approved	204	215	200
Pending [2]	120	261	276
Investigational New Animal Drug (INAD) Files [4]			
Received	2,996	3,000	3,000
Completed	3,019	2,900	3,000
Pending [2]	383	426	426
Generic Investigational New Animal Drug (JINAD) Files [4]			
Received	638	670	690
Completed	754	640	650
Pending [2]	105	190	230
Food (Animal) Additive Petitions Completed	46	80	100
Investigational Food Additive Petitions Completed	63	90	110
Adverse Drug Event (ADE) [5]			
ADE Reports Received	100,995	105,000	110,000
Post-Approval ADE Data Reviews	159	170	170

[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 & Feeds Program Activity Data (PAD)

Field Animal Drugs and Feeds Program Workload and Outputs	FY 2019 Actuals			FY 2020 Estimate			FY 2021 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	***1,385***	***165***	***1,220***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	52	52	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	119	119	0	175	175	0	175	175	0
BSE Inspections	456	0	456	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	2	0	2	25	0	25	25	0	25
Illegal Residue Program Inspections	333	0	333	450	0	450	450	0	450
Feed Manufacturing Program Inspections	209	0	209	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,267	1	1,266	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***90***	***52***	***38***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	17	17	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	40	40	0	33	33	0	33	33	0
Foreign Feed Inspections	3	0	3	5	0	5	5	0	5
BSE Inspections	4	0	4	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,475***	***217***	***1,258***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	2,808	821	1,987	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	897	1	896	867	2	865	867	2	865
Import Physical Exam Subtotal	**3,705**	**822**	**2,883**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	481,684	71,447	410,237	479,518	69,181	410,337	503,494	72,640	430,854
Percent of Import Lines Physically Examined	0.77%	1.15%	0.70%	0.97%	0.72%	1.02%	0.93%	0.68%	0.97%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***2,128***	***0***	***2,128***	***3,396***	***0***	***3,396***	***3,396***	***0***	***3,396***
State Contract Inspections: BSE	1,020	0	1,020	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	525	0	525	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	0	0	0	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	$3,458,757	0	$3,458,757	$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	**$3,458,757**	**$0**	**$3,458,757**	**$3,470,824**	**$0**	**$3,470,824**	**$3,574,949**	**$0**	**$3,574,949**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***3,606***	***217***	***3,389***	***5,134***	***367***	***4,799***	***5,134***	***367***	***4,799***

1 The FY 2019 actual unique count of foreign inspections includes 10 OIP inspections (4 for China and 6 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.

DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Devices and Radiological Health	**577,113**	**521,951**	**599,940**	**638,529**	**38,589**
Budget Authority	***387,168***	***386,733***	***395,168***	***415,828***	***20,660***
User Fees	***189,945***	***135,218***	***204,772***	***222,701***	***17,929***
Center	475,873	423,376	501,296	540,190	38,894
Budget Authority	302,163	301,738	310,163	331,393	21,230
User Fees	173,710	121,638	191,133	208,797	17,664
Prescription Drug (PDUFA)	*1,460*	*1,834*	*4,162*	*4,302*	*140*
Medical Device (MDUFA)	*165,815*	*113,370*	*180,073*	*197,459*	*17,386*
Mammography Quality Standards Act (MQSA)	*6,435*	*6,434*	*6,898*	*7,036*	*138*
Field	*101,240*	*98,575*	*98,644*	*98,339*	*-305*
Budget Authority	85,005	84,995	85,005	84,435	-570
User Fees	16,235	13,580	13,639	13,904	265
Medical Device (MDUFA)	2,240	1,800	2,358	2,398	*40*
Mammography Quality Standards Act (MQSA)	*13,995*	*11,780*	*11,281*	*11,506*	*225*
FTE	**2,120**	**2,120**	**2,302**	**2,345**	**43**

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. The Devices Program oversees development of new devices that make less-invasive treatments possible and provide new options to patients whose conditions would have been considered untreatable in the past – all while providing the assurances patients depend upon and meeting FDA's standards. The foundation of this program is medical device safety.[58]

There are 190,000 different types of medical devices on the U.S. market, manufactured at 21,000 facilities worldwide. FDA's CDRH has 1,700 dedicated employees who oversee these devices,

[58] The FDA's 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.

and handle over 20,000 submissions each year – including meeting requests – as well as reviewing over a million medical devices (adverse event/malfunction) reports. CDRH carefully reviews medical devices to assure that they meet FDA's high standards for safety and effectiveness. The Center approves or clears, on average, 12 new or modified devices every business day, authorizing and clearing thousands of products for entry into the market. This is all while promoting access, enhancing safety, and advancing innovation.

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, laser surgical devices, and artificial intelligence technologies that help with earlier detection of diseases and conditions, 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 9 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, allows FDA to act to protect patients, 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 advances innovation of high-quality, safe and effective medical devices to meet patient needs, and consistently works to protect patients and enhance safety. We are equally committed to advancing safe and effective products that can address unmet medical needs to reduce the health effects from disease. Both objectives are essential to meeting our public health mission, resulting in more lives saved and improved quality of life. 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.

To meet these objectives, the Devices program applies a total product lifecycle approach, and ensures manufacturers have a better understanding of the requirements for devices to come to market in the United States. FDA has been focused on taking steps to better clarify requirements– to better communicate about the evidence needed to demonstrate regulatory standards for marketing. 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.

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. This work has helped to reduce the time and cost of the total product life cycle of medical devices. Ultimately, CDRH's efforts better serve the needs of patients, who are at the heart of everything the Devices Program does.

The Devices Program's recent accomplishments demonstrate this ongoing commitment to improving the safety and quality of life for patients:

- Reduced the medium 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 2019.
- In September 2019, FDA announced the Safer Technologies Program for Medical Devices to promote innovation in medical devices that help advance patient safety.
- On August 2019, approved a breakthrough device for the improvement of symptoms in patients with advanced heart failure who are not suited for treatment with other heart failure devices.

CDRH's success in providing patients with new treatments and diagnostics, and more options for effective health care, are not coming at the expense of the robust non-clinical and clinical science on which we rely to make our regulatory decisions. For example, due in part to our efforts to strengthen the clinical trial enterprise and leverage real world data, in some cases we're receiving clinical evidence more quickly and more efficiently and answering postmarket questions we would not have been able to easily address in the past.

The Devices Program strategic priorities support these ongoing efforts to achieve its vision. For 2018-2020, these strategic priorities are:

- 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.

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.

Strengthen Science and Efficient Risk-Based Decision Making

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

Medical device safety remains a high priority for the FDA and the Agency remains focused on protecting patients' health by taking appropriate action when necessary, while also keeping the public informed of new risks. 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.

Artificial Intelligence

Artificial intelligence and machine learning have the potential to fundamentally transform the delivery of health care. As technology and science advance, we can expect to see earlier disease detection, more accurate diagnosis, more targeted therapies and significant improvements in personalized medicine.

On April 2, 2019, FDA announced steps toward a new regulatory framework specifically tailored to promote the development of safe and effective medical devices that use advanced artificial intelligence algorithms. The ability of artificial intelligence and machine learning software to learn from real-world feedback and improve its performance is spurring innovation and leading to the development of novel medical devices.

The goal of the framework is to assure that ongoing algorithm changes follow pre-specified performance objectives and change control plans, use a validation process that ensures improvements to the performance, safety and effectiveness of the artificial intelligence software, and includes real-world monitoring of performance once the device is on the market to ensure safety and effectiveness are maintained. We're exploring this approach because we believe that it will enable beneficial and innovative artificial intelligence software to come to market while still ensuring the device's benefits continue to outweigh it risks.

National Evaluation System for health Technology (NEST)

The FDA is collaborating with stakeholders in the medical device ecosystem to build the National Evaluation System for health Technology (NEST) to more efficiently generate better evidence for medical device evaluation and regulatory decision-making. NEST will generate evidence across the total product lifecycle of medical devices by strategically and systematically leveraging real-world evidence and applying advanced analytics to data tailored to the unique data needs and innovation cycles of medical devices.

The collaborative national evaluation system will link and synthesize data from different sources across the medical device landscape, including clinical registries, electronic health records and medical billing claims. A national evaluation system will help improve the quality of real-world evidence that health care providers and patients can use to make better informed treatment decisions and strike the right balance between assuring safety and fostering device innovation and patient access.

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 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) 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.
- 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 post-market 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.[59]

Focus on Women's Health

FDA has been working towards a better understanding of how medical devices perform in women and exploring unique issues in the regulation of medical devices related to the health of women. The Devices Program created the Health of Women Program specifically to address the steadily growing importance of sex-and gender-specific issues arising regarding medical technology design and development, clinical and non-clinical study design, and other medical device-related matters. The Devices Program also released the CDRH Health of Women Program Strategic Plan, which is open for public comment until December 23, 2019.

FDA has been working with health professional organizations, patient groups and others to establish the Health of Women Technologies Coordinated Registry Network to better evaluate and monitor devices used specifically for women. The Devices Program also held a public advisory committee meeting in November 2019 to discuss metal-containing implants and dental amalgam, which fostered public dialogue and review of the scientific evidence about immunological responses to select metals in devices, including their impact on women's health.

Advancing Consensus Standards

Consensus standards, which are developed in cooperation with a variety of stakeholders play an increasingly prominent role in ensuring that medical devices are safe and effective.

The Devices Program is expanding our already robust standards program to include a new pilot program called the Accreditation Scheme for Conformity Assessment, or ASCA. The pilot program, which is outlined in the ASCA draft guidance released on September 20, 2019, is intended to advance regulatory science in a way that could help ensure safe, effective and high-

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

quality medical devices are available to patients while reducing unnecessary delays that could preclude patient access to new and innovative devices.

Under the ASCA Pilot, the FDA would recognize qualified accreditation bodies who would accredit testing laboratories using ASCA program specifications associated with eligible consensus standards included in the Pilot. The Devices Program would recognize and grant ASCA Accreditation to qualified testing laboratories. Manufacturers could then work with these ASCA-accredited testing laboratories to perform testing to the standards included in the ASCA Pilot and use those test results to support premarket submissions to FDA.

In this way, reliance upon ASCA-accredited testing laboratories' results may increase the consistency, predictability and efficiency of the FDA's review of premarket submissions by streamlining the premarket review process while maintaining FDA's standards.

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

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, where appropriate, when they seek to bring new devices to patients.

To support modernization of the 510(k) pathway, FDA finalized guidance on the voluntary Safety and Performance Based Pathway which expands the approach long applied through the Abbreviated 510(k) Program. Under the Safety and Performance Based Pathway, a manufacturer would have the option to demonstrate aspects of substantial equivalence by showing that a new device meets FDA-identified performance criteria that reflect current technological principles and the safety and performance of modern predicate devices.

The Devices Program's goal in finalizing this pathway is to expand its use broadly across the 510(k) program. This modern framework is a direct and transparent approach to demonstrating the safety and effectiveness of low to moderate risk devices. This alternative pathway 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, this new approach 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.

Rather than looking to the past as a baseline for safety and effectiveness – and rely on predicate devices that are sometimes decades old – the Devices Program premarket review would be based on contemporary baseline. It is also expected that scientifically sound criteria can be updated as technology advances. In some cases, relying on old predicates makes 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 will help ensure new products can more easily reflect beneficial new advances.

Safer Technologies Program for Medical Devices

In September 2019, FDA announced the Safer Technologies Program for Medical Devices (STeP), which is a pilot voluntary program for certain medical devices that are reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target an underlying disease or condition associated with morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program.

The Safer Technologies Program for Medical Devices is intended to help ensure that we're giving patients timely access to safe, effective and high-quality medical devices by expediting their development, assessment and review, and by facilitating the generation of the robust evidence required to support product marketing authorizations. Spurring innovation to develop safer, more effective devices and devices that address unmet needs can also mean patients have safer options for the treatment of their conditions. Such advances should lead to more lives saved, fewer adverse events, and improved quality of life.

The Devices Program envisions that these two programs, Breakthrough and STeP, would be two different pathways—one for new devices to treat or diagnose life-threatening or irreversibly debilitating diseases or conditions that address an unmet medical need and one for devices that treat less serious conditions and innovate on safety. Still, they could have similar impact in spurring the development of and giving patients more timely access to important medical devices. If the same programmatic benefits that encourage device manufacturers to create devices to treat or diagnose a life-threatening disease could be applied to bring innovation to medical device safety for less serious conditions, the potential public safety impact could be tremendous.

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.

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.

Cybersecurity

Many medical devices include computer software either embedded or external to the device. For example, a heart pacemaker includes computer code to set the rhythm of the heart. There is a concern, that, similar to your personal computer, the software in these devices can be infected with malware (a "computer virus") that changes performance of the device. Other examples are

hacking of the device's computer code by third parties or leakage of personal health information from these devices.

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.

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.

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.

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 2019, over 80 percent of mammography facilities had no serious violations of the law and less than 1 percent of facilities were cited with the most serious violations. These MQSA-certified facilities provide nearly 39 million mammography procedures annually in the U.S.

The 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.

On March 27, 2019, FDA announced important new steps to modernize breast cancer screening and help empower patients with more information when they are considering important decisions regarding their breast health care. The agency proposed amendments to key regulations that would help improve the quality of mammography services for millions of Americans. These actions, if finalized, would expand the information mammography facilities must provide to patients and health care professionals, allowing for more informed medical decision-making. It would also modernize mammography quality standards and better position the FDA to enforce regulations that apply to the safety and quality of mammography services.

Among the proposed amendments to improve communication and medical decision making is the addition of breast density information to the mammography lay summary letter provided to patients and to the medical report provided to their referring health care professionals. Mammograms of dense breasts—breasts with a higher proportion of fibroglandular tissue compared to fatty tissue—can be difficult to interpret because the dense tissue can obscure signs of breast cancer and lower the sensitivity of the image. Dense breasts have also been identified as a risk factor for developing breast cancer. The FDA is proposing specific language that would explain how breast density can influence the accuracy of mammography and would recommend patients with dense breasts talk to their health care provider about high breast density and how it relates to breast cancer risk and their individual situation.

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, and public safety notices. On March 29, 2019, FDA proposed amendments to its regulations of electronic product reporting to better align the medical device and radiological health programs by reducing overlapping requirements.

Recent successes also include engaging with Customs and Border Protection and major online distributors to identify and prevent sale of non-compliant products, preparing outreach material to proactively engage industry and new manufacturers with information on basic safety requirements, and coordinating with the Office of Regulatory Affairs to enhance the success of inspections.

Participation in consensus standards development is a key component of the radiological health program, both to address safety issues and incorporate performance requirements and testing methods that are standard worldwide. Recent standards successes include incorporation of pediatric safety features in standards for computed tomography (CT), fluoroscopy, and general and dental radiography. In May 2019, FDA published four guidance documents that leverage the use of consensus standards to help modernize the regulatory oversight of diagnostic x-ray equipment and laser products.[60]

Case for Quality

The Devices Program advanced manufacturing and product quality through its Case for Quality Voluntary Improvement Program (CfQVIP) 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.

The CfQVIP pilot launched in January 2018, and 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). Participating companies have reported that the appraisal has helped them to develop operational excellence and metrics that will help assure better quality of their products.

Current Pilot Results include the following:

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

- CDRH has received more than 60 modified 30-Day Change notices. The pilot target was to reduce the review time from 30 days to 5 business days. To date 73% of the submissions were reviewed in less than 5 days with an average review time of 3.2 days.
- 37% of the manufacturing changes accepted were to directly improve product quality and were reviewed 21 days faster.
- 18% of the manufacturing changes were to error-proof manufacturing processes and eliminate causes of defects. Those changes were reviewed and accepted 21 days faster.
- Faster rate of 30-Day Change acceptance has resulted in product quality improvements and savings ranging from $32,000 to $286,000 per change for industry participants.
- Increased production capabilities have improved U.S. access and resulted in additional sales revenue that ranged from more than $10 million to $28 million dollars for industry participants.

In addition, participating companies have reported that the pilot and the quality provide increased value in targeting the improvements relevant to their company to increase device quality. For example, manufacturers have used the benchmarking provided by the pilot to identify gaps in various sites and implement the practices from the higher performing locations. This has increased product quality and yield in various locations. One manufacturer also reported identifying a product issue that had gone undetected and implemented a recall and internal improvement before a safety issue occurred.

Reduce the Burden of Addiction Crisis that are Threatening American Families

Devices to Prevent and Treat Opioid Use Disorder Challenge

FDA understands that medical devices will play a critical role in the agency's all hands on deck approach to confronting the opioid crisis. We believe the greatest opportunities for medical devices to address this crisis are to 1) identify patients at risk for OUD before they receive opioids, 2) manage pain to either reduce or replace opioid use, 3) prevent diversion or abuse of prescribed opioids, 4) foster development of non-opioid treatment options for OUD.

For example, the development of a diagnostic device, whether it be an *in vitro* diagnostic test or a mobile medical app, could be highly impactful in identifying those patients for whom extra caution should be exercised when considering prescribing opioids for acute or chronic pain.

In the past few years CDRH has cleared, granted, or approved more than 200 devices related to the treatment or management of pain, including 10 with new or novel technologies. Those novel devices may reduce the need to administer opioid drugs to patients suffering from either acute or chronic pain.

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

Between 2016 and 2019, 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.

Over the last year, FDA has seen a significant increase in the utilization of sprints by sponsors to address device development challenges, enable flexible clinical study designs and capitalize on FDA review team support and senior management engagement so that review of the innovative device will occur more efficiently. FDA received more breakthrough designation requests at the close of FY 2019 than received in FY 2018, which was twice as many received requests than in all of 2017.

For example, in FY 2018 FDA authorized a PMA for the OPTIMIZER Smart System manufactured by Impulse Dynamics which had previously received breakthrough device designation. This innovative device is an implantable pulse generator that delivers a novel form of electrical stimulation, known as Cardiac Contractility Modulation therapy, to patients with NYHA Class III heart failure who cannot receive cardiac resynchronization therapy.

On December 18, 2018, The Breakthrough Devices Program Final Guidance was issued describing a voluntary program for certain medical devices and device-led combination products that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. This program is intended to help patients have more timely access to these medical devices by expediting their development, assessment, and review, while preserving the statutory standards for marketing authorization, consistent with the Agency's mission to protect and promote public health.

Medical Device Development Tools (MDDT) program

One important action the FDA has taken to achieve this goal is the creation of the Medical Device Development Tools (MDDT) program at the Center for Devices and Radiological Health (CDRH). This program streamlines the medical device development and review process by advancing the development and use of scientifically validated and qualified methods, materials, and measurements for assessing how devices works.

Having a qualified tool means that product evaluation can be done more predictably and efficiently by providing innovators with the tools and techniques that FDA has found to be acceptable for their purposes. This can eliminate much of the risk and uncertainty developers often experience in product development, and helps bring high-quality, safe and effective devices to patients.

Predictability also has important implications for the timeliness of the development process. It can help accelerate any phase of the development of a new therapy or diagnostic, from the rapid screening of prototypes to streamlining clinical trial enrollment. In each case, it provides developers with greater confidence in the FDA's ability to review the data more accurately and quickly and avoiding unnecessary questions.

Before creation of the MDDT program, tools used by developers were evaluated on case-by-case basis — for each medical device submission. This added uncertainty, delay and inconsistency to the process, as well as additional costs and time to innovators and the FDA. That can now be largely averted, and FDA is looking to expand the program to as many areas as possible.

The use of a qualified tool also allows FDA regulators to concentrate on the most important aspects of the process and ensure that the end products are developed in a safe and timely manner. And, by qualifying tools for a specific use, the FDA facilitates their application for multiple medical device submissions and manufacturers, delivering greater efficiency and consistency to the community.

High Intensity Ultrasound Device Qualification Supports Greater Predictability and Reliability

One way to understand the importance of MDDTs is to consider the recent qualification by the FDA of a tool for High Intensity Therapeutic Ultrasound (HITU) Devices. Ultrasound has a long history as a medical device, with investigative products dating back to the 1940s. The ability of diagnostic ultrasounds to image in real-time, combined with its excellent safety record and modern-day portability, have led to its prominence worldwide. Recently, the development and use of new technologies in this field, such as HITU as a minimally-invasive therapeutic tool, have been accelerating. These new uses represent promising advances for patients, but they also require precision to use them safely and effectively to achieve the desired effects.

In response to these developments, FDA scientists have developed a material that can be used to mimic the behavior of tissue in a laboratory so that the effects of novel HITU devices and approaches can be assessed in a more reliable and predictable way. The mimic, known as a phantom, has recently been qualified as a MDDT. Device developers can now use this MDDT to help test the safety of their HITU device before exposing human patients in clinical studies. Understanding how their device performs early in development allows developers to improve a device's safety and make other modifications before moving to the next phase of development so those devices can be as safe as possible when they reach the market.

Empower Consumers and Patients

Patient and Caregiver Connection

The Patient and Caregiver Connection is a partnership that provides CDRH staff with broad and timely access to patient and caregiver experiences. Partner organizations will collect feedback specific issues from their members and share that feedback with CDRH. This patient feedback on the impact of the medical condition on individual patients can help provide a rich context for regulatory decision-making. CDRH developed the Patient and Caregiver Connection to obtain three types of patient feedback that can give context to the Center's regulatory activities:

- Patients' experiences living with their specific condition
- Patients' experiences with devices used for the diagnosis, treatment, or management of their condition
- Current issues or trends related to medical devices that they use or may be treated with

The program is designed to broaden CDRH staff exposure to patients' viewpoints, but not to provide policy advice, recommendations, or opinions. For example, staff may draft questions for patients, caregivers, or both, and the Partner Organizations in the Patient and Caregiver Connection will disseminate questions or surveys to their membership and collect responses. The Partner Organizations will aggregate the responses and share them with FDA, assuring no personally identifying information is included.

The feedback obtained will provide broader context and better understanding of the patient experience for FDA staff to consider throughout the course of their work. This information could also provide insights that could be useful in medical device design, clinical studies to evaluate medical devices, and post-market medical device safety monitoring and product refinement.

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.

On September 2019, FDA released final guidance Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act. This guidance provides FDA's current thinking regarding the amended device definition and the resulting effect the amended definition related to medical device software.

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.

Digital Health Software Precertification (Pre-Cert) Program

Pre-Cert is a more holistic approach to evaluating a product's safety and effectiveness. The FDA would assess both the software developer's ability to produce safe products during an organizational Excellence Appraisal and the safety of individual products during the premarket submission review process. The goal of the Excellence Appraisal is for developers to have a proven record of ensuring that their products on the market are safe or to have demonstrated that they have established strategies in place to deliver high-quality products that are consistently safe and effective.

Our digital health team has been working with patients, providers, the nine diverse companies participating in the Pre-Cert pilot program, and other stakeholders to build the software precertification framework. The Software Precertification (Pre-Cert) Program's aims are to:

- Benefit a participating organization based on its "precertified" status by offering the ability to participate in a streamlined premarket review and opportunities to collect and leverage real-world postmarket data, which encourages innovation, timely patient access, and safety and effectiveness over the product life cycle.
- Leverage and use information and data from all available sources allowing FDA and SaMD manufacturers to be more efficient and streamlined without compromising safety and effectiveness of SaMD products.
- Enable a modern and tailored approach that allows software iterations and changes to occur in a timely fashion under appropriate controls.
- Ensure high-quality software products throughout the life of the product by enabling companies to demonstrate their embedded culture of quality and organizational excellence and ability to monitor real-world performance.
- Adapt key elements and measure based on the effectiveness of the program.

Since the FDA released the Test Plan in January 2019, we have been actively analyzing test cases and working with pilot participants, with the primary intent to confirm the framework proposed in the Working Model v1.0 provides an equivalent reasonable assurance of safety and effectiveness for software products as compared to the traditional review pathway. While testing is underway, the FDA is committed to a collaborative and transparent Pre-Cert development process.

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.

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.

In December 2019, FDA formally recognized a public database, Clinical Genome Resource (ClinGen) consortium's ClinGen Expert Curated Human Genetic Data, which is funded by the National Institutes of Health (NIH), as a source of valid scientific evidence that can be used to support clinical validity in premarket submissions. This recognition by the FDA will facilitate test developers, including those that use next generation sequencing, to rely on the information available in the database to support the validity of their tests, instead of having to generate the information on their own.

Collaborative Communities

Collaborative communities are 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. Collaborative communities are equipped to perform activities such as developing best practices and robust strategies for addressing challenges; generating and evaluating evidence that supports novel approaches; and disseminating and implementing solutions.

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. The communities may also work to clarify ill-defined challenges or generate consensus on the definition and scope of the challenge which will aid in tailoring appropriate strategies to tackle those challenges. By leveraging the wide variety of resources, power and expertise of the community members, collaborative communities can help address challenges and opportunities related to medical devices.

In the next two years, the Devices Program will make building collaborative communities a standard practice. For example, on September 19, 2019, the Devices Program announce our participation as members in the first two collaborative communities: NEST Coordinating Center (NESTcc) Collaborative Community and the Ophthalmic Imaging Collaborative Community. FDA firmly believe in the opportunities offered by participating in collaborative communities, and we recognize that we serve the American public better when stakeholders in the medical device ecosystem, including the FDA, work together.

In addition, The Collaborative Communities Toolkit was published in September 2019, which serves as a collection of materials to help prospective communities in their development and effective collaboration, so that they are adequately prepared to take on health care challenges. Each component of this toolkit could help members of both new and existing communities work with one another. Collaborative Communities can contribute to improvement in areas affecting U.S. patients and healthcare and result in wide-ranging benefits for public health.

International Harmonization to Improve Efficiency and Patient Access to High-Quality, Safe and Effective Medical Devices

CDRH has been a world leader in harmonizing review and oversight practices. The Center is a founding member of the International Medical Device Regulators Forum (IMDRF). IMDRF is a group of medical device regulators from around the world that have voluntarily come together to harmonize the regulatory requirements for medical products that vary from country to country.

The current IMDRF members represent medical device regulatory authorities in: Australia, Brazil, Canada, China, Europe, Japan, Russia, Singapore, South Korea, and the United States. The World Health Organization (WHO) is an Official Observer. The Asia Pacific Economic Cooperation (APEC) Life Sciences Innovation Forum's (LSIF) Regulatory Harmonization Steering Committee, the Asian Harmonization Working Party (AHWP), and the Pan American Health Organization (PAHO) are Regional Harmonization Initiatives with IMDRF.

IMDRF develops internationally agreed upon documents related to a wide variety of topics affecting medical devices. The FDA works collaboratively with patients, industry and other members of the medical device ecosystem to implement harmonized concepts and help assure that safe and effective medical devices are available to patients in the U.S. and globally.

Medical Device Single Audit Program (MDSAP)

The Devices Program is also a founding member of the Medical Device Single Audit Program (MDSAP). MDSAP is an international coalition of trusted regulatory authorities working together to eliminate the need for multiple medical device manufacture audits and inspections. CDRH participates in this international harmonization effort with its regulatory counterparts from Australia, Brazil, Canada and Japan. The 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.

The MDSAP program saw dramatic growth in medical device firm participation over fiscal years 2017-2019, from approximately 527 firms by the end of FY2017 to 4,866 at the end of FY2019. Because participating facilities are required to be audited at least annually through MDSAP, FDA is able to remove these establishments from our annual inspection work plan without losing confidence that they were being evaluated to ensure compliance.

In FY2019, the MDSAP consortium announced a new MDSAP Affiliate Membership category for other regulatory authorities. Participation in the Affiliate membership allows regulatory authorities in other countries the ability to receive MDSAP information from participating regulatory authorities, while utilizing MDSAP audit reports for regulatory purposes. Since announcement of the Affiliate Membership in June 2019, regulatory authorities from Argentina, Colombia, Mexico, Saudi Arabia, South Korea, and Venezuela have expressed interest in joining MDSAP as Affiliate Members.

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 high quality, safe and effective for patients.[61]

Date	Docket#	Title	Description
Sep 2019	FDA-2019-D-3805	The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program	Draft Guidance describing a new pilot program designed to increase consistency and predictability in the FDA's approach to assessing conformance with ASCA-eligible standards in medical device premarket reviews.
June 2019	FDA-2017-D-5372	Marketing Clearance of Diagnostic Ultrasound Systems and Transducers: Guidance for Industry and Food and Drug Administration Staff	This guidance provides recommendations for manufacturers seeking marketing clearance of diagnostic ultrasound systems and transducers, including certain well understood types of modifications to a diagnostic ultrasound device for which FDA does not intend to enforce the requirement for a new premarket notification (510(k)), which will allow FDA to focus resources on more innovative device modifications.
Feb 2019	FDA-2017-D-6702	The Least Burdensome Provisions: Concept and Principles: Guidance for Industry and FDA Staff	This guidance describes the guiding principles of the "least burdensome" approach, that is, the minimum amount of information necessary to adequately address a relevant regulatory question or issue through the most efficient manner at the right time.
Feb 2019	FDA-2018-D-1387	Safety and Performance Based Pathway: Guidance for Industry and Food and Drug Administration	This guidance describes an optional pathway for certain, well understood device types, where a submitter would demonstrate that a new device meets FDA-identified performance criteria to demonstrate that the device is as safe and effective as a legally marketed device.
Dec 2018	FDA-2015-D-5966	Breakthrough Devices Program: 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).
Oct 2018	FDA-2018-D-3443	Content of Premarket Submissions for Management of Cybersecurity in Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff	This guidance provides updated recommendations regarding cybersecurity device design, labeling, and the documentation to be included in premarket submissions for devices with cybersecurity risk, to facilitate an efficient premarket review process and help ensure that marketed medical devices are sufficiently resilient to cybersecurity threats.

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
Nov 2019	MiSight Soft Contact Lenses	the first contact lens indicated to slow the progression of myopia (nearsightedness) in children between the ages of 8 and 12 years old at the initiation of treatment.
Aug 2019	Vertebral Body Tethering System	First of its kind device to treat pediatric patients with progressive idiopathic scoliosis.
Aug 2019	Barostim Neo System	A new. breakthrough device for the symptoms associated with advanced heart failure.
Jun 2018	MiniMed 670G hybrid closed looped system	Expanded approval of this device that monitors glucose and automatically adjusts the delivery of long acting or basal insulin to include people with diabetes who are as young as age 7.
Jun 2018	The Reset application	First of its kind mobile medical app to help treat substance use disorders (SUD).
May 2018	Imagen Technologies Inc's OsteoDetect	Artificial Intelligence (AI) Software to help providers detect wrist fractures more quickly and aid in the diagnosis of fractures.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$521,951,000	$386,733,000	$135,218,000
FY 2020 Enacted	$599,940,000	$395,168,000	$204,772,000
FY 2021 President's Budget	$638,529,000	$415,828,000	$222,701,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Devices and Radiological Health Program is $638,529,000, of which $415,828,000 is budget authority and $222,701,000 is user fees. The budget authority increases by $20,660,000 compared to the FY 2020 enacted level. User Fees increase by $17,929,000. The Center for Devices and Radiological Health (CDRH) amount in this request is $540,190,000. The Office of Regulatory Affairs (ORA) amount is $98,339,000.

FDA's focus on both safety and innovation stems from the Agency's historic mission to both protect and promote public health by assuring timely patient access to devices that are high-quality, safe and effective technologies that make less-invasive treatments possible and provide new options to patients whose conditions would have been considered untreatable in the past. Spurring innovation to develop safer, more effective devices is key to improving patient safety. The FDA is committed to advancing medical device innovation that can address unmet medical needs to reduce or prevent the adverse health effects from disease, while maintaining FDA's standards. FDA is equally committed to detecting and addressing safety risks earlier, to protect patients from harm and ensure that the Agency remains consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices. Both objectives are essential to meeting FDA's public health mission, resulting in more lives saved and improved quality of life.

The FY 2021 President's Budget Request enables the Devices Program to continue to make advances in patient safety and in the diagnosing, monitoring, and treatment provided by new devices that patients need, while enhancing safeguards at the same time. This means patients in the U.S. have access to the safe, new, high-quality devices they need to improve and extend their lives, which helps to improve the health care system in the U.S. overall.

The Devices Program continues to see 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 can understand and meet the FDA's standard. Changes in the Devices Program policies and processes have resulted in an improved medical device pipeline and innovative, safe and effective technologies.

The success of FDA in providing patients with new treatments and diagnostics, and more options for effective health care, does come at the expense of the robust non-clinical and clinical science on which FDA can rely on to make our regulatory decisions. Rather, they are due in part to FDA efforts to strengthen the clinical trial enterprise and leverage real world data. The devices program has taken actions to make evidence generation more timely, efficient and robust. In some cases, FDA is receiving clinical evidence that is more informative and more quickly and efficiently answering postmarket questions FDA would not have been able to address in the past.

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 2021 funding will enable the Devices Program to continue to support such critical advances for patients. 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 ($18.5 million/ 5 FTE)

Transform Medical Device Safety, Cybersecurity, Review, and Innovation: $18.0 million/ 4 FTE

Center: $18.0 million / 4 FTE

Innovative and complex device technologies have been driving a revolution in health care. FDA's ability to continue facilitating development of innovative, breakthrough technologies that meet its rigorous standards, and to identify, detect, and address safety signals earlier and protect patients is dependent on FDA's ability to collect and analyze good quality data – to do this, it is necessary for FDA to have a capable, modern IT system. Unfortunately, FDA's information technology systems, tools, and approaches are outdated and not designed to support our increasing cybersecurity needs and evolving technology.

Funding for the Devices Programs IT systems will allow for necessary technology modernization which will enable further creation of an integrated device innovation platform that will make the review of device applications, postmarket surveillance and detection of safety issues, and cybersecurity efforts significantly more efficient and informative. This is critical to help support shorter review cycles, the ability to more quickly identify and address safety signals and cyber vulnerabilities, and overall 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 slow the regulatory process and limit FDA's ability to make better informed decisions, support new product developments, mitigate cybersecurity threats, address safety issues for patients, 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. This existing IT infrastructure is time-consuming to use, has increasing maintenance costs, and is 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. Having so many disconnected data systems also increases the time for staff to analyze adverse event information and detect safety signals for particular devices.

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 efficiently. Patients are far better served when FDA's experts are focused on assuring the safety and effectiveness of devices, rather than navigation of outmoded technology. Digital Transformation would 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. This will enhance decision making and reduce inefficiencies.

Specifically, funding for Digital Transformation will enable FDA to build an integrated knowledge management system and portal using modern, agile information technology systems with secure cloud-based data storage. The investment will enable safety issues to be monitored throughout 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 and issues that arise during the premarket review process or are observed postmarket, 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, postmarket surveillance, 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, and providing patients more clear information about the benefits and risks of medical devices. 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 that includes appropriate safeguards for patients, 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. 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.

Modernizing Influenza Vaccines: +$0.5 million / 1 FTE

Center: +$0.5 million / 1 FTE

The FY 2021 Budget Request includes $0.5 million towards activities related to Modernizing Influenza Vaccines. This includes increased review capacity to facilitate the development and availability of medical devices to support modernizing influenza vaccines.

Crosscutting Initiatives: ($2.2 million)

Artificial Intelligence: +5.0 million/ 10 FTE
Center: (+$5.0 million / 10 FTE)

AI in medical devices promises to drive growth of the United States economy and improve patient safety and our quality of life. AI algorithms are already being used to aid in screening for diseases and to provide treatment recommendations. The ability of AI and machine learning software to learn from real-world feedback and improve its performance is spurring innovation and leading to the development of novel medical devices. FDA has granted marketing authorization for several artificial intelligence-based devices – including a device for detecting diabetic retinopathy, a device for alerting providers of a potential stroke in patients, a device to help detect wrist fractures, and most recently, a tool that can read radiographic images to identify potential cases of pneumothorax. These new devices are enabling earlier detection of medical conditions and improving accessibility and quality of care, which can lead to more safe, innovative screening options for patients, the ability for earlier interventions to manage and cure diseases, and the potential for patients to have access to screening and diagnosis that they may not have otherwise.

The authorization of these technologies is a harbinger of things to come as more medical devices incorporate advanced AI algorithms to improve their performance and safety and create new functions. AI has helped transform industries like finance and manufacturing, and will have a similar impact on our health care system if FDA supports their responsible development and assures they are safe and effective for patients. For FDA to continue to lead the world in its approach for the smart regulation of these bold, new devices and to assure their safety and that they provide consumers and our health care system with optimal benefits, it is imperative that:

- these products are designed to be customer-friendly and able to be used and understood – particularly outside the traditional health care settings, and
- we ensure there are appropriate, consensus-based international standards to bring safe products to market in a predictable, efficient, transparent, and consistent manner.

Funding in these two areas will spur responsible development, and, most importantly, maximize their safety and utility for consumers.

To encourage breakthroughs in AI technologies in healthcare, it is critical that we develop appropriate technical standards and reduce unnecessary barriers. Standards play a significant role in the efficient design, manufacture, and regulation of medical devices and are critical to advance innovation, help ensure these technologies are high-quality, safe and effective, and foster consumer confidence worldwide. Establishing standards to address common safety and effectiveness issues for product types provides transparency and clarity on expectations to device manufacturers, and allows FDA to better focus resources on the unique characteristics of a device. As medical devices grow in complexity and as international markets expand, standards are a critical mechanism to safely facilitate artificial intelligence innovations and other digital health technologies in a way that assures patient safety, while streamlining and harmonizing international regulatory oversight.

FDA will establish a Standards Acceleration Team, applying advanced analytics and AI algorithms to develop the scientific basis for new or updated standards on a continuous basis, and fostering the adoption of modern standards by other countries. These actions will strengthen the science supporting consensus standards, ensuring that AI-medical devices are safe, effective, of high quality, and perform as intended. This will also drive more efficient risk-based decision making, foster competition and more efficient innovation for safe, new and established AI and other technologies that use AI/digital health capabilities, as well as advance international harmonization.

Considering the advances in AI in medical devices and the prevalence of consumer smart devices, there is tremendous opportunity to shift health care services to where patients live and work. This is critical to enabling access for patients, particularly those who may not easily be able to access services. The ability of AI/digital heath technology to fully realize their potential and supersede the constraints of traditional health care settings to this new user environment, however, cannot be achieved without safe and intuitive user interfaces. Patients need to be able to read and interpret information provided by these devices and use them as they are intended. Human factors engineering is therefore instrumental to the successful development of AI/digital heath technologies, as it helps inform the physical, cognitive, and psychological characteristics on the design of devices and systems for human use.

In response, FDA proposes building on the Agency's Digital Health Center of Excellence by creating a program that focuses specifically on advancing and promoting the development of consumer-friendly AI/digital health medical devices through improved device-user interfaces. In this way, these technologies will ultimately make health care interventions more precise and personalized to meet patient needs and preferences.

Increasing our capacity to develop standards for AI technologies that promote safe, effective, and consumer-friendly AI will generate positive outcomes for patients and reduce the overall cost of health care. These efforts will continue to encourage innovative AI technologies and foster moving technologies out of the hospitals and clinics and into the home environment thereby benefitting patients and modernizing health care delivery while creating enormous savings to the health care system. For example, AI user interfaces have the potential to expand the use of home dialysis for patients with end stage renal disease and provide a path towards destination left ventricular assist devices for patients with heart failure. In this way life-saving AI-based medical technologies can reach 330 million US citizens rather than just a small subset.

Outreach, Training, and Organizational Excellence: -$2.8 million
Center: -$2.3 million

The Devices Program will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. The Devices Program will preserve its most critical public health and safety activities under this reduction, including post-market surveillance activities, review of premarket applications and continuing to work to meet MDUFA performance commitments.

Field: -$0.6 million

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

CURRENT LAW USER FEES

Center: +$17.6 million / Field: +$0.3 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
253203: Percentage of received Original Premarket Approval (PMA), Panel-track PMA Supplement, and Premarket Report Submissions reviewed and decided upon. (Outcome)	FY 2017: 98% in 180 days Target: 90% in 180 days (Target Exceeded)	90% in 180 days	90% in 180 days	Maintain
253204: Percentage of 180 day PMA supplements reviewed and decided upon within 180 days. (Outcome)	FY 2017: 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 2017: 99% 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 2017: 67% in 150 days (Historical Actual)	60% in 150 days	65% 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)	FY 2019: 85.7% Target: 65% (Target Exceeded)	65%	65%	Maintain
252203: Percent of total received Code Blue MDRs reviewed within 72 hours during the year. (Output)	FY 2019: 88% Target: 90% (Target Not Met)	90%	90%	Maintain
254203: Percentage of time CDRH meets the targeted deadlines for on-time recall classification (Output)	FY 2019: 84% Target: 85% (Target Not Met)	85%	85%	Maintain

252101: Number of technical analyses of postmarket device problems and performance. (Output)	FY 2019: 58 Target: 50 (Target Exceeded)	50	50	Maintain
253207: Number of technical reviews of new applications and data supporting requests for premarket approvals. (Output)	FY 2019: 2,890 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 2019: 99.3% 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)	FY 2019: 89.1% Target: 80% (Target Exceeded)	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)	FY 2019: 81.7% Target: 65% (Target Exceeded)	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 2017, 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.

Code Blue MDR Review

Code Blue MDR reports represent the most serious adverse events received. The Agency strives to have all Code Blue MDRs read within 72 hours of receipt. CDRH did not meet the FY 2019 target of having 90% of the Code Blue reports read within 72 hours. In 2019 CDRH underwent a reorganization, aligning staff with product specialty areas supporting a devices' total product lifestyle (TPLC). In support of TPLC, many staff acquired new reviewer responsibilities, requiring additional training and learning curves. During the initial months of the reorganization the 72 hour target was not always met due to the inexperience of the new staff. However, since

May 2019 we have consistently met or exceeded the 90% target on a monthly basis and believe we will be able to continue to meet this metric.

Recall Classifications

When the FDA learns of a company's correction or removal action, we review the strategy the company proposes to address the problem, determine if the problem violates applicable law, assign the recall a classification (I, II, or III) to indicate the relative degree of risk and post the information for the public. We were at 89% in FY 2018 and now 84% at FY 2019 and the target has been 85%. In 2019 CDRH underwent a reorganization, aligning staff with product specialty areas supporting a devices' total product lifestyle (TPLC). In support of TPLC, many staff acquired new reviewer responsibilities, requiring additional training and learning curves. During the initial months of the reorganization the performance target was not always met due to the inexperience of the new staff. However, since FY 2020 we have seen a 20% increase in recall processing times and believe we will be able to meet performance metrics in the future. ORA Field Performance Measures

ORA's performance goals 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

CDRH Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
Original PMAs and Panel-Track Supplements (without Advisory Committee input)			
Workload [1]	56	63	63
Total Decisions [2]	63	63	63
Approved [3]	44	46	46
Original PMAs and Panel-Track Supplements (with Advisory Committee input)			
Workload	1	3	3
Total Decisions [2]	5	4	4
Approved	1	2	2
Modular PMAs			
Workload	92	85	85
Actions [4]	71	98	98
180-day PMA Supplements			
Workload	199	199	199
Total Decisions [5]	185	193	193
Approved	176	180	180
Real Time PMA Supplements			
Workload	380	353	353
Total Decisions [6]	354	337	337
Approved	314	311	311
510(k) Premarket Notifications			
Workload	3,161	3,754	3,754
Total Decisions [7] (SE & NSE)	3,044	3,293	3,293
Cleared [9] (SE)	2,927	3,143	3,143
Humanitarian Device Exemptions (HDE)			
Workload	6	4	4
Total Decisions [2]	5	3	3
Approved	3	2	2
Investigational Device Exemptions (IDE)			
Workload	313	315	315
Total Decisions [8]	311	309	309
Approved	161	162	162
Investigational Device Exemption Supplements			
Workload	1,827	1,825	1,845
Closures [10]	1,807	1,808	1,743
Pre-Submissions			
Workload	3,253	3,412	3,578
Closures [11]	3,228	3,385	3,724
De Novo			
Workload	62	61	61
Total Decisions [14]	52	50	50
Granted	29	25	25
Standards			
Total Standards Recognized for Application Review	1,385	1,385	1,410
Medical Device Reports (MDRs) [12]			
Reports Received	1,948,717	2,598,289	2,886,987
Analysis Consults [13]	535	590	590

[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 initial and supplemental 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 Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,244***	***2,546***	***2,498***
Bioresearch Monitoring Program Inspections	201	300	300
Pre-Market Inspections	29	60	60
Post-Market Audit Inspections	19	60	60
GMP Inspections	1,214	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA) [3]	785	750	700
Domestic Radiological Health Inspections	93	50	50
Domestic Field Exams/Tests	35	100	100
Domestic Laboratory Samples Analyzed	114	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***520***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	15	14	14
Foreign Pre-Market Inspections	35	30	30
Foreign Post-Market Audit Inspections	11	20	20
Foreign GMP Inspections	436	550	550
Foreign MQSA Inspections	12	14	14
Foreign Radiological Health Inspections	47	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***2,764***	***3,159***	***3,159***
IMPORTS			
Import Field Exams/Tests	25,035	19,800	19,800
Import Laboratory Samples Analyzed	582	670	670
Import Physical Exam Subtotal	**25,617**	**20,470**	**20,470**
Import Line Decisions	22,967,758	23,852,335	25,521,999
Percent of Import Lines Physically Examined	0.11%	0.09%	0.08%
STATE WORK [2]			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,449***	***7,880***	***7,880***
Inspections (MQSA) by State Contract [5]	7,402	7,800	7,800
GMP Inspections by State Contract	47	20	20
State Contract Devices Funding	$147,250	$270,000	$278,100
State Contract Mammography Funding	$10,586,300	$10,803,540	$11,019,611
Total State Funding	**$10,733,550**	**$11,073,540**	**$11,297,711**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,213***	***11,039***	***11,039***

[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.

[5] State MQSA Non-Contract inspections have been combined into the State Contract line.

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actauls	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
National Center for Taxological Research (Budget Authority).....	66,712	66,712	66,712	66,266	-446
FTE.....	276	276	276	276	---

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 393(b) (1)); Food and Drug Administration Modernization Act; Food and Drug Administration Amendments Act of 2007; FDA Food Safety Modernization Act (P.L. 111-353)

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The National Center for Toxicological Research (NCTR) was established in 1971. As a national scientific resource, NCTR conducts peer-reviewed research to support FDA's strategic priorities to advance regulatory science and engage globally to encourage the implementation of science-based standards. Further, in support of FDA's strategic goals to Enhance Oversight and Improve Access to FDA-regulated products, NCTR enhances FDA's basis for science-based regulatory decisions by conducting collaborative research to:

- 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 and Artificial Intelligence (AI).
- Develop minimally invasive imaging capabilities to provide alternate biomarkers of toxicity.
- The following selected accomplishments demonstrate NCTR's delivery of its regulatory and public health responsibilities within the context of current priorities.[62]

Enhance Oversight

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 the area of Enhance Oversight, examples of NCTR research include Opioids, Antimicrobial Resistance and the Microbiome, Artificial Intelligence, and Compounding.

Opioids

62 Please visit FDA.gov for additional program information and detailed news items.

Drug overdose is the leading cause of death of Americans under the age of 45, with over half of these deaths attributable to opioids[63]. The FDA Opioid Action Plan[64] provides comprehensive guidance for reestablishing safe-use standards for these products. In support, NCTR has several ongoing projects related to opioid addiction and toxicity potential. In one such study, NCTR scientists are conducting research to assess perinatal opioid exposure, a concern shared in the perinatal-related FDA Drug Safety Communication[65].

NCTR, in collaboration with CDER (Center for Drug Evaluation and Research) , continues to generate data on exposure of brain cells to opioids during perinatal development. In FY 2019, hydrocodone, codeine, oxycodone, and hydromorphone were evaluated along with the positive control, valproic acid. Preliminary results suggest tested opioids have minimal effect on early stem cell growth and development. Screening of additional opioids including morphine, methadone, buprenorphine and fentanyl are planned for FY 2020.

Another CDER-collaborative project that is opioid-related began in FY 2019 and uses computational models to assess opioid structure. This project should create a better understanding of the structural requirements associated with a strong addiction potential and would allow an accurate prediction of this potential for opioids and other structurally diverse chemicals. This technology could be used to prioritize the testing of chemicals with strong addiction potentials (such as novel compounds and synthetic opioids), thus shortening the FDA regulatory-review process. This project is expected to be finalized in FY 2021.

While it has been suggested that multiple neurotransmitters play a role in the abuse-related effects of opioids, a comprehensive analysis of these effects in response to opioids has yet to be established. It is hoped that imaging technologies may help delineate an opioid's mechanism of action. In late FY 2019, NCTR began a project that will attempt to use imaging technologies to reveal the abuse-related effects of opioids.

Antimicrobial Resistance (AMR) and the Microbiome

The CDC estimates that each year roughly one in six Americans suffer illness from eating contaminated food. NCTR scientists conduct research to limit the emergence and spread of drug resistance in bacterial pathogens that compromise our ability to treat foodborne illnesses. This research supports FDA's regulatory needs related to AMR genes and bacterial pathogens in feed, foods, clinical and environmental samples, and the potential effects of transmission of resistant bacteria on human health.

63 National Vital Statistics System. Atlanta, GA: CDC, National Center for Health Statistics; 2017. Available at: https://www.cdc.gov/injury/wisqars/LeadingCauses.html
64 For more information visit: https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm
65 For more information: https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm

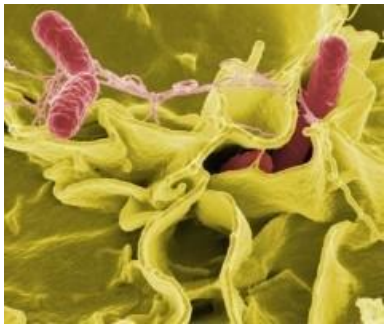


Figure 10. *Salmonella* is one of the most widely studied bacteria on Earth.

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 research area 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]. A related FY 2019 publication entitled "Draft Genome Sequences of 27 *Salmonella enterica* Serovar Schwarzengrund Isolates from Clinical Sources" can be found in *Microbiology Resource Announcements*[67].

Another ongoing AMR research project is focused on cell plasmids (cellular structures which often provide bacteria with genetic advantages) and their role in antimicrobial resistance. The long-term goal of this research is to better understand the contribution of plasmids to increased virulence (severity of a disease) among *Salmonella enterica*. This study builds upon previous NCTR studies to look at the potential for increased virulence and refine our understanding of the plasmid-associated factors. Recent FY 2019 publications related to this project can be found in *Microbial Transposon Mutagenesis*[68] and *BMC Genomics*[69].

Microorganisms associated with the human gut are known collectively as the "human microbiome" or "microbiota" and play an important role in health and disease. Throughout FY 2020 and continuing, NCTR is using state-of-the art genomic and bioinformatic approaches to determine the interactions between the human microbiome and antimicrobial agents, nanomaterials, food contaminants and FDA-regulated products. For example, 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.

NCTR is conducting a study which explores and provides research data on how fecal microbial transplantation (FMT) is an effective treatment for bacterial infections such as *Clostridium difficile*. In FY 2019, NCTR conducted experiments using next-generation sequencing techniques in a cell-culture model that showed each commensal organism in a model intestinal microbiome contributed to *C. difficile*-colonization resistance. Experiments *in vivo* models showed that the toxicity of *C. difficile* was decreased by some gut bacteria but not others. The project also

[66] For more information , please visit: https://link.springer.com/protocol/10.1007%2F978-1-4939-9570-7_12
[67] For more information, please visit: https://mra.asm.org/content/8/12/e01687-18#ack-1
[68] For more information , please visit: https://link.springer.com/protocol/10.1007%2F978-1-4939-9570-7_12
[69] For more information, please visit: https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-019-5768-0

showed that different gut bacteria fed to *C. difficile*-infected models reduced inflammation levels in their blood. Further results show that intestinal cells respond to microbiome influences during *C. difficile*-induced cell stress. Results from this project are expected in FY 2020.

In FY 2020, NCTR will also continue an CDER-collaborative study entitled "An assessment of the interactions of nanoscale (TiO2 and ZnO) materials used in sunscreens on the skin microbiome." Approximately, 95 million U.S. women aged 18 and older have used cosmetics. Recently, via the Safe Cosmetics Act of 2010[70], Congress is targeting regulation on cosmetics. Nanomaterials are now used in many cosmetic products that are already on the market including lipsticks, anti-aging creams, sunscreen, eye shadow, moisturizer, and foundation and the number of nanomaterial-containing products are increasingly rapidly. There are potential risks that externally applied cosmetics and sunscreens containing nanoscale materials could impact the microbial ecology of the skin. There is a lack of knowledge about the effects of nanoscale materials on human-skin microbiota, making this a critical area of research. This study will enhance FDA's scientific understanding of the safety and toxicity of the nanomaterials in cosmetics and provide data to be taken into consideration for safety assessment.

Other recent NCTR accomplishments related to the human microbiome include:

- Under a Broad Agency Agreement between the Arkansas Research Consortium in Nanotoxicity and FDA, NCTR scientists led a project to perform a safety assessment of carbon-based nanomaterials (CBN). The biggest technical difficulty during risk assessment of CBN is the precipitation of test material. An innovative anaerobic *in vitro* rotary cell culture system (RCCS) bioreactor was developed by NCTR that allowed a continuous interaction of microbes with CBN. A paper published in FY 2019 can be found in *ACS Applied Materials and Interfaces*[71]. The RCCS bioreactor will make it more feasible to study interactions between bacteria and nanoparticles.

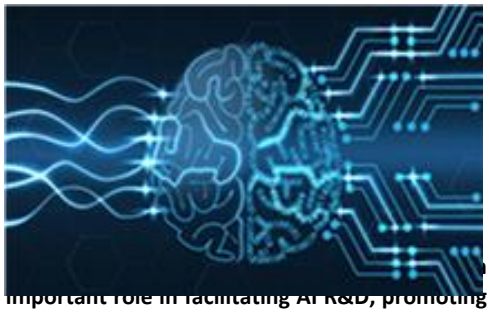
- In collaboration with scientists from the University of Arkansas at Little Rock, a risk assessment was performed to determine the effects of tomato fruits derived from plants exposed to multi-walled carbon nanotubes on the gastrointestinal epithelial-layer integrity using an *in vitro* cell-culture system. A paper summarizing the results of the study can be found in *Nanoscale*[72].

- In collaboration with the University of Arkansas for Medical Sciences, NCTR studied the hypothesis that the co-exposure of the environmental pollutant, trichloroethylene, and a high-fat diet would exacerbate the immunotoxicity, gut inflammation, and microbial dysbiosis in offspring. More information can be found in the FY 2019 publications of Journal of *Applied Toxicology*[73] and *Toxicological Sciences*[74].

[70] For more information, please visit: https://www.congress.gov/bill/111th-congress/house-bill/5786
[71] For more information, please visit: https://www.ncbi.nlm.nih.gov/pubmed/31260263
[72] For more information, please visit: https://www.ncbi.nlm.nih.gov/pubmed/30741296
[73] For more information, please visit: https://www.ncbi.nlm.nih.gov/pubmed/30187502
[74] For more information, please visit: https://www.ncbi.nlm.nih.gov/pubmed/29669109

Artificial Intelligence (AI)

AI advances in bioinformatics tools, computer software, and data science provide FDA tremendous opportunities to develop tools and technologies that will assist in fulfilling the FDA mission. NCTR looks to harness the variety of scientific opportunities available and realizes the major influence of AI on product development and regulations in the coming years. The "Executive Order on Maintaining American Leadership in Artificial Intelligence" mandates that agencies should accelerate AI adoption and invest in AI research and development[75] and explicitly states: *AI provides an approach, between observation and replication, providing another way to tackle safety and efficacy questions. The benefits and implications of underlying AI technologies cannot be fully understood without fundamental scientific research. AI could greatly increase the efficiency of screening and assessing products in a rapid, objective and reproducible means.*



important role in facilitating AI R&D, promoting the trust of the American people in the development and deployment of AI-related technologies..."

This statement highlights the need for FDA to use scientific research to harness the potential for AI in regulatory and regulatory science applications.

Applications or research areas for AI include:

- Personalized diagnostics or therapeutics
- Early disease detection
- More accurate diagnosis
- Identification of new observations or patterns on human physiology

NCTR will explore AI use cases that serve FDA priorities. For example, in collaboration with ORA and CVM, NCTR will design and develop machine-learning algorithms to assist with automated pattern recognition of persistent organic pollutants in foods and feeds. The goal of this tool is to more efficiently and quickly evaluate human and animal risk from food and feed stuffs while decreasing cost associated with sample collections. A paper, published in FY 2019, summarizing this work can be found in the *International Journal of Environmental Research and Public Health.*[76]

In collaboration with ORA and CFSAN, NCTR scientists are working to develop an intelligent system for species identification of food-contaminating beetles. Species identification is important to risk assessment for food filth inspection and analysis. Insects are often broken into small fragments during food processing and thus species identification by insect fragments is extremely difficult, even for food analysts with years of on-job experience. This lack of reliable and efficient methods becomes more difficult as vast amounts of processed food products are imported from places where the alternate preventive inspection of facilities is usually not conducted for a variety of reasons.

[75] For more information, please visit: https://www.whitehouse.gov/presidential-actions/executive-order-maintaining-american-leadership-artificial-intelligence/
[76] For more information, please visit: Int J Environ Res Public Health

This project develops a cost-effective and intelligent system for the species identification of storage pests by examining the patterns retrieved from their hard wing fragments in FDA-regulated food products. The new system integrates the latest advancements in image analysis, artificial intelligence, and information technology. The proposed system will decrease the time and cost to identify storage pest-fragments that contaminate food products, thereby greatly increasing the number of food samples that FDA can examine for extraneous materials. In FY 2019 an imaging acquisition protocol was developed after optimizing the imaging conditions. A large set of high-quality images were collected and thus improved the overall accuracy of our deep learning model to over 90%. Together with a new and more flexible user interface, the updated model will be given to ORA food analysts for field testing by the end of FY 2020. Recent publications related to this project can be found in *Computers and Electronics in Agriculture*[77], *Scientific Reports*[78], and *Analytical Chemistry*[79].

Compounding

Compounding regulation has become of great concern as we move into FY 2020[80]. Both human- and animal-compounding methodologies and products require more oversight from the FDA. NCTR is conducting research to support the regulatory responsibilities of the product centers. Specifically, NCTR is conducting peer-reviewed research to support FDA decision-making that will provide methods and strategies to reduce and rapidly detect contaminants in FDA-regulated products.

A compounding-related research project at NCTR will develop and validate a novel mass-spectrometry approach for analyzing crude samples without purification. This project is in collaboration with CDER's Division of Pharmaceutical Analysis (DPA). DPA has shown the possible utility of this analysis for examining components in creams, such as those developed in pharmaceutical compounding. Clearly a key element in the safety and efficacy of a compounded product is quality; as noted on FDA's webpage, *Compounding and the FDA: Questions and Answers*[81], "poor compounding practices can result in serious drug quality problems, such as contamination or a drug that contains too much active ingredient." A rapid means for assessing the components and contaminants of a compounded product would provide a valuable tool for protecting public health. This research is expected to be completed in FY 2022.

Another NCTR/CDER collaboration is a study titled: "Establishing Standardized Methods for Sporicidal Efficacy Assessment and Building up an Efficacy Database of Sporicidal Products to Support FDA's Regulation on Drug Compounding." Serious health problems and huge medical costs can be the consequence of inappropriate application of sporicidal agents at compounding pharmacies. While pharmaceutical manufacturers under Section 510 of FDCA are required to comply with current good manufacturing practice (CGMP) and validate the effectiveness of disinfectants at their facilities, compounding pharmacies under section 503A are exempt from

[77] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S0168169918312821?via%3Dihub

[78] For more information, please visit: https://www.nature.com/articles/s41598-018-24926-7
[79] For more information, please visit: https://pubs.acs.org/doi/10.1021/acs.analchem.8b04862
[80] For more information, please visit: https://link.springer.com/content/pdf/10.1007%2Fs40268-013-0005-9.pdf
[81] For more information, please visit: https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers

CGMP. In addition, outsourcing facilities under section 503B can follow the labeling on the disinfectants, and do not need to validate the effectiveness of disinfectants in their facilities.

This study will provide FDA a database with standard methodology, that could help FDA to accurately assess the sporicidal efficacy of disinfectants used at compounding pharmacies and outsourcing facilities. The information from this study will extend FDA's knowledge of sporicidal evaluations; help the FDA's safety assessment on the potential spore contamination in drug compounding; and further help the FDA's regulatory activities.

Improve and Safeguard Access

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 the area of Improving and Safeguarding Access, NCTR activities include: Perinatal Health Center of Excellence, Perinatal, Pediatric, and Maternal Medicine, and the Global Summit on Regulatory Science.

Perinatal Health Center of Excellence (PHCE)[82]

In FY 2019, with Congressional support, NCTR fully implemented the Virtual Center of Excellence for Perinatal and Maternal Pharmacology and Toxicology – also known as the FDA Perinatal Health Center of Excellence (PHCE). The perinatal period is the period-of-time including pregnancy, child birth, and infant/child development. The Perinatal Health Center of Excellence (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.

Pregnant women and preterm and term offspring represent understudied populations and many FDA-regulated products provided to neonates and infants, or provided to or used by pregnant mothers, have not been studied extensively in these populations. The PHCE will work to fill knowledge gaps about safety, efficacy, or potential toxicity that currently exist.

In FY 2019, the PHCE leadership council, with representatives from all FDA Centers and ORA, rigorously reviewed 22 submissions and selected 14 proposals to be funded for two years by investigators representing CBER, CDER, CDRH, CFSAN, NCTR, OC, and ORA —all with either internal or external collaborators have begun working on their funded PHCE studies and will continue into FY 2020. In addition, 3 new PHCE research projects were funded in FY2020 bringing the total to 17 PHCE projects currently funded by NCTR. Additional information about the PHCE can be found at: https://www.fda.gov/about-fda/nctr-research-focus-areas/perinatal-and-maternal-research.

Perinatal, Pediatric, and Maternal Medicine

In addition to PHCE, NCTR is providing additional 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. 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

[82] For more information, please visit: https://www.fda.gov/about-fda/nctr-research-focus-areas/perinatal-and-maternal-research

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 FDA Drug Safety Communication[83] in March 2018 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 study recently evaluated the utility of neural stem-cell models to predict the effects of pediatric anesthetics sevoflurane and isoflurane in combination with nitrous oxide. This study was finalized in late FY 2019 and a paper was published in *Neurotoxicology*. The data generated from this study further support the hypothesis that prolonged anesthesia, early in life, may increase the risk of developing cognitive impairments later in life. [84] NCTR researchers have also published data highlighting the comparative safety of general anesthesia in older individuals. These results suggest that sevoflurane does not change measured behavior and exposure to the anesthetic alone may not be sufficient to cause what is known as Postoperative Cognitive Dysfunction (POCD) in adult populations. For more information please see the publication in Neurotoxicology[85].

A closely-related study was also approved to begin in FY 2019. This study will monitor blood oxygen levels of early-life rodents during exposure to anesthetics. It is known that early-life exposure to anesthesia can cause neuronal degeneration, but no study has directly studied the associated lack of oxygen and its role in the damage. This study will provide better quality data for the FDA to use in its regulatory mission and hopefully hasten the development of safer anesthesia regimens for use in a clinical setting. A paper summarizing the results of this study are expected to be published in FY 2021.

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

[83] For more information, please visit: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-review-results-new-warnings-about-using-general-anesthetics-and

[84] For more information visit: https://pubmed.ncbi.nlm.nih.gov/30445043-early-life-exposure-to-extended-general-anesthesia-with-isoflurane-and-nitrous-oxide-reduces-responsivity-on-a-cognitive-test-battery-in-the-nonhuman-primate/?from_term=paule%2C+chelonis&from_sort=date&from_page=1&from_pos=3

[85] For more information visit: https://pubmed.ncbi.nlm.nih.gov/30605762-sevoflurane-exposure-has-minimal-effect-on-cognitive-function-and-does-not-alter-microglial-activation-in-adult-monkeys/?from_term=paule%2C+chelonis&from_sort=date&from_page=1&from_pos=2

labeling and/or best practices for pediatric general anesthesia. A summary of this research can be found in *Anesthesiology*.[86]

Most recently in the British Journal of Anesthesia87 NCTR scientists, in collaboration with scientist at the Mayo Clinic, published an analysis of results from the Mayo Anesthesia Safety in Kids (MASK) study. Despite the hypothesis that data from children would mirror animal data, this study found that there was little evidence to support that anesthesia-effects in children mirror that of young animals on the selected behavioral endpoints. However, the average length of anesthesia exposures in the MASK study were short. Animal research performed at the NCTR and elsewhere has repeatedly shown that the occurrence of anesthesia related neurotoxicity is dependent upon the duration of exposure. Accordingly, the lack of effect is in line with the animal research.

Global Summit on Regulatory Science (GSRS)

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 tenth year, the Global Summit's goal is to engage the global community and harmonize research strategies via collaborations that aim to build knowledge of and promote regulatory science, define research needs, and 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 9th Global Summit on Regulatory Science (GSRS19) on Nanotechnology and Nanoplastics was held from 24-26 September 2019, at Lago Maggiore, Stresa, Italy. The ninth annual summit was co-organized by the Global Coalition for Regulatory Science Research (GCRSR) and Joint Research Center (JRC), European Commission. GCRSR is co-chaired by Drs. William Slikker (FDA) and Marta Hugas (EFSA). The summit had 200 scientists in attendance from 34 countries representing regulatory and research institutes along with academic and industry participants to present on the regulatory science perspective, current status, knowledge gaps and future outlook. The summit topics and sessions were developed by the scientific program committee composed of GCRSR member agencies co-chaired by Drs. Anil Patri (FDA) and Birgit Sokull-Kluettgen (JRC/EC) and included plenary sessions on perspectives from regulatory agencies and others with parallel sessions on drugs, foods, devices, nanotoxicology, and standards.

The summit was a huge success with presentations from appropriate regulatory/research authorities with in-depth scientific presentations on current nanotechnology applications and panel discussions. A limited number of academic and industry presenters were invited to showcase cutting edge research, successes, ongoing clinical trials and challenges. The scientific content of the summit is unique, different from traditional scientific conferences, with a focus on regulatory science, knowledge gaps, and how to address these gaps through global collaborations and specific mechanisms utilized for this purpose. The plenary session on Nanoplastics brought

[86] For more information visit: http://anesthesiology.pubs.asahq.org/article.aspx?articleid=2679328
[87] For more information visit: https://www.ncbi.nlm.nih.gov/pubmed/30857603

together current state of the art in microplastics, the concerns, research efforts, potential health effects, emphasizing the lack of information and data on nanoplastics. There were pre- and post-meeting training sessions sponsored by JRC at their facility in Ispra, lab tours of the Nanobiotechnology Center, and an American Society for Testing and Materials (ASTM) International E56 ASTM E56 meeting on Nanotechnology standards. The scientific program committee will work on a draft summary report from the meeting and come up with summary recommendations on potential global collaborations to address the knowledge gaps.

The 10th Annual 2020 Global Summit for Regulatory Science will be held in the U.S., September 28-30 in Bethesda, MD. The meeting will focus on emerging technologies and their application to regulatory science. For updates, abstract guidelines, agenda, and more visit www.fda.gov/globalsummit.

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 Precision Medicine, Nanotechnology, Cancer, Bioinformatics and Bioinformatics Tools, and Magnetic Resonance Imaging (MRI).

Precision Medicine

NCTR studies biomarker identification and development which helps identify disease factors of demographic subpopulations, identify individualized therapies for disease, and develop new insights into preventative measures based on individual or subpopulation profiles.

Research studies are crucial to a precision-medicine approach treating neurodegenerative diseases like Alzheimer's Disease (AD). NCTR scientists presented a webcast lecture titled, "Ethnicity- and Gender-Related Differences in 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. A recording of the presentation and a brief synopsis can be found on FDA.gov[88].

Cell lines from both African-American and European-American women were used in an NCTR-conducted research study on triple-negative breast cancer (TNBC), a highly aggressive type of breast cancer that currently lacks targeted therapies. NCTR scientists have shown that FDA-approved histone deacetylase (HDAC) inhibitor, such as Vorinostat, is emerging as a possible

[88]For more information please visit: https://www.fda.gov/science-research/about-science-research-fda/ethnicity-and-gender-related-differences-alzheimers-disease-01112018-01112018

new therapy. The five TNBC subtypes, each with a different molecular profile, are known to respond differently to cancer therapies. NCTR research, showing that Vorinostat controls critical microRNAs (epigenetic targets for drug development) that play important roles in cell proliferation, drug resistance, cell invasion, and metastasis, is an important finding. This on-going work was funded by FDA's Office of Women's Health and NCTR, and current findings were presented at the 2018 Annual Meeting of the American Association of Cancer Research.

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 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. Recent publications related to this research can be found in *Pediatric Investigation*[89] and *Experimental Biology and Medicine*[90].

The potential for medicines to have adverse effects on male-reproductive capacity remains a concern in drug development. While animal tests have been useful in assessing the risk new drugs might have, faster methods would be desirable. In early FY 2019, at the meeting titled "FutureTox IV Progress to Maturity: Predictive Developmental and Reproductive Toxicology for Healthy Children," scientists from NCTR and CDER presented results of a new, *in vitro* assay where a mouse-testis organ system is used to examine the toxicity of chemicals. Further work is planned to refine this system in FY 2020 and beyond.

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 products containing nanomaterial in FDA-regulated products, staff and reviewer training and standards development through stakeholder involvement for responsible development of nanotechnology 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 drugs disseminate 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.

[89] For more information please visit: https://onlinelibrary.wiley.com/doi/epdf/10.1002/ped4.12044
[90] For more information please visit: http://journals.sagepub.com/doi/pdf/10.1177/1535370217750087

An on-going 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*[91].

The Nanocore is working on high priority collaborative-consensus standards development with support from the National Toxicology Program and stakeholder involvement from academia and industry through the ASTM E56 subcommittee on Nanotechnology and ISO Technical Committee 229. These standards on high-priority areas, such as characterization methods to ascertain reproducibility and safety, ultimately provide common ground for product developers and FDA to help facilitate the development of products containing nanomaterials. To date, several FDA-generated work items are going through the consensus process through Standards Developing Organizations (SDOs). One work item FDA developed, *Standard Practice for Performing Cryo-Transmission Electron Microscopy* of Liposomes became a standard in February 2019 and available through ASTM International. There are eight additional work items on nanotechnology under development currently through research at the Nanocore that are going through the consensus-standard process at ASTM International E56 for quality assurance and testing for biocompatibility.

Cancer

FDA scientists from NCTR and CDER are developing a sensitive method to detect mutations induced by chemicals. Mutations are changes in the DNA sequence of an organism, ranging from small-point mutations to large chromosome alterations that can cause adverse health effects, such as cancer and genetic disease. The goal of the ongoing study is to establish a new next-generation sequencing (NGS) assay that may become a powerful, rapid, and practical tool to routinely evaluate the mutagenicity of FDA-regulated products. Data from this study were interpreted and reported in the December 2018 issue of *Archives of Toxicology*.

In another cancer-related study, NCTR scientists detected the outgrowth and enrichment of mutant tumor cells clinically associated with the development of drug resistance. They cultured primary lung-tumor organoids—tiny, self-organized three-dimensional tissue cultures—in the presence of varying concentrations of erlotinib (Tarceva®), a drug used to treat lung cancer. Using this novel model and a sensitive method for mutation detection they detected increases in mutant tumor cells after culture. Better patient outcomes are being achieved using personalized cancer treatments by selecting therapies based on tumor genetics. Unfortunately, resistance to the therapy occurs frequently and limits drug efficacy. Because this lung tumor-organoid model reproduces the cellular and mutational diversity of human-lung adenocarcinomas, it has the potential to identify treatment strategies and drug combinations that reduce or eliminate drug resistance.

Scientists from NCTR, and the University of Arkansas for Medical Sciences have demonstrated that two commonly used chemotherapeutics (cyclophosphamide and doxorubicin), administered alone or in combination, did not induce behavioral alterations in an animal model reflective of

[91] For more information please visit: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5961469/pdf/ijn-13-2857.pdf

human breast-cancer patients. The study was designed to investigate the memory and attention problems that some female breast-cancer patients experience after chemotherapy — sometimes known as "chemo" brain. The lead author of the article —Timothy Flanigan, Ph.D. — was awarded the Developmental Neurotoxicology Society's "2018 Richard Butcher New Investigator Award" for this publication. The article is available in the April 2018 issue of *Toxicological Sciences.* [92]

The use of a potent chemotherapeutic drug, doxorubicin (DOX), is restricted because of the risk of heart damage in cancer patients and survivors. Using a NCTR-developed mouse model of DOX-induced heart injury, along with transcriptomics analyses, NCTR scientists identified two proteins that were elevated in plasma prior to the release of cardiac-specific injury marker known as troponin T. The study also showed that the increased levels of both proteins were mitigated and DOX effects were diminished when cardioprotective drug, dexrazoxane, was administered. These results suggest these proteins could be used as early markers of DOX cardiotoxicity. With this knowledge, there is potential for monitoring and/or predicting DOX cardiotoxicity and improved ability to design more effective treatment regimens. These results have been published in *Toxicology and Applied Pharmacology*.[93]

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 anomalies. This technology, derived from FDA-regulated MRI instruments, is called magnetic resonance spectroscopy (MRS). These methods will provide FDA with information needed for regulatory decisions and support FDA Drug Safety Communications.

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 *Neurotoxicology* [94].

NCTR, in collaboration with FDA product centers, continues to study the bioaccumulation of gadolinium in the brain. Gadolinium is an agent commonly used during MRI procedures. This research contributed to an FDA Drug Safety Communication[95] about gadolinium-based contrast agents (GBCAs) and their retention in the brain and will continue through FY 2020.

New and continuing imaging research at NCTR includes:

- Studying the relationship of MRI findings and biological fluid biomarkers of neurotoxicity.

[92] For more information please visit: https://academic.oup.com/toxsci/article/162/2/462/4706007
[93] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S0041008X18305362?via%3Dihub
[94] For more information please visit: https://www.sciencedirect.com/science/article/pii/S0161813X18300330?via%3Dihub
[95] For more information please visit: https://www.fda.gov/Drugs/DrugSafety/ucm455386.htm

- 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*[96].

- Validated a three-dimensional MRI technique to more accurately evaluate brain neurotoxicity. It will allow for minimally-invasive detection of brain lesions.

Bioinformatics and Bioinformatics Tools

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 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.

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.

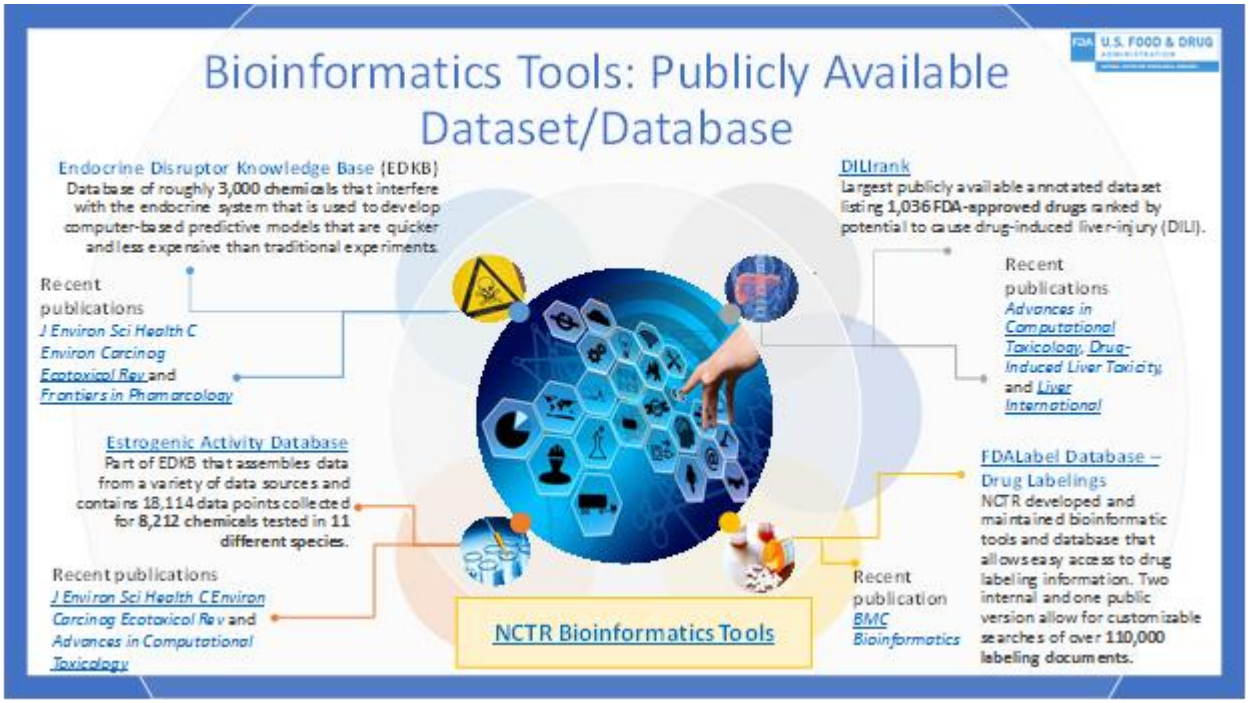
NCTR scientists, as requested by CDER reviewers, are applying text-mining techniques including pattern-matching and natural-language processing to extract information from FDA approval letters for New Drug Applications and Biologic License Applications. A relational database and web-based application have been developed to host the information for better query, review, 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 and can be found in *Drug Discovery Today* [97].

Today's consumer products are increasingly globalized, impacting public health worldwide and posing new challenges for regulatory authorities. In FY 2019, 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. 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

[96] For more information please visit: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0197213
[97] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S1359644617305858

the Investigative New Drug (IND) phase. Scientists worked on DILI caused by bile acid-related products 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*[98]. Another paper 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 published in *Liver International*[99] in FY 2019.



FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2017 Actual	$63,331,000	$63,331,000	---
FY 2018 Actual	$64,512,000	$64,512,000	---
FY 2019 Actual	$66,712,000	$66,712,000	---
FY 2020 Enacted	$66,712,000	$66,712,000	---
FY 2021 President's Budget	$66,266,000	$66,266,000	---

BUDGET REQUEST

The FY 2021 Budget Request for the National Center for Toxicological Research is $66,266,000, which is all budget authority. The budget authority is a decrease of $446,000 compared to the FY 2020 Enacted Level.

[98] For more information, please visit: https://onlinelibrary.wiley.com/doi/full/10.1111/apt.14678
[99] For more information, please visit: https://onlinelibrary.wiley.com/doi/abs/10.1111/liv.13952

The FY 2021 Budget will allow NCTR to continue research to support emerging technologies and toxicology assessments required by FDA and to maintain 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: Opioids, Antimicrobial Resistance and the Microbiome, Artificial Intelligence, Compounding, Perinatal Health Center of Excellence, Perinatal, Pediatric, and Maternal Medicine, Global Summit on Regulatory Science, Precision Medicine, Nanotechnology, Cancer, Magnetic Resonance Imaging, and Bioinformatics and Bioinformatics Tools. 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.

BUDGET AUTHORITY

At the FY 2021 President's Budget Level, NCTR's Budget Request includes a decrease in budget authority of $0.446 million. NCTR will be able to pursue activities that focus on supporting FDA's highest priorities for FY 2021 while also reducing administrative spending.

Crosscutting Initiatives: -$0.446 million

Outreach, Training, and Organizational Excellence (-$0.446 million)

NCTR will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. NCTR will preserve its most critical public health and safety activities under this reduction, including: Expediting the translation of

laboratory findings to the clinic and regulatory application; Identifying adverse effects earlier in product development and understanding the risks and benefits of nanomaterials used in FDA-regulated products; Providing strategies to reduce and rapidly detect contaminants in FDA-regulated products; Using biomarkers—biological indicators of disease—to foster precision medicine; Accelerating FDA's capability to manage and analyze research data using bioinformatics and Artificial Intelligence (AI); Developing minimally invasive imaging capabilities to provide alternate biomarkers of toxicity; and Advancing pediatric and perinatal research through collaboration and knowledge sharing.

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 Recen Result	FY 2020 Target	FY 2021 Target
263103: Conduct translational and regulatory research to advance the safety of products that FDA regulates. (Output)	FY 2019: In collaboration with CDER, data analysis regarding gadolinium experimentation was finished. Two publications are in preparation. (Target Met) FY 2019: Data on the potential neurotoxic effects of opioid exposure indicates minimal effect on neural precursor viability and proliferative ability. (Target Met)	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.	Finalize data regarding 3D molecular modeling of opioids and other chemicals.
263201: Develop science base for supporting FDA regulatory review of new and emerging technologies (Output)	FY 2019: NCTR scientists completed screening for nano-silver in 30 feminine hygiene products using 3D-mucosal models. (Target Met)	Develop a safety assessment for gene editing therapies that are pending clinical trials.	Report preliminary results on validating blood-brain-barrier-on-a-chip technology as a tool for toxicological screening of FDA-regulated products.
262401: Develop biomarkers to assist in characterizing an individual's genetic profile in order to minimize adverse events and maximize therapeutic care (Output)	FY 2019: NCTR scientists developed an accurate method to quantify hundreds of hotspot cancer driver mutations (CDMs) at once. This work was presented at the 49th Annual Environmental Mutagenesis and Genomics Society Meeting. (Target Met)	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 CDER, draft and publish a manuscript regarding biomarkers for early detection of anticancer treatment-induced heart injury.	Develop biomarkers to better assess immunotoxicity associated with FDA products containing nanomaterials.
264101: Develop risk assessment methods and build biological dose-response models in support of food protection (Output)	FY 2019: NCTR determined that some bacteria that may be present in fecal microbiota transplants inhibit *C. diff* growth and also overcome *C. diff* suppression of intracellular defense mechanisms. (Target Met)	In collaboration with CVM, develop a database and analysis tool to better understand and control *Salmonella enterica* in foods and feed.	In collaboration with CVM, identify potential ways to minimize increased virulence and antimicrobial resistance in food animals.
263104: Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates (Output)	FY 2019: NCTR scientists discovered early biomarkers of cardiotoxcity while using an effective chemotherapeutic drug. These results were published in *Toxicology and Applied Pharmacology*[100]. (Target Met)	Develop parameters to assist reviewers when evaluating applications submitted to FDA for genome assembly-based devices, products, and services.	Finalize data on the use of lipidomics to reveal factors influencing newborn susceptibility to vaccines.

[100] For more information, please visit:
https://www.sciencedirect.com/science/article/pii/S0041008X18305362?via%3Dihub

Measure	Most Recent Result / Target for Recen Result	FY 2020 Target	FY 2021 Target
263102: Develop computer-based models and infrastructure to predict the health risk of biologically active products (Output)	FY 2019: NCTR scientists established high-throughput and pathway-focused (high-content, HTHC) methods for two essential in vitro genotoxicity assays for evaluating chemical-induced DNA damage and chromosome damage. (Target Met) FY 2019: NCTR collaborated with the Spain Drug-Induced Liver Injury (DILI) registry and Duke University to investigate the influence of drug properties and host factors on delayed onset symptoms in DILI using in silico methods. A paper was published in *Liver International*[101] in 2019 and a book chapter was published in *Advances in Computational Toxicology*[102]. (Target Met)	Examine the utility of In Vitro (lab-based) to In Vivo (animal-based) Extrapolation (IVIVE) as a new tool for FDA safety assessments.	In collaboration with CDER and Elsevier, NCTR scientists will report preliminary results regarding the development of a predictive model for detecting drug induced liver injury (DILI) during the drug review process.

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 gadolinium—a heavy metal commonly used as a contrasting agent during MRI procedures. In FY 2019, NCTR continued to advance the safety of FDA-regulated products by providing data on the bioaccumulation of gadolinium in the brain and the possible adverse effects on the brain tissue. In FY 2020, NCTR scientists plan to finalize and publish results on retention and distribution of all currently marketed gadolinium-based MRI contrast agents.

Additionally, in FY 2020, NCTR scientists will gather toxicity data on FDA-approved cancer fighting molecules, called kinase inhibitors (KI). This project will provide a comprehensive picture of KI effects on the liver and heart that will help FDA better evaluate the use of KIs.

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 2019, NCTR research regarding the toxic potential of silver nanoparticles in feminine-hygiene products using 3D mucosal models was finalized. A final report discussing this work is on track to be published in FY 2020. In FY 2020, scientists plan to develop a safety-assessment for gene editing therapies that are pending clinical trials. In FY

[101] For more information, please visit: https://www.ncbi.nlm.nih.gov/pubmed/?term=The+influence+of+drug+properties+and+host+factors+on+delayed+onset+of+symptoms+in+drug%E2%80%90induced+liver+injury

[102] For more information, please visit: https://link.springer.com/chapter/10.1007/978-3-030-16443-0_13

2021, NCTR will report preliminary results on validating blood-brain-barrier-on-a-chip technology as a tool for toxicological screening of FDA-regulated products.

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 2019 research to identify human cancer mutations to help speed the development of personalized cancer treatments was conducted. NCTR scientists developed an accurate method to quantify hundreds of hotspot cancer driver mutations (CDMs) at once and presented this work at the 49th Annual Environmental Mutagenesis and Genomics Society Meeting. 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. Also in FY 2020, NCTR plans to 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.

PROGRAM ACTIVITY DATA

National Center for Toxicological Research Program Activity Data (PAD)

Program Workload and Outputs	FY 2019 Actual	FY 2020 Estimate	FY 2021 Estimate
Research Outputs			
Research Publications	152	160	160
Research Presentations	145	150	150
Patents (Industry)	5	5	5
Leveraged Research			
Federal Agencies (Interagency Agreements)	3	3	3
Nongovernmental Organizations	30	32	32
Active Research Projects	165	176	176

OFFICE OF REGULATORY AFFAIRS - FIELD ACTIVITIES

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Office of Regulatory Affairs	**1,174,811**	**1,143,329**	**1,223,286**	**1,224,180**	**894**
Budget Authority	***1,063,123***	***1,063,123***	***1,118,165***	***1,114,837***	***-3,328***
User Fees	***111,688***	***80,206***	***105,121***	***109,343***	***4,222***
Prescription Drug (PDUFA)	*10,569*	*8,688*	*10,021*	*10,303*	*282*
Medical Device (MDUFA)	*2,457*	*1,974*	*2,586*	*2,630*	*44*
Generic Drug (GDUFA)	*56,808*	*45,778*	*53,124*	*54,492*	*1,368*
Biosimilars (BsUFA)	*1,100*	*677*	*1,472*	*1,510*	*38*
Animal Drug (ADUFA)	*431*	*384*	*383*	*392*	*9*
Animal Generic Drug (AGDUFA)	*335*	---	*228*	*255*	*27*
Family Smoking Prevention and Tobacco Control Act	*14,767*	*10,534*	*14,575*	*16,575*	*2,000*
Mammography Quality Standards Act (MQSA)	*13,995*	*11,780*	*11,281*	*11,506*	*225*
Food and Feed Recall	*1,000*	---	*1,020*	*1,040*	*20*
Food Reinspection	*5,382*	---	*5,490*	*5,600*	*110*
Voluntary Qualified Importer Program	*4,320*	---	*4,406*	*4,495*	*89*
Third Party Auditor Program	*144*	---	*147*	*150*	*3*
Outsourcing Facility	*380*	*391*	*388*	*395*	*7*
FTE	**4,775**	**4,772**	**4,875**	**4,881**	**6**

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 FDA is responsible for the regulatory oversight of more than $2.5 trillion worth of food as well as medical and tobacco products consumed by Americans. The Office of Regulatory Affairs (ORA) advances the FDA's mission by conducting field operational activities on the FDA-regulated products to ensure their safety, effectiveness, and quality. As FDA's lead office for all agency regulatory 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 the FDA-regulated products offered for import into the United States,
- Oversight of recalls and execution of enforcement actions,
- Response to consumer complaints and emergencies, and
- Development and promotion of state and local partnerships.

The 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 the 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, and
- Tobacco products.

ORA has staff in 231 offices across 49 states, including the Commonwealth of Puerto Rico, with staff both temporarily and permanently assigned to foreign posts. ORA manages 13 scientific labs including two co-located medical product labs, and one tobacco lab that conducts applied research and performs specialized analyses of domestic and imported products. ORA also develops and maintains information technology systems used across the FDA that promote efficiency through information sharing and enable operational processes and decision making by employing risk-based tools. 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, share information, and enhance program capacity and infrastructure.

Recent Accomplishments

Three of ORA' most significant accomplishments from the past year are described below.

Supporting the Opioid Initiative

In response to the current opioid crisis, ORA prioritized support to increase personnel and improve space and infrastructure at the nine International Mail Facilities (IMFs) throughout the country. In FY 2018, ORA increased its presence at the IMFs by hiring 40 import investigators, thereby increasing incoming package examinations to three times more than FY 2017 levels. In addition, ORA doubled the staff of the Office of Criminal Investigations' (OCI) Import Operations Program by hiring special agents, and senior operations managers. In addition, chemists have been hired 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 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. Section 3014 of the SUPPORT Act calls for strengthening coordination and capacity between the FDA and U.S. Customs and Border Protection (CBP) on activities designed to improve detection and response to illegal controlled substances and drug imports, particularly those imported through the nine IMFs throughout the country. The FDA and CBP signed a Letter of Intent on April 4, 2019, memorializing the intent of each agency to establish and implement collaborative strategies addressing information sharing, and operational coordination for better targeting of higher-risk parcels. The FDA/ORA and CBP continue to work together to expand the scientific presence at IMFs and explore ways to enhance collaboration and efficiency of operations by sharing existing space. The FDA and CBP also agreed to explore the acquisition of parcel singulation technology where that is practicable. In FY 2018 and 2019, FDA/ORA and CBP worked with the General Services Administration to address space and capacity challenges.

Moreover, ORA participated in the 2nd Online Opioid Summit, an effort to address this public health emergency by working with internet stakeholders to crack down on internet traffic in illicit drugs. Illegal online pharmacies, drug dealers, and other criminals are increasingly using the internet to further their illicit distribution of opioids, where their risk of detection and repercussions is significantly reduced. In June 2018, then-FDA Commissioner Scott Gottlieb, M.D., invited internet stakeholders, government entities, academic researchers, and advocacy groups to attend the first Online Opioid Summit to discuss ways to collaboratively take stronger action in combatting the opioid crisis by reducing the availability of illicit opioids online. The FDA hosted a second summit on April 2, 2019, to build upon our successes and find innovative solutions to protect the American public from opioids that are illegally being offered for sale online. The focus of the summit was collaboration with internet registries and registrars. Since these entities play a role in the registration of internet domain names, they are a critical part of the solution. Further, ORA continues to notify internet stakeholders – particularly the search and social platforms - on a routine basis to alert those platforms of opioids being offered for sale to U.S. consumers.

Initiating a New Era of Smarter Food Safety

In 2018 and 2019, ORA performed inspections and oversight activities under the various Food Safety Modernization Act (FSMA) programs. Over the past two years the FSMA Accredited Third-Party Certification Program grew with an increase in participating certification bodies and subsequent audits. Foreign Supplier Verification Program (FSVP) inspections continue, with the program expanding to include inspections of produce importers and re-inspection of firms with previous FSVP inspection classifications of voluntary action indicated (VAI). ORA continues to perform inspections of domestic and foreign food facilities that are required to register under section 415 of the FD&C Act and must comply with the requirements for risk-based preventive controls mandated by FSMA. ORA also began performing inspections of applicable human and animal food manufacturers/shippers under the FSMA Sanitary Transportation Rule. Finally, the agency has released the proposed FSMA Laboratory Accreditation rule into the Federal Register for public review and comment. The laboratory accreditation program, once established, will require testing of human and animal food in certain circumstances by accredited laboratories. Accredited laboratories would be required to follow model standards and would be subject to oversight by the FDA-recognized accreditation bodies to help ensure consistently reliable testing results.

The FDA has initiated a "New Era of Smarter Food Safety" to augment and enhance the agency's ongoing efforts to implement FSMA requirements while leveraging technology to create a digital, traceable, and safer food system. The FDA has identified a diverse group of staff across the agency to participate in groups that will generate new ideas and facilitate expansion in four interconnected initiatives: Technology-Enabled Traceability and Foodborne Outbreak Response; Smarter Tools and Approaches for Prevention; Adapting to New Business Models; and Food Safety Culture. The agency has established internal mechanisms to assist each initiative and provide agency-wide communication to enhance consumer protection. In October of 2019, FDA held a public meeting to hear from broad cross-section of stakeholders on this new modern approach to strengthen our protection of the food supply. The input received during the public meeting along with comments submitted to the Federal Register document will help shape our blueprint for a New Era of Smarter Food Safety.

Expanding FDA Medical Product Safety

ORA has advanced two key initiatives, both domestic and international, in the area of medical product safety. First, ORA supports the FDA's Center of Excellence on Compounding for Outsourcing Facilities. The Drug Quality and Security Act of 2013 established a new, voluntary category of compounders known as "outsourcing facilities," which are held to quality standards (e.g., current good manufacturing practice) to protect patient health. Outsourcing facilities are intended to produce a reliable supply of compounded drugs needed by hospitals, clinics, and other providers. It is particularly important that this sector be able to meet provider needs for compounded drugs distributed without patient-specific prescriptions. To help this industry grow to meet its intended function, the FDA created a Center of Excellence on Compounding for Outsourcing Facilities and will be expanding FDA engagement with outsourcing facilities and state regulatory bodies in training and development of this new industry sector. ORA continues to support this center in areas such as the development of content for the delivery of planned outreach and trainings.

The second initiative that ORA continues to advance, in collaboration with FDA centers, is the Mutual Recognition Agreement (MRA). The amended Pharmaceutical Annex of the 1998 U.S.–European Union (E.U.) Mutual Recognition Agreement (MRA), implemented on November 1, 2017, allows participating countries to use each other's good manufacturing practice inspections of pharmaceutical and certain biological drug manufacturing facilities. As of July 2019, the FDA announced that human drug capability assessments have been completed for the 28 E.U. member states under the MRA for pharmaceuticals, and all 28 regulatory authorities are now recognized. The full implementation of the human MRA with Europe will increase efficiency, avoid duplicative inspections, allow the reallocation of resources to areas with higher public health risks, and thereby enable greater market access and improve international harmonization. Additionally, efforts are underway to expand the MRA with E.U. to include veterinary medicines and the FDA is currently conducting capability assessments of E.U. veterinary agencies.

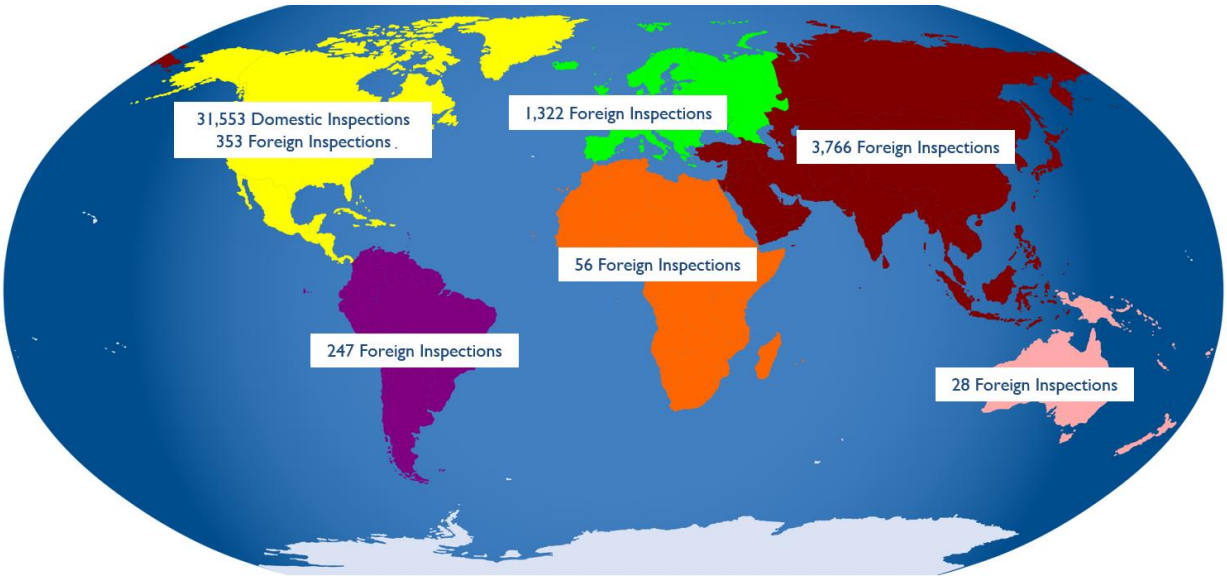


Figure 12 FY 2019 FDA Inspections by Continent. *Numbers as of December 2019

Strengthening Science and Increasing Efficiency Via Risk-Based Decision-Making in the Surveillance of FDA-Regulated Products

ORA works with each FDA Center to 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), including civil investigators
- Compliance officers
- Laboratory analysts
- Recall coordinators
- Occupational safety and health officers
- Consumer complaint coordinators
- Criminal investigators
- State cooperative program specialists
- Public affairs and communication specialists

FDA's foreign inspections are a critical component of protecting the health and safety of U.S. citizens. These inspections ensure that FDA-regulated products produced in foreign countries intended for the market meet the same regulatory standards as those manufactured domestically.

In FY 2019, ORA added a dedicated foreign inspection cadre for conducting Bioresearch Monitoring (BIMO) inspections abroad. This cadre consists of eight investigators who have completed 119 foreign BIMO inspections, representing 39% of the total number of foreign BIMO

inspections conducted in FY 2019. This new cadre allows ORA to quickly respond to application-driven inspection assignments with short review dates and develop specialized skills. 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.

Protecting the U.S. food supply requires an integrated approach for identifying, investigating, and responding to foodborne illnesses and food-related incidents. The integrated 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, minimizes the loss of consumer confidence, and lessens 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 2019, ORA conducted 127 inspections of compounding facilities, which resulted in 32 recalls, and the issuance of 21 warning letters and 33 state referral letters as we continue our collaborative efforts with the states to oversee compounding facilities throughout the U.S.

Also, four permanent injunctions were entered in FY 2019:

- On May 22, 2019, the Northern District of Illinois entered a consent decree of permanent injunction between the United States and PharMedium Services, LLC, headquartered in Lake Forest, Ill., as well as Scott Aladeen, the company's president, and Warren Horton, vice president for Quality and Research and Development after FDA issued previous warnings and inspections revealed PharMedium continued to violate the law. The company has four registered 503B outsourcing facilities located in Memphis, TN.; Cleveland, MS.; Sugar Land, TX and Dayton, NJ.
- On May 22, 2019, the Southern District of Texas signed and entered a consent decree of permanent injunction, ordering Pharm D Solutions, LLC, Texas, and its owners to stop producing compounded drugs intended to be sterile until the company complies with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and other requirements after FDA inspections revealed the firm continued to violate the law despite previous warnings from the FDA.
- On March 12, 2019, a federal court ordered Guardian Pharmacy Services, Texas, to stop producing compounded drug products intended to be sterile until the company complies with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and other requirements after FDA inspections revealed the firm continued to violate the law despite previous warnings from the FDA.
- On February 06, 2019, the Western District of Pennsylvania entered a consent decree of permanent injunction between the United States and Ranier's Rx Laboratory Inc., doing

business as Ranier's Compounding Laboratory, of Jeanette, Pennsylvania, and pharmacist Francis H. Ranier, who owns the compounding facility after FDA investigators observed the firm manufacturing purportedly sterile drug products under insanitary conditions.

In April 2019, former chief executive Paul J. Elmer, of Pharmakon Pharmaceuticals, Noblesville, Indiana, was convicted of conspiracy to defraud the federal government and adulterating drugs after the FDA consumer safety officers testified that during inspections of the facility, they observed several violations of federal regulations and informed Elmer of their existence. Over a three-year period, Pharmakon Pharmaceuticals distributed over- and under-potent drugs to hospitals across the country. On February 16, 2016, the FDA was alerted of serious adverse events in three infants associated with the use of recalled morphine sulfate products from Pharmakon.

Additionally, ORA participated in outreach meetings including the June 2019 Outsourcing Facility Briefing and Listening Session. ORA actively participates in working groups for the Center of Excellence on Compounding for Outsourcing Facilities tasked to produce training materials for in-person and web-based training for Outsourcing Facilities.

Enforcing FDA Authorities

ORA's Office of Criminal Investigations (OCI) has the primary responsibility for criminal investigations conducted by the FDA and for all law enforcement and intelligence issues pertaining to threats against FDA-regulated products and industries. In FY 2019, the criminal investigative efforts of OCI resulted in:

- 249 domestic arrests,
- 8 foreign arrests,
- 239 convictions, and
- More than $2.3 billion in forfeiture, fines, and restitutions.

Given the increasingly global nature of crime related to FDA-regulated commodities, ORA's OCI has implemented a multitiered strategy emphasizing three complimentary areas: (1) international engagement to ensure the safety of the FDA-regulated supply chain; (2) combating cybercrime on the surface net and dark nets; and (3) import operations to detect and seize violative products prior to their entering domestic markets. One example of the intersection of these three pivotal areas is OCI's ongoing bilateral initiative with its law enforcement counterparts from the United Kingdom (U.K.) to disrupt the large-scale shipment of illicit medicine to the United States from and through the United Kingdom. The underlying OCI criminal investigations, which served as the genesis for this initiative, prosecuted a U.K. importation nexus and many involved bad actors misusing the internet to distribute non-FDA-approved drugs and medical devices. As a byproduct of this initiative, in September 2019, the FDA placed an OCI Special Agent within the U.S. Embassy in London.

In recognition of a similar threat to public health and safety, in June 2019, OCI also received approval from the U.S. Department of State to place an OCI Special Agent within the U.S. Embassy in New Delhi, India. If concurrently approved by the government of India, this would

give OCI three international postings. The third posting, OCI's first, is at EUROPOL, The Hauge, Netherlands.

OCI's international engagement efforts have expanded to include inviting law enforcement representatives from the U.K. and India to attend its Special Agent Training Program at the Federal Law Enforcement Training Center, Charleston, South Carolina. OCI continues to support regional training programs around the world, which it often co-organizes with the U.S. Department of Justice and U.S. Patent and Trademark Office. In FY 2019 alone, OCI facilitated and/or participated in:

- "7th meeting of the Task Force on Countering Illicit Trade held by the Organization for Economic Co-Operation and Development (OECD)", 70-80 attendees, Paris, France, March 2019;
- "Asia Regional Workshop on Enforcement Against Trade in Counterfeit Food, Beverages, Cosmetics, and Fast Moving Consumer Goods", 130-150 attendees; Ho Chi Minh City, Vietnam, April 2019;
- "Workshop for Public Prosecutors on Intellectual Property Criminal Enforcement", 30-40 attendees, Bangkok, Thailand, June 2019;
- The Third Emirates International Conference on Falsified and Substandard Medical Products," involved representatives from more than 12 countries, Dubai, United Arab Emirates, April 2019
- "Asia Regional Workshop on Enforcement Against Trade in Counterfeit Goods", 80 – 90 attendees, Bangkok, Thailand, September 2019.

OCI's Internet-related criminal investigations are led by its Cybercrime Investigations Unit (CcIU), which strategically targets online transnational criminal networks that threaten the public health of Americans. In September 2019, CcIU hosted an intensive cybercrime training seminar that combined international counterparts from Canada, India, and the U.K., with OCI's cybercrime specialists and experts from the online ecosystem. Augmenting ORA's international efforts, OCI's Senior Operation Manager for CcIU was elected to lead the Permanent Forum of International Pharmaceutical Crime (PFIPC). PFIPC is an international network that links OCI with direct law enforcement counterparts from around the world and enables Special Agents to work nimbly on investigations covering the globe.

OCI's Import Operations Program (IOP), detects violative shipments of FDA-regulated products entering our domestic ports and facilities. IOP's priorities include responding to international mail facilities, fast parcel carriers, sea and land ports, and mail hubs. IOP Special Agents routinely conduct joint enforcement activities, including internationally, and serve as a critical component within the FDA's support of the overall U.S. government-wide effort to combat cross-border crime. IOP also frequently provides training to its foreign law enforcement counterparts, U.S. government partner agencies, as well as local- and state-level law-enforcement personnel and regulated industry.

Compliance Activities

ORA issued 12 warning letters and five online advisory letters to foreign and domestic companies that were illegally selling more than 58 unapproved new drugs and/or misbranded

drugs that claim to prevent, treat, or cure Alzheimer's disease and a number of other serious diseases and health conditions. Several of the actions were taken jointly with the Federal Trade Commission. As part of ongoing efforts to protect consumers, the FDA has issued more than 40 warning letters in the past five years to companies marketing unapproved products for the cure, mitigation, treatment, or prevention of Alzheimer's disease on websites, social media, and in stores.

ORA created 61 immediate public notifications to alert consumers and health care providers about products marketed as dietary supplements discovered by FDA labs to contain undeclared drug ingredients. Many of these products were discovered during examinations of international mail shipments.

ORA issued and published 18 domain registrar abuse complaints and published those complaints on the FDA website. These abuse complaints are submitted to the respective domain registrar under the Internet Corporation for Assigned Names and Numbers (ICANN) Registrar Accreditation Agreement regarding the use of domain names for illegal purposes. The abuse complaints were issued to registrars of websites offering opioids and unapproved oncology and antiviral drugs for sale to U.S. consumers.

IFSS and Program Standardization

The FDA collaborates with other federal, SLTT, regulatory and public health association partners to advance an IFSS with the goal of protecting public health and reducing foodborne illness. The Partnership for Food Protection provides the collaborative forum for FDA and its partners to establish a collective vision and approach for a sustainable IFSS. The bedrock of an effective IFSS is having the assurance that the FDA and its regulatory partners are building and maintaining consistent, quality, and capable programs necessary to ensure public health. As of November 2019, FDA has 273 cooperative agreements/grants with 49 states, American Samoa, and 11 associations to accomplish this objective in FY2020. In addition, in FY 2019, to leverage the resources of our state/territorial regulatory partners to ensure domestic oversight of the nation's domestic food supply, the FDA has executed, 87 contracts that included 45 states and Puerto Rico. These contracts enabled approximately 17,000 inspections, site visits, and sample collections, including 444 human food preventive controls inspections (up from 231 in FY 2018) and 95 animal food preventive controls inspections.

The FDA continues to work collaboratively with its SLTT partners to develop, revise, and promote conformance with the Manufactured Food Regulatory Program Standards (MFRPS), Animal Feed Regulatory Program Standards (AFRPS), and Voluntary National Retail Food Regulatory Program Standards (VNRFRPS). Programs enrolled in the standards are taking meaningful steps to ensure they have the regulatory foundation and framework necessary to protect public health. Hence, conformance with the standards is a foundational element of an effective IFSS. As of November 2019, 43 SLTT programs are enrolled in the MFRPS, 23 in the AFRPS, and 855 in the VNRFRPS. There are 28 SLTT programs in full conformance with the MFRPS, four that has fully implemented the AFRPS, and five in full conformance with the VNRFRPS.

Another 2019 key achievement was the launch of international and domestic inspections for large farms growing produce covered by the FSMA Produce Safety Rule. In FY 2019, the FDA has cooperative agreements with 47 states and one territory to plan, establish, and/or enhance state and territorial produce safety programs. FDA continues to collaborate with our SLTT and association partners to develop guidance to ensure national consistency for the implementation of produce inspections, compliance, and enforcement.

The Animal Drugs and Feeds Program provided approximately $14 million in grants since FY 2011 to support the activities of the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), a network of 44 state and university veterinary diagnostic labs. The collaboration of veterinary diagnostic labs has helped the FDA prevent and respond to animal food emergencies by carefully investigating the clinical aspects of the reported illness. Such partnerships expand the FDA's ability to protect animal and human health.

The FDA has continued to integrate outbreak response by developing rapid response teams (RRTs) with state partners. RRTs are multi-agency, multi-disciplinary teams that operate using Incident Command System (ICS)/National Incident Management System (NIMS) principles and a Unified Command structure to respond to human and animal food emergencies. The purpose of this program is to minimize the time between notification of a human or animal food contamination event and implementation of effective control measures to prevent harm to consumers. In an emergency, RRTs coordinate efforts to align the response activities of agencies that have overlapping jurisdiction. Since FSMA was passed, the RRT program has grown from nine funded states (in 2009) to 18 funded states (in 2019), and an additional six states participate in the program voluntarily (outside of the funded cooperative agreement).

The use of new and evolving digital information sharing platforms and technologies will play a pivotal role in the timeliness of information sharing. Access to key information during an outbreak will help us trace the origin of contaminated food quickly, conduct timelier root-cause analysis and apply these lessons to prevent future incidents.

The FDA has also developed and led the domestic and international effort to build a first-of-its-kind network of labs that can sequence the genomes of foodborne pathogens and upload the genomic sequence and geographic location from which the pathogen was gathered, into a publicly accessible database. Known as the GenomeTrakr Network, this new tool is a paradigm-changing development that facilitates foodborne outbreak investigations. The network currently includes 15 federal labs, 25 state health and university labs, one U.S. hospital lab, and two additional U.S. labs, 20 international labs, and collaborations with independent academic researchers with the intent for more labs to join the network.

Import Operations

Over the last decade, there has been a 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.

Table 2: Number of Import Lines by Program Area: FY 2014 through FY 2022 (Est.)

Program Area	2015	2016	2017	2018	2019	5 Yr Actual Percent Growth*	2019 Percent of Total Lines	Estimate 2020	Estimate 2021	Estimate 2022
Foods	13,080,429	13,952,537	15,251,687	16,859,790	17,722,742	6%	39.24%	18,608,879	19,539,323	20,516,289
Cosmetics	2,930,682	2,939,034	2,625,555	2,729,584	2,762,411	-1%	6.12%	2,900,532	3,045,558	3,197,836
Human Drugs	688,208	739,309	789,853	871,212	838,267	4%	1.86%	880,180	924,189	970,399
Animal Drugs & Feeds	416,860	434,384	426,484	456,684	410,237	0%	0.91%	430,749	452,286	474,901
Biologics	150,673	151,911	157,080	170,575	181,328	4%	0.40%	190,394	199,914	209,910
Medical Devices & Rad Health	17,252,283	18,757,725	20,584,138	22,291,902	22,967,758	6%	50.85%	24,575,501	26,295,786	28,136,491
Tobacco Products	16,680	32,972	199,066	281,097	280,901	129%	0.62%	294,946	309,693	325,178
Total	34,535,815	37,007,872	40,033,863	43,660,844	45,163,644	25%	100.00%	47,881,181	50,766,750	53,831,004

*5 Yr Actual is based off a 5-year average (FY 2014 - FY 2019)

ORA works with the U.S. Customs and Border Protection (CBP) through 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), designed to promote interagency collaboration to target high-risk shipments and increase compliance with federal standards and regulations.

The FDA and CBP continue to work together to assess recommendations from the 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. COAC considers issues such as:

- Global supply-chain security and trade facilitation
- CBP modernization and automation; air cargo security
- Customs broker regulations
- Trade enforcement
- U.S. government approach to trade and safety of imports
- Agriculture inspection
- Protection of intellectual property rights

Under the FSMA framework, ORA has successfully implemented the Voluntary Qualified Importer Program (VQIP) in conjunction with the Centers for Food Safety and Nutrition (CFSAN) and Center for Veterinary Medicine (CVM). The VQIP application portal was launched in FY 2018 through fda.gov and remained open to accept completed VQIP applications through July 31, 2019, for importer benefits beginning in FY 2020. In future years, the VQIP Application portal will be open between January 1 and May 31. 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 the FDA to focus its resources on food entries that pose a higher risk to public health.

The FDA has developed and implemented an account management system within the Industry Trade Auxiliary System (ITACS), which allows for bilateral communications with importers and other industry stakeholders. The ITACS system and its use by trade is voluntary. The ITACS system allows trade to communicate directly with FDA to submit additional information and obtain information on shipments. In FY 2019, industry held over 1,450 accounts, thereby enhancing communication capabilities between FDA and Trade. ITACS also supports sending FDA Notices of Action electronically 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.

Risk-Related Prevention Focus

Because of the large volume and variety of imports, ORA must allocate inspectional resources based on estimates of risk associated with specific domestic and foreign firms. Using a preventive model to prioritize resources, ORA thus can efficiently focus inspection efforts, in conjunction with the FDA centers, in its efforts to protect public health. In addition, ORA advocates for enhanced collaboration with federal, SLTT, and global public health regulatory partners.

Strengthening the domestic network of regulators allows ORA to apply its investigators to 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 the FDA understand risks, assess the value of strategies to control those risks, and prevent contaminated products from reaching consumers. The process serves as a mechanism to actively identify risks and areas where preventive controls should be placed to protect public health. As the 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 Drug Evaluation and Research (CDER) and ORA continue to collaborate under an Concept of Operations (ConOps) agreement to integrate facility evaluations and inspections for human drugs. The agreement, titled 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, reducing the time to issue advisory and enforcement actions. For example, between FY17 to FY19, the median time from end of inspection to warning letter issuance decreased from 8 months to 6 months.

Additionally, CDER and ORA are working together to develop a new inspection and reporting paradigm to better assess and record the state of quality in manufacturing facilities. This 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 on October 29, 2018. The new protocols do not change the role of the investigator. Instead they 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. As NIPP data is collected and analyzed, it is expected to reveal anomalies, patterns, and correlations that will help drive decision-making and further reduce risks related to drug quality.

ORA and CDER are also collaborating to implement the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54), which 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 the 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 by the end of CY 2019.

To maximize ORA's medical device inspectional resources, and reduce the likelihood of 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 its medical device inspectional staff of approximately 130 investigators on products and facilities identified as highest risk through CDRH's risk-model. This model considers the medical device malfunctions, industry compliance trends, and public health concerns. ORA continues to work with CDRH to transition 21 CFR 820 regulations to ISO 13485:2016.

Mammograms are critical to early detection of breast cancer. More than 39 million mammograms are performed on patients annually. Each year, the FDA and inspectors in 44 states evaluate the level of compliance at more than 8,500 mammography facilities. RadHealth 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, the FDA participates in a five-country (United States, Australia, Brazil, Canada, and Japan) Medical Device Single Audit Program (MDSAP), which allows a third-party auditing organization to conduct a single regulatory facility audit of a medical device manufacturer, even if the manufacturer has multiple facilities in different countries. Approximately 2,900 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 that appropriate "For Cause" inspections are initiated.

In FY 2019, having conducted inspections of more than 1,014 U.S. blood establishments, ORA's oversight plays an important role in maintaining the safety of the U.S. 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 United States in 2015.

ORA is also responsible for inspections and investigations of human cells, tissues, and cellular and tissue-based products (HCT/Ps) and conducted 558 HCT/P establishment inspections in FY 2019.

The FDA's oversight of foreign facilities plays an important part in maintaining a safe human and animal food supply here in the United States. In FY 2019, ORA accomplished more than 1,700 foreign inspections of human and animal foods. ORA's foreign inspections found violations that led to a variety of compliance actions including warning letters, voluntary recalls, and on import alert listings. The agency is on target to meet the FY 2020 foreign inspection goals in the human and animal food programs by completing more than 1,450 inspections this fiscal year.

In FY 2019, ORA conducted inspections of 27 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 United States.

Under the Bioresearch Monitoring Program, ORA conducts more than 1,100 domestic and 315 foreign inspections each fiscal year. These are driven by risk-based selection models developed in each of the FDA's six 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 post-marketing adverse drug experience (PADE) reporting, and risk evaluation and mitigation strategies (REMS) to ensure patients continue to be protected after products are available on the market.

Premarket Medical Product Activities

To ensure products are produced as outlined in medical product applications, ORA inspects manufacturing facilities as part of the application review process. CDER and ORA have streamlined the process for Pre-Approval Facility Evaluation and inspections, through the ConOps strategic framework. This framework addresses how CDER and ORA work together on application review, inspections, and any associated compliance activities. This directly supports the assessment of marketing applications by ensuring that the application data is accurate, complete, and any named manufacturing facility in the application conforms to current Good Manufacturing Practice (cGMP) requirements.

The FDA Reauthorization Act of 2017 (FDARA) requires FDA to publicly report information on facility inspections, which are required for approval of a particular drug or a device. FDARA's section 902 requires that the FDA post annual reports on the agency website regarding facility inspections related to drug and device approvals. The inaugural CY 2017 report was published March 1, 2018. The CY 2018 report was published on March 12, 2019. The information and metrics contained in this report provide benchmark data to industry stakeholders regarding inspections related to product application approvals.

Developing Workforce and Leaders

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.

In FY 2019, the ORA Office of Training Education and Development's (OTED) quality program supported the awarding of International Association for Continuing Education and Training-accredited continuing education units for 222 training courses for more than 4,950 students. At the same time, ORA advanced the Associate Commissioner for Regulatory Affair's (ACRA) quality and strategic initiatives in records management and office-wide policy and procedure evaluation toward continuous improvement of training design, development, and delivery processes.

To prepare ORA's future leaders 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 pursuing a management career or career advancement. In continued support of ORA management succession planning, OTED completed the first Leadership Excellence Advancement Program to assist first-line supervisors in developing skills for second-level management. In addition, OTED successfully completed the fourth cohort of the Potential Supervisors Program (PSP), providing knowledge and skills to non-supervisory employees who may be considering management as a career path. Thirty-nine participants attended PSP in FY 2019.

ORA continues to map job functions to determine the specific 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 in chemistry for analysts. In FY 2019, job task analyses were completed for microbiology, state liaisons, and imports, and job analysis updates were completed for 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 FY 2020 and FY 2021. Additionally, ORA has redesigned the National Advanced Import course to reflect recent changes in the import arena including advanced technology needs. ORA also optimized the New Hire Fundamentals Training (NHFT) program in FY 2019. The NHFT program provides newly hired investigators with foundational knowledge about FDA, the laws we enforce, and field activities and will afford investigative consistency across all medical product and food programs.

Reduce the Burden of Addiction Crises that are Threatenin*g American Families*

Enhancing Opioids Enforcement

Section 3022 of the SUPPORT Act added section 801(u) [21 U.S.C. § 381(u)] to the FD&C Act, giving the FDA/ORA authority to treat an FDA-regulated article as a drug if it is or contains an Active Pharmaceutical Ingredient (API) in an approved drug or licensed biologic or an API in a drug or biologic that has been granted an investigational use exemption and for which a substantial clinical trial has been instituted and made public, if the article is an "ingredient that presents significant public health concern." During FY 2019, ORA worked with CDER to develop an initial list of nine APIs that meet both the "significant public health concern" and the

approval/investigational use authorization conditions described above. FDA will update the API list, as additions are approved throughout FY 2020.

ORA implemented this new authority using the initial list of indicated APIs at the IMFs on March 4, 2019. As of the end of September 2019, FDA has applied the section 801(u) authority in the IMFs to almost 10,000 violative drugs, representing approximately 43% of the drugs reviewed for admissibility by the FDA in the IMFs during that time. The implementation of 801(u) is an unquestioned success: in FY 2018 we destroyed approximately 6% of refused drug products; in FY 2019, prior to implementing 801(u), that number was about 16%. Since 801(u) implementation (through September 2019), ORA raised its overall destruction rate to more than 48% of violative drug products and expect that percentage to rise to 50% in early FY 2020.

The SUPPORT Act also provides new mandatory recall authority for controlled substances, including opioids, as well as authority to debar a person who has been convicted of a felony involving illegal importation of drugs or controlled substances, or who has engaged in a pattern of importing certain adulterated or misbranded drugs or controlled substances. Policies and procedures for implementing these authorities continue to be developed. The FDA has issued several notices of debarment for felony convictions involving the illegal importation of a drug. The FDA is currently processing the first debarment order under that new authority.

During the opioid crisis, consumers began seeking medication and treatments for opioid addiction and withdrawal. In 2018, the FDA teamed with other federal agencies to identify and warn dietary supplement product manufacturers who were marketing questionable opioid treatment remedies with violative claims about treating, mitigating, or preventing opioid addiction and opioid withdrawal. This work continues today through ongoing inspections of those firms.

Additionally, in FY2018 and FY2019 ORA completed three Opioid Quality Survey assignments intended to survey the pharmaceutical supply chain of opioid products to identify potential quality risks or economically motivated adulteration in the supply chain. Compounding assignments were also updated to include collection of information regarding the firm's purchase, production and distribution history of opioid Active Pharmaceutical Ingredients.

Enhancing Tobacco Enforcement

The "Deeming Rule," published May 10, 2016, in the Federal Register, extended FDA's authority to "deem" electronic cigarettes, cigars, hookah, and pipe tobacco and their components and parts tobacco products. ORA's tobacco operations staff completed 131 inspections of domestic tobacco product manufacturers, 188 investigations and investigated ten free-sample events in FY 2019. 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 FD&C Act. FDA's Center for Tobacco Products (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 FY 2020, ORA's tobacco operations staff will conduct at least 200 manufacturing inspections and investigations and will investigate a minimum of seven free sample events.

Foster Competition and Innovation

Cultivating a Global Regulatory Network

The 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.

The FDA fosters the 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.

The 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, and
- 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 sample collections. The 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 participates as an active member of Pharmaceutical Inspection Cooperation Scheme (PIC/S), the multinational organization that now contains 52 participating authorities representing the pharmaceutical inspectorate. In addition, FDA continues to participate in the MRA with the EU. The full implementation of the human MRA with Europe will increase efficiency, avoid duplicative inspections, allow the reallocation of resources to areas with higher public health risks, and thereby enable greater market access and improve international harmonization. Additionally, efforts are underway to expand the MRA with EU to include veterinary medicines and FDA is currently conducting capability assessments of EU veterinary agencies

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 United States have cooperated on joint inspections, joint traceback investigations, and environmental assessments, in addition to enhancing laboratory capacity.

Leveraging Laboratory Capabilities

ORA provides oversight of regulatory science standards in labs using 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 labs in building their capability and capacity to respond to large-scale food contamination events. FDA currently funds 26 FERN network laboratories, some of which cover multiple disciplines, including 14 microbiological, 14 chemical, and 5 radiological labs. In addition, ORA provides cooperative agreements to 55 state human and animal food testing labs to meet and maintain lab accreditation through the International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC) 17025:2005.

Figure 13 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 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 new technology. To promote this technology further, ORA works with state regulatory partners to initiate and use WGS in state labs on a national level. In addition, ORA, in collaboration with CFSAN, provides cooperative agreements to 11 state laboratories to support the development of a stronger international rapid surveillance system for pathogen traceback through whole genome sequencing.

Enhancing IT Systems and Initiatives

ORA is committed to supporting expanded regulatory authorities, increasing productivity, and maintaining program integrity through our information technology systems and initiatives.

ORA's approach is to make both incremental and continual progress to enhance and modernize its information technology (IT) portfolio while expanding functionality to encompass and support new regulatory requirements and business initiatives. The ORA IT governance boards direct the IT activities to achieve maximum benefits from IT innovations and projects. The modernization approach focuses on the top-level strategic goals of the agency and office, including:

- Increase information-sharing capabilities with internal and external partners to strengthen mutual reliance and support progress towards an IFSS;
- Improve ORA's application of data-driven analytical capabilities by advancing data standardization, reporting, search, and predictive analytics;
- Advance field data collection, detection, lab, and surveillance tools and systems;
- Improve IT efficiencies for end-users by aligning with and advancing the core business capabilities; and
- Ensure the IT infrastructure is adequate to share and secure information locally, across the field organizations, among the states, and with regional and global partners.

ORA has enhanced external information sharing and management capability including collaboration with seven partner states to pilot the National Food Safety Data Exchange (NFSDX), a system that enables data sharing to support food safety programs across produce safety and other FSMA programs. This also includes an externally facing web portal to provide one-stop shopping for partner states to access FSMA functionalities and maintain state user profiles and access control, a dashboard for monitoring exchange status and history, as well as notifications and system alerts.

ORA has implemented an electronic document management and internal information exchange to include use of Document Retrieval and Management Service (DRMS), a system that allows the FDA to share documents with internal and external partners. DRMS also provides states, external agencies, and internal FDA partners the ability to electronically submit the FDA inspection reports and other artifacts related to inspections.

Strides have been made to improve business intelligence capabilities such as records management and information access. Examples include enhancements to ORA's modern Commercial Off-the-Shelf (COTS) tool (Informatica™) to maintain the approximately 13 million FDA-regulated firm records. In addition, enhancements were made to ORA's Online Search and Retrieval (OSAR), a Google-like search capability, to easily view and access structured and unstructured data maintained in 25 different universes related to post-market regulatory functions.

ORA is developing the System for Entry Review and Import Operations (SERIO) to meet the needs of ORA's Import Investigational and Compliance staff. The SERIO project will consolidate some of the currently fragmented system functionality distributed across import systems and instead develop a system flexible enough to run on multiple devices, and allow for the end-to-end processing of entries (entry review, investigation, compliance) in one integrated system. The system will have capabilities to record and process field examination and sample collection activities while offline which will be later synched with the online web application and database systems. The mobile pilot to support entry review at ports and international mail facilities has been successfully completed and the mobility component will be rolled out in January 2020.

ORA approved and funded approximately 35 development/modernization projects over the past two years in support of these strategic goals. Additional ongoing IT enhancement projects include:

- Establishing Importer Industry account management functionality, which allows electronic communications between importers, filers, and the FDA staff, thus saving both postage and staff resources.
- Establishing and supporting an industry portal with the capability to look-up the FDA Firm Establishment Identifier (FEI) number to support data submission requirements for FDA-regulated products submitted for import into the United States.
- Delivering capabilities to support the regulatory authorities of FSMA to include functionality to support Import Certification and Third-Party Accreditation, VQIP, FSVP, and Preventive Controls for Human and Animal Food.
- Advancing tools and applications to support new regulations and improve operational effectiveness to include enhancement of the eNSpect platform to enable new inspection protocols (IPs) or guided inspections intended to standardize and improve inspection data.
- Delivering and improving the FDA Data Dashboard, which provides greater transparency to the public about the 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.
- Developing an integrated system for the scheduling and logistical support for Foreign Inspections.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$1,143,329,000	$1,063,123,000	$80,206,000
FY 2020 Enacted	$1,223,286,000	$1,118,165,000	$105,121,000
FY 2021 President's Budget	$1,224,180,000	$1,114,837,000	$109,343,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Office of Regulatory Affairs Program is $1,224,180,000, of which $1,114,837,000 is budget authority and $109,343,000 is user fees. The budget authority decreases by $3,328,000 compared to the FY 2020 Enacted Level. User Fees increase by $4,222,000. The FY 2021 budget allows FDA to continue to ensure that the food, feed, and medical products available to the American public are safe and effective.

Budget Authority

Food Safety (+$2.0 million / +5 FTE)

Cannabis and Cannabis Derivatives: Field Foods: + $2.0 million/ 5 FTE
This funding would provide ORA additional resources to regulate and inspect establishments manufacturing FDA regulated products containing cannabis and cannabis-derived compounds. The Agriculture Improvement Act of 2018 helped preserve FDA's authorities under the Food Drug and Cosmetic Act (FD&C) and section 351 of the Public Health Service Act. While these products are not controlled under the Controlled Substance Act, they are subject to the same authorities and requirements as FDA-regulated products containing any other substance. This allows the FDA to continue enforcing the law to protect patients and the public while also providing potential regulatory pathways, to the extent permitted by law, for products containing cannabis and cannabis-derived compounds.

While many products containing cannabis and cannabis ingredients remain illegal under the FD&C Act, there has been a proliferation of such products since the Farm Bill passed, putting a strain on agency resources. In many cases, product developers make unproven claims to treat serious or life-threatening diseases, and patients may be misled to forgo otherwise effective, available therapy and opt instead for a product that has no proven value or may cause them serious harm. New funding will enable FDA to better regulate the usage of cannabis-derived substances, such as cannabidiol (CBD), in FDA-regulated products such as dietary supplements and when used as unapproved food additives. The initiative will support regulatory activities, including developing policies and continue to perform its existing regulatory responsibilities including review of product applications, inspections, enforcement, and targeted research. FDA must support oversight of increasing numbers of marketed FDA-regulated products containing cannabis-derived substances that may put the public at risk.

Crosscutting Initiatives: (-$5.3 million / 1 FTE)

Artificial Intelligence and Other Emerging Technologies: Field Foods: + $2.1 million/ 1 FTE
The tremendous shift to a more global market for foods and medical products has introduced important new challenges. In addition to growth in the sheer volume of imports and the number of foreign facilities, the variety and complexity of imported products has increased, and the number of countries involved in producing these products has expanded to include many with less sophisticated regulatory systems than our own. Simultaneously, the supply chain from manufacturer to consumer has become increasingly complex — with an expanding web of consolidators and redistributors — making oversight significantly more difficult by both FDA as well as industry managing its own supply chain. The implementation of Artificial Intelligence (AI) is expected to improve FDA and industry's capabilities to respond to these complexities while also ensuring trade isn't adversely impacted.

ORA will focus on incorporating AI modeling (machine learning) into the import screening process for food commodities. Full incorporation of AI into ORA's import screening tools is dependent upon both a modernized screening system as well as development of machine learning models across all commodities. The proposed funding will allow ORA to modernize its current

screening tool called PREDICT. This modernization is intended to incorporate AI as well as update the software supporting entry screening functionality.

Outreach, Training, and Organizational Excellence: $7.444 million/ 0 FTE
Field Foods: -$5.025 million/ 0 FTE

Field Human Drugs: -$1.091 million/ 0 FTE

Field Biologics: -$0.282 million/ 0 FTE

Field Animal Drugs and Foods: -$0.476 million/ 0 FTE

Field Devices and Radiological Health: -$0.570 million/ 0 FTE

ORA will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. ORA will preserve its most critical public health and safety activities under this reduction, including training new and existing staff on emerging technologies used in industry, and pursuing productive global partnerships in the future.

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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 95.9% Target: 80% (Target Exceeded)	80%	80%	Maintain
224221: Percentage of Human and Animal Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 85.5% Target: 80% (Target Exceeded)	80%	80%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2019: 90.0% Target: 70% (Target Exceeded)	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)	FY 2019: 89.1% Target: 80% (Target Exceeded)	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)	FY 2019: 80.6% Target: 65% (Target Exceeded)	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)	FY 2019: 68.8% Target: 55% (Target Exceeded)	55%	55%	Maintain
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2019: 85.7% Target: 65% (Target Exceeded)	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)	FY 2019: 81.7% Target: 65% (Target Exceeded)	65%	65%	Maintain
253221: Percentage of Bioresearch Monitoring (BIMO) follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2019: 85.7% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2019: 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 2019: 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.

ORA Field Performance Measures

ORA's performance goals 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

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY2019 Actuals	FY2020 Estimate	FY2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***7,254***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	4,961	**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	114		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	207		
Domestic Fish & Fishery Products (HACCP) Inspections	740		
Import (Seafood Program Including HACCP) Inspections	187		
Juice HACCP Inspection Program (HACCP)	164		
Interstate Travel Sanitation (ITS) Inspections	803		
Domestic Field Exams/Tests	1,986	2,500	2,500
Domestic Laboratory Samples Analyzed	16,419	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,747***	***1,400***	***1,400***
All Foreign Inspections	1,747	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***9,001***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	141,905	168,200	168,200
Import Laboratory Samples Analyzed	17,770	35,300	35,300
Import Physical Exam Subtotal	**159,675**	**203,500**	**203,500**
Import Line Decisions	17,722,742	17,702,780	18,587,918
Percent of Import Lines Physically Examined	0.90%	1.15%	1.09%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	80,013	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***7,485***	***9,062***	***9,062***
State Contract Food Safety (Non HACCP) Inspections	6,627	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	757	1,000	1,000
State Contract Juice HACCP	50	100	100
State Contract LACF	101	100	100
State Contract Foods Funding	$13,359,092	$13,756,200	$13,893,762
Number of FERN State Laboratories	33	33	33
Annual FERN State Cooperative Agreements/Operations Funding	$8,894,886	$15,865,891	$15,865,891
Total State & Annual FERN Funding	**$22,253,978**	**$29,622,091**	**$29,759,653**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***16,486***	***18,462***	***18,462***

[1] The FY 2019 actual unique count of foreign inspections includes 133 OIP inspections (67 for China, 59 for India, & 7 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 Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***73***	***100***	***100***
Domestic Inspections	73	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***2***	***0***	***0***
Foreign Inspections	2	0	0
IMPORTS			
Import Field Exams/Tests	4,586	1,600	1,600
Import Laboratory Samples Analyzed	249	400	400
Import Physical Exam Subtotal	**4,835**	**2,000**	**2,000**
Import Line Decisions	2,762,411	2,866,063	3,009,366
Percent of Import Lines Physically Examined	0.18%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***75***	***100***	***100***

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,569***	***1,695***	***1,695***
Pre-Approval Inspections (NDA)	62	100	100
Pre-Approval Inspections (ANDA)	89	90	90
Bioresearch Monitoring Program Inspections	625	600	600
Drug Processing (GMP) Program Inspections	589	650	650
Compressed Medical Gas Manufacturers Inspections	35	50	50
Adverse Drug Events Project Inspections	73	88	88
OTC Monograph Project and Health Fraud Project Inspections	17	70	70
Compounding Inspections[1]	127	127	127
Domestic Laboratory Samples Analyzed	936	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1265***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	99	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	220	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	284	255	255
Foreign Drug Processing (GMP) Program Inspections	722	900	900
Foreign Adverse Drug Events Project Inspections	6	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,834***	***3,055***	***3,055***
IMPORTS			
Import Field Exams/Tests	7,617	10,000	10,000
Import Laboratory Samples Analyzed	843	620	620
Import Physical Exam Subtotal	**8,460**	**10,620**	**10,620**
Import Line Decisions	838,267	845,143	904,303
Percent of Import Lines Physically Examined	1.01%	1.26%	1.17%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***2,834***	***3,055***	***3,055***

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

[2] The FY 2019 actual unique count of foreign inspections includes 141 OIP inspections (69 for China, 70 for India, and 2 for Latin America).

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,734***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	93	100	100
Blood Bank Inspections	770	900	900
Source Plasma Inspections	216	190	190
Pre-License, Pre-Market Inspections	93	55	55
GMP Inspections	48	28	28
GMP (Device) Inspections	8	7	7
Human Tissue Inspections	552	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***65***	***47***	***47***
Bioresearch Monitoring Program Inspections	8	11	11
Foreign Human Tissue Inspections	3	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	9	7	7
GMP Inspections (Biologics & Device)	38	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,799***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	107	45	45
Import Line Decisions	181,328	179,104	188,059
Percent of Import Lines Physically Examined	0.06%	0.03%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,799***	***1,939***	***1,939***

Field Animal Drugs & Feeds Program Activity Data (PAD)

Field Animal Drugs and Feeds Program Workload and Outputs	FY 2019 Actuals			FY 2020 Estimate			FY 2021 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	***1,385***	***165***	***1,220***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	52	52	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	119	119	0	175	175	0	175	175	0
BSE Inspections	456	0	456	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	2	0	2	25	0	25	25	0	25
Illegal Residue Program Inspections	333	0	333	450	0	450	450	0	450
Feed Manufacturing Program Inspections	209	0	209	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,267	1	1,266	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***90***	***52***	***38***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	17	17	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	40	40	0	33	33	0	33	33	0
Foreign Feed Inspections	3	0	3	5	0	5	5	0	5
BSE Inspections	4	0	4	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,475***	***217***	***1,258***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	2,808	821	1,987	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	897	1	896	867	2	865	867	2	865
Import Physical Exam Subtotal	**3,705**	**822**	**2,883**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	481,684	71,447	410,237	479,518	69,181	410,337	503,494	72,640	430,854
Percent of Import Lines Physically Examined	0.77%	1.15%	0.70%	0.97%	0.72%	1.02%	0.93%	0.68%	0.97%
STATE WORK [2]									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***2,128***	***0***	***2,128***	***3,396***	***0***	***3,396***	***3,396***	***0***	***3,396***
State Contract Inspections: BSE [3]	1,020	0	1,020	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	525	0	525	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue [4]	0	0	0	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	$3,458,757	0	$3,458,757	$3,470,824	0	$3,470,824	$3,574,949	0	$3,574,949
State Contract Tissue Residue Funding [4]	$0	0	$0	$0	0	$0	$0	0	$0
Total State Funding	**$3,458,757**	**$0**	**$3,458,757**	**$3,470,824**	**$0**	**$3,470,824**	**$3,574,949**	**$0**	**$3,574,949**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***3,606***	***217***	***3,389***	***5,134***	***367***	***4,799***	***5,134***	***367***	***4,799***

[1] The FY 2019 actual unique count of foreign inspections includes 10 OIP inspections (4 for China and 6 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 Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,244***	***2,546***	***2,498***
Bioresearch Monitoring Program Inspections	201	300	300
Pre-Market Inspections	29	60	60
Post-Market Audit Inspections	19	60	60
GMP Inspections	1,214	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA) [3]	785	750	700
Domestic Radiological Health Inspections	93	50	50
Domestic Field Exams/Tests	35	100	100
Domestic Laboratory Samples Analyzed	114	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***520***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	15	14	14
Foreign Pre-Market Inspections	35	30	30
Foreign Post-Market Audit Inspections	11	20	20
Foreign GMP Inspections	436	550	550
Foreign MQSA Inspections	12	14	14
Foreign Radiological Health Inspections	47	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***2,764***	***3,159***	***3,159***
IMPORTS			
Import Field Exams/Tests	25,035	19,800	19,800
Import Laboratory Samples Analyzed	582	670	670
Import Physical Exam Subtotal	**25,617**	**20,470**	**20,470**
Import Line Decisions	22,967,758	23,852,335	25,521,999
Percent of Import Lines Physically Examined	0.11%	0.09%	0.08%
STATE WORK [2]			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,449***	***7,880***	***7,880***
Inspections (MQSA) by State Contract [5]	7,402	7,800	7,800
GMP Inspections by State Contract	47	20	20
State Contract Devices Funding	$147,250	$270,000	$278,100
State Contract Mammography Funding	$10,586,300	$10,803,540	$11,019,611
Total State Funding	**$10,733,550**	**$11,073,540**	**$11,297,711**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,213***	***11,039***	***11,039***

[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.

[5] State MQSA Non-Contract inspections have been combined into the State Contract line.

TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Tobacco	**666,832**	**686,991**	**661,739**	**762,612**	**100,873**
Center	652,065	676,457	647,055	747,765	100,710
Family Smoking Prevention and Tobacco Control Act	*652,065*	*676,457*	*647,055*	*647,765*	*710*
Expand tobacco products (Proposed)	---	---	---	*100,000*	*100,000*
Field	14,767	10,534	14,684	14,847	163
Family Smoking Prevention and Tobacco Control Act	*14,767*	*10,534*	*14,684*	*14,847*	*163*
FTE	**942**	**942**	**1,016**	**1,068**	**52**

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 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 false or misleading tobacco product labeling and advertising.

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.

Almost 90 percent of adult smokers start smoking by the age of 18,[103] and approximately 1,600 youth aged 12 to 17 smoke their first cigarette every day in the United States.[104] 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 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: to prevent access to - and use of - tobacco products, particularly e-cigarettes by children and teens
- science-based review of tobacco products.

Reduce the Burden of Addition Crises That Are Threatening American Families

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 (NTSO).

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

[103] 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.

[104] Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data

products, including electronic nicotine delivery systems (ENDS) - such as e-cigarettes, cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels.

This rule helps implement the goals of the Tobacco Control Act and enables FDA to improve public health and protect future generations from the dangers of tobacco use in a number of ways, including restricting the sale of these tobacco products to minors nationwide.

Figure 14

FDA has issued guidance documents that state the Agency's compliance policy with respect to premarket review of certain deemed products. The compliance policy applies to deemed products that are not "grandfathered" (i.e., on the market as of February 15, 2007) and were on the market prior to the effective date of the final deeming rule (August 8, 2016). When FDA announced its comprehensive plan for tobacco and nicotine regulation in 2017, the deadlines for premarket review of certain deemed products were extended, in part, so FDA could issue guidance and foundational rules to support the submission of product applications and to allow manufacturers of currently marketed deemed products more time to prepare product applications. FDA's concerns were clear about kids' use of e-cigarettes 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 would rise so sharply.

According to findings from the 2018 National Youth Tobacco Survey (NYTS), there was a dramatic increase in youth use of e-cigarettes: 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.[105] FDA's ongoing oversight of e-cigarettes and other ENDS products is critical to the Agency's public health mission and, especially, to protecting kids from the dangers of nicotine and tobacco-related disease and death. While certain ENDS products may hold some promise in helping addicted adult smokers transition away from combustible tobacco to a potentially less harmful form of nicotine delivery, these products – like all tobacco products – pose risk, and should not be used by kids. Years of progress to combat youth use of tobacco – to

[105] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625917.htm

prevent lifetimes of addiction to nicotine – is now threatened by an epidemic of e-cigarette use by kids.

Therefore, on November 15, 2018, FDA outlined updates to its policy framework to address the large increase in youth use of tobacco products. FDA's focus is on youth appeal and youth access to flavored tobacco products.

On July 12, 2019, a U.S. District Court judge in Maryland issued a decision that, among other things, vacated FDA's previous compliance policy guidance and requires makers and importers of e-cigarettes and other ENDS and certain other tobacco products like cigars, pipe tobacco and hookah to submit applications for their currently marketed products to the Agency within 10 months (May 12, 2020). FDA stands ready to accelerate the review of e-cigarettes and other new tobacco products.

FDA remains committed to tackling the epidemic of youth vaping using all available regulatory tools at our disposal. Recently published 2019 NYTS data in the *Mortality and Morbidity Weekly Reports (MMWR)*[106] shows that e-cigarettes remain the most commonly used tobacco product: 27.5 percent of high school students and 10.5 percent of middle school students were current e-cigarette users. Additionally, as in previous years, the 2019 NYTS shows a disturbing rate of youth use of non-tobacco flavored e-cigarettes.

On January 2, 2020, FDA issued a final guidance for industry entitled "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization."[107] Amid the epidemic levels of youth use of e-cigarettes and the popularity of certain products among children, FDA issued a policy prioritizing enforcement against certain unauthorized flavored e-cigarette products that appeal to kids, including fruit and mint flavors. Under this policy, companies that do not cease manufacture, distribution and sale of unauthorized flavored cartridge-based e-cigarettes (other than tobacco or menthol) within 30 days risk FDA enforcement actions.

FDA intends to prioritize enforcement against illegally marketed ENDS products by focusing on the following groups of products that do not have premarket authorization:

Any flavored, cartridge-based ENDS product (other than a tobacco- or menthol-flavored ENDS product);

- All other ENDS products for which the manufacturer has failed to take (or is failing to take) adequate measures to prevent minors' access; and
- Any ENDS product that is targeted to minors or likely to promote use of ENDS by minors.

[106] Wang TW, Gentzke AS, Creamer MR, et al. Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2019. MMWR Surveill Summ 2019;68(No. SS-12):1–22. DOI: http://dx.doi.org/10.15585/mmwr.ss6812a1

[107] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-delivery-system-ends-and-other-deemed-products-market

Cartridge-based ENDS products are a type of ENDS product that consists of, includes, or involves a cartridge or pod that holds liquid that is to be aerosolized when the product is used. For purposes of this policy, a cartridge or pod is any small, enclosed unit (sealed or unsealed) designed to fit within or operate as part of an ENDS product.

Importantly, FDA's enforcement priorities are not a "ban" on flavored or cartridge-based ENDS. FDA has already accepted and begun review of several premarket applications for flavored ENDS products through the pathway that Congress established in the Tobacco Control Act. Manufacturers that wish to market any ENDS product – including flavored e-cigarettes or e-liquids – are required by law to submit an application to FDA that demonstrates that the product meets the applicable standard in the law, such as whether the product is appropriate for the protection of the public health.

In addition, on December 20, 2019, the President signed legislation to amend the Federal Food, Drug, and Cosmetic Act, and raise the federal minimum age of sale of tobacco products from 18 to 21 years. It is now illegal for a retailer to sell any tobacco product – including cigarettes, cigars and e-cigarettes – to anyone under 21. FDA will provide additional details on this issue as they become available.

Further, as part of FDA's comprehensive plan for regulation of nicotine and tobacco, FDA is actively working on foundational rules to, among other things, make the Agency's science-based review process more efficient, predictable, and transparent for manufacturers, while upholding the Agency's public health mission. For example, FDA has issued proposed rules regarding Premarket Tobacco Product Applications (PMTA) and the content and format of Substantial Equivalence (SE) Reports. In addition, as described in the Unified Agenda, FDA is working towards product standards for electronic nicotine delivery systems (ENDS, including e-cigarettes) and other tobacco products, as well as drafting a proposed rule regarding requiring manufacturers to establish tobacco product manufacturing practices.

The Tobacco Control Act also requires the FDA to include new warning labels on cigarette packages and in cigarette advertisements. On August 16, 2019, FDA published a proposed rule to require new health warnings on cigarette packages and in advertisements to promote greater public understanding of the negative health consequences of smoking. The proposed warnings, which feature photo-realistic color images depicting some of the lesser-known, but serious health risks of cigarette smoking, stand to represent the most significant change to cigarette labels in more than 35 years. When finalized, this rule would fulfill a requirement in the Family Smoking Prevention and Tobacco Control Act and complement additional important work the FDA is undertaking to advance the health of America's families.

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).

FDA continues to take steps to strengthen the product review process. This includes holding public meetings, issuing regulations and guidance, and providing other information to assist the public in understanding the process.

To provide more clarity to applicants and support efficient and predictable review of SE Reports, FDA issued a proposed rule on April 2, 2019, entitled "Content and Format of Substantial Equivalence Reports; Food and Drug Administration Actions on Substantial Equivalence Reports." The proposed rule, if finalized, would:

- establish requirements for the content and format of reports intended to demonstrate the substantial equivalence of a tobacco product;
- establish the information an SE Report must include so that FDA may make a substantial equivalence determination;
- establish the general procedures FDA intends to follow when evaluating SE Reports; and
- include procedures that would address communications with the applicant and the confidentiality of data in an SE Report.

In June 2019, FDA issued a guidance, "Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS)," intended to assist persons submitting premarket tobacco product applications (PMTAs) for ENDS under section 910 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 387j).

In September 2019, FDA issued a proposed rule to set forth requirements related to the content, format and FDA's review and communications procedures for PMTAs as part of the agency's continued commitment to its oversight of e-cigarettes and other tobacco products. When finalized, this proposed rule will help to ensure that PMTAs contain sufficient information for evaluation such as details regarding the physical aspects of a tobacco product and information on the product's potential public health benefits and harms. It also would codify the procedures by which the agency would review PMTAs and establish the requirements for manufacturers to maintain records related to the legal marketing status of their tobacco products.

Similarly, FDA intends to issue a proposed rule that would establish basic content and format requirements for modified risk tobacco product applications (MRTPAs). The proposed rule would help to ensure that MRTPAs contain sufficient information for FDA to determine whether it should issue an order for a modified risk tobacco product (MRTP).

On October 28 and 29, 2019, FDA held a public meeting to provide information on FDA's expectations for tobacco product applications with a particular focus on deemed tobacco products

including product review policies, procedures, and general scientific principles. Information was presented about the tobacco product application review programs including lessons learned, process improvements, and observations that may inform further improvements in submissions and the review process.

In November 2019, FDA issued a final guidance, "Compliance Policy for Limited Modifications to Certain Marketed Tobacco Product," that describes FDA's compliance policy for premarket review requirements for certain modifications manufacturers can make to their tobacco products: (1) to address a voluntary industry battery standard (UL 8139) and (2) to comply with the Child Nicotine Poisoning Prevention Act of 2015 (CNPPA) requirements related to safe packaging of liquid nicotine products, known as flow restrictors. FDA encourages these limited safety-related modifications because they are intended to ensure the public is protected from risks such as battery explosions or accidental exposure to toxic levels of nicotine. The guidance provides clarity to manufacturers considering these limited safety-related modifications to their electronic nicotine delivery system products by outlining our compliance policy for premarket review requirements for such modifications.

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.

On April 30, 2019, FDA announced it has authorized the marketing of four new tobacco products through the PMTA pathway. Through its rigorous science-based review of the applications, FDA determined that these non-combusted cigarette products produce fewer or lower levels of some toxins than combusted cigarettes. To prevent youth access and exposure to the products, the Agency has placed stringent marketing restrictions on the products.

On December 17, 2019, FDA announced it has authorized the marketing of two additional new tobacco products through the PMTA pathway. These products are combusted, filtered cigarettes that contain a reduced amount of nicotine compared to typical commercial cigarettes. Following a rigorous science-based review of the applications, FDA determined that authorizing these reduced nicotine products is appropriate for the protection of the public health because of, among several key considerations, the potential to reduce nicotine dependence in addicted adult smokers, who may also benefit from decreasing nicotine exposure and cigarette consumption. In addition, the Agency determined that non-smokers, including youth, are unlikely to start using the products, and those who experiment are less likely to become addicted than people who experiment with conventional cigarettes. To prevent youth access and exposure to the products, the Agency is placing stringent restrictions on how the products are marketed – particularly via websites and through social media platforms.

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[108] 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.

In FY 2019, 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 implemented new performance measures for these reports and met those goals 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.

FDA continues scientific review of provisional SE Reports.[109] 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. As of October 31, 2019, 1,393 reports have been removed from review. This 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.

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.

In April 2019, FDA posted on its website six appendices containing common issues found in SE Reports, broken down by product type. To assist manufacturers preparing SE Reports, the appendices highlight common deficiencies that may result in an unfavorable SE decision.

Beginning in July 2019, in response to public interest, FDA began to post on its website reviewer guides and science policy memoranda. These documents offer a snapshot in time of FDA's thinking regarding details on key areas of tobacco regulatory science, and although not a

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108 http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm

109 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.

comprehensive manual for manufacturers preparing or anticipating review of a tobacco product application, these documents can serve as a resource to manufacturers.

Modified Risk Products

In addition to the three marketing pathways, before marketing a tobacco product 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.

On October 22, 2019, FDA announced that, for the first time, it has authorized the marketing of eight snus smokeless tobacco products through the MRTPA pathway. FDA made this authorization after reviewing scientific evidence submitted by the company that supports the claim that using the product "instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis". In an effort to help prevent youth access and exposure, the agency has also placed stringent advertising and promotion restrictions on the products, including a requirement to restrict advertising to adults. In addition, the products' packaging and advertising must also bear the warning statements required for all smokeless tobacco products.

Status of Submitted Applications

The following table is a summary of tobacco product applications received through October 31, 2019.

Application Status	**Product Class**[110]	**Cumulative through 10/31/2019**			
		Regular SE Reports	**Provisional SE Reports**	**Premarket Tobacco Applications**	**Modified Risk Tobacco Applications**
Received	Cigarettes	1,298	2,362	11	14
	RYO	1001	646	4	0
	Smokeless	413	589	14	19
	Other	349	18	403	9
	Total	**3,061**	**3,615**	**432**	**42**
Open	Cigarettes	50	415	2	6
	RYO	16	13	0	0
	Smokeless	22	113	6	7

[110] Other includes deemed products and products not under CTP jurisdiction.

	Other	53	0	34	0
	Total	**141**	**541**	**42**	**13**
Closed[111]	Cigarettes	1,248	1,947	9	8
	RYO	985	633	4	0
	Smokeless	391	476	8	12
	Other	296	18	369	9
	Total	**2,920**	**3,074**	**390**	**29**

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 2019, FDA invested more than $226 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:

- Chemistry and Engineering: understanding the chemical constituents in tobacco products and the methods for measuring them across products with diverse characteristics
- 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
- 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 regarding the health effects of tobacco products and nicotine (including addiction), through media campaigns, and digital media
- Marketing Influences: understanding the impact of marketing on susceptibility to using tobacco products (both classes of products and products within classes) and transitions between experimentation, 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,

[111] Closed includes refuse-to-accept, refuse-to-file, remove from review, issuance of an order, deficiency, environmental information request, response, withdrawn, or closure due to administrative issues.

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.

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.

FDA has also undertaken efforts to further the discussion and understanding around how the Agency can help those kids who are already addicted to the nicotine in e-cigarettes quit. This included holding a public hearing[112] and a separate scientific workshop[113] to discuss efforts to eliminate youth e-cigarette use as well as other tobacco product use, with a focus on the potential role of drug therapies to support cessation and the issues impacting the development of such therapies for youth.

NIH Tobacco Regulatory Science Program (TRSP)

FDA enhances scientific research capability through a collaboration with NIH by tapping into its well-established infrastructure for the solicitation, review, and management of scientific research. In FY 2019, FDA funded 112 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.

[112] https://www.fda.gov/media/118868/download

[113] https://www.federalregister.gov/documents/2019/04/02/2019-06323/youth-tobacco-cessation-science-and-treatment-strategies-public-scientific-workshop-request-for

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 2019, FDA funded 41 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 nine Tobacco Centers of Regulatory Science (TCORS). 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 National

Figure 15 Population Assessment of Tobacco and Health logo

Institute on Drug Abuse (NIDA), with both agencies collaborating on the scientific aspects of the study. The PATH Study is an ongoing nationally representative, longitudinal cohort study of approximately 46,000 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. Research topics in the PATH Study related to reducing harm include evaluating patterns of tobacco use over time, such as switching products and using multiple products, as well as seeking to understand perceptions, knowledge, attitudes and use of modified risk tobacco products.

Data is collected in "Waves" and the questionnaire data are made available to researchers and the public. Data were initially collected annually, with data collection moving to every two years starting in FY 2017 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, data collection for a sub-study of adult e-cigarette users began in March 2018 and was completed in June 2019.

Wave 4 questionnaire data were released to researchers in May 2019 and to the public in November 2019. Biomarker data from Wave 2 of the PATH Study were released to researchers in March 2019.

Laboratory Analyses

FDA partners with CDC to address priority research needs and with the Division of Laboratory Sciences at CDC on 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 and the toxicity of tobacco products via cell culture and animal models.

CTP partners 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. On November 5, 2019, data from this survey were published in the *Mortality and Morbidity Weekly Reports (MMWR)*[114] shows that e-cigarettes remain the most commonly used tobacco product, showing that 27.5 percent of high school students and 10.5 percent of middle school students were current e-cigarette users. 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).

CTP plans to continue the collaboration with CDC's National Center for Chronic Disease Prevention and Health Promotion, Division of Reproductive Health on the use of e-cigarettes and hookah among recently pregnant women in the Pregnancy Risk Assessment Monitoring System (PRAMS) survey.

CTP also 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.

[114] Wang TW, Gentzke AS, Creamer MR, et al. Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2019. MMWR Surveill Summ 2019;68(No. SS-12):1–22. DOI: http://dx.doi.org/10.15585/mmwr.ss6812a1

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 to youth.

Since the beginning of FY 2019, as part of the Youth Tobacco Prevention Plan, FDA has taken the following actions to stop youth use of, and access to, JUUL and other e-cigarette products:

- conducted well over 150,000 retail inspections to crack down on the sale of tobacco products, including e-cigarettes, to minors at both brick-and-mortar and online retailers
- issued thousands of warning letters and civil money penalties to retailers for illegally selling e-cigarette products to minors
- identified large retail chains that sell tobacco in the U.S. with violation rates above 15 percent and sent letters to corporate leadership requesting a plan to prevent tobacco sales to minors
- issued 30-day NTSO complaints for repeated violations to two companies identified as having violation rates above 15 percent
- partnered with the Federal Trade Commission (FTC) to issue warning letters to e-liquid manufacturers for violations related to online posts by social media influencers on the companies' behalf
- issued warning letters to e-liquid manufacturers whose products used misleading, kid-appealing imagery that caused the products to appear ingestible by imitating food products such as candy
- issued warning letters to e-liquid manufacturers whose products use misleading imagery that caused the products to appear ingestible by imitating cough syrups
- 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 more than 80 companies that may be illegally marketing more than 110 products, including ENDS, to youth
- issued seven warning letters to companies for illegally marketing over 100 unauthorized tobacco products in FY 2019
- issued a warning letter in October 2019 to a company for illegally marketing nearly 100 unauthorized ENDS products
- issued a warning letter to JUUL Labs for marketing unauthorized modified risk tobacco products via a presentation given to youth at a school
- sent a letter to JUUL Labs requesting more information about the company's outreach and marketing targeted at students, tribes, health insurers, and employers.

Figure 16 Example of misleadingly labeled e-liquids resembling cough syrups

FDA has also been working tirelessly alongside CDC and other federal, state, and local partners to investigate the distressing incidents of severe lung injuries and deaths associated with the use of vaping products. To date, the Agency has taken, or continues to take, the following actions:

- following up with patients and health care professionals to collect details about products or substances involved, where they were purchased, and how they were being used
- traveling throughout the country and attempting to gather any available evidence, including devices, pods/cartridges, diluting agents
- identifying any compounds that are present in the samples
- reaching out directly to the states that have submitted samples and is providing them high-level aggregate data in the form of status reports on preliminary analytical findings
- activating an Incident Management Group and is working alongside CDC's Incident Management System to serve as a focal point for emergency management and information sharing.

Tobacco Retailer Inspection Program

As of October 31, 2019, FDA had contracts for tobacco retailer compliance check inspections in 54 states and territories, and one tribal jurisdiction. 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 700 commissioned inspectors.

Although most tobacco retailers comply with FDA's tobacco laws and regulations, FDA conducts compliance check inspections and issues advisory and enforcement actions such as Warning Letters, Civil Money Penalties, and No-Tobacco-Sale-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 2019 Actuals	FY 2020 (as of 10/31/2019)	Total Since the Program's Inception (as of 10/31/2019)
Retailer Inspections	146,905	10,890	1,146,970
Warning Letters	14,673	845	93,986
ENDS Products Only	4,423	242	10,639
Civil Money Penalties	4,707	443	23,960
ENDS Products Only	829	805	1,655
No-Tobacco-Sale-Orders	13	2	171

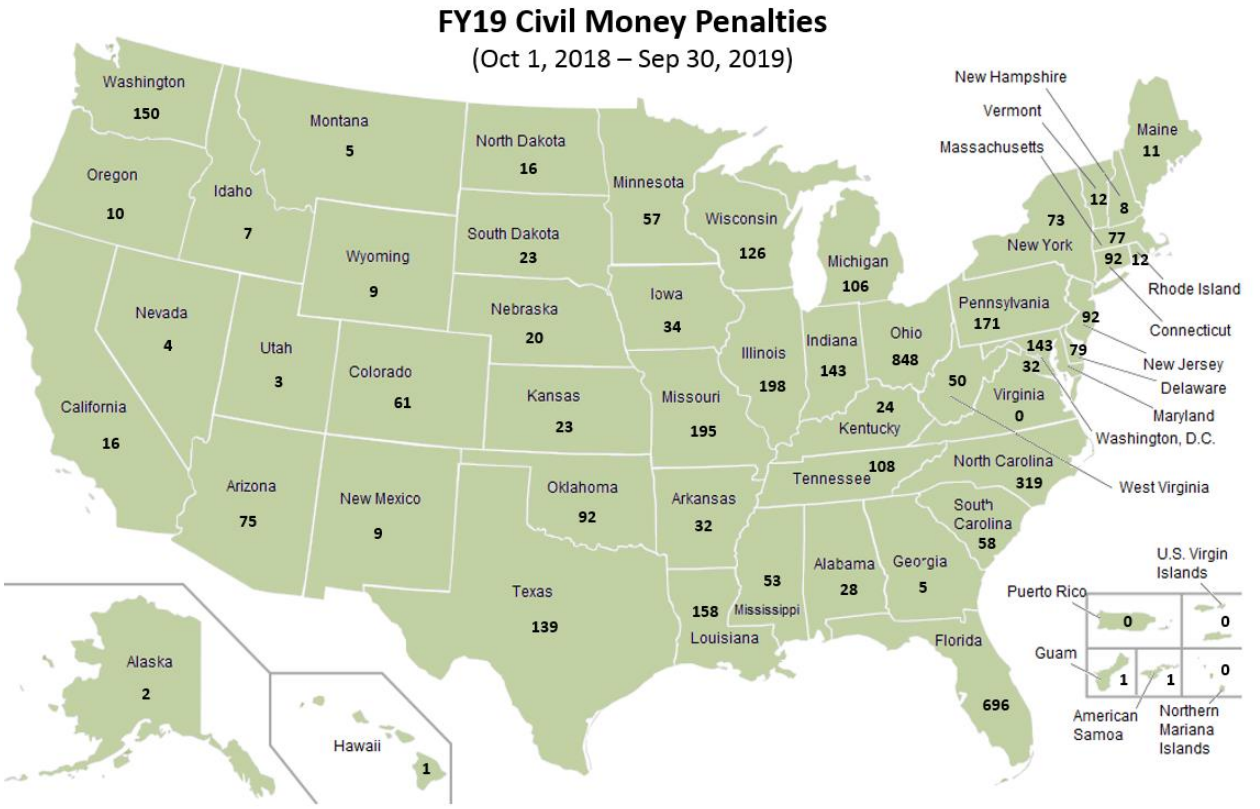

Figure 17 The number of Civil Money Penalty Complaints filed by the Center for Tobacco Products in FY 2019 by state.

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. It complements the tobacco sales compliance efforts of the Tobacco Retailer Inspection Program. The program includes a free set of resources, such as a digital calendar, designed to support retailers' efforts to educate staff on enforcing federal laws and regulations. In spring 2019, digital programmable calendars were mailed to tobacco retailers nationwide. The calendar enables retailers to set the age on the digital calendar to match their local tobacco laws.

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, 2019, CTP has overseen the completion of more than 2,000 inspections of vape shops to verify whether they were engaged in manufacturing activities, and ORA has completed over 650 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, 2019, FDA has issued over 790 warning letters as a result of these surveillance activities. In FY 2019, more than 100 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 more than 70 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.

FDA's current public education campaigns:

Campaigns	Launch date	Description
"The Real Cost" Cigarette Campaign	February 2014	Educate at-risk youth aged 12 to 17 about the harmful effects of cigarette 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. Since "The Real Cost" launched in 2014, the campaign has used a robust media strategy to effectively reach teens and change their tobacco-related knowledge, attitudes, beliefs, and behaviors. The campaign continues nationally across TV, radio, print, web, and social media, and will launch new advertising in Summer 2020.

Under the brand, “The Real Cost”, FDA educates male youth 12-17 to shift their knowledge, attitudes, and beliefs about the dangers associated with smokeless tobacco use. In January 2019, the FDA expanded its reach from 35 counties and 600,000 at-risk rural male teens to nearly 3 million across 20 states using a primarily digital media strategy.

Figure 18 "The Real Cost" campaign logo

Preliminary evaluation data indicates that 85.9 percent of the target audience is aware of at least one of the campaign’s videos. Data also shows increased agreement with specific campaign-targeted attitudes and beliefs that are correlated with reduced odds of smokeless tobacco use – key indicators of campaign effectiveness.

In September 2018, FDA further extended “The Real Cost” brand to prevent youth e-cigarette use. The campaign targets 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. The campaign launched with national digital advertising and posters placed in school bathrooms. In 2019, campaign advertising expanded to television. The campaign distributed e-cigarette prevention information to over 700,000 high school administrators and teachers, including fact sheets and lesson plans in 2018. In the 2019-2020 school year, the campaign is delivering new lesson plans and resources for both high school and middle school teachers, students, and parents.

Since its launch, “The Real Cost” E-Cigarette Prevention Campaign is showing positive results for reach and engagement. The campaign, which originally focused on digital and social media sites popular among teens, has generated nearly 2 billion teen views in 9.5 months. Across social media platforms, the FDA has engaged teen audiences with more than 850,000 likes, 115,000 shares, and 47,000 comments. Additionally, the agency began driving teens who want to quit vaping to Teen.SmokeFree.gov in July 2019. Since the web pages on quitting vaping launched, there have been over 250,000-page views.

A nationally recognized campaign, “The Real Cost” Smokeless campaign earned a silver Effie in 2019 in the Youth Marketing category of the North American Effie Awards. The Effies are the advertising industry’s most prestigious award, recognizing marketing ideas that work and have demonstrated effectiveness. In 2019, “The Real Cost” Cigarettes campaign also received a BrandBlazer award from Verizon Media for its youth marketing and gaming advertising. The BrandBlazer award recognizes excellence from brands in the advertising field.

Fresh Empire

"Fresh Empire" educates the nearly five million multicultural youth who are open to smoking

or are already experimenting with cigarettes about the harms of tobacco use. The campaign uses broadcast TV, radio, digital advertising, and social media to reach the audience with aspirational messaging that tobacco use is not a necessary part of the hip hop lifestyle. "Fresh Empire" advertising focuses on addiction caused by smoking.

Figure 19 "Fresh Empire" campaign logo

In 2019, the "Fresh Empire" campaign received platinum and gold Hermes awards for the social marketing and Twitter categories respectively. Hermes is an international competition that honors excellence in communications and marketing.

This Free Life

LGBT young adults are nearly twice as likely to use tobacco as other young adults, ultimately resulting in the loss of tens of thousands of LGBT lives to tobacco use each year. The "This Free Life" campaign is designed to reach occasional or "social" smokers through print and digital advertising, and social media to help prevent tobacco-related death and disease in the LGBT community.

Figure 20 "This Free Life" campaign logo

In 2019 the campaign received a Gold Hermes Award for its engagement-focused digital and social media content.

Every Try Counts

FDA's first adult cessation campaign, "Every Try Counts,"

Figure 21 "Every Try Counts" campaign logo

is aimed at encouraging cigarette smokers to quit through messages of support that underscore the health benefits of quitting. These messages are displayed in and around gas stations or

convenience stores – retail locations where smokers face a multitude of triggers and that typically feature cigarette advertisements. Select campaign print ads are available for use via both CTP's content sharing platform, the Exchange Lab, and the Centers for Disease Control and Prevention (CDC)'s Media Campaign Resource Center (MCRC). The Exchange Lab and MCRC provides access to advertisements for use by states and/or other public health organizations and agencies. The "Every Try Counts" campaign has partnered with the Detroit Pistons to amplify the campaign message in the Detroit area. As part of the partnership, the Pistons will donate up to $15K to the Henry Ford Tobacco Treatment Service and feature in-arena campaign signage, social media messages, and PSA videos.

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 National Cancer Institute (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.

An evaluation found that in the first 2 years of the "The Real Cost" campaign more than 587,000 youth aged 11 to 19 were prevented from initiating cigarette smoking – half of whom might have gone on to become established smokers – saving more than $53 billion by reducing smoking-related costs like early loss of life, costly medical care, lost wages, lower productivity, and increased disability. 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 $180 for every dollar of the nearly $250 million invested in the first two years of the campaign. FDA has also recently concluded data collection for separate outcome evaluations of "The Real Cost" Smokeless campaign messaging, the "Fresh Empire" campaign, and the "This Free Life" campaign.

For "The Real Cost" Smokeless campaign evaluation, the FDA surveyed a longitudinal cohort of male youth aged 11 to 16 at baseline from January 2016 through December 2018 to changes in attitudes and beliefs for respondents in intervention markets to control markets. At final follow-up, agreement with some campaign-targeted attitudes increased significantly in the intervention markets and with male youth aged 15 and older. Based on prior literature showing the predictive relationship between attitudes and longer-term behavior change, these findings suggest that the campaign could have an effect on smokeless tobacco use among rural boys. Additional analysis using media-market level data is ongoing.

Results from the "Fresh Empire" and "This Free Life" outcome evaluations will be made available after the data are analyzed. The evaluation for the "Every Try Counts" campaign is currently in progress. These evaluations measure whether exposure to campaign messaging creates positive changes in tobacco-related knowledge, attitudes, beliefs, and intentions among the target audiences.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2017 Actual	$754,076,000	---	$754,076,000
FY 2018 Actual	$625,406,000	---	$625,406,000
FY 2019 Actual	$686,991,000	---	$686,991,000
FY 2020 Enacted	$661,739,000	---	$661,739,000
FY 2021 President's Budget	$762,612,000	---	$762,612,000

BUDGET REQUEST

The FY 2021 Budget Request is $762,612,000 all from user fees. This amount is $100 million above the FY 2021 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 $100,873,000 above the FY 2020 Enacted Budget.

The Center for Tobacco Products amount in this request is $747,765,000. 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. This additional funding will strengthen actions FDA is taking to combat youth use of tobacco products, including the epidemic of youth use of e-cigarettes, through our Youth Tobacco Prevention Plan, which bolsters compliance and enforcement efforts for all tobacco products, and to expand public education campaigns and science and research programs. To ensure that resources keep up with new tobacco products, the proposal would also index future collections to inflation. This proposal would ensure that FDA has the resources to address today's alarming rise in youth e-cigarette use as well as new public health threats of tomorrow.

In FY 2021, CTP will continue implementing the FDA-wide Comprehensive Plan for Tobacco and Nicotine Regulation, which is consistent with the Center's 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

FDA-wide Comprehensive Plan for Tobacco and Nicotine Regulation

FDA's comprehensive plan serves as a multi-year roadmap to protect youth and significantly reduce tobacco-related disease and death. FDA regulates a broad range of nicotine-delivering products, from cigarettes to medicinal nicotine gum and patch. FDA is pursuing an integrated, agency-wide policy on nicotine- containing products that is public health based and recognizes the continuum of risk among such products.

FDA will continue to implement the comprehensive plan by:

- considering regulatory guidance on premarket review policy based on the principle of relative toxicity and risk
- implementing the Youth Tobacco Prevention Plan, to prevent access to - and use of - tobacco products, particularly e-cigarettes by children and teens
- conducting science-based review of tobacco products
- working on foundational rules such as proposed rules on Substantial Equivalence, Tobacco Product Manufacturing Practices, PMTAs and MRTPs.

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, especially given the epidemic-level use of e-cigarettes by children and adolescents.

FDA is continuing efforts with the Nicotine Steering Committee; this committee includes representatives from CTP, FDA's Center for Drug Evaluation and Research (CDER), and FDA's Office of the Commissioner. Efforts include:

- continuing work to develop options for a comprehensive regulatory approach to nicotine containing products
- considering potential policies for regulation of products made from nicotine from sources other than tobacco.

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[115] tobacco products:

- by demonstrating they are appropriate for protection of the public health, or
- by demonstrating substantial equivalence[116] to certain commercially marketed products, or
- by demonstrating they are exempt from the requirements of substantial equivalence.

CTP is 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 review, including new performance measures effective in FY 2019 for provisional SE Reports. CTP also regularly evaluates the application review process to identify areas where process improvements could enhance CTP work efficiencies. Further, CTP is hiring additional scientific and regulatory staff to review product applications.

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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 and exploring potential product standards for addictiveness, toxicity, and appeal in a strategic effort to yield strong standards and improve public health.

[115] A "new tobacco product" is any tobacco product (including those products in test markets) that was not commercially marketed in the United States as of February 15, 2007; or any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007.

[116] A pathway to market for new tobacco products where the applicant has to demonstrate that the characteristics of the new tobacco product(s) are the same as the corresponding predicate product(s) (which is a product that was commercially marketed in the United States as of February 15, 2007 (other than for test markets), or a product previously found to be substantially equivalent) or the characteristics are different, but the new product does not raise different questions of public health.

FDA also is actively considering the need for other product standards. For example, FDA is working on ENDS safety standards, including standards for toxicants and impurities. In addition, FDA is working on a proposed rulemaking to ban characterizing flavors in cigars.

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 have expanded to include messages 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 2021, 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 expanding education efforts, such as "The Real Cost" campaign, to educate youth about the dangers of using tobacco products, including e-cigarettes
- 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 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 will continue to take vigorous enforcement actions aimed at ensuring e-cigarettes and other tobacco products are not being marketed to, or sold to, kids.

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
- continuing inspections and investigations at brick and mortar locations and online websites
- continuing a sustained campaign to monitor, penalize, and prevent ENDS sales in convenience stores and other retail sites that violate the FD&C Act and regulations

- 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 inspections of tobacco manufacturing facilities
- inspecting vape shops to ensure that they are in compliance with the requirements of the FD&C Act and regulations
- enforcing promotion, advertising, and labeling requirements
- referring potential criminal activity to FDA's Office of Criminal Investigations
- Investing in Human Capital

Investing in Human Capital

FDA is focused on growing our workforce to support our strategic initiatives and continues 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.

To address the critical hiring need to support our mission, FDA/CTP requested and received approval of the Direct Hire Authority (DHA) from the Office of Personnel Management (OPM) for scientific, Consumer Safety Officers, and information technology positions through October 2021. This will significantly increase CTP's ability to hire talented staff.

Additional Support Activities

FDA will continue to:

- partner with other agencies, including NIH, CDC, and FDA's NCTR to expand the tobacco regulatory science base and fund priority Tobacco Regulatory Science (TRS) research
- 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
- conduct targeted priority research with contract research organizations
- continue to develop enterprise IT systems to support the tracking, management, and review of product applications
- conduct tobacco product surveillance by reviewing all reports submitted by the public through the Safety Reporting Portal to identify new or concerning trends.

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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
280005: Total number of compliance check inspections of retail establishments in States under contract. *(Outcome)*	FY 2019: 146,905 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 2019: 96% Target: 80% (Target Exceeded)	80%	80%	Maintain
280007: Educate at-risk youth (12-17 year olds) about the harmful effects of tobacco use. *(Output)*	FY 2019: Reached 75% of general market at risk 12-17 year olds with campaign messaging. (Target Met)	Reach 75% of 12-17 year olds with campaign messaging within 1 year.	Reach 75% of 12-17 year olds with campaign messaging within 1 year.	Maintain

Compliance Check Inspections

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 2019. Although this number was much higher than the expected FY 2019 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 2020, 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 2020 and FY 2021 targets consider these challenges and will therefore remain at the FY 2019 target levels.

Regular SE Reports

"Review and act on" includes issuing a Deficiency letter (deficiency notification), Cancellation, Closure, SE Order or NSE Order.

Educate At-Risk Youth 12-17 Year Olds

FDA's public education campaigns help educate the public—especially youth—about the dangers of regulated tobacco products. FDA has four active youth campaigns in market - “The Real Cost” Cigarettes campaign, “The Real Cost” Smokeless campaign, “The Real Cost” E-Cigarette Prevention campaign, and the “Fresh Empire” campaign.

PROGRAM ACTIVITY DATA

CTP Workload and Outputs	FY 2019 Actuals	FY 2020 Target	FY 2021 Target
Tobacco Retailer Inspections			
Number of Inspections	146,905	130,000	130,000
Tobacco Manufacturer Inspections			
Number of Inspections[1]	276	300	300
Substantial Equivalence Reviews			
Number of Regular SE Reports	302	100	100

[1] Outyear estimates are based on the number of firms registered with FDA. FDA inspects each registered firm biennially.

FDA HEADQUARTERS

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
FDA Headquarters	**311,133**	**307,092**	**319,487**	**326,070**	**6,583**
Budget Authority	***180,220***	***187,776***	***185,420***	***186,713***	***1,293***
User Fees	***130,913***	***119,316***	***134,067***	***139,357***	***5,290***
Prescription Drug (PDUFA)	*56,391*	*66,425*	*56,756*	*58,501*	*1,745*
Medical Device (MDUFA)	*8,463*	*8,411*	*9,219*	*9,833*	*614*
Generic Drug (GDUFA)	*35,243*	*31,790*	*32,834*	*33,691*	*857*
Biosimilars (BsUFA)	*632*	*2,004*	*1,331*	*1,364*	*33*
Animal Drug (ADUFA)	*1,004*	*948*	*914*	*938*	*24*
Animal Generic Drug (AGDUFA)	*785*	*708*	*756*	*845*	*89*
Family Smoking Prevention and Tobacco Control Act	*27,012*	*9,030*	*30,867*	*30,867*	*---*
Mammography Quality Standards Act (MQSA)	*92*	*---*	*74*	*76*	*2*
Food and Feed Recall	*75*	*---*	*77*	*78*	*1*
Food Reinspection	*480*	*---*	*489*	*499*	*10*
Voluntary Qualified Importer Program	*277*	*---*	*283*	*287*	*4*
Third Party Auditor Program	*39*	*---*	*40*	*40*	*---*
Outsourcing Facility	*420*	*---*	*427*	*438*	*11*
Innovative Food Products (Proposed)	*---*	*---*	*---*	*1,900*	*1,900*
FTE	**961**	**961**	**927**	**930**	**3**

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.

Protect and Promote the Safety and Health of Families

FDA protects and promotes the safety and health of families by working to:

- reduce harms from opioid addiction and abuse
- implement a Comprehensive Nicotine Strategy and Youth Use/Enforcement Strategy
- implement a food safety program
- ensure safety of medical devices
- combat antimicrobial resistance
- reduce pathogens
- monitor post market safety of drugs
- monitor safety of compounding 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[117].

New Era of Smarter Food Safety

In April 2019, FDA announced a new approach to food safety to leverage technology, and other tools, to create a more digital, traceable and safer food system. This approach will build on the progress that continues to be made in FDA's implementation of the Food Safety Modernization Act (FSMA), while advancing the use of technologies that are currently used in society and business sectors all around us, such as blockchain, sensor technology, the Internet of Things, and artificial intelligence. In September 2019, FDA released a "Food for Thought" document outlining initial ideas on how to begin a "New Era of Smarter Food Safety" by addressing issues such as tech-enabled traceability for foodborne outbreak response, smarter tools and approaches

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

for prevention, evolving food business models, and food safety culture.[118] In October 2019, FDA held a public meeting and opened a Federal Register docket to hear from a broad cross-section of stakeholders on how this approach will strengthen its protection of the food supply. In early 2020, FDA plans to release a blueprint that will outline critical steps to protect public health and keep pace with the ever-changing global food supply chain.

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. Through the seven foundational rules finalized in 2015 and 2016, FSMA guides the food safety system in implementing effective measures to prevent contamination and engages all domestic and foreign participants in the food system to do their part to minimize the likelihood of harmful contamination.

In 2019, FDA carried out activities to support the compliance dates for these foundational rules, many of which took effect this past year. For example, in 2019, FDA and its state regulatory counterparts began conducting routine inspections of large farms for the Produce Safety Rule established by FSMA. Under cooperative agreements with FDA and state regulatory partners, almost 1,000 large farm inspections have been completed. The first routine inspections of small farms are set to begin in January 2020. FDA also remains focused on education, training and outreach to farms. This outreach includes about 1,400 On-Farm Readiness Reviews that National Association of State Departments of Agriculture (NASDA) developed in collaboration with the FDA and state partners to help farmers assess their readiness to comply with the rule.

In February 2019, the agency released the "FDA Strategy for the Safety of Imported Foods," describing our comprehensive approach to imported food safety. Our new strategy is designed to meet four important goals: preventing food safety problems in the foreign supply chain prior to entry into the U.S.; effectively detecting and refusing entry of unsafe foods at U.S. borders; responding quickly when the FDA learns of unsafe imported foods; and measuring our progress to ensure that our imported food safety program remains effective and efficient. To support the goal of preventing imported safety problems prior to entry into the U.S., FDA began inspections for the Foreign Supplier Verification Programs (FSVP) rule. This program requires importers to verify that their suppliers are meeting U.S. food safety standards. In addition, FDA's launch of the Accredited Third-Party Certification program provides a framework for audits of foreign food facilities to verify compliance with U.S. food safety standards, which can be used by importers to establish eligibility in the Voluntary Qualified Importer Program (VQIP). The VQIP offers importers expedited review and entry of their food based on the safety assurances that the audits provide. The program also provides additional data and intelligence that helps FDA plan oversight activities based on a more accurate assessment of risk.

In August 2019, FDA issued a letter calling on all sectors of the papaya industry (growers, packers, shippers and retailers) to review their operations and make all necessary changes to strengthen public health safeguards. Since 2011, American consumers have been exposed to eight outbreaks caused by Salmonella serotypes linked to imported, fresh papaya. In addition to

[118] https://www.fda.gov/media/131682/download

the papaya industry letter, FDA also issued a warning letter to the distributor of the papayas implicated in the outbreak.

In September 2019, FDA launched a Food Safety Dashboard designed to track the impact of the seven foundational FSMA rules, measure their progress, and help FDA continue to refine FSMA implementation. The dashboard is available as part of the FDA-TRACK program, FDA's agency-wide performance management system. Presently, the Food Safety Dashboard will track outcomes from three of the FSMA rules: preventive controls for both human food and food for animals, and imported food safety, including data relevant to the "Foreign Supplier Verification Program" (FSVP) rule. Additional measures and data will be added in the future.

Emergency Preparedness and Response

FDA HQ coordinates Agency emergency response to adverse events associated 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 a nationwide, 24-hour, 7 day-a-week emergency response system, including around-the-clock 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 2019, FDA HQ coordinated emergency response to 108 significant incidents including:

- 7 serious adverse or injury event incidents
- 57 natural disasters
- 43 man-made disasters
- 4 National Special Security Event

In FY 2019, FDA HQ also activated Incident Management Groups (IMGs) to provide headquarters coordination for Hurricanes Michael and Dorian and 2019 Vape Products.

FDA HQ evaluated 3,832 consumer complaints (including 25 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 2019, FDA HQ:

- coordinated 23 Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products.

- addressed four draft notices of Public Health Emergency of International Concern (PHEIC) from the HHS International Health Regulations Program.
- responded to and coordinated 185 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.
- conducted, evaluated and reported on Table Top and Full Scale Exercises for two Center Select Agent Laboratory facilities, including a medically downed patient in a High Containment Laboratory.
- conducted, evaluated and reported on a second Table Top Exercise (TTX) involving a fire in the high containment area, with the resulting after action reports emphasizing the need for additional training.
- created and presented three training sessions for laboratory researchers on patient assessment, monitoring, movement and turn over to medical authority.
- conducted a Radiation Laboratory Security TTX.
- supported the Shaken Fury inter-agency exercise.
- supported the Crimson Contagion inter-agency exercise.
- 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 (FEMA) led exercise that examined tribal, local, state and federal capabilities in 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 Fiscal Year 2019, along with the publication of the proposed and final rules themselves, FDA published the economic analyses for rules related to medical device and human drug products:

- Medical Device Classification Procedures: Incorporating FDA Safety and Innovation Act Procedures
- Classification of In Vitro Diagnostic Device for Bacillus Species Detection
- Medical Device De Novo Classification Process
- Sunscreen Drug Products for Over-The-Counter Human Use
- 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
- Safety and Effectiveness of Consumer Antiseptic Rubs; Topical Antimicrobial Drug Products for OTC Human Use
- Biologics License Applications and Master Files

The support provided by these economic analyses spanned more than five years and informed policy decisions throughout the rulemaking process. Data analysis and economic modeling provide vital inputs to our analyses and play a key role in the publication of proposed and final rules that foster innovation and clarify regulatory uncertainty among the regulated industry.

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, journalists, policymakers, regulated industry, and others.

From May 2018 through November 2019 FDA HQ issued:

- 300 MedWatch Safety Alerts (FDA's second largest e-list) to more than 440 thousand subscribers;
- More than 500 News Releases and other press announcements in English and/or Spanish to more than 100 thousand subscribers;
- 69 FDA Voice Blogs with more than 61, thousand subscribers;
- About 120 Consumer Updates (both new and updated content) in English and Spanish to more than 116 thousand subscribers;
- 20 Consumer Videos uploaded to YouTube with 213,929 views and nearly 40 thousand subscribers; and
- More than 70 newsletters, which reach over 83,000 Health care professionals, consumers and patients and targeted emails to specific organizations.
- Published about 125 tweets per month, 100 Facebook posts per month, and our posts are seen about 5 million times a month.
- We have 1 million followers on OMA accounts, and 2.5 million followers when you count all the social media accounts across FDA.

MedWatch Update Reporting: FDA's ongoing work to promote MedWatch present numerous opportunities to increase awareness about the importance of health professional, patient and consumer reporting adverse events and problems with medical products to the FDA.
FDA HQ has worked to make updates to the MedWatch forms simplifying the reporting, image attaching of suspected products, and submitting a MedWatch report for health professionals, patients and consumers. FDA has also released a newly translated Form FDA 3500B in Spanish to reach additional users.

FDA Office of Women's Health (OWH) addresses FDA priority areas by promoting women's health and safety information through social medial platforms and disseminating health education materials to external stakeholders. OWH's resources help women make informed health decisions throughout their lifespan. Notable FY 2019 accomplishments include:

- Disseminating FDA safety alerts and health information via the OWH twitter account to approximately 73 thousand followers,
- Reaching women through presentations and outreach to over 32 national healthcare professional, research and women's advocacy conferences and meetings,
- Receiving over 1.7 million twitter impressions and approximately 1 million website visits and engagement,
- Distributing over 2 million print materials via the Government Publishing Office, or GPO. Over 300,000 of these materials were in Spanish. The following are the top requests, publications for the period:
- Mammograms - Fact Sheet – 145,000
- Heart Health for Women - Fact Sheet – 125,000
- Diabetes Medicines – Booklet – 93,570

OWH began the development of its new campaign, KNOWH (Knowledge and News on Women's Health) The Difference. This campaign builds on increasing an understanding of sex

and gender differences as they pertain to women with respect to medical conditions that are unique to women or that impact women differently. The first focus area in this campaign series is cardiovascular disease. This features a video called "Getting a Beat on What Women Know about Heart Health", available on various media platforms, to help raise awareness about heart disease among women and correct any misconceptions viewers may have about the disease.

The Office of Minority Health and Health Equity (OMHHE) develops culturally and linguistically tailored health education materials for racial and ethnic minority, underserved, and under-represented consumer groups, written at low literacy levels. These communications are designed to strengthen consumer's decision-making process regarding FDA-regulated products and include items like brochures, fact sheets, post cards, and digital content.

In FY 2019, over 5,000 health education materials were disseminated to over 20 organizations, with over 9 health educational materials translated into 10 languages. OMHHE also reached 5 million consumers through digital outreach like social media messages, 7 Twitter chats, 4 blogs, 3 newsletters, and 20 e-alerts focused on health topics disproportionately impacting minority groups. OMHHE also continued promotion of 2 public service announcements and a podcast as part of the Minorities in Clinical Trials Campaign featuring veterans sharing their stories to promote clinical participation that reached over 126,000 consumers.

In addition, OMHHE educated and trained 60+ staff on strategies to create culturally tailored health education materials through a workshop entitled "Communicating with Confidence: Strategies to Create Effective Communications for Diverse Audiences". This training supports building a culturally competent workforce and will continue in FY 2020 with a focus on cultural biases.

Support for FDA's Priority Rulemakings and Guidance Documents

In 2019, FDA's Office of Policy (OP) continued to advance the agency's public health mission through support for priority policies, including policies to combat addiction to opioids, advance FDA's framework for regulation of tobacco products, and empower consumers and patients.

As part of the FDA's ongoing commitment to assess the benefit-risk of opioid pain medications, OP coordinated the issuance of the draft guidance "Opioids Analgesic Drugs: Consideration for Benefit-Risk Assessment Framework" and a notice announcing a public hearing on the future of opioid analgesics to treat pain and addiction. Information received in response to the guidance and the hearing will inform how FDA assesses the benefit-risk and public health risks associated with use and misuse of these drugs.

As part of FDA's work to advance a comprehensive framework for the regulation of tobacco products and to combat use youth of tobacco, OP coordinated the issuance of foundational rulemaking and guidance, including the proposed rule "Content and Format of Substantial Equivalence Reports" and the final guidance, "Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems." These foundational policies will help make FDA's science-based regulatory review process more efficient, predictable, and transparent for manufacturers, while upholding the agency's public health mission.

As part of HHS's and FDA's Safe Importation Action Plan, OP led FDA's efforts to develop a draft guidance recommending a pathway by which manufacturers could use importation to offer lower-cost versions of their drugs originally intended for foreign markets. OP also coordinated the agency's efforts to draft a Notice of Proposed Rulemaking (NPRM) to rely on section 804 of the Federal Food, Drug, and Cosmetic Act to authorize the importation of drugs from Canada. The Guidance and NPRM, if finalized, would provide two pathways to provide safe, lower-cost drugs to consumers.

To empower consumers and patients, OP coordinated the issuance of key aspects of FDA's Nutrition Innovation Strategy, including the final guidance "Declaration of Added Sugars on Honey, Maple Syrup, Single Ingredient Sugars and Syrups and Certain Cranberry Products." A component of FDA's strategy to provide information that consumers need to make better-informed decisions about eating, this guidance will help consumers better understand the amount of sugar in single-ingredient products like powdered sugar, pure maple syrup and honey.

In addition, OP continued to support all the agency's components in the development and issuance of regulations, guidances, and other Federal Register documents, which, in total, routinely exceed 700 or more actions per year. Between October 2018 - July 2019, OP facilitated issuance of more than 600 documents in the Federal Register.

Foster Competition and Innovation

FDA foster's competition and innovation by:

- pricing/access with biosimilars
- supporting biotech innovation
- harnessing real-world evidence
- continuing to implement FDARA and 21st Century Cures Act
- 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 good clinical practices and 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.

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants
In FY 2019, FDA HQ:

- received 520 first-time requests for orphan drug designation and designated 348 promising drugs and biological products for rare diseases
- received 26 first-time requests for Humanitarian Use Device designations and designated 10 promising devices for rare diseases and conditions
- received 54 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 44 drugs and biologics for rare pediatric disease's[119]
- funding 75 clinical studies of promising therapies for rare diseases and 12 new clinical trial grant awards
- funding 2 natural history grant awards to inform medical product development by better understanding how specific rare diseases progress over time
- funding 5 pediatric device consortia with 3 real world evidence projects to provide multidisciplinary advice and funding to assist pediatric device innovators and bring technological advances in medical devices to children
- 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.

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

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 pediatric rare disease populations study design considerations and informed consent requirements.

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 completing 67 pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews).

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.

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.

FDA HQ developed the Research Impact and Outcomes (RIO) Framework to evaluate the performance of programmatic initiatives, including funded research portfolios. The RIO Framework has been successfully applied to establish prospective metrics to select proposals for funding with the highest impact. It is currently being used retrospectively to evaluate the Office's research portfolio and identify areas of improvement and existing knowledge/research gaps. In addition, since the establishment of the Office of Women's Health, FDA HQ has distributed $45.5 million to 421 projects. Scientific data from many of these research projects have contributed to FDA guidance development and labeling changes.

The Office of Women's Health partners with several external organizations to investigate sex differences and its impact on health, medication and use of health data. It also develops additional gender specific data to inform clinical trials and studies. The Office of Women's Health is also piloting the OWH Women's Health Fellowship program, officially launching in 2020, which will fund full-time research fellows to conduct research directly with Center investigators.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ 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 2019 program accomplishments include:

- Leading a quarterly Scientific Speaker Series to promote the inclusion of sex and gender differences in research, professional education, and consumer information, which improves attendee knowledge by 30 to 60%
- In honor of Women's Health Week 2019, leading a scientific discussion focusing on the science and statistics of sex differences in the microcosm of space exploration. This research is vital not only to the success of NASA's missions, but also human endeavors in challenging environments on Earth and healthy aging for both men and women.

OWH also serves as the FDA representative to the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)[120], established in 2016 by the 21st Century Cures Act[121] (PRGLAC) to advise the Secretary of Health and Human Services (HHS). In September 2018, PRGLAC submitted to the HHS Secretary and Congress its report and 15 recommendations[122]. The taskforce has been renewed for an additional two years by the Secretary of Health and Human Services and will provide advice and guidance to the HHS Secretary on the implementation of these recommendations.

OWH co-founded a symposium with CDER/DPMH in November 2019 on the safety of asthma medications during pregnancy. FDA brought in outside expert speakers for a full day of discussions on research priorities and methodologies with emphasis on study designs to fill evidence gaps and developing a research agenda.

OWH supported the 2019 FDA Science Forum planning committee and incorporated women's health topics into the panel and poster session on Precision Health.

[120] For more information please visit https://www.nichd.nih.gov/about/advisory/PRGLAC

[121] For more information please visit https://uscode.house.gov/view.xhtml?path=&req=%28title:42+section:289a-2+edition:prelim%29+OR+%28granuleid:USC-prelim-title42-section289a-2%29&f=treesort&fq=&num=0&hl=false&edition=prelim

[122] Report is available at https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf

Minority Health Research Engagement

The Office of Minority Health and Health Equity (OMHHE) works with FDA Centers, offices and extramural partners to reduce health disparities by supporting, conducting, and funding minority-health focused research, education, and scientific exchanges. Research studies provide insight into scientific basis for individual therapies, provide future directions for research, and aid regulatory decision-making. OMHHE amplifies research through strategic partnerships that advance the health of diverse populations. OMHHE also partners with diverse stakeholders like academia, professional associations, non-profit organizations, among others to collaborate on health equity projects.

In FY 2019, OMHHE collaborated across FDA product Centers and funded and/or participated in 9 health disparity-focused research projects through the FDA Centers for Excellence in Regulatory Science and Innovation (CERSI), Office of the Chief Scientist Challenge Grant mechanisms, FDA's Broad Agency Announcement, and other mechanisms on product labeling, health literacy, pharmacogenomic biomarkers, nonalcoholic fatty liver disease, chronic pain, and nutrition and food safety.

OMHHE also leads strategic collaboration with federal partners around issues that impact minority and vulnerable populations. OMHHE collaborated with the Veterans Health Administration on a research project aimed at understanding minority Veterans' use of opioids and adverse events. In addition, OMHHE collaborated with the FDA Genomics workgroup to host a National Human Genome Research Institute (NHGRI) and FDA meeting to support advancing strategic planning, collaborations, and partnerships.

To provide awareness about research, programs, and initiatives that address issues which adversely impact racial and ethnic minority populations, OMHHE hosted 5 lectures on topics including clinical trials, tobacco use among tribal communities, precision medicine, sickle cell disease, and asthma drug response under the "Health Equity Lecture Series". These lectures provided continuing education credits for physicians, pharmacists, nurses, and health educators. OMHHE also partnered with NHGRI to co-host a Genomics and Health Disparities Lecture Series.

OMHHE has participated and/or exhibited at over 40 meetings and conferences and presented on a range of topics such as minority health focused research findings that have also been communicated through peer reviewed journals and posters including a recent publication on social media and FDA archival data in Social and Administrative Pharmacy (October 2019). OMHHE met with multiple stakeholders on an ongoing basis including regulated industry to advance racial and ethnic minority participation in clinical trials as well as community engagement efforts to advance clinical trial diversity.

To advance social and behavioral sciences, OMHHE partnered with the Office of the Chief Scientist by collaborating to co-chair the FDA Social and Behavioral Sciences Work Group including hosting an internal symposium in November 2019 to advance social and behavioral science efforts for the Agency. Other efforts to advance regulatory science and minority health include supporting the CFSAN Summer Science Teachers program by funding 3 teachers to develop curricula for students in underserved areas, funding 3 NCTR summer students that

conducted a range of projects to advance regulatory science, and precepting 2 pharmacy students and three Yale University interns.

In partnership with the Center for Tobacco Products, to support efforts to reduce death and disease caused by tobacco use, selected 15 peer reviewed journal articles on interventions, research, and strategies to address tobacco use among diverse populations. Articles will be featured in an upcoming Health Promotion Practice Supplemental Journal Issue on tobacco and health equity that will publish in January 2020 (includes 3 articles by FDA researchers). FDA will host a panel session at the Society for Public Health Education annual meeting in March 2020 to promote the featured research.

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. During the summer of 2016, FDA held a public meeting to have a robust and interactive discussion with openFDA users to obtain feedback on the openFDA platform.

OpenFDA provides access to:

- Drug Adverse events – over 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
- device registration and listing – over 230,000 records
- recalls and enforcement report data, containing information from public notices about recalls

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[123]

Communication with Stakeholders - Improvements to FDA.gov

FDA launched a redesigned FDA.gov website in April 2019. The redesign of the public-facing website centered on the transition to Drupal, a state-of-the-art content management system (CMS). The Drupal platform offers 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 makes 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.

Communicating with Stakeholders - Eloqua Email Delivery Service

FDA HQ continues to use the Eloqua email delivery system to send priority agency announcements and 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 150 content topics available and over 1.7 million stakeholders who have subscribed to receive information. The topic of Recalls currently has more than 405,000 subscribers.

Stakeholder Outreach Activities

Since June 2018, FDA HQ has conducted approximately 85 meetings/activities with a wide range of stakeholders. Noteworthy among these has been meetings or interactions with Consumer Groups, Healthcare Professional Organizations, Patient Advocacy groups, and Research and Policy Institutions.

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

FDA HQ has also used social media to engage with our stakeholders, via Facebook, multiple Twitter accounts, YouTube, and other channels. The agency conducted five Twitter chats, including three targeting a bilingual (English- and Spanish-speaking) audience.

FDA's Scientific Data and Information about Products Containing Cannabis or Cannabis-Derived Compounds Public Hearing: During Spring of 2019 FDA HQ coordinated, facilitated and moderated the agencies first public hearing on CBD. Nearly 140 speakers – formal presentations (with accompanying slide deck) or oral comments (with no slide deck) – were presented during the public hearing session. Over 600 individuals attended the hearing in person, while over 2000 tuned in remotely.

Listening Sessions on Drug Shortages: FDA HQ facilitated several individual listening sessions for the Shortages Task Force from September - October 2018, to gather information concerning the economic and clinical impact of drug shortages. Over 50 organizations traveled to FDA's White Oak Campus to participate, including groups from: Industry & GPOs, Distributors & Payers, Pharmacies & Hospitals, Manufacturers & Trade Associations, Think Tanks & Experts.

Listening Session on Counterfeits Products: FDA HQ coordinated several listening sessions during the Summer of 2019 to gather stakeholder concerns, feedback and useful information regarding counterfeit FDA-regulated products. Over 35 stakeholder groups participated.

Speaker Requests: FDA HQ manages 1,337 speaker requests received from over 142 trade associations and industry-based groups for issues that cut across the FDA's organizational and product lines, as well as major meetings that involve various FDA Centers and offices subject matter experts' participation in external meetings, conferences, and workshops.

FDA's Office of Minority Health and Health Equity amplifies the voice of the agency by hosting, exhibiting, and presenting at national meetings and conferences to showcase FDA's portfolio of minority health programs and initiatives.

In FY 2019, OMHHE participated and/or exhibited at over 40 meetings and conferences as well as participating in a media interview that reached more than 25,000 Hispanic consumers, and collaborated to support the 2019 Puerto Rico Clinical Research Summit to share best practices on clinical investigation.

OMHHE also hosted a Public Meeting on "Strategies to Improve Health Equity Amidst the Opioid Crisis" to share information and obtain the public's perspectives on the current opioid crisis and how it affects minority, underrepresented, and underserved populations across the country, approaches to prevent and treat opioid use disorder, and emerging research to improve care, and explore how FDA can support those efforts. Over 250 participants attended/viewed the meeting via webcast. Senior leaders including, the U.S. Surgeon General, FDA's Chief Scientist, and FDA's Associate Commissioner for Minority Health gave remarks; plus 23 speakers representing patients, patient advocacy groups, Department of Health and Human Services Agencies, Department of Justice, and the Veterans Health Administration gave presentations on their unique efforts to address the opioid crisis.

To advance partnerships and collaborations, OMHHE established a MOU with The Alliance of Multicultural Physicians to collaborate on developing educational, outreach, and training initiatives for physicians and the patients they serve to advance health equity and diverse participation in clinical trials. OMHHE also continued to advance efforts through a MOU with Yale University to advance the Yale Cultural Ambassadors Program and engagement of community partners to increase diverse participation in clinical research.

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 history interviews of selected staff to more completely document and explain the past; educates the public and staff through publications, exhibits, presentations, and exhibits; and provides counsel on precedents to regulations, statutes, policies, actions, and legal cases.

Since June 2018 the FDA HQ installed a permanent exhibit, "Our Story: The Food and Drug Administration," at FDA Headquarters, featuring a rich collection of historical artifacts, images, films, stories and multimedia displays that convey important aspects of the agency's development and current regulatory work. This exhibit was designed with the help of the Smithsonian Institution to serve as an educational tool for all FDA employees and visitors to HQ and is accompanied by a portfolio of digital assets on fda.gov, YouTube and Flickr to serve those employees who are unable to visit the White Oak campus, as well as public stakeholders. The historians frequently tour this exhibit for staff and visitors to the campus. In support of the FDA's educational goals, the agency also curated exhibits on the 25th anniversary of the Office of Women's Health, World AIDS Day; the AIDS Memorial Quilt, featuring a display of one of its sections; the Chamber of Horrors and the 1938 Food, Drug, and Cosmetic Act; the 50th anniversary of the Animal Drug Amendments; and the History of FDA and PHS collaborations, Part I: 1906-1962. In addition, FDA completed a video (in collaboration with the CDRH studio) and a video blog (in collaboration with OEA) on the Chamber of Horrors, as well as a video introducing the public to the "Our Story" exhibit. To document the agency's institutional memory, FDA recorded the reorganization of the Office of Regulatory Affairs through oral histories with approximately 30 principal officials, including Center Directors, the ACRA, and other officials from HQ and the field. The anniversary of the Office of Women's Health and its 25-year history was captured in a series of interviews with former Directors of the Office. Public access to and improved use of the corpus of more than 250 oral history transcripts was facilitated by the migration of these records to fda.gov with enhanced search functionality. In furtherance of the agency's historical preservation needs, FDA digitized 500 tapes in the oral history collection representing 250 interviews, as well as 3400 A/V recordings, and acquired over 3000 artifacts. In advance of information migration to a White House-mandated, public-facing collection database for the agency's scientific collections, FDA converted catalog information on roughly 6,000 objects to spreadsheets and created a database template to accommodate approximately 13,000 objects. FDA also participated in the Interagency Working Group on Scientific Collections to study the economics of the government's scientific collections. FDA provided bi-weekly in-person and online-based training on agency history to new hires; perspective on product-oriented regulatory developments in human and animal drugs, food labeling, medical devices, and other areas to staff and outside groups; and historical background to print and broadcast media interested in agency policy.

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[124]

Congressional Engagement

OL has worked closely with Congress to ensure FDA can implement legislative proposals to lower the cost of prescription drugs, many of which are novel such as those related to drug importation, exclusivity, price disclosure, publication of biologic patents, the use of citizen petitions, access to reference listed drugs, and biosimilars. OL has assisted Congress as it shaped legislation that could impact medical product approval standards and regulatory pathways in an effort to expedite getting innovative products onto the market, including the passage by the House of Representatives of legislation to reform the approval of over-the-counter drugs, and the passage into law of legislation to reauthorize the animal drug user fee programs, regulate products containing hemp and its extracts, and prepare for disaster and emergency response health activities. OL also provided information requested by Congress in order to inform policymaking on new issues in the food space. Through OL, the Agency has worked diligently to provide timely feedback to authorizing committees and other Congressional offices on these and many other issues of concern to them.

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

Engagement with State, Local, Territorial and Tribal Officials

The Intergovernmental Affairs (IGA) staff works to facilitate the Agency's communication and collaboration with state, local, territorial and tribal officials and regulatory partners. In addition to proactively providing timely information on the important activities of the Agency, the IGA staff works to serve as a primary entry point for these important stakeholders on issues of significant concern to states, localities, territories and tribes, and to ensure that questions from these stakeholders related the Agency's policies and programs are addressed. In FY 2020, significant engagement by the IGA team with these important stakeholders related to issues such as the regulation of cannabis and cannabis-derived products, tobacco products, device sterilization, opioids and other controlled substances, food safety, and compounded drugs. With respect to the last of these issues, the IGA team is the facilitator of the annual intergovernmental meeting on drug compounding issues which brings together regulators from across the country, as well as representatives from key state associations, to discuss pressing issues in the compounding space. The 8th such meeting was held in FY 2020 (October 10-11, 2019) and brought together regulatory officials from 43 states, the District of Columbia and the U.S. Virgin Islands, as well as staff from the National Association of State Boards of Pharmacy. The meeting featured sessions on finalizing the state Memorandum of Understanding, information-sharing concerning the interstate distribution of compounded drugs, current good manufacturing practices, the modernization of outsourcing facilities, and implementation of the Drug Supply Chain Security Act. Regarding food safety, the IGA team interfaces with Governors' offices, health departments and state departments of agriculture (in coordination with Agency program staff) to ensure that important information regarding food recalls, outbreaks of foodborne illnesses, and other important food safety issues are shared in a timely manner.

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, to the extent applicable and permissible, given FDA's and HHS's different statutory mandates.[125]

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 regulation and results reporting on ClinicalTrials.gov (42 CFR part 11). FDA HQ provided consultation to NIH to support two reports required under the Cures Act related to ClinicalTrials.gov.

[125] 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.[126] 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.[127] 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[128]	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[129]	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 –	This guidance provides recommendations for submission of information when clinical data from device investigations conducted within or outside the US are submitted to support

[126] 83 FR 7366; https://www.gpo.gov/fdsys/pkg/FR-2018-02-21/pdf/2018-03244.pdf

[127] 83 FR 57378; https://www.gpo.gov/fdsys/pkg/FR-2018-11-15/pdf/2018-24822.pdf%20

[128] https://www.fda.gov/RegulatoryInformation/Guidances/ucm623197.htm

[129] https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM512761.pdf

Publication Date	Formal Title	Description
	Frequently Asked Questions[130]	research or marketing applications or other submission.
January 2018	Payment and Reimbursement to Research Subjects – Information Sheet Guidance[131]	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 FDA's website[132].

In addition, FDA HQ annually provides over 100 formal inter-Center ethics consultations on a wide variety of ethical issues identified during the review for clinical trials and marketing applications submitted to the FDA.

Geographic Information System Mapping

In FY 2019 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 2019 Hurricane Season. FDA HQ completed maps for 92 GIS project requests involving FDA-regulated industry.

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,

[130] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm597273.pdf

[131] https://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm

[132] https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm

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. MCMi Regulatory Science Program activities in FY 2019 – FY 2020 include:

- developing gastrointestinal, bone marrow, and lung models based on 'organs-on-a-chip' technology for evaluation of MCMs drugs to treat acute radiation syndrome, including a better understanding of sex-based differences in responses to ARS medical countermeasures
- developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during public health emergencies
- developing new methods of respiratory protective devices decontamination for potential reuse in emergency situations resulting in the first ASTM consensus standard for UV surface decontamination
- expanding a database of regulatory-grade nucleic acid sequences to include antimicrobial-resistant organisms as well as Ebola- and Zika-related sequences
- developing and improving animal models for emerging infectious diseases
- developing a toolkit to assess efficacy of Ebola vaccines and therapeutics
- supporting survivor studies to better understand the after-effects of Ebola and Zika infection, and applying new technologies, to help find new treatments
- exploring how the Sentinel System may inform study protocols for MCM safety and effectiveness, and provide a baseline for comparison during a public health emergency
- in collaboration with DoD, working to better understand the microbial pathogenesis of Ebola, Marburg, Rift Valley fever, Crimean Congo hemorrhagic fever, Chikungunya, and Zika viruses
- conducting the largest Ebola virus and host gene expression (i.e., transcriptomics) study to date, using the latest sequencing technologies, including single-cell sequencing methods, to assess how Ebola virus evolves and spreads within the body
- developing a unique biobank of clinical Ebola-related samples from over 2,500 participants, including investigational Ebola vaccinees and Ebola survivors, to characterize the durability and correlates of vaccine-induced and natural immunity to Ebola virus disease
- 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 2019 – FY 2020 that support MCM availability and access include:

- implementing and responding to questions related to FDA's Material Threat Medical Countermeasure Priority Review Voucher program
- using FDA's 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
- supporting FDA MCM-related collaborations, including enhanced DoD collaborations under Public Law 115-92, and drafting memoranda of understanding (MOUs) to provide frameworks for various FDA collaborations (e.g., DoD, NASA, Office of the Assistant Secretary for Preparedness Response)
- working with the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare and Medicaid Services (CMS) to collaborate on and address issues related to the implementation of EUA diagnostic tests in clinical and public health laboratories during public health emergencies
- participating in the Global Health Security Agenda's implementation of a National Action Plan to advance the World Health Organization goal to build national capacities required to rapidly identify and act quickly to respond to public health emergencies and the Global Health Security Initiative MCM Task Force's effort to establish a generic framework for sharing medical countermeasures
- clarifying regulatory issues around building frameworks for conducting clinical studies during public health emergencies.

FDA HQ continued to facilitate 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 – including facilitating the authorization of the use of a rapid, single-use diagnostic test for the detection of Ebola virus, which was 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 supported the issuance of 6 amendments to current EUAs upon request from the product manufacturers to add additional instruments or specimen types or make clarifications, and 4 EUA revocations, when diagnostics previously available under EUA were authorized for marketing.

FDA HQ also developed policies for the development, use, and export of investigational MCMs as necessary. 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 work to resolve MCM shortages as quickly as possible when they occurred. For example, FDA continued to collaborate with U.S. government partners and the product manufacturer of auto-injectors used for the treatment of nerve agent and insecticide poisoning to help prevent shortages of these products after quality issues were identified in the manufacturing process. FDA reviewed applicable scientific data and determined that, if properly stored, certain lots of this manufacturer's auto-injectors held for emergency use could continue to be used beyond the original labeled expiration date for a period specified by FDA, to help ensure ready access to these products. Based on its review of scientific data, FDA also identified certain lots that are no longer usable and, therefore, should be properly disposed of. FDA also responded to numerous inquiries on nerve agent auto-injector expiry dating extensions to assist in determinations about whether stockpiled auto-injector products made by the same manufacturer should be retained.

FDA HQ also continued to advance efforts to facilitate the development and availability of medical products to support American military personnel. For example, FDA HQ 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 [133].

Office of Regulatory Science and Innovation

Centers of Excellence in Regulatory Science and Innovation

FDA HQ provides leadership, coordination and support for four academic Centers of Excellence in Regulatory Science and Innovation to provide FDA scientists ready access to leading researchers to assist in addressing high priority regulatory science questions. The four Centers of Excellence are Johns Hopkins University, Yale-Mayo Clinic, University of Maryland, and the University of California San Francisco-Stanford University. Recently established collaborative research projects include addressing real world evidence, opioids, bulk compounding, and digital health.

Technology Transfer Program

The FDA Technology Transfer Program (FDATT) activities fulfill the Agency's federal technology transfer mandate under 15USC3710 and related legislation. FDATT provides intellectual property guidance for the Agency, especially in the area of inventions and data rights, and provides technology transfer policy and leadership for FDA. FDATT assists FDA researchers and external collaborators to interact in the development and transfer of FDA invented technologies that improve public health. Through Cooperative Research and

[133] More information about these efforts is available on the FDA website at: https://www.fda.gov/medicalcountermeasures

Development Agreements (CRADAs) and out-licensing of FDA technologies, the Agency advances regulatory science and innovation in all areas of FDA's mission, including medical therapies, human and animal food safety, medical devices, and enhancement of regulatory processes.

Foster Competition and Innovation: International Inspections, Information Sharing and Strategic Engagement, and Continued Implementation of China Safety Initiative

FDA strategically engages with global regulatory counterparts and stakeholders to ensure that products coming to the U.S. market are safe, effective and of high quality. FDA's Office of Global Policy and Strategy (OGPS) is comprised of three headquarters offices (Office of Diplomacy and Partnerships; Office of Global Operations; and Office of Trade, Mutual Recognition, and International Arrangements) and four foreign offices (China, Europe, India and Latin America) in seven locations: Beijing, China; New Delhi, India; Brussels, Belgium; Amsterdam, Netherlands; Mexico City, Mexico; San Jose, Costa Rica and Santiago, Chile that report up through the Office of Global Operations. OGPS collaborates with FDA Centers and Offices to ensure that global issues are reflected in policy and regulatory actions, and that priority regulatory initiatives are advanced and implemented globally.

OGPS activities include announced and unannounced inspections in China, India, and Latin America; strategic engagements (trainings, seminars, etc.) and observed inspections with regulatory counterparts to enhance global inspectional capacity; advocacy in bilateral and multilateral settings for how strong regulatory systems enhance public health and facilitate international trade; represent regulatory equities in trade negotiations and at the WTO; the negotiation and development of international arrangements or agreements which facilitate the exchange of regulatory intelligence with our global counterparts; and continued implementation of the China Safety Initiative by the FDA China Office.

International Inspections

FDA foreign office staff as well as ORA investigators on short-term assignment to the China, India, and Latin America offices conduct international inspections. These inspections provide valuable in-country insights and information which supports FDA's risk-based inspection models workplan, helping to direct inspections to the highest risk facilities and strengthening FDA's regulatory knowledge. During FY 2019, a total of 135, 126, and 6 inspections were conducted by FDA investigators based in-country or on short-assignments in China, India and Latin America respectively.

In FY 2019, the India Office conducted an analysis on inspection trends, export data, and seasonal harvesting leading to a better understanding of how to target inspections of FDA regulated commodities. They also developed a Foreign Export Inspection Guidance to support FDA investigators conducting inspections in India.

India Office has also played an instrumental role in conducting inspections at facilities in India that manufacture the so-called "Angiotensin II Receptor Blockers" or ARBs. Pursuant to findings of trace levels of impurities in valsartan, losartan and other ARBs, the office participated in inspections of nine manufacturing facilities, all of which resulted in multiple-

observation FDA 483's with further regulatory action(s) currently under consideration. The India Office also collected samples representing multiple lots of ARBs from multiple manufacturers to be tested by FDA, including urgent samples required due to discrepant test results. The testing of these samples resulted in targeted initiation of for-cause inspections.

The China Office conducted regulator-to-regulator capacity-building workshops to strengthen relationships and improve mutual understanding of the approaches to conducting inspections with the China National Drug Administration's Center for Food and Drug Inspection in Beijing. In addition, the India and China Offices collaborated with ORA to conduct workshops to share inspectional experiences and challenges. It also conducted high-profile inspections that led to warning letters.

Information Sharing and Strategic Engagement

FDA engages strategically to ensure that accurate and timely information can be exchanged among regulators in support of information-driven decisions and actions. As part of cooperative regulatory activities, the Agency maintains international arrangements with selected regulators around the globe. International arrangements including confidentiality commitments and Cooperative Arrangements facilitate regulatory cooperation, including the sharing of certain kinds of non-public information with foreign authorities.

During FY 2019, FDA established two 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) with the European Commission and European Union Member States. The MRA facilitates the exchange of non-public information related to human drugs in the area of good manufacturing practices (GMP) inspections, while the other one was signed to facilitate the exchange of non-public information related to veterinary drugs in GMP inspections.

FDA signed a Cooperative Arrangement in FY 2019 with Mexico's Federal Commission for the Protection against Sanitary Risk (COFEPRIS) to facilitate regulatory activities related to shellfish exported from Mexico to the United States. The Latin America Office was instrumental, working with COFEPRIS, CFSAN, and OGPS headquarters staff to identify any proposed amendments and clarify any elements of proposed changes which were either not clear or not aligned with the other Agency agreements. This is the third time that Mexico's COFEPRIS and FDA have renewed their commitment to protect food from hazards that could endanger public health, and which provides for periodic audits to confirm compliance.

Continued Implementation of China Safety Initiative

The China Safety Initiative allows FDA to strengthen its efforts to regulate the quality, safety and efficacy of FDA-regulated products exported to the United States from China. The China Office conducts high-risk, for-cause, and follow-up priority inspections, collects regulatory information, conducts regulatory trend analysis to support risk-based decision making This contributes to FDA regulatory policies and actions, providing critical regulatory intelligence to Centers and ORA to mitigate public health risks, and promote greater oversight of products manufactured in China. The China Office also assists in vetting all Chinese firms identified on

the ORA workplans, cutting the "washout rate" of inspections that could not be completed by over 90% for medical products and over 75% for foods in FY 2019.

Strengthen Science and Efficient Risk-Based Decision Making: International Partnerships and Leveraging the Authority of Foreign Regulators

FDA collects, analyzes and shares high-quality information to strengthen science, enhance risk-management of FDA regulatory resources and to improve FDA oversight through better surveillance and reliance on foreign regulatory authorities' information. This increases FDA's understanding of complex global supply chains and strengthens its capacity to better detect and manage public health risks through regulatory actions. FDA utilizes OGPS offices to foster global partnerships and where appropriate, leverage the authority of foreign regulatory authorities.

International Partnerships

FDA builds strategic partnerships to raise awareness and understanding of the role strong regulatory systems play in ensuring public health and facilitating international trade. FDA advocates for foreign national policy makers to invest in and support regulatory systems strengthening in their respective countries. In FY 2019, FDA's partnerships include multilateral institutions such as the World Health Organization, the Pan American Health Organization, the World Bank, the Organization of Economic Cooperation and Development, and the Inter-American Institute for Cooperation on Agriculture (IICA)across FDA-regulated commodities. FDA also engages with a range of other institutions, including the World Economic Forum, the Bill & Melinda Gates Foundation, and the National Academies of Science, Engineering and Medicines.

For example, OGPS commissioned studies to catalyze global dialogue and understanding around regulatory systems and capacity. These included a World Bank Report on the Food Safety Imperative to accelerate progress in Low- and Middle-Income Countries (2018); a PAHO analytical landscape on the state-of-play of medical products regulation and production in the Americas Region (to be released early 2020); and NASEM Reports on mutual recognition and reliance in the regulation of medicines, and regulatory system strengthening (released in 2019 and 2020). Working with other governments in 2019, FDA led delegations to WHO/FAO/African Union and World Trade Organization (WTO) Global Summits on food safety where the roles of technology/innovation, science and trade to foster stronger food safety systems were addressed.

During FY 2019, OGPS, in collaboration with FDA Centers, catalyzed global efforts such as whole-genome sequencing of foodborne pathogens; the need to explore the role of regulatory authorities in the regulation of artificial intelligence within a global context; and the exploration of mobile-accessible information platforms to strengthen regulatory competency and capacity, e.g., in support of FSMA rules compliance and making the case for risk-based surveillance for substandard and falsified medical products through economic modeling.

FDA assures that U.S. Government trade positions promote regulations that are efficient, transparent, predictable, and ground in robust science and which balance our public health regulatory priorities with the export related objectives of the trade promoting agencies. OGPS

serves as FDA's policy lead for the negotiation of new trade obligations and for discussions on the implementation of existing free trade and WTO obligations, collaborating with relevant FDA Centers and Offices. This advances FDA policy positions at the USG interagency level where negotiations occur between trade agencies and regulators.

Leveraging the Authority of Foreign Regulators

FDA leverages partnerships to protect and promote public heath through diplomacy and global leadership. Its efforts increase compliance of relevant foreign stakeholders with FDA regulations and guidance and understanding of the links between well-functioning regulatory systems and public health, development and trade.

OGPS is the agency lead for the negotiation of Mutual Recognition Agreements (MRAs) which allow FDA to recognize foreign government inspections under Title VII, Section 712 of the Food and Drug Administration Safety and Innovation Act (FDASIA). In FY 2019, the Europe Office and Office of Trade, Mutual Recognition, and International Arrangements were instrumental in assuring that FDA met its obligations to complete capability assessments of all 28 member states in the MRA with the European Union, paving the way for the recognition of human drug good manufacturing practice (GMP) inspections. OGPS also worked with CVM in FY 2019 to identify a pathway to move forward on the recognition of animal drug GMP inspections in FY 2020.

The Europe Office also plays a key role is enhancing U.S. understanding of the regulation of biotechnology in food products. In FY 2019, the Europe Office and relevant USG agencies, brought together other regulators from Europe, Latin America and elsewhere to explore areas of opportunity for potential collaboration and alignment in biotech product regulation.

Through the leadership and efforts of the Latin America Office in FY 2019, the implementation of FSMA's rules for produce safety and third-party verification continue to make sustainable inroads. These included a Produce Safety Partnership with Mexican regulatory authorities, farm-readiness workshops in Chile, and train-the-trainer capacity building in collaboration with IICA to enhance competencies of food producers and manufacturers exporting to the United States. 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 completed 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; and
- 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.

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 70 years ago.

Similarly, many of FDA's leased lab facilities were leased and constructed more than 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 as leases expire. 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; and
- requesting resources needed to carry out high priority projects.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$307,092,000	$187,776,000	$119,316,000
FY 2020 Enacted	$319,487,000	$185,420,000	$134,067,000
FY 2021 President's Budget	$326,070,000	$186,713,000	$139,357,000

BUDGET REQUEST

The FY 2021 President's Budget Request is $326,070,000, of which $186,713,000 is budget authority and $139,357,000 is user fees. The budget authority increases by $1,293,000 compared to the FY 2020 Enacted level. User Fees increase by $5,290,000.

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

Food Safety: +$2.0 million / 1 FTE

Artificial Intelligence and Other Emerging Technologies: +$1.5 million / 0 FTE

OFPR: +$1.5 million / 0 FTE

Artificial Intelligence (AI) and other emerging technologies hold tremendous potential to "drive growth of the United States economy, enhance our economic and national security, and improve our quality of life," as per the Executive Order on Maintaining American Leadership in Artificial Intelligence. The recent outbreaks related to romaine lettuce underline the urgent need to evaluate new technologies and upgrade our abilities to rapidly track and trace food through the supply chain. This component of the AI initiative invests in tech-enabled outbreak response and modernized track and track capabilities.

When it comes to food traceability, many in the food system utilize a largely paper-based system of taking one step forward to identify where the food has gone and one step back to identify the source. The use of new and evolving digital technologies may play a pivotal role in tracing the origin of a contaminated food to its source in minutes, or even seconds, instead of days or weeks, when contamination does occur.

If it is possible to get back to source quickly and determine the root cause of an outbreak, factors contributing to past outbreaks could be incorporated into advanced analytical tools to help predict future outbreaks. As industry begins investment in these new tools, they are actively asking FDA to provide direction on issues like interoperability and common data elements, as a lack of harmonization could greatly reduce the effectiveness of these new tools.

Recognizing the rapidly changing landscape of technologies available and the growing need for FDA's engagement on how these technologies can be most impactful, FDA launched an initiative called the New Era of Smarter Food Safety in 2019, which is being led by the Office of Food Policy and Response (OFPR) in close collaboration with CFSAN, CVM, and ORA. Advancing tracing technologies is the heart of this initiative, as it is critical that FDA invest resources now to ensure that the systems currently being developed will be set up in a way that will allow FDA to expeditiously use information in an emerging outbreak.

The FY 2021 Budget Request is $1.5 million, an investment to expand FDA's engagement with stakeholders on these new technologies and to begin proof-of-concept testing to ensure that FDA can receive and efficiently process new data streams, particularly in urgent outbreak scenarios. This investment will enable FDA to support the goals of the Executive Order by driving "development of appropriate technical standards and reduce barriers to the safe testing and deployment" of new "technologies in order to enable the creation of new AI-related industries and the adoption of AI" and other emerging technologies "by today's industries." While small, this investment will therefore have a large impact on public health, reduce greater long-term costs, and help ensure American leadership for the application of AI and other emerging technologies.

Cannabis and Cannabis Derivatives: +$0.5 million / 1 FTE

OFPR: +$0.5 million / 1 FTE
FDA is seeing a significant increase in activity relating to the marketing of unlawful cannabis-derived products, especially those containing cannabidiol (CBD), since the Farm Bill passed. In many cases, product developers make unproven claims to treat serious or life-threatening diseases, and patients may be misled to forgo otherwise effective, available therapy and opt instead for a product that has no proven value or may cause them serious harm.

This initiative will enable FDA to continue regulating the usage of cannabis-derived substances, such as cannabidiol (CBD), in FDA-regulated products such as dietary supplements and when used as unapproved food and feed additives. The initiative will support regulatory activities, including developing policy, and continue to perform its existing regulatory responsibilities including review of product applications, inspections, enforcement, and targeted research. FDA must support oversight of increasing numbers of marketed FDA-regulated products containing cannabis-derived substances that may put the public at risk.

Medical Products Safety: +$2.0 million

Modernizing Influenza Vaccines: +$2.0 million

OCS/OCET: +$2.0 million

This request, which reflects additional funding above the FY 2020 Enacted level, will allow FDA to advance regulatory science necessary to support the implementation of Executive Order 13877, "Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health," to help make the United States influenza vaccine supply more robust, secure, and nimble to combat seasonal influenza epidemics and potential influenza pandemics.

Crosscutting: -$1.2 million / 0 FTE

Outreach, Training, and Organizational Excellence: -$1.2 million
FDA HQ: -$1.2 million

FDA HQ will reduce Outreach, Training, and Organizational Excellence activities while maintaining the most critical programmatic activities. FDA HQ will preserve its most critical public health and safety activities under this reduction, including investments in high priority education and outreach activities, essential employee training and development, legal and litigation support to core program activities, and responding to Congressional inquiries.

USER FEES
Current Law User Fees: +$7.3 million / 2 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 2020 Target	FY 2021 Target	FY 2021 +/- FY 2020
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products. *(Output)*	FY 2019: Developed 92 mapping products to support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinated 108 incidents involving FDA regulated products during the year. Participated in seven 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 seven 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.	Maintain
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 2019: FDA completed annual milestones for 7 additional projects, for a total of 52 intramural research projects under the Nanotechnology CORES program to promote cross-center and external collaborative regulatory science research opportunities, focusing on studies evaluating	58 CORES projects with completed annual milestones Complete review of 80% of Medical Product nanotechnology standards	64 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards	+6 +20%

	nano-materials. (Target Met)			
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship programs. (Outcome)	FY 2019: 86% Target: 50% (Target Exceeded)	50%	20%	-30%
293205: Percentage of requests for combination product designations processed within the 60-day statutory requirement. *(Output)*	FY 2019: 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 2019: 169 Target: 45 (Target Exceeded)	100	100	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 2019: 54 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 result in support of	FY 2019: 50 Target: 25 (Target Met)	35	35	Maintain

FDA's global mission. *(Outcome)*				
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2019: 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 nanotechnology. 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.

Traineeship and Fellowship Programs

To support the Department's mission and FDA's scientific expertise, FDA is 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. As FDA transitions to the new agency-wide Traineeship program, which will be greater in number and scope than the previous Fellowship program, FDA needs to reset the retention target to 20% in FY 2021 to reflect the new program's expected baseline. Additionally, it is important to realize that 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.

INFRASTRUCTURE - GSA RENT, OTHER RENT, AND WHITE OAK

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
FDA White Oak Consolidation	**50,587**	**49,255**	**53,913**	**63,411**	**9,498**
Budget Authority	***43,044***	***43,044***	***45,914***	***55,717***	***9,803***
User Fees	***7,543***	***6,211***	***7,999***	***7,694***	***-305***
Prescription Drug (PDUFA)	*3,810*	*3,810*	*3,848*	*3,886*	*38*
Medical Device (MDUFA)	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	*3,733*	*2,401*	*4,151*	*3,808*	*-343*
Other Rent and Rent Related	**123,735**	**120,201**	**132,970**	**151,359**	**18,389**
Budget Authority	***71,943***	***71,943***	***80,173***	***98,518***	***18,345***
User Fees	***51,792***	***48,258***	***52,797***	***52,841***	***44***
Prescription Drug (PDUFA)	*26,127*	*25,912*	*26,389*	*26,652*	*263*
Medical Device (MDUFA)	*5,239*	*5,239*	*5,291*	*5,344*	*53*
Generic Drug (GDUFA)	*13,075*	*12,243*	*13,206*	*13,338*	*132*
Biosimilars (BsUFA)	*1,070*	*932*	*1,081*	*1,092*	*11*
Animal Drug (ADUFA)	*790*	*624*	*797*	*805*	*8*
Animal Generic Drug (AGDUFA)	*264*	*132*	*266*	*269*	*3*
Family Smoking Prevention and Tobacco Control Act	*4,752*	*3,137*	*5,283*	*4,847*	*-436*
Food and Feed Recall	*43*	---	*44*	*45*	*1*
Food Reinspection	*204*	---	*208*	*212*	*4*
Voluntary Qualified Importer Program	*170*	---	*173*	*177*	*4*
Third Party Auditor Program	*24*	*5*	*24*	*25*	*1*
Outsourcing Facility	*34*	*34*	*35*	*35*	---
GSA Rental Payments	**238,665**	**218,907**	**240,549**	**236,970**	**-3,579**
Budget Authority	***170,208***	***170,208***	***171,208***	***167,119***	***-4,089***
User Fees	***68,457***	***48,699***	***69,341***	***69,851***	***510***
Prescription Drug (PDUFA)	*35,341*	*22,716*	*35,695*	*36,052*	*357*
Medical Device (MDUFA)	*8,312*	*4,812*	*8,395*	*8,479*	*84*
Generic Drug (GDUFA)	*12,720*	*12,720*	*12,847*	*12,975*	*128*
Biosimilars (BsUFA)	*451*	*451*	*455*	*460*	*5*
Animal Drug (ADUFA)	*839*	*839*	*847*	*856*	*9*
Animal Generic Drug (AGDUFA)	*307*	*307*	*310*	*314*	*4*
Family Smoking Prevention and Tobacco Control Act	*9,671*	*6,845*	*9,960*	*9,866*	*-94*
Food and Feed Recall	*73*	---	*74*	*76*	*2*
Food Reinspection	*348*	---	*355*	*362*	*7*
Voluntary Qualified Importer Program	*290*	---	*296*	*302*	*6*
Third Party Auditor Program	*47*	*9*	*48*	*49*	*1*
Outsourcing Facility	*58*	---	*59*	*60*	*1*

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.

Although a new master plan for the Federal Research Center was approved by the National Capital Planning Commission on December 6, 2018, GSA does not anticipate receiving funding to construct additional office space on Campus in the foreseeable future. Therefore, FDA is working with GSA to lease space close to Campus to house the staff growth associated with headquarters programs until funding for federal office construction is available.

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 39,000 regulated products and manufacturers annually
- Collecting and analyzing more than 43,000 samples of regulated products annually
- Recalling unsafe products, like the 7,562 recalls in FY 2018 alone
- Reviewing more than 43 million distinct product lines offered for entry into the U.S.
- Swiftly identifying the causes of foodborne illnesses that threaten the health and lives of Americans, like the recent outbreaks caused by frozen ground tuna and pre-cut melons contaminated by Salmonella and the multistate outbreak of E. coli O157:H7 infections linked to romaine lettuce from the Yuma growing region
- Interdicting opioids at International Mail Facilities (IMFs) to combat the addiction crisis, which is the dominant public health problem in the U.S., killing more than 130 Americans daily
- Conducting criminal investigations, which resulted in 317 arrests, 215 convictions, $114 million of assets forfeited and seized, and $2.2 billion in fines and restitution in FY 2018 alone.

FDA occupies almost 6.8 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 267 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 2019, FDA:

- completed the construction for the relocation of the ORA laboratory near San Francisco, California, to replace an aging facility and improve lab operations for food sensory and microbiological, elemental, chemistry, and product sterility analysis
- continued coordinating the construction for the relocation of the ORA laboratory near Kansas City, Kansas, to replace an aging facility and improve lab operations for analyzing food items, including infant and toddler foods
- initiated design activities required 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, with the responsibility to uphold the mandates of the Tobacco Act through analytical support and tobacco-related research in support of the Center for Tobacco Products (CTP)
- occupied two new leased office locations near the White Oak Campus to house FDA's workforce growth resulting from its expanding mission and authorities
- coordinated design and construction activities to create a training center 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
- worked with GSA to submit a prospectus lease proposal to OMB for new office space near the White Oak Campus to house FDA's workforce growth resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- coordinated leasing four new locations for ORA resident posts and border stations to expand inspection operations that protect public health
- coordinated relocating seven ORA resident posts to facilitate inspection operations that protect public health
- coordinated leasing, design, and construction activities required to expand ORA's presence in nine IMFs, enhance opioid interdiction efforts, and combat the addiction crisis threatening American families
- coordinated the expansion CDER's laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis
- coordinated leasing a new CDER laboratory near the White Oak Campus to house a pilot plant for simulating the processing of drug substances and products manufacturing
- coordinated 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.

In FY 2020, FDA plans to:

- continue coordinating the construction for the relocation of the ORA laboratory near Kansas City, Kansas
- continue coordinating the design and construction activities required to replace an aging facility and improve the operations of the ORA laboratory near Atlanta, Georgia, that houses the Southeast Food and Feed Laboratory and the Southeast Tobacco Laboratory
- begin coordinating the design and construction activities required to replace an aging facility and improve operations of ORA's human and animal foods laboratory near Denver, Colorado
- begin coordinating the design and construction activities required to renovate and expand operations at ORA's Forensic Chemistry Center located in Cincinnati, Ohio
- initiate design and construction activities for a prospectus-level office lease near the White Oak Campus to house FDA's workforce growth resulting from its expanding mission and authorities, FDARA, and the 21st Century Cures Act
- coordinate leasing seven new locations for ORA resident posts and border stations to expand inspection operations that protect public health
- coordinate relocating eight ORA resident posts and a District Office to facilitate inspection operations that protect public health
- continue coordinating leasing, design, and construction activities required to expand ORA's presence in nine IMFs, enhance opioid interdiction efforts, and combat the addiction crisis threatening American families
- continue coordinating the expansion of CDER's laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis
- coordinate design and construction of a new CDER laboratory near the White Oak Campus to house a pilot plant for simulating the processing of drug substances and products manufacturing
- continue coordinating the renovation of 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, maintaining , and securing FDA and GSA facilities located nationwide. Costs include:

- operation and maintenance contracts
- operation and maintenance repairs
- janitorial and grounds maintenance contracts
- DHS basic and building specific security and guard services
- 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 provided the utilities needed to 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 nearing completion.

FDA completed an investment-grade audit for our facilities at the Muirkirk Road Campus to identify facilities projects. We awarded a UESC for approximately $5.9 million to address urgent projects for replacement of air handling units supporting FDA laboratories as well as other projects identified by the audit. FDA initiated a facility improvement project to replace and upsize four emergency generators at the MRC as well as the obsolete panelboards, providing better reliability during outages with contract award projected in FY 2020. FDA will be initiating a feasibility study in FY 2020 to address additional facility improvements such as: cooling tower improvements; air handling unit replacement; boiler stack economizer metering and boiler venting improvements; pump enhancement for office heating; boiler deaerator pump improvements; heat exchanger and valve enhancements; lighting and controls retrofits; window control joints and connections repair and HVAC pneumatic controls replacement. 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 research, 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

Most of FDA Headquarters operations are on the White Oak Campus. Occupied in phases between 2003 and 2014, the Campus replaced geographically disparate, out-of-date facilities with new, state-of-the-art laboratories, office buildings, and support facilities in one location. The total number of employees currently assigned to the White Oak Campus is approximately 11,000

as a result of occupying the last phase, the LSBC (two office and two lab buildings), in FY 2014 and instituting alternative office strategies, including increased telework.

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 22 State-of-the-Art Laboratories at White Oak

Figure 23 State-of-the-Art Laboratories at White Oak

Figure 24 Anechoic Chambers Laboratory

Figure 25 Nuclear Magnetic Resonance Laboratory Supporting CBER and CDER

Figure 26 State-of-the-Art White Oak Infrastructure: Advanced Air Terminal Units Supporting Laboratories

Figure 27 Flow Cytometry Core Facility: Highly Specialized and Expensive Equipment for Vaccine and Cell Therapy Studies

The GSA appropriation funds the design and construction of new base buildings and the operations and maintenance of existing base buildings at White Oak. FDA's White Oak budget funds Campus above-standard infrastructure, building fit-out, specialized equipment, move costs, alterations, 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.

In addition to funding Campus operations, FDA White Oak funding supports above-GSA-standard repair and improvement projects required by FDA's specialized functions to ensure that facilities do not degrade, remain state-of-the-art, and support program requirements.

FUNDING HISTORY – GSA RENTAL PAYMENTS

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$218,907,000	$170,208,000	$48,699,000
FY 2020 Enacted	$240,549,000	$171,208,000	$69,341,000
FY 2021 President's Budget	$236,970,000	$167,119,000	$69,851,000

FUNDING HISTORY - OTHER RENT AND RENT-RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$120,201,000	$71,943,000	$48,258,000
FY 2020 Enacted	$132,970,000	$80,173,000	$52,797,000
FY 2021 President's Budget	$151,359,000	$98,518,000	$52,841,000

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$49,255,000	$43,044,000	$6,211,000
FY 2020 Enacted	$53,913,000	$45,914,000	$7,999,000
FY 2021 President's Budget	$63,411,000	$55,717,000	$7,694,000

BUDGET REQUEST

The FY 2021 President's Budget Request for the Infrastructure Program is $451,740,000, of which $321,354,000 is budget authority and $130,386,000 is user fees. The budget authority increases by $24,059,000 compared to the FY 2020 Enacted Budget. User Fees increase by $249,000.

The request will cover rent costs that the agency anticipates in FY 2021 related to market changes, including new Occupancy Agreements replacing those expiring in FY 2020 and FY 2021 for approximately 60 GSA Occupancy Agreements that will cause rental rates to reset to market rates. The increase in OR&RR is needed to meet cost escalations associated with security, operations and maintenance contracts, utilities, and Energy Savings Performance Contract payments for its owned and leased buildings nationwide. In addition, the OR&RR increase is also needed to address more demands for repairs and non-standard maintenance requests as FDA's owned buildings continue to age and equipment and systems failures occur. Operating costs at the White Oak Campus continue to increase with inflation and because several of the buildings on Campus are 10 or more years old. Accordingly, the FY 2021 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 of approximately 19,700 staff 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.

GSA Rental Payments

The FY 2021 President's Budget Request for GSA Rental Payments is $236,970,000, of which $167,119,000 is budget authority and $69,851,000 is user fees. The budget authority decreases by -$4,089,000 compared to the FY 2020 Enacted Budget. User Fees increase by $510,000.

The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2021 Budget Request for GSA Rental Payments covers the cost of

rental payments to GSA for FDA's almost 6.8 million square feet of GSA-managed space. The reduction in budget authority is due to current rent estimates.

Other Rent and Rent-Related

The FY 2021 President's Budget Request for Other Rent and Rent-Related is $151,359,000, of which $98,518,000 is budget authority and $52,841,000 is user fees. The budget authority increases by $18,345,000 compared to the FY 2020 Enacted Budget. User Fees increase by $44,000.

The FY 2021 Budget will allow FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support the FDA mission. It will also provide additional funding to address increased utility and maintenance costs associated with FDA's aging owned buildings.

White Oak

The FY 2021 President's Budget Request for White Oak is $63,411,000, of which $55,717,000 is budget authority and $7,694,000 is user fees. The budget authority increases by $9,803,000 compared to the FY 2020 Enacted Budget. User Fees decrease by -$305,000.

The FY 2021 Budget provides the necessary resources for increased above GSA-standard repairs and improvements as well as White Oak Campus utility infrastructure capacity and reliability improvements. It also provides needed funding for daily mission support services for the over 11,000 employees, contractors and visitors on the White Oak Campus. In summary, the FY 2021 Budget request will fund Campus infrastructure improvements, 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.

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BUILDINGS AND FACILITIES

(Dollars in Thousands)	FY 2019 Final	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 President's Budget (+/-) FY 2020 Enacted
Buildings and Facilities (Budget Authority).....	11,788	11,477	31,788	13,788	-18,000

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 FDA's 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 28 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.

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 2019 and Planned for FY 2020

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 2019, FDA initiated projects to:

- replace floor finishes in the main lab building
- replace the perimeter security gate
- install fire alarm and sprinkler systems in the aquaculture building.

In FY 2020, FDA will initiate projects to:

- replace heating water pipe and insulation
- replace AC units using R22 refrigerant that are being phased out with units that use refrigerant 410
- provide supplemental funding, if required, for Non-Recurring Expenses Fund project to design and construct 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 Laboratory (ARKL). Additional details of the vital scientific research that takes place at the Complex can be found in the NCTR Narrative.

ARKL provides analytical laboratory support to FDA's regulatory mission in the Southwest Region.

In FY 2019, FDA initiated projects to:

- design a new Data and Disaster Recovery Center
- design and repair a main sewer line on the west side of the site
- complete modifications to the site master plan
- repair and improve the site water treatment plant
- design and replace the campus motor control center
- complete renovation of a critical toxicology lab.

In FY 2020, FDA plans to initiate projects to:

- complete design/re-design of a new Data and Disaster Recovery Center
- repair the motor control center on the site electrical loop
- relocate operations to prepare space for roof repair
- replace an air handling unit in a lab building
- renovate Campus dorms used for visiting scientists
- design roof replacements for several buildings

- design reroute of steam and air systems for ARKL
- abate steam lines to prepare for future projects
- install a new domestic water well
- additional repairs to site infrastructure (roadways, drainage, sidewalks)
- design renovations to a critical pathology lab.

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 2019, FDA initiated projects to:

- convert labs to offices to support mission needs
- design and construct replacement of substation housing and switchgear
- provide supplemental funding for Non-Recurring Expenses Fund project to replace AHUs.

In FY 2020, FDA will initiate projects to:

- replace electrical feeders on campus
- provide supplemental funding for Non-Recurring Expenses Fund project to replace generators and panelboards.

Pacific Southwest Laboratory – Irvine, California

The Pacific Southwest Laboratory provides analytical laboratory support to FDA's regulatory mission in the Pacific Region.

In FY 2019, FDA initiated a project to design the replacement of the cooling tower system.

In FY 2020, FDA will initiate projects to:

- replace the security gates at building exits

- replace (construction) the cooling tower system
- design two additional steam boilers for N+1 redundancy
- 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 Pharmaceutical Laboratory – San Juan, Puerto Rico

The San Juan Pharmaceutical 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 2019, FDA provided supplemental funding to a Non-Recurring Expenses Fund project to design and construct a new ORA District Office Building (Toro 2).

In FY 2020, FDA will initiate a project to design the repair of the seawall adjacent to the Boat House.

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.

FDA is in the process of executing a design-build project to replace the existing WEAC facilities on the same site. No FY 2019 B&F Projects were performed at this facility.

- In FY 2020, FDA will provide supplemental funding for the Non-Recurring Expenses Fund project to support construction of the new WEAC facility.

FDA Owned Facilities Condition Assessment and Seafood-Related Projects

In FY 2020, FDA will initiate a project to assess the condition of all FDA owned facilities and provide a report that will include the updated Condition Index (CI) and Backlog of Maintenance and Repair (BMAR) for each facility.

FDA will also initiate appropriate studies, designs, construction, repairs, improvements, alterations, and demolition of FDA-owned facilities used for operations associated with seafood safety.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2017 Actual	$9,243,000	$9,243,000	---
FY 2018 Actual	$14,618,000	$14,618,000	---
FY 2019 Actual	$11,477,000	$11,477,000	---
FY 2020 Enacted	$31,788,000	$31,788,000	---
FY 2021 President's Budget	$13,788,000	$13,788,000	---

BUDGET REQUEST

The FY 2021 President's Budget Request is $13,788,000, consisting solely of budget authority, which is a decrease of $18,000,000 compared to the FY 2020 Enacted Budget.

FDA will continue to sustain the current condition of FDA's six mission-critical, owned facilities, including the site infrastructure and buildings. At this funding level, FDA will continue to prioritize the most urgent and critical needs across owned building and facilities. At the Gulf Coast Seafood Laboratory facility, FDA will:

- replace boat launch with a boat lift
- provide design and oversight services to convert existing offices to labs and renovate existing labs to create more efficient space.

At the Jefferson Labs Complex, FDA will:

- replace roofs for Buildings 53A and 53B
- design roof replacements for Buildings 53C, 5B and 5D
- renovate lab building to support Pathology operations
- complete second phase of renovations of Campus dorms used for visiting scientists
- complete second phase of repairs of the motor control center on the site electrical loop
- upgrade the hot water, steam, and deionized water systems in Buildings 53B, C, D, and E
- design the office tower portion of the Scientific Computational Facility that houses staff supporting the new Data and Disaster Recovery Center.

At the Muirkirk Road Complex, FDA will:

- construct replacement of substation housing and switchgear, and electrical feeders
- replace flooring in Building A
- design and construct modifications to the BRF building loading dock.

In the Pacific Regional Laboratory Southwest, FDA will:

- correct facility condition deficiencies
- design additional steam boiler for N+1 redundancy

- provide additional cooling for the telecom closets to address additional heat generated due to server upgrades
- sound insulate select offices
- replace vacuum pumps in the basement
- replace lab nitrogen system.

In the San Juan District Office and Laboratory, FDA will:

- modify distribution of fume hood ductwork for manifolded distribution.

In Winchester Engineering Analytical Center, FDA will:

- provide for miscellaneous building contingencies to keep existing lab building operational until replacement building is complete.

In FY 2021, FDA will initiate the evaluation and assessment of the condition of FDA-owned facilities.

The following table provides an allocation plan by site for use of the FY 2021 funds.

FY 2021 BUILDINGS AND FACILITIES ALLOCATION PLAN

BUILDINGS AND FACILITIES ALLOCATION PLAN FY 2021 Congressional Justification	
Site	**Total**
CFSAN Gulf Coast Seafood Laboratory – Dauphin Island, AL	$600,000
Jefferson Laboratories Complex (NCTR & ORA Arkansas Lab) – Jefferson, AR	$6,894,000
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	$3,275,000
ORA Pacific Laboratory SW – Irvine, CA	$1,819,000
San Juan District Office and Laboratory – San Juan, PR	$100,000
Winchester Engineering and Analytical Center – Winchester, MA	$100,000
Multiple Sites Facility Condition Assessments	$1,000,000
B&F Project Total	**$13,788,000**

In FY 2021, 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 2021 will help reduce Scope 1, 2, and 3 greenhouse gas emissions by replacing or repairing aged, inefficient roofs and building equipment

PROGRAM ACTIVITY DATA

Program Activity Data[1]

Facility	Average FCI Score		
	FY 2019 Actual	FY 2020 President's Budget	FY 2021 Request
CFSAN Gulf Coast Seafood Laboratory	87	87	87
Jefferson Laboratories Complex	64	63	65
Muirkirk Road Complex	47	47	47
ORA Pacific Regional Laboratory Southwest	95	95	95
San Juan District Office and Laboratory	74	74	74
Winchester Engineering And Analytic Center	63	62	62

[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 requested in FY 2020 and FY 2021, FDA's remaining total BMAR after FY 2021 is estimated to be $233.83 million, with 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.

Authorizing Legislation: The FY 2018 Appropriation included the legislative language needed to establish and put a WCF into operation at the beginning of FY 2019.

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 eventual 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.

NON-RECURRING EXPENSES FUND

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 fund replacement of 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 leased 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 additional $89 million in FY 2019 NEF resources that were received will advance the ongoing laboratory relocation project at ORA's Southeast Laboratory in Atlanta. Funding will also support construction and facilities needs at ORA's leased 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 continues to work to:

- identify ongoing laboratory replacement, relocation, repair, and improvement projects;
- prioritize these projects; and
- develop resource requests to implement the highest priority projects.

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SUPPLEMENTARY TABLES

OBJECT CLASSIFICATION TABLES

Budget Authority

(Dollars in Thousands)	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	889,379	970,847	977,236
Other than full-time permanent (11.3)	91,043	99,383	100,037
Other personnel compensation (11.5)	41,232	45,009	45,305
Military personnel (11.7)	59,257	60,798	62,379
Special personnel services payments (11.8)	995	1,087	1,094
Subtotal, Personnel Compensation	**1,081,908**	**1,177,124**	**1,186,051**
Benefits:			
Civilian benefits (12.1)	335,942	366,714	369,127
Military benefits (12.2)	32,578	33,425	34,294
Benefits to former personnel (13.0)	57	400	400
Subtotal, Benefits	**368,577**	**400,539**	**403,822**
Total Personnel Compensation and Benefits	**1,450,485**	**1,577,664**	**1,589,873**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	49,266	47,099	47,636
Transportation of things (22.0)	2,735	2,615	2,645
Rental payments to GSA (23.1)	170,208	171,208	167,119
Rent payments to others (23.2)	633	606	612
Communication, utilities, and misc. charges (23.3)	18,035	17,241	17,438
Printing and reproduction (24.0)	1,820	1,740	1,760
Subtotal, Contractual Services	**242,697**	**240,509**	**237,210**
Other Contractual Services:			
Consulting services (25.1)	44,109	42,169	42,650
Other services (25.2)	428,483	409,642	414,307
Purchase of goods and svcs from Govt Acts. (25.3)	505,641	483,406	488,911
Operation and maintenance of facilities (25.4)	139,232	133,110	134,626
Research and Development Contracts (25.5)	20,258	19,367	19,588
Operation and maintenance of equipment (25.7)	34,892	33,357	33,737
Subsistence and support of persons (25.8)	---	---	---
Subtotal, Other Contractual Services	**1,172,615**	**1,121,051**	**1,133,818**
Supplies and Materials:			
Supplies and materials (26.0)	39,660	37,916	38,348
Equipment (31.0)	63,078	60,304	60,991
Land and Structures (32.0)	3,324	3,178	3,214
Grants, subsidies, and contributions (41.0)	232,328	222,111	224,641
Insurance claims and indemnities (42.0)	2,335	2,232	2,258
Interest and dividends , Refunds (43.0, 44.0)	---	---	---
Subtotal, Supplies and Materials	**340,724**	**325,742**	**329,451**
Total Contractual Services and Supplies	**1,756,036**	**1,687,302**	**1,700,479**
Total Budget Authority by Object Class	**3,206,521**	**3,264,966**	**3,290,352**

User Fee

(Dollars in Thousands)	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	650,269	711,064	718,652
Other than full-time permanent (11.3)	98,507	107,717	108,866
Other personnel compensation (11.5)	74,106	81,034	81,899
Military personnel (11.7)	51,954	53,305	55,021
Special personnel services payments (11.8)	188	206	208
Subtotal, Personnel Compensation	**875,024**	**953,325**	**964,646**
Benefits:			
Civilian benefits (12.1)	261,547	286,000	289,051
Military benefits (12.2)	32,996	33,854	34,944
Benefits to former personnel (13.0)	---	---	---
Subtotal, Benefits	**294,543**	**319,853**	**323,995**
Total Personnel Compensation and Benefits	**1,169,567**	**1,273,179**	**1,288,641**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	16,467	17,731	20,713
Transportation of things (22.0)	684	737	860
Rental payments to GSA (23.1)	48,699	69,341	69,851
Rent payments to others (23.2)	162	174	204
Communication, utilities, and misc. charges (23.3)	3,391	3,651	4,265
Printing and reproduction (24.0)	4,918	5,296	6,186
Subtotal, Contractual Services	**74,321**	**96,930**	**102,080**
Other Contractual Services:			
Consulting services (25.1)	82,836	89,196	104,195
Other services (25.2)	473,993	510,387	596,213
Purchase of goods and svcs from Govt Acts. (25.3)	450,497	485,087	566,659
Operation and maintenance of facilities (25.4)	22,902	24,660	28,807
Research and Development Contracts (25.5)	43,716	47,073	54,988
Operation and maintenance of equipment (25.7)	24,834	26,741	31,238
Subsistence and support of persons (25.8)	---	---	---
Subtotal, Other Contractual Services	**1,098,778**	**1,183,144**	**1,382,101**
Supplies and Materials:			
Supplies and materials (26.0)	15,876	17,095	19,970
Equipment (31.0)	9,446	10,171	11,882
Land and Structures (32.0)	---	---	---
Grants, subsidies, and contributions (41.0)	87,069	93,754	109,520
Insurance claims and indemnities (42.0)	311	335	391
Interest and dividends , Refunds (43.0, 44.0)	---	---	---
Receivables-collected (61.7)	---	---	---
Subtotal, Supplies and Materials	**112,702**	**121,355**	**141,763**
Total Contractual Services and Supplies	**1,285,801**	**1,401,430**	**1,625,943**
Total Reimbursable by Object Class	**2,455,368**	**2,674,609**	**2,914,584**

Total Program

(Dollars in Thousands)	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	1,539,648	1,681,911	1,695,888
Other than full-time permanent (11.3)	189,550	207,099	208,903
Other personnel compensation (11.5)	115,338	126,044	127,204
Military personnel (11.7)	111,211	114,103	117,400
Special personnel services payments (11.8)	1,183	1,292	1,302
Subtotal, Personnel Compensation	**1,956,932**	**2,130,449**	**2,150,697**
Benefits:			
Civilian benefits (12.1)	597,489	652,714	658,179
Military benefits (12.2)	65,574	67,279	69,238
Benefits to former personnel (13.0)	57	400	400
Subtotal, Benefits	**663,120**	**720,393**	**727,817**
Total Personnel Compensation and Benefits	**2,620,052**	**2,850,842**	**2,878,514**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	65,733	64,831	68,349
Transportation of things (22.0)	3,419	3,352	3,505
Rental payments to GSA (23.1)	218,907	240,549	236,970
Rent payments to others (23.2)	795	780	816
Communication, utilities, and misc. charges (23.3)	21,426	20,893	21,703
Printing and reproduction (24.0)	6,738	7,036	7,946
Subtotal, Contractual Services	**317,018**	**337,440**	**339,289**
Other Contractual Services:			
Consulting services (25.1)	126,945	131,366	146,845
Other services (25.2)	902,476	920,029	1,010,520
Purchase of goods and svcs from Govt Acts. (25.3)	956,138	968,493	1,055,570
Operation and maintenance of facilities (25.4)	162,134	157,770	163,433
Research and Development Contracts (25.5)	63,974	66,440	74,576
Operation and maintenance of equipment (25.7)	59,726	60,098	64,975
Subsistence and support of persons (25.8)	---	---	---
Subtotal, Other Contractual Services	**2,271,393**	**2,304,196**	**2,515,919**
Supplies and Materials:			
Supplies and materials (26.0)	55,536	55,011	58,318
Equipment (31.0)	72,524	70,475	72,872
Land and Structures (32.0)	3,324	3,178	3,214
Grants, subsidies, and contributions (41.0)	319,397	315,866	334,161
Insurance claims and indemnities (42.0)	2,646	2,567	2,649
Interest and dividends , Refunds (43.0, 44.0)	---	---	---
Receivables-collected (61.7)	---	---	---
Subtotal, Supplies and Materials	**453,426**	**447,097**	**471,214**
Total Contractual Services and Supplies	**3,041,837**	**3,088,733**	**3,326,422**
Total Program Level by Object Class	**5,661,889**	**5,939,575**	**6,204,936**

SALARY AND EXPENSES

(Dollars in Thousands)	FY 2019 Actuals	FY 2020 Enacted	FY 2021 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	889,379	970,847	977,236
Other than full-time permanent (11.3)	91,043	99,383	100,037
Other personnel compensation (11.5)	41,232	45,009	45,305
Military personnel (11.7)	59,257	60,798	62,379
Special personnel services payments (11.8)	995	1,087	1,094
Subtotal, Personnel Compensation	**1,081,908**	**1,177,124**	**1,186,051**
Benefits:			
Civilian benefits (12.1)	335,942	366,714	369,127
Military benefits (12.2)	32,578	33,425	34,294
Benefits to former personnel (13.0)	57	400	400
Subtotal, Benefits	**368,577**	**400,539**	**403,822**
Total Personnel Compensation and Benefits	**1,450,485**	**1,577,664**	**1,589,873**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	49,266	47,099	47,636
Transportation of things (22.0)	2,735	2,615	2,645
Rent payments to others (23.2)	633	606	612
Communication, utilities, and misc. charges (23.3)	18,035	17,241	17,438
Printing and reproduction (24.0)	1,820	1,740	1,760
Subtotal, Contractual Services	**72,489**	**69,301**	**70,091**
Other Contractual Services:			
Consulting services (25.1)	44,109	42,169	42,650
Other services (25.2)	428,483	409,642	414,307
Purchase of goods and svcs from Govt Acts. (25.3)	505,641	483,406	488,911
Operation and maintenance of facilities (25.4)	139,232	133,110	134,626
Research and Development Contracts (25.5)	20,258	19,367	19,588
Operation and maintenance of equipment (25.7)	34,892	33,357	33,737
Supplies and materials (26.0)	39,660	37,916	38,348
Total Contractual Services and Supplies	**1,284,764**	**1,228,269**	**1,242,256**
Rental payments to GSA (23.1)	**170,208**	**171,208**	**167,119**
Grand Total, Salaries and Expense and Rent	**2,735,249**	**2,805,932**	**2,832,130**
Direct FTE	**9,915**	**9,939**	**10,000**

*For FY 2019 and FY 2020, 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 2021, FDA proposes to discontinue the transfer.

DETAIL OF FULL-TIME EQUIVALENTS

	FY 2019 Actuals			FY 2020 Estimate			FY 2021 Estimate		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Food Safety and Applied Nutrition	1,056	41	1,097	1,103	41	1,144	1,168	41	1,209
Center for Drug Evaluation and Research	4,845	517	5,362	5,095	517	5,612	5,192	517	5,709
Center for Biologics Evaluation and Research	1,131	58	1,189	1,121	58	1,179	1,130	58	1,188
Center for Veterinary Medicine	680	12	692	713	12	725	714	12	726
Center for Devices and Radiological Health	1,532	82	1,614	1,714	82	1,796	1,757	82	1,839
National Center for Toxicological Research	276	---	276	276	---	276	276	---	276
Office of Regulatory Affairs	4,424	348	4,772	4,527	348	4,875	4,533	348	4,881
Headquarters and Office of the Commissioner	897	64	961	863	64	927	866	64	930
Export Certification	23	---	23	26	---	26	26	---	26
Color Certification	33	---	33	37	---	37	37	---	37
Family Smoking Prevention and Tobacco Control Act	855	39	894	908	39	947	960	39	999
Priority Review Vouchers (PRV) Pediatric Disease	11	---	11	11	---	11	11	---	11
MCMi - No Year	10	---	10	---	---	---	---	---	---
Opiods - No Year	73	---	73	---	---	---	---	---	---
21st Century Cures (BA Only)	136	---	136	136	---	136	100	---	136
Total	**15,983**	**1,161**	**17,144**	**16,530**	**1,161**	**17,691**	**16,770**	**1,161**	**17,967**

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 70 reimbursable and 26 PEPFAR.

DETAIL OF POSITIONS

	FY 2019 Actuals	FY 2020 Enacted	FY 2021 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	**$187,918**	**194,495**	**$194,495**
Executive Service (ES)			
Executive Service	57	59	60
Total Executive Service	**57**	**59**	**60**
Total - ES Salary	**$10,711,326**	**$11,465,636**	**$11,657,077**
General Schedule (GS)			
GS-15	1,440	1,489	1,514
GS-14	3,948	4,083	4,151
GS-13	4,921	5,089	5,174
GS-12	2,082	2,153	2,189
GS-11	681	705	716
GS-10	11	11	11
GS-9	438	453	461
GS-8	57	59	60
GS-7	246	254	258
GS-6	23	24	24
GS-5	54	56	57
GS-4	33	34	34
GS-3	20	20	21
GS-2	9	9	9
GS-1	6	6	6
Total General Schedule	**13,968**	**14,446**	**14,687**
Total - GS Salary	**$1,608,834,240**	**$1,722,131,079**	**$1,750,885,355**
Administrative Law Judges (AL)	---	---	---
Scientific/Senior Level (ST/SL)	5	5	5
Senior Biomedical Research Service (RS)	45	47	47
Scientific Staff Fellows (RG) (Title 42)	941	973	989
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	154	159	162
Former Performance Mgmt Recognition System Employees (GM)	1	1	1
Physicians and Dentists - (GP) (Title 38)	772	798	812
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06	290	290	290
Commissioned Corps - Other	871	871	871
Total Commissioned Corps	**1,161**	**1,161**	**1,161**
Administratively Determined (AD) (includes Title 42)[2]	5	5	5
Wage Grade	13	13	14
Consultants[2]	21	22	22
Total FTE (End of Year)[1]	**17,144**	**17,691**	**17,967**
Average ES Level	3	3	3
Average ES Salary	$187,918	194,495	194,495
Average GS grade	13	13	13
Average GS Salary	$115,180	119,211	119,211
Average GM Salary	$152,352	157,684	157,684
Average GP Salary	$218,255	225,894	225,894

[1] Does not include an estimated 70 reimbursable 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.

GOOD ACCOUNTING OBLIGATION IN GOVERNMENT ACT (GAO-IG ACT; PUBLIC LAW 115-414)

Appendix 1: OIG-GAO Open Recommendations							
Report Number	**Report Title**	**Report Date**	**Recommendation Text**	**Concur / Non-Concur**	**Implementation Timeline**	**Implementation Status**	**Implementation Updates and Constraints**
GAO-09-190	Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process	1/15/2009	The Secretary of Health and Human Services should direct the FDA Commissioner to expeditiously take steps to issue regulations for each class III device type currently allowed to enter the market through the 510(k) process. These steps should include issuing regulations to (1) reclassify each device type into class I or class II, or requiring it to remain in class III, and (2) for those device types remaining in class III, require approval for marketing through the PMA process.	Concur	NA	In progress	In 2018, FDA published the final order reclassifying electroconvulsive therapy devices for certain indications and requiring a PMA for those indications remaining in class III. At of the end of 2018, the Agency has completed the action for 25 of 26 device types as identified on FDA's website, which also provides links to the orders, panel transcripts and other relevant materials (https://www.fda.gov/about-fda/cdrh-transparency/515-program-initiative). The remaining device to reclassify or require a PMA is the cranial electrotherapy stimulator. We held the required panel meeting in 2012 and published the proposed order in 2016. We anticipate that the final order will be published in 2019.
GAO-10-246	Food Safety: FDA Should Strengthen Its Oversight of Food Ingredients Determined to Be Generally Recognized as Safe (GRAS)	2/3/2010	To better ensure FDA's oversight of the safety of GRAS substances, the Commissioner of FDA should develop a strategy to minimize the potential for conflicts of interest in companies' GRAS determinations, including taking steps such as issuing guidance for companies on conflict of interest and requiring information in GRAS notices regarding expert panelists' independence.	Concur	NA	In progress	On November 16, 2017, FDA published a notification of availability for the draft guidance "Best Practices for Convening a GRAS Panel: Guidance for Industry," with a request for comments on the draft guidance by May 15, 2018. FDA indicated that the draft guidance represents FDA's current thinking on strategies to minimize the potential for conflicts of interest in companies' GRAS conclusions, including assessing potential GRAS panel members for conflicts of interest. As of June 2019, FDA had not yet finalized the guidance, so we are leaving the recommendation open.

GAO-10-960	FDA Administration: Overseas Offices Have Taken Steps to Help Ensure Import Safety, but More Long-Term Planning Is Needed	9/30/2010	To help ensure that FDA's overseas offices are able to fully meet their mission of helping to ensure the safety of imported products, the Commissioner of FDA should ensure, as it completes its strategic planning process for the overseas offices, that it develops a set of performance goals and measures that can be used to demonstrate overseas office contributions to long-term outcomes related to the regulation of imported products and that overseas office activities are coordinated with the centers and Office of Regulatory Affairs (ORA).	Concur	NA	In progress	OIP has reorganized and is now called the Office of Global Policy and Strategy (OGPS). The Monitoring and Evaluation Staff is now integrated into the Planning and Evaluation Staff (P&E) in OGPS. This Staff leads and supports strategic planning and performance measurement efforts across OGPS. Progress continues to be made to strengthen OGPS' capacity to systematically plan, track and measure program results, ensure alignment with agency priorities, and effectively demonstrate change and impact over time through use of data and analytics. Over the past year, the framework and metrics were updated to reflect the organization's current priorities and expected outcomes. The P&E Staff utilized the capturing of intermediate outcomes to inform end outcomes, connecting the two categories. Discussions have been held to emphasize the importance of planning, monitoring and evaluation at many levels. Short and long-term planning conversations were held at the OGPS leadership retreat across Centers and internally. Discussions were held with individual offices to show offices how intermediate outcomes can lead to end outcomes and how to describe these in their quarterly reporting. Training and intermittent meetings are held to ensure that staff have the tools they need to track program results. The Staff has also focused on the integration of intermediate outcomes and consequential end outcomes and subsequent contributions to narratives (see attachment). The Staff plans to continue this conversation and training in the future.

GAO-12-346	Information Technology: FDA Needs to Fully Implement Key Management Practices to Lessen Modernization Risks	3/15/2012	To help ensure the success of FDA's modernization efforts, the Commissioner of FDA should direct the CIO to, in completing the assessment of Mission Accomplishments and Regulatory Compliance Services (MARCS), develop an integrated master schedule (IMS) that (1) identifies which legacy systems will be replaced and when; (2) identifies all current and future tasks to be performed by contractors and FDA; and (3) defines and incorporates information reflecting resources and critical dependencies.	Concur	NA	In progress	FDA is meeting with GAO in November 2019 to discuss how best to implement this recommendation.
GAO-13-244	Dietary Supplements: FDA May Have Opportunities to Expand Its Use of Reported Health Problems to Oversee Products	3/18/2013	To enhance FDA's ability to use AERs and to oversee dietary supplement products, the Secretary of the Department of Health and Human Services should direct the Commissioner of FDA to incorporate a mechanism to collect information on when AERs are used to support and inform consumer protection actions (i.e., surveillance, advisory, and regulatory actions).	Concur	NA	In progress	Due to unanticipated IT issues, delays in clearance of the modernized portal, and the government shut-down, FDA has needed to push back the January 2019 target date for the implementation of the modernized AE portal and mechanism for tracking compliance actions associated with AERs. FDA is in the final review stages of the new portal for public and industry reporting of AERs. FDA anticipates that this new portal will be released to the public in early FY 20 to aid in the collection of more structured public health data. This is the first phase for improving FDA's ability to quickly assess and determine risk of reported problems/illnesses. In order to best determine how to systematically collect data linking compliance actions to AERs, FDA is currently conducting a comprehensive analysis of IT and business processes as part of a multi-year initiative to improve tracking and coordination related to the AERs received about dietary supplements. This includes the development of requirements for system and business workflow mechanisms that will track and document public health actions taken in response to AERs that are processed.

GAO-13-723	New Tobacco Products: FDA Needs to Set Time Frames for Its Review Process	10/21/2013	To improve CTP's ability to operate efficiently, achieve effective results, and plan appropriately, the Secretary of Health and Human Services should direct the Commissioner of FDA to monitor FDA's performance relative to those time frames, such as evaluating whether staff are performing reviews of these submissions efficiently and effectively.	Concur	NA	In progress	In April 2018, FDA established performance measures for the review of provisional SE submissions. Beginning Fiscal Year 2019, FDA intends to meet the following goals for the review of all remaining provisional SE Reports: Issue Withdrawal Acknowledgement letter within 21 days of receiving withdrawal request; and Issue Advice/Information letter, Preliminary Finding letter, Cancellation, Closure, SE Order, or NSE Order within 120 days of scientific review commencing. FDA's progress in meeting these goals will be updated at the end of each fiscal year. More information on these performance measures, including the release of new performance measure data for review of regular SE applications from FY18, is available on CTP's performance measures webpage:
GAO-14-194	Drug Shortages: Threat to Public Health Persists, Despite Actions to Help Maintain Product Availability	2/10/2014	To enhance its oversight of drug shortages, particularly as the agency fine-tunes the manner in which it gathers data on shortages and transitions from its database to a more robust system, the Commissioner of FDA should conduct periodic analyses using the existing drug shortages database (and, eventually, the new drug shortages information system) to routinely and systematically assess drug shortage information, and use this information proactively to identify risk factors for potential drug shortages early, thereby potentially helping FDA to recognize trends, clarify causes, and resolve problems before drugs go into short supply.	Concur	NA	In progress	As FDA has transitioned to a more robust database that is supported by the Agency, we are able to conduct periodic analyses on a routine basis and gather shortage data. This allows us to see what the common reasons for shortages are and what is needed to better mitigate and prevent shortages. From these analyses, we continue to see that most shortages are due to manufacturing issues. Others have been due to raw material issues or natural disasters. We are currently targeting much of our effort on developing two guidances for industry to better prevent and mitigate shortages. One guidance provides additional recommendations on shortage notifications and what information the Agency is looking for to assist its efforts in preventing and mitigating shortages. The other guidance emphasizes the need for industry to put risk mitigation plans as well as a significant degree of redundancy in place. These industry efforts are anticipated to help prevent and mitigate shortages.

GAO-15-183	Food Safety: Additional Actions Needed to Help FDA's Foreign Offices Ensure Safety of Imported Food	2/27/2015	To help ensure the safety of food imported into the United States, the Commissioner of Food and Drugs should complete an analysis to determine the annual number of foreign food inspections that is sufficient to ensure comparable safety of imported and domestic food. If the inspection numbers from that evaluation are different from the inspection targets mandated in FSMA, FDA should report the results to Congress and recommend appropriate legislative changes.	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-15-38	Food Safety: FDA and USDA Should Strengthen Pesticide Residue Monitoring Programs and Further Disclose Monitoring Limitations	11/6/2014	To better inform users of the annual monitoring report about the frequency and scope of pesticide tolerance violations, the Secretary of Health and Human Services should direct the Commissioner of FDA to disclose in the agency's annual pesticide monitoring program report which pesticides with EPA-established tolerances the agency did not test for in its pesticide monitoring program and the potential effect of not testing for those pesticides.	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-15-671	Drug Compounding for Animals: FDA Could Improve Oversight with Better Information and Guidance	9/28/2015	To help ensure that FDA has relevant and timely information to support management decisions, including the critical information necessary to ensure the safety and effectiveness of drugs compounded for animals, the Secretary of Health and Human Services should direct the Commissioner of the FDA to develop policy or guidance for agency staff that specifies circumstances under which FDA will or will not enforce compounding regulations for animals and clearly define key terms.	Concur	NA	In progress	Barring unforeseen circumstances, FDA anticipates being able to publish draft Guidance for Industry #256 for public comment this calendar year.

GAO-15-671	Drug Compounding for Animals: FDA Could Improve Oversight with Better Information and Guidance	9/28/2015	To help ensure that FDA has relevant and timely information to support management decisions, including the critical information necessary to ensure the safety and effectiveness of drugs compounded for animals, the Secretary of Health and Human Services should direct the Commissioner of the FDA to consistently document the bases for FDA's decisions about how or whether it followed up on warning letters, adverse event reports, and complaints about drug compounding for animals.	Concur	NA	In progress	When CVM's guidance is finalized, we intend to develop a risk-based compliance program to address compounding of animal drugs from bulk drug substances. As part of that compliance program, CVM intends to consistently document the bases for our decisions about what actions are taken, for example, warning letters, adverse event reports, and complaints
GAO-16-182	Information Technology: FDA Has Taken Steps to Address Challenges but Needs a Comprehensive Strategic Plan	12/17/2015	To help ensure that FDA's IT strategic planning activities are successful in supporting the agency's mission, goals, and objectives, the Commissioner of FDA should require the CIO to implement the plan to ensure that expected outcomes of the agency's key IT initiatives are achieved.	Concur	NA	In progress	FDA is meeting with GAO in November 2019 to discuss how best to implement this recommendation.

GAO-16-192	Drug Safety: FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement	1/14/2016	To improve the data on tracked safety issues and postmarket studies that are needed for required reporting and for systematic oversight of postmarket drug safety, the Secretary of HHS should direct the Commissioner of FDA to work with stakeholders within FDA to identify additional improvements that could be made to FDA's current database or future information technology investments to capture information in a form that can be easily and systematically used by staff for oversight purposes.	Concur	NA	In Progress	Using experience and feedback gained from the 15-month pilot, FDA is configuring an IT system to track postmarket drug safety issues with oversight CDER's Business Informatics Governance (BIG) Board. The target completion for the first release is spring 2020. The IT system developed will be evaluated as part of the contractor assessment referenced above. Future releases will add enhancements and capabilities to IT system.Postmarketing Requirements (PMRs) and Postmarketing Commitments (PMCs)In January 2019, CDER's Business Informatics Governance Board (BIG) selected an information technology (IT) system that has workflow and content management capabilities to support the New Drug Regulatory Program Modernization effort. BIG also established an integrated project team (IPT) to provide oversight and to develop, implement, and successfully operate the IT system. The IPT is establishing project teams to address specific concerns of the new drug process, including establishing a project team to evaluate and address the needs of CDER's postmarketing requirement (PMR) and postmarketing commitment (PMC) program. CDER is developing test cases which will inform whether or not the IT system will meet CDER's needs. The project team for PMRs and PMCs is expected to be established by the end of calendar year 2020, or the beginning of calendar year 2021. Once the project team for PMRs and PMCs is established, the project team will create a plan for how to develop and implement support of the PMR/PMC program, as well as a timeline for completion.In the meantime, CDER continues to work with its stakeholders to improve tracking and data accuracy related to PMRs and PMCs. Some of the actions that CDER has taken in recent months include:• Entering into final clearance the "Annual Status Report Information and Other Submissions for Postmarketing Requirements and Commitments: Using Forms FDA 3988 and FDA 3989 Guidance for

							Industry" and the Notice of Availability o Guidance and Notice of Availability proceeding through CDER clearance• Finalizing FDA Form 3988 (Transmittal of PMR/PMC Submissions for Drugs and Biologics), a standardized fillable form that supports electronic signature. Providing complete and accurate information on Form 3988 will help to expedite routing of the submission for FDA review and any necessary follow-up actions. Additionally, the form allows for automated processing. o Form 3988 has completed functional testing• Finalizing FDA Form 3989 (PMR/PMC Annual Status Report for Drugs and Biologics), a standardized fillable form supporting electronic signature. FDA Form 3989 includes fields where applicants can provide data that they are required to provide annually, as well as fields for optional data. The form also allows for automated processing. o Form 3989 has completed functional testingContinuing collaboration with internal stakeholders to identify and implement changes or targeted training to improve the accuracy of PMR/PMC data entry coding issues (e.g., providing the correct code for the PMR/PMC-related submissions, individualized training).L15
GAO-16-399	Imported Food Safety: FDA's Targeting Tool Has Enhanced Screening, but Further Improvements Are Possible	5/26/2016	To further enhance FDA's PREDICT tool and its ability to ensure the safety of imported food, the Secretary of Health and Human Services should direct the Commissioner of FDA to document the process for identifying the type of open source data to collect, obtaining such data, and determining how PREDICT is to use the data.	Concur	NA	In progress	FDA established a project charter with the goal of developing an SOP in coordination with FDA field offices. The draft SOP is under review and we anticipate finalizing it in the first quarter of FY2020.

GAO-16-432	Medical Product Oversight: FDA Needs More Strategic Planning to Guide its Scientific Initiatives	6/15/2016	In order to improve FDA's strategic planning for regulatory science efforts, we recommend the Secretary of Health and Human Services direct the Commissioner of FDA to develop and document measurable goals, such as targets and time frames, for its regulatory science efforts so it can consistently assess and report on the agency's progress in regulatory science efforts.	Concur	NA	In progress	At the agency level, as part of the agency's cyclical strategic planning, FDA is currently revisiting its strategic regulatory science priorities contained in the 2011 Strategic Plan for Regulatory Science. In addition, as detailed below, FDA medical product centers have made significant progress towards implementing GAO's recommendation 1 to develop measurable goals, objectives, and priorities while enhancing research governance.
GAO-16-432	Medical Product Oversight: FDA Needs More Strategic Planning to Guide its Scientific Initiatives	6/15/2016	In order to improve FDA's strategic planning for regulatory science efforts, we recommend the Secretary of Health and Human Services direct the Commissioner of FDA to systematically track funding of regulatory science projects across each of its priority areas.	Concur	NA	In progress	The FDA relies on individual Centers to manage and track their funds, which are distributed from the Agency to the Centers for allocation to specific regulatory science efforts. The medical product centers have made progress towards implementing Recommendation 2.
GAO-16-500	FDA: Comprehensive Strategic Planning Needed to Enhance Coordination Between Medical Product Centers	6/15/2016	To ensure that FDA can effectively coordinate and integrate its medical product centers' programs and emerging issues, the Secretary of Health and Human Services should direct the Commissioner of FDA to engage in a strategic planning process to identify challenges that cut across the medical product centers and document how it will achieve measurable goals and objectives in these areas.	Concur	NA	In progress	In January 2018, FDA published its Strategic Policy Roadmap, which outlines the cross-cutting policy priorities that FDA planned to pursue in the next two years. The document was the product of a close collaboration across the medical product centers as well as the foods and tobacco programs. FDA's Strategic Policy Roadmap was intended to optimize FDA's resources to achieve clear deliverables that would yield results in a timely manner.
GAO-16-79	Critical Infrastructure Protection: Sector-Specific Agencies Need to Better Measure Cybersecurity Progress	11/19/2015	To better monitor and provide a basis for improving the effectiveness of cybersecurity risk mitigation activities, informed by the sectors' updated plans and in collaboration with sector stakeholders, the Secretaries of Agriculture and Health and Human Services (as co-SSAs) should direct responsible officials to develop performance metrics to provide data and determine how to overcome challenges to monitoring the food and agriculture sector's cybersecurity progress.	Concur	NA	In progress	We have little to no information to provide to GAO because there is no requirement for USDA or FDA-regulated entities to implement cybersecurity practices within their operations. We have shared information with our Sector membership (Federal, State, Local, Tribal and Territorial government; academia; private industry) regarding general cybersecurity measures but it is entirely up to individual entities to address cybersecurity vulnerabilities as they deem appropriate.

GAO-17-143	Drug Safety: FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of Its Foreign Offices	1/17/2017	To help ensure that FDA's foreign offices are able to fully meet their mission of helping to ensure the safety of imported products, as the agency continues to test performance measures and evaluate its Office of International Programs (OIP) strategic workforce plan, the Commissioner of FDA should assess the effectiveness of the foreign offices' contributions by systematically tracking information to measure whether the offices' activities specifically contribute to drug safety-related outcomes, such as inspections, import alerts, and warning letters.	Concur	NA	In progress	OIP has reorganized and is now called the Office of Global Policy and Strategy (OGPS). The Monitoring and Evaluation Staff is now integrated into the Planning and Evaluation Staff (P&E) in OGPS. This Staff leads and supports strategic planning and performance measurement efforts across OGPS. Progress continues to be made to strengthen OGPS' capacity to systematically plan, track and measure program results, ensure alignment with agency priorities, and effectively demonstrate change and impact over time through use of data and analytics. Over the past year, the framework and metrics were updated to reflect the organization's current priorities and expected outcomes. The P&E Staff utilized the capturing of intermediate outcomes to inform end outcomes, connecting the two categories. Discussions have been held to emphasize the importance of planning, monitoring and evaluation at many levels. Short and long-term planning conversations were held at the OGPS leadership retreat across Centers and internally. Discussions were held with individual offices to show offices how intermediate outcomes can lead to end outcomes and how to describe these in their quarterly reporting. Training and intermittent meetings are held to ensure that staff have the tools they need to track program results. The Staff has also focused on the integration of intermediate outcomes and consequential end outcomes and subsequent contributions to narratives (see attachment). The Staff plans to continue this conversation and training in the future. In addition to focusing on outcomes in the past year, OGPS was focused on implementation of consistent performance measures in 2019, and efficiencies were gained through continuous data quality management and the continuous development and improvements to our system for activity tracking, planning and reporting.

GAO-17-189	Antibiotics: FDA Has Encouraged Development, but Needs to Clarify the Role of Draft Guidance and Develop Qualified Infectious Disease Product Guidance	3/2/2017	In order for drug sponsors to benefit from FDA's revised guidance on antibiotic development and take full advantage of the QIDP designation, FDA should develop and make available written guidance on the QIDP designation that includes information about the process a drug sponsor must undertake to request the fast track designation and how the agency is applying the market exclusivity incentive.	Concur	NA	In progress	FDA is in the process of finalizing the Qualified Infectious Disease Product Designation Questions and Answers draft guidance, taking into account the comments that were received on the draft guidance. It is important to the Agency to provide drug sponsors and other stakeholders with clarity and transparency. To fulfill this aim FDA has held and continues to hold public workshops to discuss the development of drug products for certain bacterial or fungal diseases or for certain populations (unmet needs, neonates, or single species). These public meetings inform FDA's thinking on important drug development issues and help to ensure transparency. Examples of recent workshops can be found here: https://www.fda.gov/about-fda/center-drug-evaluation-and-research/oap-regulatory-science-activities. These workshops provide insight into areas where consensus has been reached by the scientific community and areas where questions remain. FDA uses information gleaned from these workshops to develop guidances that provide consensus opinion and to answer questions we have heard at workshops. One example of this work is the meeting in September 2016, on Coordinated Development of Antimicrobial Drugs and Antimicrobial Susceptibility Test Devices, which resulted in the publication of the recently published final guidance of the same name.

GAO-17-192	Antibiotic Resistance: More Information Needed to Oversee Use of Medically Important Drugs in Food Animals	3/16/2017	The Secretary of Health and Human Services should direct the Commissioner of FDA to develop performance measures and targets for actions to manage the use of antibiotics such as revising the veterinary feed directive and developing guidance documents on judicious use.	Non-Concur	NA	In progress	FDA agrees that performance measures and targets for actions are needed to help gauge the success of antimicrobial stewardship efforts and guide their continued evolution and optimization. As part of implementation of GFI #213, "New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209," and the VFD final rule, FDA set the target to remove all production indications from affected applications and to bring all 292 new animal drug application under veterinary oversight. In January 2017, FDA reported that all affected drug applications have either aligned with the recommendations outlined in GFI #213, or their approvals have been voluntarily withdrawn. Because of these changes, these products cannot be used for production (e.g., growth promotion) purposes and may only be used under the authorization of a licensed veterinarian. Of the 292 new animal drug applications initially affected by GFI #213: • 84 were completely withdrawn • Of the remaining 208 applications, o 93 applications for oral dosage form products intended for use in water were converted from over-the-counter to prescription status, o 115 applications for products intended for use in feed were converted from over-the-counter to veterinary feed directive status • Production (e.g., growth promotion) indications were withdrawn from all (31) applications that included such indications for use The implementation of GFI #213 is a significant milestone in national efforts to address the use of medically important antimicrobials in food-producing animals. Additionally, following the successful implementation of GFI #209, "The Judicious Use of

							Medically Important Antimicrobial Drugs in Food-Producing Animals," GFI #213, and the Veterinary Feed Directive final rule, in December 2018 FDA's Center for Veterinary Medicine (CVM) announced that domestic sales and distribution of all medically important antimicrobials intended for use in food-producing animals have: • decreased by 33 percent from 2016 through 2017 • decreased by 43 percent from 2015 (the year of peak sales) through 2017 • decreased by 28 percent from 2009 (the first year of reported sales) through 2017 While sales data do not necessarily reflect antimicrobial use, the reduction in sales volume is an important indicator that ongoing efforts to support antimicrobial stewardship are having a significant impact.
GAO-17-192	Antibiotic Resistance: More Information Needed to Oversee Use of Medically Important Drugs in Food Animals	3/16/2017	The Secretary of Health and Human Services should direct the Commissioner of FDA to establish steps to increase veterinary oversight of medically important antibiotics administered in routes other than feed and water, such as injections and tablets.	Non-Concur	NA	In progress	As previously noted, in September 2018 FDA released a broad, five-year plan outlining the activities and important steps it intends to take to support stewardship of medically important antimicrobials in veterinary settings. As part of that plan, FDA's CVM intends to publish a draft strategy, likely in the form of draft guidance for industry, to bring all dosage forms (such as injectables and tablets) of medically important antimicrobial drugs under veterinary oversight. FDA believes this is an important step in fostering the judicious use of these important drugs. The Agency plans to issue this draft strategy no later than the end of fiscal year 2019. This draft GFI will provide the framework, including proposed timelines, for transitioning from over-the-counter to prescription marketing status for all approved medically important antimicrobial drugs that are not yet subject to

							veterinary oversight. In conjunction with issuing this draft strategy, CVM intends to publish a list of affected new animal drug applications.
GAO-17-192	Antibiotic Resistance: More Information Needed to Oversee Use of Medically Important Drugs in Food Animals	3/16/2017	The Secretary of Health and Human Services should direct the Commissioner of FDA to develop a process, which may include time frames, to establish appropriate durations of use on labels of all medically important antibiotics used in food animals.	Non-Concur	NA	In progress	In September 2018, FDA announced its five-year action plan for supporting antimicrobial stewardship in veterinary settings. This plan builds upon the important steps FDA has taken to eliminate production uses of medically important antimicrobials used in the feed or water of food-producing animals, and to bring all remaining therapeutic uses of these drugs under the oversight of licensed veterinarians. It also supports the judicious use of antimicrobials in food-producing animals and is driven by the concept that medically important antimicrobial drugs should only be used in animals when necessary for the treatment, control, or prevention of specific diseases.As part of the five-year action plan, FDA continues its efforts to establish appropriately targeted durations of use for medically important antimicrobial drugs used in the feed or in water of food-producing animals. Action 1.1.1 of the five-year plan, "publish a list of medically important antimicrobial drugs administered in the feed or drinking water of food-producing animals that are approved for indications that lack a defined duration of use," has already been completed. Action 1.1.2, "issue a draft strategy (e.g., Guidance for Industry [GFI]) to ensure that all medically important antimicrobial drugs used in the feed or drinking water of food-producing animals have an appropriately targeted duration of use," is expected to be published by the end of September 2020. We expect this draft guidance will propose a process, including deadlines, for sponsors to submit applications to revise the approved conditions of use of affected new animal drugs accordingly.While FDA is committed to advancing this initiative as quickly as possible, we believe these revisions to the approved conditions of use need to be based on sound scientific data and information.

							Understanding that such data and information are currently limited, FDA published a Request for Applications (RFA) on April 1, 2019, soliciting study proposals to help establish more targeted or defined durations of use for approved medically important antimicrobial drugs used in the feed of food-producing animals. There are currently no such products approved for use in water with an undefined duration of use. Given the significant scientific and technical challenges, including the potential need to generate appropriate supporting information, we anticipate that this initiative will require substantial time to fully complete. Our primary objective is to update product dosage regimens to better target when and for how long the drug may be used. Defining more targeted durations of use supports the FDA's ongoing efforts to slow the development of antimicrobial resistance by fostering the judicious use of medically important antimicrobial drugs in animals.
GAO-17-443	Imported Seafood Safety: FDA and USDA Could Strengthen Efforts to Prevent Unsafe Drug Residues	10/2/2017	The Commissioner of FDA should pursue formal agreements with countries exporting seafood to the United States that commit these countries to test for drugs of concern to FDA and the corresponding maximum residue levels (MRLs) that FDA established for these drugs.	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-17-443	Imported Seafood Safety: FDA and USDA Could Strengthen Efforts to Prevent Unsafe Drug Residues	10/2/2017	The Commissioner of FDA should coordinate and communicate with FSIS in developing drug residue testing methods and corresponding maximum residue levels for imported seafood that may also be applicable to imported catfish.	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-17-445	Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks	5/23/2017	The Secretary of Health and Human Services should direct the Commissioner of the Food and Drug Administration to consolidate information from individual diagnostic test labels and make this information available in a form that enables users to more readily compare information across tests.	Concur	NA	In Progress	The Food and Drug Administration is working to consolidate and make available on its website information for Zika virus diagnostic tests that have emergency use authorization and plans to recommend to sponsors of Zika virus diagnostic tests that they provide a description of the comparator assay.

GAO-17-445	Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks	5/23/2017	The Secretary of Health and Human Services should direct the Commissioner of the Food and Drug Administration to require manufacturers to list the identity of comparator assays on their diagnostic test labels.	Concur	NA	In progress	Food and Drug Administration plans to recommend to sponsors of Zika virus diagnostic tests that they provide a description of the comparator assay.
GAO-17-87	FDA Facilities: Planning Efforts for White Oak Campus Should Further Incorporate Leading Practices to Address Ongoing Challenges	1/3/2017	In order to ensure that the agency is adequately protecting the White Oak campus as a designated high-risk facility and strategically planning for the White Oak campus's future, as FDA moves forward with its proposed planning efforts, the Commissioner of FDA, in consultation with the Administrator of GSA, should implement vehicular access control measures on the White Oak campus to meet the requirements of the high-risk facility level designation assigned in the 2014 risk assessment report, or fully document the rationale for any deviations from these requirements.	Concur	NA	Awaiting Disposition	GAO has informed FDA that it plans to close the recommendation as implemented.
GAO-17-87	FDA Facilities: Planning Efforts for White Oak Campus Should Further Incorporate Leading Practices to Address Ongoing Challenges	1/3/2017	In order to ensure that the agency is adequately protecting the White Oak campus as a designated high-risk facility and strategically planning for the White Oak campus's future, as FDA moves forward with its proposed planning efforts, the Commissioner of FDA, in consultation with the Administrator of GSA, should further incorporate leading strategic facilities planning practices into FDA's proposed planning efforts by ensuring that FDA establish strategic linkage between its strategic priorities and its facilities plans.	Concur	NA	Awaiting Disposition	GAO has informed FDA that it plans to close the recommendation as implemented.

GAO-17-87	FDA Facilities: Planning Efforts for White Oak Campus Should Further Incorporate Leading Practices to Address Ongoing Challenges	1/3/2017	In order to ensure that the agency is adequately protecting the White Oak campus as a designated high-risk facility and strategically planning for the White Oak campus's future, as FDA moves forward with its proposed planning efforts, the Commissioner of FDA, in consultation with the Administrator of GSA, should document the key information related to daily operational activities and ongoing benefits and challenges that are needed to inform FDA's proposed planning efforts in the areas of needs assessment, gap identification, and alternatives analysis, and incorporate into proposed planning efforts a detailed strategy for collecting and analyzing this information.	Concur	NA	Awaiting Disposition	GAO has informed FDA that it plans to close the recommendation as implemented.
GAO-18-140	FDA Medical Device Reviews: Evaluation is Needed to Assure Requests for additional Information Follow a Least Burdensome Approach	1/16/2018	The Commissioner of FDA should develop performance metrics and use them to evaluate the implementation of the least burdensome requirements, such as during its planned audits of medical device deficiency letters	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-18-174	Food Safety and Nutrition: FDA Can Build on Existing Efforts to Measure Progress and Implement Key Activities	3/5/2018	The Commissioner of FDA should ensure that FVM Program staff uniformly document the bases for their decisions for issuing either regulations or guidance related to food safety and nutrition, such as by using concept papers or guidance initiation sheets.	Concur	NA	Awaiting Disposition	FDA has provided GAO with an update indicating that the recommendation has been implemented.
GAO-18-174	Food Safety and Nutrition: FDA Can Build on Existing Efforts to Measure Progress and Implement Key Activities	3/5/2018	The Commissioner of FDA should ensure that the FVM Program develops performance measures with associated targets and time frames for all eight of FDA's food safety- and nutrition-related objectives.	Concur	NA	In Progress	Consistent with GAO's recommendation, the Agency has been actively working to expand the use of outcome-based performance measures. Implementation of FSMA-based preventive controls standards is a top priority for the Agency and a key component of the FVM Program's strategic plan. For this reason, FSMA-related performance metrics have been prioritized, and the first performance measures to be implemented will be for the Preventive Controls (PC) for Human Food and PC for Animal Food rules. FDA is using inspections and compliance data to assess the impact of the FSMA

							regulations on food safety. A set of these measures will be published via FDA's Agency-wide performance management system in 2019.
GAO-18-174	Food Safety and Nutrition: FDA Can Build on Existing Efforts to Measure Progress and Implement Key Activities	3/5/2018	The Commissioner of FDA should complete an implementation plan that includes specific actions, priorities, and milestones for the FVM Program's strategic plan.	Concur	NA	In Progress	The Agency is currently developing an implementation plan that aligns with the FVM Strategic Plan. Due to organizational and leadership changes, the Agency had to delay the release of the implementation plan to ensure the plan aligns with leadership priorities. The plan will be released in 2019.
GAO-18-199	Food Safety: Federal Efforts to Manage the Risk of Arsenic in Rice	4/16/2018	The Commissioner of FDA should develop a timeline for updating the risk assessment on arsenic in rice.	Concur	NA	In Progress	FDA will provide an update on the risk assessment at the time the final guidance is issued.
GAO-18-199	Food Safety: Federal Efforts to Manage the Risk of Arsenic in Rice	4/16/2018	The Commissioner of FDA should develop a timeline for finalizing the draft guidance on arsenic in infant rice cereal.	Concur	NA	In Progress	FDA has prepared a final guidance document and, consistent with FDA's regulations, intends to announce the final guidance document's availability through a notice in the Federal Register. As of July 26, 2019, the final guidance document and notice are undergoing review and clearance prior to publication, and we hope to make the final guidance document publicly available in the near future.
GAO-18-199	Food Safety: Federal Efforts to Manage the Risk of Arsenic in Rice	4/16/2018	The Commissioner of FDA should develop a mechanism for working with relevant agencies to identify their roles and responsibilities for coordinating risk assessments of contaminants in food, including arsenic in rice.	Concur	NA	Awaiting Disposition	FDA currently is designing a new reporting process, using data collected in existing FDA systems, to record the date that FDA learns of certain potentially hazardous food. For foods in the first category, it will be the date that the final lab classification is entered into the Field Accomplishments and Compliance Tracking System (FACTS), based on analytical results from an FDA laboratory or a mutually reliant state regulatory laboratory. For foods in the second category, it will be the date that the traceback investigation has produced actionable information about the source of the product. We will consider how best to document these dates in our data systems, including whether to add new data fields in RES. We expect this new reporting process to be fully implemented by the end of the calendar year 2020.

A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA develop a policy for defining and a procedure for identifying retrospectively the date that FDA learns of a potentially hazardous product and consider adding a field for the date to the RES or another FDA system so that FDA staff involved in managing a recall have access to this information.	Concur	2020	In progress	FDA currently is designing a new reporting process, using data collected in existing FDA systems, to record the date that FDA learns of certain potentially hazardous food. For foods in the first category, it will be the date that the final lab classification is entered into the Field Accomplishments and Compliance Tracking System (FACTS), based on analytical results from an FDA laboratory or a mutually reliant state regulatory laboratory. For foods in the second category, it will be the date that the traceback investigation has produced actionable information about the source of the product. We will consider how best to document these dates in our data systems, including whether to add new data fields in RES.
A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA establish performance measures for the amount of time between the date FDA learns of a potentially hazardous product and the date a firm initiates a voluntary recall, monitor performance, and refine operating procedures, as needed.	Concur	2021	In progress	FDA will establish performance measures for the amount of time between the date FDA learns of a potentially hazardous food, as described in response to Recommendation 10, and the date a firm initiates a voluntary recall. Once we have finalized the design of the new report, we will begin monitoring performance against the metric and will refine operating procedures as needed.
A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA develop procedures to determine whether a reconciliation of distribution lists to shipping records is necessary to ensure that FDA uses complete and accurate distribution lists when assigning audit checks.	Concur	2019	In progress	The FDA is continuing to work on developing procedures to determine whether a reconciliation of distribution lists to shipping records is necessary. Factors to consider would include evidence of malfeasance by the firm; whether audit checks at direct consignees audited from the original distribution list provided by the recalling firm claim to not carry the recalled product; and whether FDA has received reports from direct consignees not listed on the original distribution list provided by the recalling firm, indicating that they were not notified of the recall. Should FDA determine that the original distribution list provided by the recalling firm was incorrect, FDA would request that the recalling firm notify the correct consignees. FDA would re-evaluate the original audit check assignment and adjust it to audit the corrected distribution list.

A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA ensure, through its recall audit plan, that audit checks are issued at the level specified in the FDA audit program.	Concur	2019	In progress	FDA is working to make changes in its recall audit plan to include a verification that audit checks are issued at the level specified for that recall. The FDA is also reviewing the process to see if it would be feasible and effective to standardize the number of recall audit checks that should be completed based on the number of direct consignees that were identified as having received the recalled product, resources available to conduct recall audit checks, and the hazard of the recalled product.
A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA implement procedures to request status reports at the initiation of the recall and, through its recall audit plan, ensure FDA monitoring district offices follow up with firms that do not provide timely or complete status reports.	Concur	2019	In progress	The FDA reviewed the existing RPM procedures, and as a result, revised and added procedures intended to increase the consistency with which the FDA will request, and firms will provide, status reports to the FDA. The RPM was updated in April 2019 to include procedures for divisions to request status reports at the initiation of a recall using a written acknowledgement of the firm's recall (Section 7-7-1 #2 and Exhibit 7-8), to track whether firms are submitting requested status reports and to send reminders to firms that have not submitted periodic status reports. Additionally, the FDA is pursuing RES improvements which would send emails reminding firms to send status reports. Once these improvements are made, the RPM will be updated to instruct the divisions to use RES to send the reminders
A-01-16-01502	The Food and Drug Administration's Food-Recall Process Did Not Always Ensure the Safety of the Nation's Food Supply	12/22/2017	We recommend that FDA increase the use of third-party audit checks through its recall strategic plan.	Concur	2019	Awaiting Disposition	The FDA concurs with, and has implemented, this recommendation. FDA will be awarding a new indefinite delivery, indefinite quantity contract that will soon go into effect. The new contract includes an increase of approximately 3,300 third-party audits as compared to the previous contract and allows the contractor to conduct audits by visit and by phone. In addition, the new contract allows the contractor to conduct recall audit checks at points of distribution, not just the retail level
OEI-01-08-00510	Challenges to FDA's Ability To Monitor and Inspect Foreign Clinical Trials	6/1/2010	FDA should require standardized electronic clinical trial data and create an internal database	Concur	2021	In Progress	In February 2018, FDA published draft industry guidance entitled Standardized Format for Electronic Submission of NDA and BLA Content for the Planning and Conduct of Bioresearch

							Monitoring (BIMO) Inspections for CDER Submissions to support inspection planning and conduct.
OEI-01-11-00210	Dietary Supplements: Structure/Function Claims Fail To Meet Federal Requirements	10/2/2012	FDA should seek explicit statutory authority to review substantiation for structure/function claims to determine whether claims are truthful and not misleading	Non-Concur	2019	Awaiting Disposition	FDA is not currently seeking explicit statutory authority to review substantiation for structure/function claims beyond its existing authorities. As noted in the report, under section 403(r)(6) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), a manufacturer must have substantiation that a structure/function claim used in the labeling of a supplement is truthful and not misleading, and must notify FDA of the claim no later than 30 days after the first marketing of the supplement with the claim. FDA can request that manufacturers voluntarily submit substantiation for structure/function claims, and has done so in the past, but these requests are not always granted. FDA also has a right to review and inspect a firm's substantiation records as part of our general records inspection authority, should we have concerns about a particular structure/function claim. In addition, FDA collaborates with and supports Federal Trade Commission efforts to enforce the substantiation requirements.
OEI-01-11-00211	Dietary Supplements: Companies May Be Difficult To Locate in an Emergency	10/2/2012	FDA should seek statutory authority to impose civil monetary penalties on companies that do not comply with registration requirements	Non-Concur	2019	Awaiting Disposition	The Food Safety Modernization Act (FSMA), P.L. 111-353 failed to include civil monetary penalties. Given the continued lack of congressional support for civil penalties linked to the failure to register, FDA does not plan to pursue this further.
OEI-01-14-00390	FDA is Issuing More Postmarketing Requirements, but Challenges with Oversight Persist	7/20/2016	FDA should build capacity in DAARTS to support PMR oversight	Concur	2020	In Progress	CDER is strengthening its data management for the PMR and PMC program on several fronts, including implementation of streamlined procedures for data entry, a revised Annual Status Report (ASR) review form and related MAPP, and improvements to DARRTS.
OEI-01-14-00390	FDA is Issuing More Postmarketing Requirements, but Challenges with Oversight Persist	7/20/2016	FDA should provide a standardized form for ASRs, ensure that they are complete, and require sponsors to submit them electronically	Concur	2020	In Progress	CDER is strengthening its data management for the PMR and PMC program on several fronts, including implementation of streamlined procedures for data entry, a revised Annual Status Report (ASR) review form and related MAPP, and improvements to DARRTS.

OEI-02-08-00080	FDA Inspections of Domestic Food Facilities	4/1/2010	FDA should consider seeking statutory authority to impose civil penalties through administrative proceedings against facilities that do not voluntarily comply with statutory and regulatory requirements.	Concur	2019	Awaiting Disposition	The Food Safety Modernization Act (FSMA), P.L. 111-353 failed to include civil monetary penalties. Given the continued lack of congressional support for civil penalties linked to the failure to register, FDA does not plan to pursue this further.
OEI-02-14-00420	Challenges Remain in FDA's Inspections of Domestic Food Facilities	9/25/2017	FDA should conduct timely follow-up inspections to ensure that significant inspection violations are corrected.	Concur	2022	In Progress	FDA remains committed to implementing the inspection frequency mandate for high- and non-high risk domestic food facilities and has provided OIG with an action plan that describes ongoing activities directly responsive to this recommendation.
OEI-02-14-00420	Challenges Remain in FDA's Inspections of Domestic Food Facilities	9/25/2017	FDA should improve the timeliness of FDA's actions, including warning letters, so that facilities do not continue to operate under harmful conditions.	Concur	2022	In Progress	FDA remains committed to implementing the inspection frequency mandate for high- and non-high risk domestic food facilities and has provided OIG with an action plan that describes ongoing activities directly responsive to this recommendation.
OEI-02-14-00420	Challenges Remain in FDA's Inspections of Domestic Food Facilities	9/25/2017	FDA should take appropriate action against all facilities with significant inspection violations	Concur	2022	In Progress	FDA remains committed to implementing the inspection frequency mandate for high- and non-high risk domestic food facilities and has provided OIG with an action plan that describes ongoing activities directly responsive to this recommendation.
OEI-02-14-00420	Challenges Remain in FDA's Inspections of Domestic Food Facilities	9/25/2017	FDA should improve how it handles attempted inspections to ensure better use of resources	Concur	2022	In Progress	FDA remains committed to implementing the inspection frequency mandate for high- and non-high risk domestic food facilities and has provided OIG with an action plan that describes ongoing activities directly responsive to this recommendation.
OEI-04-10-00480	FDA's Clearance of Medical Devices Through the 510(k) Process	9/19/2013	FDA should, in accordance with the law, finish classifying the remaining 19 types of Class III preamendment devices that include devices still used as predicates in the 510(k) process	Concur	2019	In progress	In 2018, FDA published the final order reclassifying electroconvulsive therapy devices for certain indications and requiring a PMA for those indications remaining in class III. At of the end of 2018, the Agency has completed the action for 25 of 26 device types as identified on FDA's website, which also provides links to the orders, panel transcripts and other relevant materials (https://www.fda.gov/about-fda/cdrh-transparency/515-program-initiative). The remaining device to reclassify or require a PMA is the cranial electrotherapy stimulator. We held the required panel meeting

							in 2012 and published the proposed order in 2016. We anticipate that the final order will be published in 2019.
OEI-04-11-00510	FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety	2/12/2013	Identify REMS that are not meeting their goals and take appropriate actions to protect the public health.	Concur	2019	In progress	FDA has developed two FDA draft guidance documents to address this recommendation.
OEI-04-11-00510	FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety	2/12/2013	Ensure that assessment reviews are timely.	Concur	2020	In progress	FDA is developing a Manual of Policies and Procedures that will delineate the timeframes for conducting reviews of REMS assessments.
OEI-04-11-00510	FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety	2/12/2013	Seek legislative authority to enforce FDA assessment plans.	Concur	2019	Awaiting Disposition	FDA has had no opportunities to pursue legislative changes to the statutory provisions that describe the requirements for REMS assessments. FDA would like OIG to close this recommendation as "not implemented".
OEI-04-11-00510	FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety	2/12/2013	Develop and implement a plan to identify, develop, validate, and assess REMS components.	Concur	2019	In progress	FDA has developed two FDA draft guidance documents to address this recommendation.
OEI-04-11-00510	FDA Lacks Comprehensive Data To Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety	2/12/2013	Clarify expectations for sponsors' assessments in FDA assessment plans.	Concur	2019	In progress	FDA has developed two FDA draft guidance documents to address this recommendation.
OEI-05-07-00730	The Food and Drug Administration's Oversight of Clinical Investigators' Financial Information	1/1/2009	FDA should require that sponsors submit financial information for clinical investigators as part of the pretrial application process	Non-Concur	2019	Awaiting Disposition	FDA believes that clinical investigator financial disclosures are being appropriately identified and managed during the study planning process and that additional disclosure to and review by FDA at that time is not

							needed and would not be an efficient use of FDA resources
OEI-05-14-00640	Drug Supply Chain Security: Wholesalers Exchange Most Tracing Information	9/12/2017	FDA should provide technical assistance on requirements regarding direct purchase statements	Concur	2021	In progress	FDA intends to provide additional information related to direct purchase statements in a guidance document for industry
OEI-05-14-00640	Drug Supply Chain Security: Wholesalers Exchange Most Tracing Information	9/12/2017	FDA should provide technical assistance regarding the exchange of drug product tracing information for sales to 340-B-covered entities that use 340-B contract pharmacies	Concur	2021	In progress	FDA will explore options for clarifying the types of products that are exempt from the DSCSA. FDA will also consider providing suggestions for how trading partners might resolve or prevent disagreements about whether a particular product has exempt status.
OEI-05-14-00640	Drug Supply Chain Security: Wholesalers Exchange Most Tracing Information	9/12/2017	FDA provide technical assistance regarding exempt products	Concur	2021	In progress	FDA intends to provide additional information on third-party agreements in a guidance document for industry.
OEI-05-16-00550	Drug Supply Chain Security: Dispensers Received Most Tracing Information	3/26/2018	Provide educational outreach to dispensers about DSCSA requirements for receiving drug product tracing information	Concur	2020	In progress	FDA will review its dispenser communications plan and identify and create opportunities to work with dispenser-centric trade and professional organizations to provide additional education and outreach.
OEI-09-16-00220	FDA Should Further Integrate Its Review of Cybersecurity Into the Premarket Review Process for Medical Devices	9/10/2018	FDA should include cybersecurity documentation as a criterion in FDA's Refuse-to-Accept checklists	Concur	2020	In progress	FDA will update the RTA checklist and the accompanying guidance to specifically identify cybersecurity as an item in the checklist during the next update of these items.
OEI-09-16-00220	FDA Should Further Integrate Its Review of Cybersecurity Into the Premarket Review Process for Medical Devices	9/10/2018	FDA should promote the use of presubmission meetings to address cybersecurity-related questions	Concur	2020	In progress	While FDA believes that discussions on cybersecurity are already encompassed broadly in the presubmission program, FDA will specifically mention cybersecurity in the next planned update of the presubmission guidance to further promote the use of presubmissions for cybersecurity questions.
OEI-09-16-00220	FDA Should Further Integrate Its Review of Cybersecurity Into the Premarket Review Process for Medical Devices	9/10/2018	FDA should include cybersecurity as an element in the Smart template	Concur	2019	In progress	FDA has updated the Smart Template to include a specific section on cybersecurity.

GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should develop department policies for managing hazardous biological agents in high-containment laboratories that contain specific requirements for training and inspections for all high-containment component agency laboratories and not just for their select-agent-registered laboratories; or direct the Director of CDC to provide these requirements in agency policies.	Concur	2020	In Progress	Guidance pulled from clearance for revisement to remove lab training section and embed in overall CDC training policy. Internal comments have been addressed in clearance process.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should direct the Director of NIH and the Commissioner of FDA to require routine reporting of the results of agency laboratory inspections--and in the case of FDA, require routine reporting of select agent inspection results--to senior agency officials.	Concur	NA	In progress	FDA has a standing policy for managing hazardous biological agents in high-containment laboratories that includes reporting requirements (SMG 2130.8 and Directive 201710.2). In 2019, FDA began piloting a standardized Agency-wide laboratory safety inspection checklist to ensure that all laboratories are inspected rigorously and consistently. As part of the pilot, all laboratories are to be inspected during Q1-Q3 of the calendar year. Any corrective/preventative actions will be tracked and resolved locally during this inaugural year. The results of the inspections will be aggregated, and trends and significant findings will be reported to Agency senior leadership in Q4 of 2019. Beginning in 2019, OLS is committed to independently inspecting all high-containment and select agent laboratories and 1/3 of all other laboratories each year to ensure compliance with all laws, regulations, and consensus standards. (In other words, all laboratories will be inspected at least once every three years)

GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should develop department policies for managing hazardous biological agents in high-containment laboratories that contain specific requirements for reporting laboratory incidents to senior department officials, including the types of incidents that should be reported, to whom, and when, or direct the Director of CDC and the Commissioner of FDA to incorporate these requirements into their respective policies.	Concur	NA	In progress	FDA has a standing policy for managing hazardous biological agents in high-containment laboratories that includes reporting requirements (SMG 2130.8, Directives 201710.2 and 2019.3). FDA also implemented a mechanism for incident reporting electronically to facilitate the investigation, resolution, and reporting of incidents. FDA continues to work with the Biosafety and Biosecurity Coordinating Council to establish a process for the routine reporting of the results of agency and select agent laboratory inspections to senior department officials.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should require routine reporting of the results of agency and select agent laboratory inspections to senior department officials.	Concur	NA	In Progress	NIH has provided documentation to GAO as evidence they have implemented this recommendation.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should require routine reporting of incidents at CDC, FDA, and	Concur	NA	In progress	In August 2019, FDA reported that it continues to work with the Biosafety and Biosecurity Coordinating Council to establish a process for the routine reporting of these results but had not yet completed its actions.

			NIH laboratories to senior department officials.				

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SIGNIFICANT ITEMS

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (116-107)

1. 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 FDA to establish a separate U.S. Standard of Identity for different grades of olive oil (e.g. extra virgin, virgin, and refined) and olive-pomace oils. As the Committee is particularly concerned with the number of different oil state standards for olive oils in the U.S., it is important to determine if establishing a uniform set of the standards would better inform and protect consumers. 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 to ensure the integrity of these products for U.S. consumers.

FDA Response:
Under the U.S. Food and Drug Administration's (FDA) 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 plans to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity in 2020. 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.

In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. In June and September 2019, FDA met with the North American Olive Oil Association, American Olive Oil Producers Association, and Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA continues to discuss this matter with industry representatives.

Further, FDA is reviewing a citizen petition related to olive oil that was submitted in November 2019 by the American Olive Oil Producers Association (Docket No. FDA-2019-P-5191). The petition requests FDA to establish a standard of identity for olive oil and olive pomace oil that includes compositional requirements and analytical testing. No decision has been made on the petition.

2. Electrical Stimulation Devices

The Committee is concerned about the delay in issuing a final rule prohibiting the use of electrical stimulation devices on persons with intellectual and developmental disabilities, especially in light of the agency's statement that ''these products present an unreasonable and substantial risk to public health.'' Given this risk, the Committee directs the agency to issue the final rule no later than December 31, 2019, consistent with the Spring 2019 Unified Agenda of Regulatory and Deregulatory Actions.

FDA Response:
Medical device safety is a key priority for FDA. The agency carefully reviewed the comments submitted to the public docket in connection with the proposed ban on electrical stimulation devices, including lengthy comments on scientific and legal issues. FDA has been working to issue the final rule as closely as possible to the plan announced in the Fall 2019 Unified Agenda.[134] Issuing this final rule remains a priority for FDA. Finalizing the proposed rule Banned Devices; Proposal To Ban Electrical Stimulation Devices Used To Treat Self-Injurious or Aggressive Behavior (81 FR 24385), would ban both new electrical stimulation devices and devices already in distribution and use.

3. Corrosive Chemicals

The Committee remains concerned over reports that meat and poultry workers are being harmed by corrosive chemicals, such as peroxyacetic acid. The Committee urges the USDA, FDA, and EPA to enter into a memorandum of under-standing concerning plant worker and FSIS employee safety and approval of antimicrobials in the meat and poultry industry.

FDA Response:
Several peroxyacetic acid solutions are the subject of pre-market authorizations by the FDA for use as antimicrobials applied to meat and poultry in food processing facilities. FDA shares jurisdictional authority with the U.S. Department of Agriculture (USDA) over this use of antimicrobials, and such products must also go through USDA's approval process prior to use. In addition, certain antimicrobial uses on meat and poultry may require registration as a pesticide with the Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

FDA has an information sharing memorandum of understanding (MOU) with FSIS to facilitate concurrent premarket review of food additives, color additives, generally recognized as safe (GRAS) substances, and food contact substances intended for use in the production of FSIS-regulated meat, poultry, and egg products. As part of its review, FDA's role is to assess the safety of the use of the substance when consumed in food. As provided in Section 409 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA approves the use of a food additive

[134] https://www.reginfo.gov/ublic/do/eAgendaViewRule?pubId=201910&RIN=0910-AI22

after careful review of the scientific data establishing the safety of its intended use in food, including the safety of the expected dietary exposure to the food additive over a consumer's lifetime. This review does not include an evaluation of non-dietary exposure, such as worker exposure as a result of the use of food additives in food manufacturing facilities. FDA does not have the authority or expertise to consider employee safety as part of its review.

4. Dairy Standard of Identity for Certain Products

The Committee is pleased that the FDA has begun a deliberative process to review how it will enforce the standards of identity for dairy products. The Committee continues to hear concerns with the labeling of certain foods and beverages as dairy products when the products are plant-based rather than derived from an animal. As such, the Committee urges the FDA to continue its work toward ultimately enforcing standards of identity for dairy products.

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 FDA examine the labeling of plant-based dairy alternatives, in September 2018, FDA issued a request for comments and data from stakeholders about consumer perceptions of these products, including nutritional considerations, when labeled with names that include the names of dairy foods. The comment period closed in January 2019, and FDA recently finished reviewing the approximately 13,000 comments received. These comments are helping to inform FDA's next steps on appropriate labeling of plant-based dairy alternatives.

5. Glass Packaging

The Committee urges FDA to continue to work with glass packaging suppliers and pharmaceutical manufacturers to evaluate and promote streamlined approval requirements designed to expedite the adoption and use of innovative glass pack-aging technologies with the capacity to improve product quality, reduce product recalls, reduce drug shortages, and protect public health. Such streamlined approval requirements should address stability testing and other relevant types of data to be submitted in support of product approval.

FDA Response:
FDA engages companies working on developing new glass designs for use in pharmaceutical containers with the goal of addressing quality issues, such as the formation of glass lamellae. In addition, the Office of Pharmaceutical Quality (OPQ), within the Center for Drug Evaluation and

Research (CDER), developed methodology and conducted studies to evaluate the performance characteristics of glass containers for injectable drug products (See https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm607223.htm).

These laboratory studies will help inform future quality assessments and provide insight for feedback that can be provided to companies as they work on developing their products. FDA remains committed to enabling the use of innovative products and approaches that support drug quality, and we will continue to meet with companies through CDER's Emerging Technology Program to support the development of novel manufacturing technologies.

In general, prior to adopting any new packaging technology, an application holder for a drug or biological product needs to conduct testing to ensure the suitability of the new packaging when used with a specific drug or biological product and the specific processing equipment. It is important that the packaging is tested based on the specific drug or biological product that the packaging will be used with to prevent interactions between the product and packaging, such as impurities extracting or leaching from the packaging. Interactions like these may result in recalls and could potentially harm patients. Testing is required to help avoid such interactions.

FDA has existing mechanisms intended to lead to improved product quality for companies developing innovative technologies. CDER's Emerging Technology Program and the Center for Biologics Evaluation and Research's Advanced Technologies Team were created to encourage companies that are pursuing innovative approaches to pharmaceutical product design and manufacturing to engage with the Agency early in the development process. These programs foster early communication and collaboration to help identify and discuss scientific and regulatory challenges prior to a regulatory submission, streamlining the application submission process. In addition, CDER OPQ can expedite assessment of submissions that, if approved, may help mitigate or prevent drug shortages.

6. Epinephrine Auto Injector Shortage

The Committee is concerned by the national shortage of epinephrine auto injectors, which pose a serious threat to those at risk of allergic reactions. The Committee is encouraged by FDA's actions to address availability of these drugs, both by approving a new generic and safely extending the expiration dates for existing medications. The Committee urges FDA to aggressively combat this drug shortage to ensure epinephrine auto injectors are readily available to meet the growing number of prescriptions.

FDA Response:
FDA has been working closely with Mylan (which markets EpiPen) to understand the status of EpiPen product supply and has been in contact with the other manufacturers of epinephrine auto-injectors regarding their supply status. FDA continues to be aware of reports of localized supply disruptions and Mylan has reported intermittent manufacturing constraints. However, Mylan continues to release the product, and they have provided a phone number which is posted on our

website to help pharmacies and patients locate EpiPens.[135] In August, after reviewing stability data provided by the manufacturer of EpiPen (Pfizer), the Agency alerted health care professionals and patients of updated dates through which some EpiPens and the authorized generic version may be used beyond the manufacturer's labeled expiration date. FDA posted product availability information for all epinephrine auto-injectors on our website due to the intermittent supply disruptions Mylan has reported.
FDA continues to keep the Drug Shortages website updated with the latest supply information as we receive it. This includes a list of epinephrine auto-injector products that are available from all manufacturers, including contact information for those manufacturers.

7. 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:
FDA's Oncology Center of Excellence (OCE), Immuno-oncology Therapeutics Program (IOTP), brings together existing expertise across FDA, including expertise from the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research, and promotes development of new therapeutics that harness the immune system to engage new, more efficacious treatment paradigms for patients with cancer. While immuno-oncology (IO) products have changed the treatment paradigm of many cancers, and more patients are starting to receive IO products as standard of care as well as investigational products in clinical trials evaluating novel IO combinations, the full spectrum of potential side effects (toxicities) are being realized. IOTP initiatives to standardize the toxicity evaluation and reporting include:

- Leveraging the experience within FDA in review of cancer immunotherapeutics, including immune checkpoint inhibitors (ICI) with over 1,500 clinical trials evaluating ICIs and nearly 60 new or supplemental FDA approvals in oncology across seven approved ICIs, to provide recommendations for standardizing templates for the identification and reporting toxicities cancer immunotherapy trials.

135 https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Epinephrine%20Injection,%20Auto-Injector&st=c

- Forming an immune-mediated toxicity group that is addressing key concerns for standardization of identification and management of immune-mediated toxicities with IO products.

- Publicly engaging with multiple stakeholders such as 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.

8. Homeopathic Draft Guidance

The Committee urges FDA to consider the views of patients in finalizing its draft guidance.

FDA Response:

In the Federal Register on December 20, 2017 (82 FR 60403), FDA announced the availability of a draft guidance for FDA staff and industry entitled "Drug Products Labeled as Homeopathic." This draft guidance was intended to describe how FDA aims to prioritize enforcement and regulatory action with regard to drug products, including biological products, labeled as homeopathic and marketed in the United States without the required FDA approval that potentially pose higher risk to public health.

In an effort to further consider the issues raised in the draft guidance, FDA revised the draft guidance and reissued it for public review and comment, including by patients, before it is finalized. In particular, the Agency added a definition of "homeopathic drug product" for purposes of the guidance, added additional explanation of some of the safety issues that contributed to the development of the draft guidance, and clarified the intent to use risk-based factors to prioritize enforcement and regulatory actions involving homeopathic products that are marketed without required FDA approval. The comment period for this guidance closes January 23, 2020.

9. Lower-Cost Insulin Products and Transition to the Biologics Price Competition and Innovation Act and Approval Pathway

To ensure patient access to lower-cost insulin, the Committee urges FDA to undertake the following measures: (1) ensure any pending application for a proposed insulin product with a goal date prior to March 23, 2020 is reviewed in accordance with the ''Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs'' (''the Program''), (2) work to identify and promote efficiencies in the review of any application submitted under the Public Health Service Act for a proposed insulin product that previously was submitted under the FFDCA with a goal date prior to March 23, 2020, and that failed to meet the requirements for final approval under the FFDCA by March 23, 2020, and (3) act quickly to evaluate stakeholder feedback and recommendations from its May 13, 2019 public meeting on the future of insulin biosimilars.

FDA Response:

FDA is committed to continuing our efforts to help increase market competition among insulin products, which may potentially lower costs for patients and payors and increase access and

product choice. The Agency is working to implement the statutory provision in the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) that requires that on March 23, 2020, an approved marketing application for a biological product under the FD&C Act (such as insulin) will be deemed to be a license for the biological product under the Public Health Service Act. FDA is approaching this transition in a manner that minimizes burden, helps ensure stability for patients using currently marketed products, and facilitates the development of products that are biosimilar to, or interchangeable with these transitioned biological products in order to increase competition. The Agency has issued guidance providing recommendations to sponsors to facilitate alignment of product development plans with FDA's interpretation of this statutory provision, as well as provide clarity and predictability to manufacturers. In addition, the Agency has met with sponsors of proposed products that may be affected by the transition to discuss and provide recommendations on their development programs on a product-specific basis.

FDA intends to review any pending new drug application (NDA) for a proposed insulin product with a goal date prior to March 23, 2020, in accordance with the review timelines established in the PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022 (PDUFA VI Commitment Letter) and, if applicable, the "Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs." FDA has further described its draft recommendations on good review management principles and practices for the review of NDAs and BLAs more generally in FDA's draft guidance for industry and review staff, "Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications" (Draft GRMP Guidance). Consistent with these recommendations, FDA has carefully considered steps it may take to minimize the disruption to any application that may be pending at the time of the transition. More recently, section 607 of the Further Consolidated Appropriations Act, 2020, amended section 7002(e)(4) of the BPCI Act to provide that, with respect to an application for a biological product submitted under section 505 of the FD&C Act that is filed not later than March 23, 2019, and is not approved as of March 23, 2020, FDA shall continue to review such application under section 505 of the FD&C Act after March 23, 2020.

FDA has communicated through guidance that FDA intends to assist applicants who may be affected by the statutory transition provision, where feasible and appropriate. For example, FDA has explained in guidance that during the review of a biologics license application (BLA) submitted after the transition date for a proposed biological product that was previously submitted, but not approved, in an application under section 505 of the FD&C Act, FDA intends to consider any previously conducted scientific review by the Agency of such previous application under the FD&C Act, to the extent that such review is relevant to, and consistent with, applicable requirements of section 351 of the PHS Act. As noted above, section 607 of the Further Consolidated Appropriations Act, 2020, recently amended section 7002(e)(4) of the BPCI Act to provide for continued review under section 505 of the FD&C Act for any applications described by such section 607.

In May 2019, FDA held a public meeting to hear input from patients, families, healthcare providers, and other stakeholders about the challenges and opportunities the Agency should consider as FDA prepares for the submission and review of applications for biosimilar and interchangeable insulin products, and also to hear from manufacturers and other stakeholders

about the development process for biosimilar and interchangeable insulin products. The Agency received valuable stakeholder feedback on these topics, which has informed and will continue to inform our next steps and help advance access to more affordable insulin products.

In November 2019, FDA issued a draft guidance for industry, "Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products," that explains that FDA generally would not expect comparative clinical immunogenicity studies to support a demonstration of biosimilarity or interchangeability for certain proposed insulin products in the circumstances described in the guidance. The thinking on this issue described in the draft guidance can result in significant cost and time savings in developing biosimilar and interchangeable insulin products seeking licensure in 351(k) BLAs after the transition.

10. Opioid Abuse

The abuse, misuse, and diversion of opioid pain-killers continue to drive an epidemic in the United States. The CDC indicates that one American loses his or her battle with addiction every twelve and a half minutes. The Committee continues to be pleased that, with the Opioids Action Plan, Opioid Policy Steering Committee, and several significant regulatory actions, FDA is doing its part to help stem the tide of abuse. The use of opioids as first-line therapies for any form of pain has led to over-prescribing, and the CDC has made clear that clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh the risks to the patient. The Committee hopes that FDA will continue to support the development of alternative and non-addictive alternatives to opioid analgesics and, when opioids are medically necessary, will continue to incentivize development and use of abuse-deterrent formulations. The Committee notes that every patient's treatment regimen should be tailored by his or her doctor to his or her unique needs. The federal government, therefore, should promote the full suite of available treatment options, including abstinence-based models and non-opioid medications. Finally, the Committee continues to be supportive of naloxone distribution among trained, licensed healthcare professionals and emergency responders. When considering the appropriateness of providing naloxone over-the-counter, the Committee urges the FDA to ensure that the administration of naloxone serves as a point of intervention to spur an honest conversation between the patient and his doctor about addiction and treatment.

FDA Response:
FDA remains committed to fighting the opioid crisis and will continue to advance using a multipronged strategy. FDA is focusing on 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 continues to support 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 to advance efforts to make naloxone more broadly available. Naloxone is currently a prescription drug nationwide. In January 2019, FDA took an unprecedented step in helping to encourage development of OTC naloxone products. To encourage drug companies to

enter the OTC market, FDA designed, tested and validated the key labeling requirements necessary to approve an OTC version of naloxone. To do this, FDA developed a model Drug Facts label (DFL) with pictogram instructions, so anyone with access to the drug can better understand how to administer it. To ensure the pictograms are easy to understand, FDA also conducted label comprehension testing with consumers. This was the first time the FDA proactively developed and tested a DFL to support development of an OTC product.

With one of the key components for OTC availability now in place, drug companies can use this information as part of an application to obtain approval for OTC naloxone. Furthermore, FDA continues to work with industry partners who are interested in developing these OTC naloxone products.

FDA also held an advisory committee meeting in December 2018 on various options for increasing access to naloxone, weighing logistical, social and economic aspects of this important issue. There was overwhelming support from meeting participants to remove barriers to obtaining naloxone, particularly OTC naloxone, and to support community activities that expand its availability. As a result, FDA is currently exploring more ways to increase the availability of all forms of naloxone, such as working with manufacturers to see if shelf-life extensions for naloxone products are possible; conducting additional research on naloxone; and considering situations where co-prescribing of naloxone may be appropriate, including possible updated product labeling. Also, as recommended at the advisory committee meeting, FDA is exploring ways to encourage prescribers to discuss naloxone with their patients, assess the need for personal access to naloxone, and prescribe naloxone, as warranted, based on risk factors for overdose.

11. Patient Experience in Drug Reviews

The Committee is aware the FDA is implementing policies to promote public access to information about how patient experience information factored into the review of approved products. The Committee supports this step forward and encourages FDA to continue refining the instrument and ways to improve its visibility. The Committee also requests that FDA consider ways to include patient-experience information in relevant labeling and accompanying documentation to inform patient/provider decision making and payer determinations.

FDA Response:
FDA is committed to including the views of patients during the medical product development process and considering patient perspectives in regulatory decision-making.

FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) are currently implementing the provisions of section 3001 of the 21st Century Cures Act (Cures Act), by making public a brief statement regarding the patient experience data and related information, if any, submitted and reviewed as part of new drug applications (NDAs) and biologics license applications (BLAs) reviewed and approved after mid-June 2017. This information is made public along with the NDA or BLA approval package posted on FDA's website.

The Centers are also working to support development and sponsor submission of patient experience data that is sufficiently reliable and representative of the indicated population, and relevant to the assessment of the benefits and risks of the new drug or biological product under review, so that it can be used in decision making and included in the labeling. FDA is doing this by developing a series of guidance documents that implement provisions of section 3002 of the Cures Act and will help interested parties to create helpful and reliable representative patient experience data.

To implement provisions (c)(1) through (4) of section 3002, CBER and CDER are developing a series of four methodological patient-focused drug development (PFDD) guidance documents to address, in a stepwise manner, how stakeholders can collect patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision making. Work on these guidances and related public workshops is well under way. FDA held the public workshop for the first guidance in December 2017, issued the draft guidance for public comment in June 2018 and is working to publish the final guidance in calendar year 2020. FDA held the public workshops for the second and third guidances in October 2018. The second guidance was issued as draft for public comment in October 2019. FDA anticipates issuing the third guidance in draft by September 2020. In addition, FDA held the public workshop for the fourth guidance in the series in December 2019, and its development is now underway. For more information on the methodological PFDD guidance series, including resources related to the public workshops (e.g., agendas, recordings), please visit: https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical.

To implement provision (c)(5) of section 3002 of the Cures Act, FDA held a public workshop in March 2018, to inform the development of FDA guidance to assist stakeholders seeking to develop and submit a proposed draft guidance relating to patient experience data for consideration by FDA. FDA issued the draft guidance for public comment in December 2018 and is working toward publication of the final guidance in calendar year 2020. For more information, please visit: https://www.fda.gov/drugs/development-approval-process-drugs/developing-and-submitting-proposed-draft-guidance-relating-patient-experience-data.

To complement the PFDD work outlined above, FDA plans to further advance the quality and utility of sponsor-submitted patient experience data for regulatory decision making with its new pilot grant program to support the development of publicly available core sets of clinical outcome assessments and their related endpoints for specific disease indications. In September 2019, FDA made three awards under this grant program in the areas of: (1) migraine, (2) acute pain in infants and young children, and (3) physical function applicable across a range of chronic conditions. For each award, it is expected that a standard core set be publicly available by the end of the grant period, at no cost or nominal cost. FDA hosted a public workshop in December 2019 to provide an opportunity for the grantees funded under this grant program to share their development plans for the standard core sets and to receive feedback from stakeholders, including patients and caregivers. For more information, please visit: https://www.fda.gov/drugs/development-approval-process-drugs/cder-pilot-grant-program-standard-core-clinical-outcome-assessments-coas-and-their-related-endpoints.

The Center for Devices and Radiological Health (CDRH) launched its initiative to include patient preference information as part of the medical device regulatory decision-making process in September 2013 and has witnessed increasing evidence of the benefits of soliciting patient feedback. Patient preference information (PPI) is designed to identify and develop methods for assessing patient valuations of benefit and risk as well as outcomes that matter most to patients related to specific device types and specific illnesses and conditions that can be used to inform regulatory decisions. Part of FDA's public health mission is to help patients be more aware of the health care options available to them. Alongside industry, patient groups, and other government agencies, FDA is actively engaging patients to help them understand how a disease or condition impacts their daily lives and their caregiver's lives, and the types of treatment benefits and risks that matter the most to them.

Below are some key examples of CDRH's efforts in this space.

- Through the Medical Device Innovation Consortium (MDIC), FDA developed a framework for incorporating PPI through the device lifecycle. This report has more than 1,500+ unique downloads and was used to inform FDA guidance on incorporating patient preferences into premarket benefit/risk assessments.
- For the years 2016-2017, patient science and engagement was a CDRH strategic priority. In that time, CDRH staff participated in numerous patient interaction opportunities involving 48 patient groups/organizations; more than 96% of CDRH staff interacted with patients.
    - Additionally, 100% of premarket approval (PMA), De Novo and humanitarian device exemption (HDE) pre-market decisions made by CDRH now include a public summary of available and relevant patient perspective data. This helps ensure that reviewers take patient perspective data into account, and that this information is transparent to the public.
    - Over those two years, CDRH increased by 75% the number of investigational device exemptions (IDEs) with patient-reported outcomes (PROs) and issued a report on the value of PROs and a compendium of 135 commonly seen PRO measures in device submissions.

- CDRH also established the Patient Engagement Advisory Committee. The Committee provides advice on complex issues relating to medical devices, the regulation of devices, and their use by patients and may consider topics such as: Agency guidance and policies, clinical trial or registry design, patient preference study design, benefit-risk determinations, device labeling, unmet clinical needs, available alternatives, patient-reported outcomes, device-related quality of life or health status issues, and other patient-related topics.
- CDRH established the Patient & Caregiver Connection which is a process that connects patient organizations with CDRH staff to address time-sensitive questions about living with a medical condition as well as the diagnostic and therapeutic devices with which they interface in identifying, managing, and treating the condition.
- The Center has encouraged sponsors to include patient preference information in their regulatory submissions resulting in 15 studies completed or in the pipeline. All 15 studies were initiated by medical device manufacturers.

- One proton pump inhibitor drug study led to expanding the labeled indication to give patients with end-stage kidney disease the freedom to dialyze at home without a care partner.
- Another study was used to help set the primary clinical endpoint that ultimately led to a label expansion to treat patients who suffer from blood vessels blocked by blood clots in the brain.

12. Sunscreen Ingredients

The Committee continues to track the actions of the FDA related to sunscreen ingredients. The Committee recognizes the agency's efforts in generating and posting consumer and public health resources regarding health benefits of sunscreen use. The Committee urges FDA to clarify its messaging concerning currently marketed sunscreen ingredients to ensure the continued use of sunscreens. In addition, the Committee encourages FDA to work with stakeholders.

FDA Response:
FDA agrees that public health messaging regarding sun protection measures is especially important. Therefore, FDA has generated and posted considerable consumer and public health resources regarding sunscreens on our website and has disseminated these resources with public health and stakeholder groups.[136] Concurrent with and since publication of the recent proposed sunscreen rule in February 2019, FDA has issued consistent messaging that, given the public health benefits of sunscreen use, Americans should continue to use broad spectrum sunscreen with SPF values of at least 15 with other sun protective measures[137] while the rulemaking proceeds. FDA plans to continue similar messaging supporting sun safety and the importance of continuing to use broad spectrum sunscreens with SPF values of at least 15 along with other sun protection measures.

Medical and public health groups, such as American Academy of Dermatology, Skin Cancer Foundation, Consumer Union, and Environmental Working Group have supported FDA's rulemaking, and importantly, many have echoed FDA's message regarding sun protective measures and the importance of continuing to use broad spectrum sunscreens with SPF values of at least 15. FDA will continue to work with industry and public health stakeholders to help make sure that consumers have access to safe and effective sunscreens.

13. The Real Cost

The Committee supports FDA's ''The Real Cost'' youth e-cigarette prevention campaign which to date has been directed at youth ages 12–17, and directs the FDA to explore expanding the advertising to the general public.

FDA Response:

[136] *Tips to Stay Safe in the Sun: From Sunscreen to Sunglasses* webpage at: https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm049090.htm

[137] https://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/UCM631712.pdf

The Agency does not have concerns about exploring the expansion of its e-cigarette youth prevention campaign to the general public as it aligns with current efforts to provide information about dangers of vaping e-cigarettes to parents, teachers, and other adults working with youth. While "The Real Cost" campaign is highly targeted to its youth audience, with ads running on teen-focused broadcast programming, digital platforms and in location-targeted advertising in and around middle and high schools, some of these media channels will also reach adult populations.

To reach adults with prevention messages for youth, FDA joined forces with Scholastic, the global children's publishing, education and media company, to distribute posters in 2018 and 2019 to the nation's 31,000 high schools with e-cigarette prevention messages for display in high school bathrooms, the epicenter for teen vaping. In 2018, FDA developed and distributed fact sheets and lesson plans to more than 750,000 high school administrators and teachers. In fall of 2019, FDA expanded the effort to include resources for middle school educators and new resources for high school educators, reaching 1.3 million educators. Resources included lesson plans and activity sheets to help teachers start educational conversations about the harms of youth e-cigarette use. In addition, these resources, as well as a teacher resource guide and youth addiction and cessation materials, are available online at no cost.

The Agency also developed and disseminated posters and resources for doctors, youth groups, religious institutions, state and local public health agencies, and others on the dangers of youth e-cigarette use and has worked to advance discussion and understanding around how to help those kids who are already addicted to e-cigarettes to quit. These educational resources are available to the public on FDA's website.

Adults, including parents and teachers, are an important audience for e-cigarette education and they also see e-cigarette vaping prevention messages via "The Real Cost" campaign, which is promoted via paid media, Scholastic, and public health stakeholders at the state and local level.

14. <u>Youth E-Cigarette Use</u>

The Committee is troubled by the dramatic increase in youth e-cigarette use and notes that flavors are the most common reason youth use e-cigarettes. The Committee urges FDA to expedite the pre-market review of e-cigarettes and other newly deemed tobacco products that were on the market as of August 8, 2016 and to remove from the market any deemed tobacco product introduced after August 8, 2016 that has not under-gone a pre-market review.

FDA Response:

FDA shares the Committee's concern about the epidemic of youth use of electronic nicotine delivery system (ENDS) products. The magnitude of this problem was revealed by the data from the 2018 National Youth Tobacco Survey (NYTS). FDA is committed to addressing this epidemic of youth use of ENDS products.

On January 2, 2020, the Agency issued a policy prioritizing enforcement against certain unauthorized ENDS products that appeal to kids, including fruit and mint flavored products. Under this policy, companies that do not cease the manufacture, distribution, and sale of unauthorized flavored, cartridge-based ENDS products (other than tobacco or menthol) within 30 days risk FDA enforcement actions. More specifically, the policy outlined in a final guidance

document[138] noted that beginning 30 days from the publication of the notice of availability of this guidance in the *Federal Register*, FDA intends to prioritize enforcement against these illegally marketed ENDS products by focusing on the following groups of products that do not have premarket authorization:

- Any flavored, cartridge-based ENDS product (other than a tobacco- or menthol-flavored products);
- All other ENDS products for which the manufacturer has failed to take (or is failing to take) adequate measures to prevent minors' access; and
- Any ENDS product that is targeted to minors or whose marketing likely to promote use of ENDS by minors.

By focusing on these priorities, the Agency has attempted to balance the public health concerns related to youth use of ENDS products with considerations regarding addicted adult cigarette smokers who may try to use ENDS products to transition away from combustible tobacco products. In addition to data showing that cartridge-based ENDS products are most commonly used among youth, important findings from the 2019 *Monitoring the Future*[139] survey focusing on youth use of JUUL indicate that youth preference for menthol- and tobacco-flavored e-cigarettes is much lower than that for mint- and fruit-flavored e-cigarettes. Because of the relatively low numbers of youth using both menthol- and tobacco-flavored cartridge-based ENDS products, as well as non-cartridge-based ENDS products, they are not among the current enforcement priorities. Should FDA become aware of an increase of youth using any other unauthorized tobacco products (both cartridge-based or otherwise), the Agency will take appropriate action to address youth use of those products if necessary.

In July 2019, a U.S. District Court in Maryland issued an order directing FDA to require that premarket authorization applications for all new deemed tobacco products (e.g., e-cigarettes, cigars, pipe tobacco, hookah tobacco) that were on the market as of August 8, 2016, be filed with FDA no later than May 12, 2020. The court order also provided for a one-year period in which products with timely filed applications might remain on the market pending FDA review, but, in a subsequent order, also clarified that FDA may enforce the premarket review provisions against deemed products prior to May 12, 2020, or during the one-year review period.

No ENDS product in the United States is on the market legally. To be legally marketed, the product would need to undergo FDA scientific review and meet the applicable statutory standard for marketing authorization—for example, the product is appropriate for the protection of the public health with respect to the risks and benefits to the population as a whole, including users and nonusers, and taking into account, among other things, the likelihood that those who do not use tobacco products will start using them. Alternatively, an ENDS product that is marketed as a

[138] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-delivery-system-ends-and-other-deemed-products-market

[139] https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2019.17968?guestAccessKey=6cd13a73-46aa-460e-95c7-0cb2d9b66fdf&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=110519

drug, such as to help cigarette users quit smoking, would need to be reviewed under FDA's drug authorities and approved for such marketing.
In addition, since the beginning of FY 2019, as part of the Youth Tobacco Prevention Plan, FDA has taken the following actions to address the marketing of tobacco products to youth and to help prevent youth use of, and access to, tobacco products, including e-cigarette products:

- Conducted over 150,000 retail inspections to crack down on the sale of tobacco products, including e-cigarettes, to minors at both brick-and-mortar and online retailers
- Issued thousands of warning letters and civil money penalty complaints to retailers for illegally selling e-cigarette products to minors
- Identified large retail chains that sell tobacco in the U.S. with violation rates above 15 percent and sent letters to corporate leadership requesting a plan to prevent tobacco sales to minors
- Issued 30-day No-Tobacco-Sale Order complaints for repeated violations to two companies identified as having violation rates above 15 percent
- Partnered with the Federal Trade Commission (FTC) to issue warning letters to e-liquid manufacturers for violations related to online posts by social media influencers on the companies' behalf
- Issued warning letters to e-liquid manufacturers whose products used misleading, kid-appealing imagery that caused the products to appear ingestible by imitating food products such as candy
- Issued warning letters to e-liquid manufacturers whose products use misleading imagery that caused the products to appear ingestible by imitating cough syrups
- 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
- Issued a warning letter to JUUL Labs for marketing unauthorized modified risk tobacco products via, for example, a presentation given to youth at a school
- Sent a letter to JUUL Labs requesting more information about the company's outreach and marketing targeted at students, tribes, health insurers, and employers.

15. <u>Rare Cancer Therapies</u> (OC/OCE/CBER/CDER)

FDA's Oncology Center of Excellence was formed to streamline the development of cancer therapies. It creates a unified and collaborative scientific environment to advance the development and regulation of oncology products for cancer patients. However, there continues to be a significant development gap for rare cancer therapies. Therefore, the Committee includes an additional $5,000,000 to address gaps in the system, streamline resources, accelerate the development of rare cancer therapies and advance the field of cancer research overall, mirroring the efforts of the National Cancer Institute's Developmental Therapeutics Program. FDA is directed to build lines of communications and processes between these two agencies in order to expedite review of rare cancer therapies.

FDA Response:

FDA's Oncology Center of Excellence (OCE) recognizes the challenges of developing therapies for patients with rare oncology diseases and appreciates the additional resources provided by the Committee. OCE has collaborated with both inter-agency and intra-agency partners to work toward accelerating development of rare cancer therapies and will continue this mission. Ongoing OCE initiatives include:

- Developing inter-agency alliances to expedite review of rare cancer therapies, including with the National Institutes of Health (NIH) and National Cancer Institute (NCI).
- Exploring drug repurposing as a strategy for expedited development of therapies for patients with rare diseases. OCE participated in a recent FDA-NCATS/NIH workshop to explore pathways and collaborations that can support these efforts.
- Engaging with patient advocacy groups to gather feedback and input on patient experiences and priorities for treatments. These interactions have occurred through various venues supported by OCE including symposia and workshops.
- Exploring the role of "real world data" for drug development for rare oncology diseases and use when applicable.
- Establishing an "Orphan Products Liaison" role for FDA's Office of Orphan Products Development (OOPD) to facilitate communication, collaboration and consistency between OCE and OOPD.

OCE is committed to facilitate and support the development of products intended for patients with rare oncology diseases.

16. Food Safety and the Food Safety Modernization Act (FSMA) Funding

The Government Accountability Office (GAO) released a report in January 2019 entitled ''Food Safety and Nutrition: FDA Can Build on Existing Efforts to Measure Progress and Implement Key Activities.'' The report documents spending and shows a steady increase in spending for food safety. A majority of this spending relates to activities surrounding FSMA development and implementation activities. FSMA implementation places additional requirements on state governments and private stakeholders, and therefore urges the FDA to provide sufficient resources to state and non-profit education and inspection programs to address these needs.

FDA Response:

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 their suppliers meet U.S. safety standards.

FDA finalized all seven foundational FSMA rules by 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.[1]

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

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country in building an Integrated Food Safety System (IFSS). Forty-seven (47) cooperative agreements have been awarded under the State Produce Implementation Cooperative Agreement Program (State CAP) to state and territorial government organizations. A three-year total of approximately $85 million has been awarded and divided among the 47 state and territorial applicants based on the size of the produce industry covered by the regulation in each jurisdiction. The primary goal of this program is to provide awardees with the resources to develop a state produce safety regulatory program, including necessary infrastructure, farm inventory, outreach, education, and technical assistance. Another key goal for FDA's CAP program is to create an inspectional system in which the state experts who are most familiar with local farming practices conduct the bulk of the inspections. To that end, most states have opted to elect into this funding mechanism to conduct produce farm inspections.

In addition, in FY 2019, to leverage the resources of our state/territorial regulatory partners to ensure oversight of the nation's domestic food supply, FDA executed 87 contracts that included 45 states and Puerto Rico. These contracts enabled FDA's counterparts in state government to complete inspections, site visits, and sample collections, including 444 human food preventive controls inspections (up from 231 in FY 2018) and 95 animal food preventive controls inspections in the initial year of the contracts. FDA is also developing additional future cooperative agreements for states to further support and develop their programs to advance the prevention-oriented approach called for by FSMA.

FDA continues to advance food safety through several collaborative efforts with its state, local, tribal, and territorial (SLTT) partners. The Agency continues to develop, revise, and promote conformance with the Manufactured Food Regulatory Program Standards (MFRPS), Animal Feed Regulatory Program Standards (AFRPS), and Voluntary National Retail Food Regulatory Program Standards (VNRFRPS). The SLTT programs that are enrolled in these standards are taking meaningful steps to ensure they have the regulatory foundation and framework necessary to protect public health. Hence, conformance with the standards is a foundational element of an effective IFSS. As of November 2019, 43 SLTT programs are enrolled in the MFRPS, 23 in the AFRPS, and 855 in the VNRFRPS. There are 30 SLTT programs in full conformance with the MFRPS, five that have fully implemented the AFRPS, and five in full conformance with the VNRFRPS. FDA also plans to work with the National Association of State Departments of Agriculture (NASDA) and Association of Food and Drug Officials (AFDO) under a cooperative agreement to begin development of Produce Safety Regulatory Program Standards beginning in 2021. Additionally, FDA continues to provide guidance and resources to SLTT and association partners to protect the nation's food supply:

- FDA has launched routine international and domestic inspections for large farms growing produce covered by the FSMA Produce Safety Rule.
- The Animal Drugs and Feeds Program has provided approximately $14 million in grants since FY 2011 to support the activities of the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), a network of 44 state and university veterinary diagnostic labs.
- FDA has entered into a cooperative agreement with NASDA to develop an implementation framework for state animal food programs to modernize their regulatory program to prevention-oriented programs aligned with the FSMA Preventive Controls for Animal Food regulation.

- FDA has continued to integrate outbreak response by developing rapid response teams (RRTs) with state partners. RRTs are multi-agency, multi-disciplinary teams that operate using Incident Command System (ICS)/National Incident Management System (NIMS) principles and a Unified Command structure to respond to human and animal food emergencies. RRTs minimize the time between notification of a human or animal food contamination event and implementation of effective control measures. Since FSMA was enacted, the RRT program has grown from nine funded states (in 2009) to 18 funded states (in 2019), and an additional six states participate in the program voluntarily (outside of the funded cooperative agreement).

FDA is working with stakeholder groups to develop national regulatory program standards for shellfish and shell eggs. In conjunction with the Interstate Shellfish Sanitation Conference (ISSC), the Voluntary National Shellfish Regulatory Program Standards (VNSRPS) for the Plant Sanitation element of the National Shellfish Sanitation Program (NSSP) has been developed, piloted, and formally approved by the states. FDA only provides consultation for these standards with no funding obligations at this time as they are voluntary and managed by ISSC.

In addition, in FY 2017 ORA awarded two cooperative agreements to states to develop recommendations for national shell egg regulatory standards. The cooperative agreements required the states to conduct egg regulatory program self-assessments of their own state regulations and systems and to identify the gaps and areas of improvement between federal and state egg regulatory programs. FDA is now working with the National Egg Regulatory Organization (NERO) to finalize the Egg Safety Regulatory Program Standards in FY 2020 and will assist state regulatory programs with implementation through a new cooperative agreement in FY 2021.

17. Traceability of Food

The Committee is aware that FDA has not put forward a comprehensive food-traceability system. The Committee directs FDA to work with stakeholders on a wide-scale traceability system that could help companies and government agencies more rapidly access data crucial to tracking foods implicated in disease outbreaks and subject to recalls.

FDA Response:
Improving wide-scale traceability of foods to rapidly respond to foodborne illness outbreaks and recalls is a key focus of the Agency. To advance these efforts, on April 30, 2019, FDA released a joint statement from Acting FDA Commissioner Ned Sharpless, M.D., and Deputy Commissioner for Food Policy and Response Frank Yiannas on the New Era of Smarter Food Safety.[140]

[140] See "Statement from Acting FDA Commissioner Ned Sharpless, M.D., and Deputy Commissioner Frank Yiannas on steps to usher the U.S. into a new era of smarter food safety" (April 30, 2019), available at

FDA intends the New Era of Smarter Food Safety initiative to enhance the Agency's ongoing efforts to implement the FDA Food Safety Modernization Act (FSMA) by encouraging a more digital, traceable, and safer system to help protect consumers from contaminated food. FDA expects this work to build on the advances that have been, and are being, made in FDA's implementation of FSMA while advancing the use of technologies that are currently used in society and business sectors all around us, such as blockchain for traceability, sensor technology, the Internet of Things, and artificial intelligence.

FDA is committed to working with stakeholders on the New Era of Smarter Food Safety initiative, and held a public meeting[141] on October 21, 2019, to discuss, seek input, and share ideas on our overall strategy and specific initiatives. The input received at this meeting and in comments submitted to the docket is being used to shape an FDA Blueprint for a New Era of Smarter Food Safety, which we plan to issue in early 2020. FDA expects this Blueprint to outline how this modern approach will address public health challenges, ranging from being able to trace sources of contaminated foods to using new predictive analytics tools like artificial intelligence to assess risks, and to help prioritize the Agency's work and resources.

FDA is also working expeditiously to complete a rulemaking required by FSMA on traceability for certain foods, with a proposed rule scheduled to issue in September 2020. This will be followed by three public meetings to solicit stakeholder input, which will inform the final rule, which is scheduled to issue in November 2022. Although the final rule will only create requirements for certain foods, it will help establish a foundation for the use of consistent food tracing terminology across all stakeholders, and a universal understanding of the types of data needed for a standardized, efficient, and rapid system for traceability. Given the work on the FSMA rulemaking and the broader traceability effort under the New Era of Smarter Food Safety initiative, FDA is working with stakeholders to advance wide-scale adoption of traceability.

https://www.fda.gov/news-events/press-announcements/statement-acting-fda-commissioner-ned-sharpless-md-and-deputy-commissioner-frank-yiannas-steps-usher.

[141] See "A New Era of Smarter Food Safety; Public Meeting, Request for Comments," 84 Fed. Reg. 49111, Docket No. FDA-2019-N-4187 (Sept. 18, 2019), available at *https://www.federalregister.gov/documents/2019/09/18/2019-20229/a-new-era-of-smarter-food-safety-public-meeting-request-for-comments*.

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Senate Appropriations Committees Significant Items

SENATE COMMITTEE REPORT (116-110)

1. Modeling and Simulation in Clinical Trials

The Committee commends the FDA for its continued support for and use of computer enabled in silico modeling and simulation in clinical trials and for its close affiliation with academic institutional leaders in this field. Partnership in this endeavor allows the development of personalized medical interventions, optimizes the regulatory process, and bridges gaps in the current regulatory infrastructure, which may advance the availability of new generic drugs, biological products, and devices to market at a potentially reduced cost. The Committee directs the FDA to further invest in advancing these applications and deepening its academic affiliations to this end.

FDA Response:
FDA appreciates the Committee's continued support for use of modeling and simulation in clinical trials, and the Agency's continued establishment of affiliations with academic institutions having expertise in this field. These collaborations and partnerships facilitate the development of personalized medical interventions, optimize the regulatory process, and bridge gaps in FDA's current regulatory infrastructure. The Agency looks forward to continuing to advance these methodologies and techniques to best take advantage of the benefits for continued product innovation and more rapid introduction of life saving technology to US patients.
FDA recognizes the public health benefits offered by modeling and simulation, including those in the area of in silico clinical trials (using individualized computer simulation in development and or regulatory evaluation of medical products). Modeling and simulation play a critical role in, among other areas, organizing diverse data sets, exploring alternate study design strategies, and predicting performance, so that safe and effective new therapeutics can advance more efficiently, from preclinical studies through clinical trials to market.

FDA routinely advises industry on using modeling and simulation to, for example: 1) predict clinical outcomes, 2) inform clinical trial designs, 3) support evidence of effectiveness, 4) identify the most relevant patients to study, and 5) predict product safety. In some cases, in silico clinical trials are used to replace human clinical trials, especially those that are intended to evaluate the risk of drug interactions. The Agency will continue to advance these methodologies and techniques to support product innovation and more rapid introduction of life-saving technology to our nation's patients.
FDA has demonstrated the Virtual Patient Model as one framework for in silico clinical trials, by creating a virtual population to enable computer-based simulations for medical devices. Additionally, the Agency has recently demonstrated the ability to conduct a clinical trial entirely in silico, and the framework is already in everyday use in the medical device community. 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 plans to develop guidances and standards related to use of modeling and simulation in device and drug development and evaluation.

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.

FDA's Center for Drug Evaluation (CDER) and Research and Center for Biologics Evaluation and Research (CBER) launched a Model-Informed Drug Development (MIDD) pilot for new drugs and biologics, to 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. FDA also plans to develop guidance related to use of advanced computer models and simulations in device and drug development.

For generic drugs, user fee supported research has helped to develop modeling and simulation approaches that aid the development and assessment of complex generic products. Potential applicants that want to employ modeling and simulation have met with FDA through the pre-ANDA meeting process. Modeling and simulations can inform science and risk-based bioequivalence (BE) standards, support in vitro based BE approaches, and identify sensitive and clinically relevant BE metrics. FDA is exploring how Virtual BE simulations based on validated empirical and mechanic models can serve as evidence for complex generic approval.
FDA will continue to explore the utility of in silico clinical trials for new purposes. These include enhancing the mechanistic understanding of disease progression and the complex interplay between genetics and predictive biomarkers with response to therapy.

2. Deemed Biological Products

The Committee is concerned that the FDA's interpretation of the Biologics Price Competition and In-novation Act [BPCIA] related to the transition of biological products to the biologic product regulatory review pathway will result in delayed access to lower-cost biosimilar products, including insulin. Further, the Committee is concerned that the FDA's interpretation and guidance related to this transition will create a scenario where sponsors of applications for biological products submitted as a new drug application under section 505 of the Federal Food, Drug, and Cosmetic Act (Public Law 75–717) that have not received final approval before March 23, 2020 would have to resubmit the application as a biological license application under the bio-logic product review pathway created under the BPCIA. This could have significant public health consequences and delay access to lower-cost biosimilar products, such as insulin, for millions of Americans. To address these concerns and ensure patients' access to lower-cost biosimilar drugs, such as insulin, the Committee directs the FDA to undertake the following

measures: (1) ensure final review of all such pending applications for biological products to be deemed a licensed biological product pursuant to the BPCIA are completed prior to March 23, 2020; (2) provide that applications submitted under section 505 of the Federal Food, Drug, and Cosmetic Act, but did not receive a complete review prior to March 23, 2020, receive priority review under section 351 of the Public Health Service Act (Public Law 78–410) and are allowed to rely on FDA's prior review and any data submitted under the new drug application submitted pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act (Public Law 75–717); and (3) provide flexibility in deeming follow-on insulin products to be biological products or biosimilar biologic products after March 23, 2020.

FDA Response:
FDA is working to implement the statutory provision in the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) that requires that on March 23, 2020, an approved marketing application for a biological product under the FD&C Act (such as insulin) will be deemed to be a license for the biological product under the Public Health Service Act. FDA is approaching this transition in a manner that minimizes burden, helps ensure stability for patients using currently marketed products, and facilitates the development of products that are biosimilar to, or interchangeable with these transitioned biological products in order to increase competition.

The BPCI Act describes procedures for submission of a marketing application for certain biological products during a 10-year transition period ending on March 23, 2020. FDA interprets section 7002(e)(4) of the BPCI Act (redesignated as section 7002(e)(4)(A) of the BPCI Act by section 607 of the Further Consolidated Appropriations Act, 2020) to plainly mean that, on March 23, 2020, only "approved" new drug applications (NDAs) will be deemed to be biologics license applications (BLAs). FDA has issued guidance providing recommendations to sponsors to facilitate alignment of product development plans with FDA's interpretation of this statutory provision, as well as provide clarity and predictability to manufacturers. In addition, FDA has met with sponsors of proposed products that may be affected by the transition to discuss and provide recommendations on their development programs on a product-specific basis.

With respect to FDA's review of any pending applications prior to the March 23, 2020, transition date, the Agency notes that timelines for review of NDAs, including NDAs for proposed biological products such as insulin, are established in the PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022 (PDUFA VI Commitment Letter) and, if applicable, the "Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs." FDA has further described its draft recommendations on good review management principles and practices for the review of NDAs and BLAs more generally in FDA's draft guidance for industry and review staff, "Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications" (Draft GRMP Guidance). Consistent with these recommendations, FDA has carefully considered steps it may take to minimize the disruption to any application that may be pending at the time of the transition. FDA also notes that section 607 of the Further Consolidated Appropriations Act, 2020, recently amended section 7002(e)(4) of the BPCI Act to provide that, with respect to an application for a biological product submitted under section 505 of the FD&C Act that is filed not later than March 23, 2019, and is not approved as of March 23, 2020, FDA shall continue to review such application under section 505 of the FD&C Act after March 23, 2020.

With respect to the availability of priority review under section 351 of the PHS Act for any applications submitted under section 505 of the FD&C Act that did not receive a complete review prior to March 23, 2020, FDA has communicated through guidance that the Agency intends to assist applicants who may be affected by section 7002(e) of the BPCI Act, where feasible and appropriate. For example, FDA has explained in guidance that during the review of a BLA submitted after the transition date for a proposed biological product that was previously submitted, but not approved, in an application under section 505 of the FD&C Act, FDA intends to consider any previously conducted scientific review by the Agency of such previous application under the FD&C Act, to the extent that such review is relevant to, and consistent with, applicable requirements of section 351 of the PHS Act. However, FDA does not believe that any such applications necessarily would meet established standards for priority review. As noted above, section 607 of the Further Consolidated Appropriations Act, 2020, recently amended section 7002(e)(4) of the BPCI Act to provide for continued review under section 505 of the FD&C Act for any applications described by such section 607.

With respect to the deeming of follow-on insulin products on March 23, 2020, FDA has explained in draft guidance that its interpretation that an approved 505(b)(2) application for a biological product (including a "follow-on" biological product) will be deemed to be a 351(a) BLA reflects the statutory requirement that both types of applications contain full reports of investigations of safety and effectiveness. This approach also reflects FDA's view that it is more appropriate to regulate a biological product approved through the 505(b)(2) pathway that may differ in certain respects (e.g., different strength, dosage form, or route of administration or conditions of use) from a previously approved product under the statutory and regulatory framework for 351(a) BLAs because these differences are not permitted under the statutory framework for 351(k) BLAs for biosimilar and interchangeable products. Moreover, FDA's approval of a 505(b)(2) application reflects FDA's evaluation of the data against a different statutory standard than the requirements under section 351(k) of the PHS Act.

We note that in November 2019 FDA issued a draft guidance for industry, "Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products," that explains that FDA generally would not expect comparative clinical immunogenicity studies to support a demonstration of biosimilarity or interchangeability for certain proposed insulin products in the circumstances described in the guidance. The thinking on this issue described in the draft guidance can result in significant cost and time savings in developing biosimilar and interchangeable insulin products seeking licensure in 351(k) BLAs after the transition.

3. Innovative Glass Packaging

The Committee directs the FDA to work with glass packaging suppliers and pharmaceutical manufacturers to evaluate and promote streamlined approval requirements designed to expedite the adoption and use of innovative glass pack-aging technologies with the capacity to improve product quality, reduce product recalls, reduce drug shortages, and protect public health. Such streamlined approval requirements should address stability testing and other relevant types of data to be submitted in support of product approval.

FDA Response:
FDA engages companies working on developing new glass designs for use in pharmaceutical containers with the goal of addressing quality issues, such as the formation of glass lamellae. In addition, the Office of Pharmaceutical Quality (OPQ), within the Center for Drug Evaluation and Research (CDER), developed methodology and conducted studies to evaluate the performance characteristics of glass containers for injectable drug products (See https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm607223.htm). These laboratory studies will help inform future quality assessments and provide insight for feedback that can be provided to companies as they work on developing their products. FDA remains committed to enabling the use of innovative products and approaches that support drug quality, and we will continue to meet with companies through CDER's Emerging Technology Program to support the development of novel manufacturing technologies.
In general, prior to adopting any new packaging technology, an application holder for a drug or biological product needs to conduct testing to ensure the suitability of the new packaging when used with a specific drug or biological product and the specific processing equipment. It is important that the packaging is tested based on the specific drug or biological product that the packaging will be used with to prevent interactions between the product and packaging, such as impurities extracting or leaching from the packaging. Interactions like these may result in recalls and could potentially harm patients. Testing is required to help avoid such interactions.

FDA has existing mechanisms intended to lead to improved product quality for companies developing innovative technologies. CDER's Emerging Technology Program and the Center for Biologics Evaluation and Research's Advanced Technologies Team were created to encourage companies that are pursuing innovative approaches to pharmaceutical product design and manufacturing to engage with the Agency early in the development process. These programs foster early communication and collaboration to help identify and discuss scientific and regulatory challenges prior to a regulatory submission, streamlining the application submission process. In addition, CDER OPQ can expedite assessment of submissions that, if approved, may help mitigate or prevent drug shortages.

4. <u>Polypharmacy</u>

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 inter-actions 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:
FDA routinely assesses the potential for drug-drug interactions (DDIs), and considers those that result from polypharmacy, as a part of new drug evaluation. 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.

FDA, as part of the clinical trial process, generally expects full reporting by sponsors of INDs of all concomitant medications used by study subjects and takes this information into consideration, as appropriate, when evaluating both the efficacy and safety of the study drug. The Agency

agrees that the risk of drug-drug interactions may increase with routine usage of multiple medications. FDA provides guidance and recommendations 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 Guidance for Industry".* This draft guidance was developed to help sponsors of investigational new drug applications and applicants of new drug applications consider how to evaluate DDIs during drug development. More recently in June 2019, the Agency published a draft guidance entitled: *"Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs".* This draft guidance, when finalized, will provide guidance to industry on broadening clinical trial eligibility criteria to increase diversity in clinical trial enrollment, including, as appropriate, participants who are on multiple concomitant medications (including the elderly) so that we better understand the safety and efficacy of new drugs and biologics for these patients.

5. <u>Tuberculosis</u>

The Committee directs the agency to work with the Centers for Disease Control to explore interagency mechanisms to mitigate TB drug shortages, including centralizing procurement and supply, securing resources to maintain the limited emergency TB drug stockpile, developing policies to allow for the importation of needed quality-assured drugs, and formalizing a patient assistance program for accessing treatments.

FDA Response:
FDA and CDC continue to collaborate and engage in regular discussions regarding Tuberculosis (TB) drug availability. This includes working with CDC on our drug shortage strategies for TB drugs on a continuing basis. Per the Committee's direction, FDA will continue our collaborations with CDC to ensure TB drug shortages are addressed to the fullest of our authorities.

6. <u>Olive Oil</u>

The Committee is particularly concerned with the number of different standards for olive oil and directs the FDA to consult with domestic producers and importers of olive oil to develop a science-based Standard of Identity for the different grades (e.g. extra virgin, virgin, and refined) of olive oil and olive-pomace oils.

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 plans to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity in 2020. 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.

In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. In June and September 2019, FDA met with the North American Olive Oil Association, American Olive Oil Producers Association, and Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA continues to discuss this matter with industry representatives.

Further, FDA is reviewing a citizen petition related to olive oil that was submitted in November 2019 by the American Olive Oil Producers Association (Docket No. FDA-2019-P-5191). The petition requests FDA to establish a standard of identity for olive oil and olive pomace oil that includes compositional requirements and analytical testing. No decision has been made on the petition.

7. Seafood Labeling

The Committee is concerned about imitation seafood products being marketed as seafood. As the FDA continues to update the standards of identity for certain foods, the Committee directs the FDA Commissioner to coordinate with the seafood industry to ensure that such products are properly labeled in accordance with such standards of identity.

FDA Response:
FDA takes seriously its responsibilities under federal law to protect consumers from misbranded food and understands the Committee's concern regarding the proper labeling of foods. FDA is mindful of the importance of working with our stakeholders to ensure that food is labeled in accordance with the FD&C Act and regulations and that the labeling is truthful and not misleading.

Section 403(i)(1) of the FD&C Act requires food labels to bear the common or usual name of the food, if such a name exists. Common or usual names are generally established by common usage, though in some cases are established by regulation. In the absence of a common or usual name, the label of a food in packaged form must bear a statement of identity that accurately describes the food. The name or statement of identity must not cause the labeling to be misleading.

In determining whether labeling is false or misleading, FDA generally considers the terms used within the context of the entire label. This applies to different types of seafood and to plant-based products or other seafood alternatives. FDA may also consider consumer data and information indicating whether or not the words or representations may cause consumers to confuse products not derived from fish or other seafood with those that are. FDA is not aware of such data at this time and welcomes additional information about this matter.

FDA is also currently reviewing a citizen petition that asks FDA to issue regulations clarifying how food names may reference the names of other foods. This relates to whether, for example, plant-based seafood alternatives may be labeled with names that include the common or usual names of fish and shellfish or any other name established by regulation for fish and shellfish – regardless of whether the fish or shellfish is standardized.

The Agency will continue to assess products on the market to help ensure that consumers are not misled by labeling. One tool that FDA uses when determining appropriate names for seafood sold in interstate commerce is *The Seafood List*.[142] The "acceptable market name" list in *The Seafood List* is a name the Agency recognizes as suitable for the product's statement of identity, its ingredient list, and the allergen labeling requirements under the Food Allergen Labeling and Consumer Protection Act of 2004 for a seafood species.

8. Thermal Packaging

Food and pharmaceutical delivery is one of the fastest growing shipping markets, and with that come a significant increase in packaging waste. The Committee is aware of design-forward approaches that merge sustainability and functionality for entities shipping time-sensitive materials, and accordingly, directs the FDA to provide awareness on the economic and environmental benefits of sustainable thermal packaging alternatives.

FDA Response:
FDA is responsible for the review and approval of food contact packaging materials, with the goal of assuring that any migration of food contact substances into food is safe for the consumer. FDA's authority is limited to food safety, and FDA does not have authority over packaging used in shipping if the packaging does not contact food directly. FDA has approved certain types of biodegradable and/or recyclable polymers in the same manner as the Agency reviews all industry submissions for new packaging, without encouraging or discouraging any particular type of submission. Further, it is not within FDA's purview to promote the use of any particular type of packaging.
As an impartial regulator, the Agency remains neutral with respect to the benefits of any particular type of packaging where such benefits are unrelated to food safety. FDA is not legally or operationally in a position to provide awareness on the economic and environmental benefits of sustainable thermal packaging alternatives as described in the report language.

9. Opioid Epidemic

The Committee is deeply concerned about the opioid abuse epidemic that has taken the lives of more than 70,000 Americans. As previously noted, the Committee recommendation includes additional funding to support ongoing efforts to address the opioid crisis, as well as support existing investments and additional lab needs for the International Mail Facilities initiative. The Committee notes that fifty million Americans suffer from chronic pain and that living with chronic pain can be life-altering and deeply impact people on many levels. The current state of chronic pain management is often inadequate for many patients and places an economic burden on the healthcare system, costing the U.S. $560,000,000,000 a year. Management of chronic pain often requires both non-pharmacological treatment, as well as medicines. Unfortunately, the current pharmacological options do not meet the needs of all patients, and additional treatments

[142] Guidance for Industry: The Seafood List (July 2012), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-seafood-list.

are needed. Therefore, the Committee directs the FDA to comply with Section 3001 of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities [SUPPORT] Act, which directs the FDA to hold public meetings and issue guidance regarding the challenges and barriers of developing non-addictive medical products intended to treat pain or addiction and expects the agency to comply with this directive. The Committee also notes that the FDA has a responsibility to seek the advice of experts on the safety and efficacy of both new opioid medications as is required under the Comprehensive Addiction and Recovery Act. Therefore, 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 also supports the FDA's efforts to transition from the conventional opioid analgesic formulations that dominate the market today to safer products, including, but not limited to, more effective abuse-deterrent opioid analgesic formulations. The Committee directs the FDA to comply with Section 3032 of the SUPPORT Act (Public Law 115–271) and explore other safety-enhancing features, like special packaging or disposal options, that could assist with deterring abuse, misuse, and diversion. The Committee also encourages the FDA to continue to monitor the effectiveness of existing Opioid Analgesic Risk Evaluation and Mitigations Strategy to determine whether further modifications are necessary. The Committee is also aware of concerns pertaining to the use of opioid analgesics with ultra-high doses and directs the FDA to evaluate potential safety issues associated with higher dose opioid analgesics, as well as potential adverse or public health con-sequences associated restrictions on higher dose opioid analgesics.

FDA Response:

SUPPORT Act Section 3001

FDA agrees that the development of novel, potent non-opioid pain therapies is paramount, and is committed to doing its part to spur this development. Pursuant to section 3001 of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act, FDA convened an advisory committee meeting on November 15, 2018, to discuss the assessment of opioid analgesic sparing outcomes in clinical trials of acute pain. FDA also issued draft guidance on June 20, 2019, "Opioid Analgesic Drugs: Considerations for Benefit-Risk Assessment Framework," which describes the application of the benefit-risk assessment framework that the agency uses in evaluating applications for opioid analgesic drugs and summarizes the information that can be supplied by opioid analgesic drug applicants to assist the agency with its benefit-risk assessment, including considerations about the broader public health effects of these products in the context of this crisis. In addition, FDA held a public hearing on September 17, 2019, "Standards for Future Opioid Analgesic Approvals and Incentives for New Therapeutics to Treat Pain and Addiction," to receive stakeholder input on the approval process for new opioids and how FDA might best consider the existing armamentarium of therapies, among other factors, in reviewing applications for new opioids to treat pain.

Furthermore, FDA plans to hold one or more additional public meetings and issue more guidances regarding the challenges and barriers of developing non-addictive medical products intended to treat pain or addiction.

Advisory Committees

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").

SUPPORT Act Section 3032

FDA agrees that exploring safety-enhancing features, like special packaging or disposal options could assist with deterring abuse, misuse, and diversion. Pursuant to section 3032 of the SUPPORT Act, FDA opened a public docket on May 30, 2019, to request information on requiring fixed-quantity blister packaging for certain opioid pain medicines to help decrease unnecessary exposure to opioids. Currently, FDA is analyzing comments from the docket and will take action as appropriate.

Opioid Analgesic Risk Evaluation and Mitigations Strategy (OA REMS)

FDA agrees with the Committee and continues to monitor the effectiveness of the current OA REMS. The goal of the OA REMS is to educate prescribers and other healthcare providers (including pharmacists and nurses) on the treatment and monitoring of patients with pain. Under the OA REMS, sponsors must submit REMS Assessments annually from the date of the approval of the REMS (09/18/2018).

Higher-Dose Opioid Analgesics

The Agency is also aware of concerns pertaining to the use of opioid analgesics with doses of 90 MME or greater. The Agency has a pending citizen petition on this issue (which also asks FDA to take action regarding opioid analgesics that allow for daily doses of 90 MME or greater), and cannot comment on its deliberations. However, please be assured that the Agency prioritizes public health issues concerning opioids; FDA is and has been actively examining epidemiological data, analyzing the risk management framework, and evaluating potential safety issues associated with higher dose opioid analgesics, as well as potential adverse consequences associated with proposed restrictions. In addition, the Agency held an advisory committee meeting in June 2019 to discuss issues pertaining to higher-dose opioid analgesics.

FDA further notes that, as a scientific and regulatory agency, it must work within the Agency's legal and policy framework to make the best decisions it can in the face of a very complicated public health challenge. Given the complex and inter-related nature of pain management, opioid use disorder, and overdose in a rapidly evolving drug landscape in the U.S., FDA scientists and legal and policy experts are carefully considering all facets of the issues surrounding higher-dose opioid analgesics and look forward to the public discussion of these issues at the upcoming advisory committee meeting. Once FDA has concluded its analysis, it will take any action on higher-dose opioid analgesics it deems appropriate.

FDA understands that medical devices will play a critical role in the agency's all hands-on deck approach to confronting the opioid crisis. We believe the greatest opportunities for medical devices to address this crisis are to 1) identify patients at risk for Opioid Use Disorder (OUD) before they receive opioids, 2) manage pain to either reduce or replace opioid use, 3) prevent diversion or abuse of prescribed opioids, 4) foster development of non-opioid treatment options for OUD. For example, the development of a diagnostic device, whether it be an in vitro diagnostic test or a mobile medical app, could be highly impactful in identifying those patients for whom extra caution should be exercised when considering prescribing opioids for acute or chronic pain.
In the past few years CDRH has cleared, granted, or approved more than 200 devices related to the treatment or management of pain, including 10 with new or novel technologies. Those novel devices may reduce the need to administer opioid drugs to patients suffering from either acute or chronic pain.

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 OUD—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 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. 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. 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 OUD. 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.

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JOINT EXPLANATORY STATEMENT SIGNIFICANT ITEMS

1. Olive Oil Standards of Identity

The agreement acknowledges the submission of a comprehensive petition pending at the FDA to establish a separate U.S. Standard of Identity for different grades of olive oil (e.g., extra virgin, virgin, and refined) and olive-pomace oils. With a pending petition now at the FDA, the agreement directs the FDA to complete work on this petition as expeditiously as possible.

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 plans to reopen the comment period on a proposed rule seeking to establish general principles to update the framework for standards of identity in 2020. 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.

In October 2018, FDA met with olive oil producer Deoleo SA to discuss their interest in a standard of identity for olive oil. In June and September 2019, FDA met with the North American Olive Oil Association, American Olive Oil Producers Association, and Deoleo SA to discuss their interest in a standard of identity for olive oil. FDA continues to discuss this matter with industry representatives.

Further, FDA is reviewing a citizen petition related to olive oil that was submitted in November 2019 by the American Olive Oil Producers Association (Docket No. FDA-2019-P-5191). The petition requests FDA to establish a standard of identity for olive oil and olive pomace oil that includes compositional requirements and analytical testing. No decision has been made on the petition.

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FDA SPECIFIC ITEMS

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES

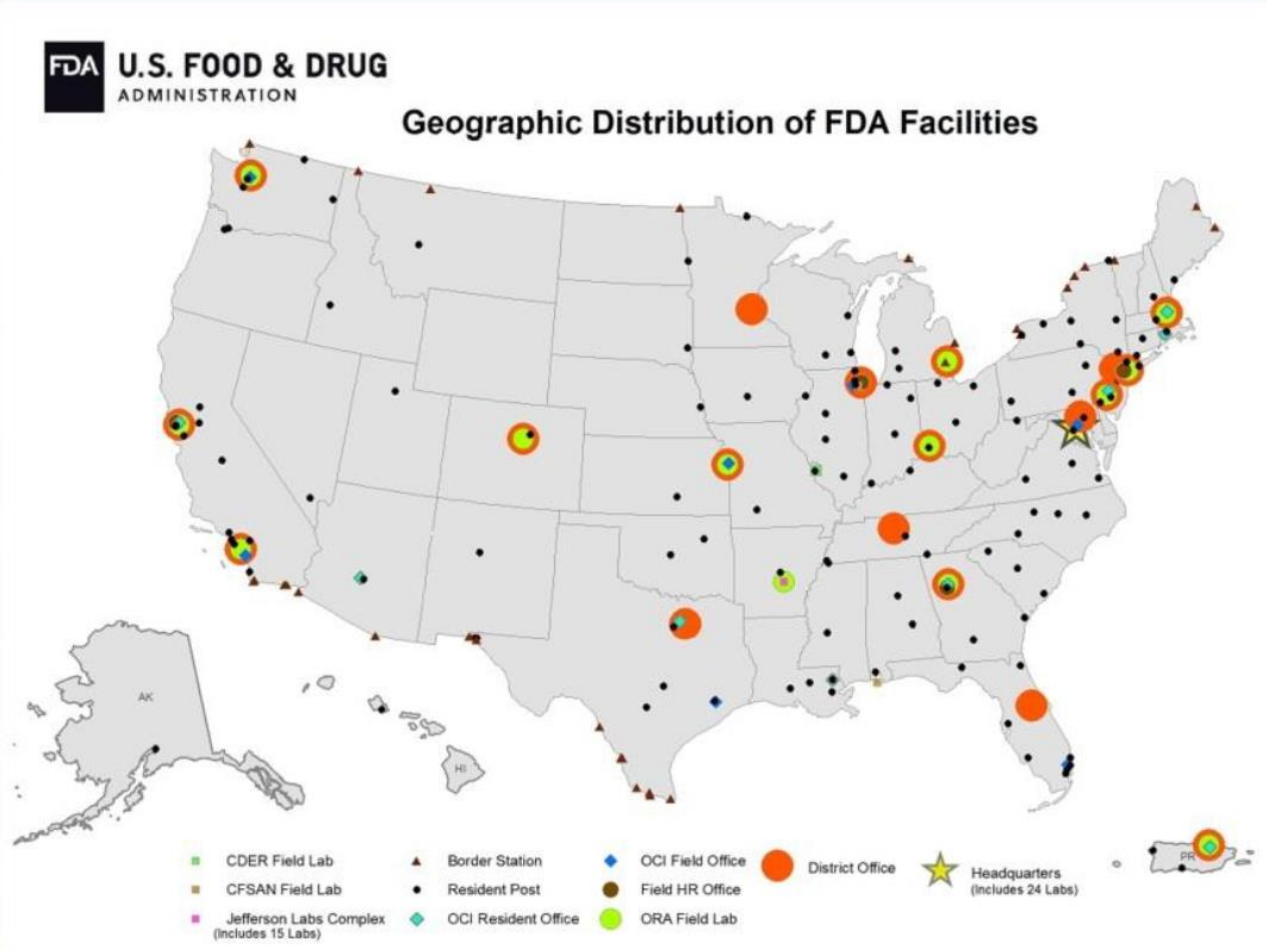

Figure 1 Geographical Distribution of FDA Facilities

HIV/AIDS FUNCTIONAL TABLE

Food and Drug Administration
HIV/AIDS Resource Funding
(Dollars in Thousands)

Program	FY 2019 Estimate	FY 2020 Estimate	FY 2021 Estimate
Human Drugs	$29,869	$29,869	$29,869
Biologics	$28,462	$31,665	$30,725
Medical Devices	$414	$318	$431
Field Activity	$36,300	$36,300	$37,620
Other Activities	$3,395	$3,395	$3,395
Total HIV/AIDS	**$98,440**	**$101,547**	**$102,040**

*FY 2020 Estimates consistent with FY 2020 CJ

CROSSCUTS

FY 2019-FY 2021 Crosscutting Information
(Program Level in Thousands)

(dollars in thousands)	**FY 2019 Estimate**	**FY 2020 Estimate**	**FY 2021 Estimate**
Alzheimer's Disease	5,113	5,379	5,137
HIV/AIDS	98,440	101,547	102,040
Antimicrobial Resistance	46,488	48,587	48,670
Bioterrorism-Medical Countermeasures	108,151	114,632	119,632
Cosmetics	14,014	13,998	13,998
Diabetes	22,934	23,806	24,019
Drug Abuse	13,700	15,615	15,715
Global Health	160,344	161,206	160,909
Immunization	30,562	30,861	31,088
Mental Health	20,599	21,077	20,940
Minority Health	1,852	2,646	2,627
Opioids 1/	67,011	75,011	75,011
Pandemic Influenza	43,981	43,342	48,779
Patient Safety	541,703	574,358	574,993
Pediatric Drugs	10,962	10,905	9,781
Tobacco	712,000	712,000	812,000
Women's Health	102,500	101,567	102,416

*Crosscut estimates are based on FDA's current level of effort at time of publication and are subject to change based on application review, inspection workload, and response efforts

**All estimates reflect total Program Level, including BA and UF, where applicable

***Total Program Level differs from the FDA Operating Plan due to inclusion of UF estimates

1/ Opioids BA estimates shown are consistent with the FY 2020 Operating Plan

CENTRAL ACCOUNTS

Program (dollars in thousands)	FY 2019 Actuals		FY 2020 Estimates		FY 2021 Estimates	
	BA	UF	BA	UF	BA	UF
Foods	**16,960**	-	**17,480**	-	**16,539**	-
Center	5,003	-	5,437	-	5,154	-
Field	11,957	-	12,043	-	11,385	-
Human Drugs	**19,894**	**49,064**	**21,748**	**54,395**	**20,622**	**51,605**
Center	16,481	48,183	17,118	53,139	16,201	50,405
Field	3,414	881	4,630	1,255	4,421	1,200
Biologics	**6,104**	**5,144**	**6,656**	**5,515**	**6,311**	**5,226**
Center	5,120	5,099	5,635	5,468	5,345	5,181
Field	984	45	1,021	47	966	44
Animal Drugs and Feeds	**4,003**	**868**	**4,099**	**1,078**	**3,877**	**1,027**
Center	2,605	868	2,695	1,078	2,550	1,027
Field	1,398	-	1,404	-	1,327	-
Devices and Radiological Health	**10,554**	**4,507**	**11,114**	**5,095**	**10,524**	**4,837**
Center	8,376	4,370	8,891	4,957	8,422	4,707
Field	2,179	138	2,223	138	2,102	130
National Center for Toxicological Research	730	-	800	-	759	-
Family Smoking Prevention and Tobacco Control Act	-	**5,602**	-	**6,115**	-	**5,798**
Center	-	5,516	-	5,985	-	5,674
Field	-	86	-	130	-	124
FDA Headquarters	10,592	7,827	12,207	6,273	11,596	5,914
Total	**68,838**	**73,012**	**74,104**	**78,470**	**70,228**	**74,406**

HHS CHARGES AND ASSESSMENTS

Food and Drug Administration

Department of Health and Human Services Charges and Assessments
Fiscal Year 2019 Actuals

Assessments:	**250,173**
NIH eRA Grants Management System Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	246,781
Federal Audit Clearinghouse	3,392
Fee For Service:	**65,134,490**
Program Support Center/ Office of the Secretary Provides various services to the FDA, including some Information and Systems Management Services	**17,889,770**
Financial Management Portfolio (FMP)	584,389
Real Estate and Logistics Portfolio Includes building operations, shredding, storage, property disposal,	9,814,810
Equal Employment Opportunity Compliance and Operations Includes Complaint Investigations, FAD/Counseling, Mediation	510,000
Miscellaneous Services Includes AIM, Category Mgmt., Commissioned Corps Force Mgmt (CCFM), Departmental Contracts Information System Program (DCIS), Ethics Program, Grants, Broadcast studio, HPO, Media Monitoring, OGC Claims, Small Business Consolidation, Strategic Planning, TAGGS	6,980,571
Federal Occupational Health (FOH): FDA agency health units and services	**2,467,228**
Information & System Management Services	**36,707,093**
Freedom of Information (FOIA)	144,091
Unified Financial Management Systems (UFMS) Includes services for Consolidated Financial Reporting System (CFRS), Financial Business Intelligence System (FBIS), Governance and UFMS O&M support	13,099,027
HCAS Operations and Maintenance HCAS O&M services provide support for daily operations of the HCAS application.	2,670,353
Information Technology Infrastruction & Operations (ITIO) Telecommunications team offers expertise on Network / Telecomunnications / Security.	2,752,442
Office of IT Strategy, Policy & Governance	2,110,922
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	4,979,495
Office of Information Security (OIS) Includes computer security incident reponse center. Trusted Internet Connections and IT Security.	4,611,885
Digital Communications Web Crawler, Web Media	6,338,878
Office of Human Resource Services Includes HR Center services teir I, payroll liaison, systems planning and implemenation	**8,070,400**

Jointly Funded Projects:	**3,438,861**
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	**2,207,702**
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.	496,057
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
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	225,000
NIH Negotiation of Indirect Cost Rates Agreement with NIH/OD to support costs associated with the negotiation of indirect cost rates with commercial organizations	40,000
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.	120,597
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.	80,956
Implementation of the DATA Act (PMO)	56,173
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
Secretary's Tribal Advisory Committee Outreach with Tribal Governments and Organizations; communication and coordination of HHS activities and initiatives, which enhance the government-to-government relationship that HHS has with Indian Tribes. In addition IEA will find ways to educate HHS and guide the Department in developing future programs, initiatives, and other interactions with tribal governments and tribal organizations.	-

HHS Charges and Assessments: FY 2019 – FY 2021

Activity	FY 2019 Actual	FY 2020 Estimate	FY 2021 Estimate
Assessments	**$ 250,173**	**$ 282,496**	**$ 314,819**
Fee for Service	**$ 65,134,490**	**$ 66,324,394**	**$ 68,714,061**
Program Support Center/OS	$ 17,889,770	$ 19,352,289	$ 20,589,070
Federal Occupational Health	$ 2,467,228	$ 1,531,000	$ 1,576,930
Information System Management Service	$ 36,707,093	$ 37,128,593	$ 37,986,174
Human Resource Center – Rockville, Maryland	$ 8,070,400	$ 8,312,512	$ 8,561,887
Jointly Funded Services	**$ 3,438,861**	**$ 3,590,621**	**$ 3,624,033**
International Health - Bilateral Agreement	$ 1,231,159	$ 1,500,000	$ 1,500,000
Other Jointly Funded Projects	$ 2,207,702	$ 2,090,621	$ 2,124,033
Total	**$ 68,823,524**	**$ 70,197,511**	**$ 72,652,913**

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GLOSSARY

Acronyms

ACE	Automated Commercial Environment
ACRA	Associate Commissioner of Regulatory Affairs
ADUFA	Animal Drug User Fee Amendment
AFRPS	Animal Feed Regulatory Program Standards
AHRMM	Association for Healthcare Resources and Materials Management
AHWP	Asian Harmonization Working Party
AMP	Asset Management Plan
AMR	Antimicrobial Resistance
ANAB	ANSI-ASQ National Accreditation Board
ANDA	Abbreviated New Drug Application
ANPRM	Advance Notice of Proposed Rulemaking
ANSI	American National Standards Institute
APEC	Asia Pacific Economic Cooperation
ARIA	Active Risk Identification and Analysis
ARS	Acute Radiation Syndrome
ASPR	Assistant Secretary for Preparedness and Response
ASTM	American Society for Testing and Materials
BAP	Biosimilars Action Plan
BARDA	Biomedical Advanced Research and Development Authority
BEST	Biologics Effectiveness and Safety
BIMO	Bioresearch Monitoring
BLA	Biologics License Application
BMAR	Backlog of Maintenance and Repair
BPD	Biosimilar Product Development
CAERS	CFSAN Adverse Event Reporting System
CASEL	Center for Coordination of Analytics, Science, Enhancement and Logistics
CATT	CBER Advanced Technologies Team
CBER	Center for Biologics Evaluation and Research
CBN	Carbon-Based Nanomaterials
CBP	Customs and Border Protection
CBRN	Chemical, Biological, Radiological, Nuclear
CDC	Centers for disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CFSAN	Center for Food Safety and Applied Nutrition
CGMP	Current Good Manufacturing Practice
CID	Complex Innovative Designs
CMS	Center for Medicare and Medicaid Studies
CNDA	China National Drug Administration
COAC	Commercial Operations Advisory Committee
COO	Chief Operating Officer
CORE	Coordinated Outbreak Response and Evaluation

COTS	Commercial Off-the-Shelf
CRCPD	Council of Radiation Program Control Directors
CRN	Coordinated Registry Networks
CSI	China Safety Initiative
CTAC	Commercial Targeting and Analysis Center
CTP	Center for Tobacco Products
CUP	Central Utility Plant
CVM	Center for Veterinary Medicine
DAC	Data Analytics Commons
DBT	Digital Breast Tomosynthesis
DCAP	Drug Competition Action Plan
DCM	Dilated Cardiomyopathy
DDT	Drug Development Tools
DHA	Docosahexaenoic Acid
DHS	Department of Homeland Security
DILI	Drug-Induced Liver injury
DOD	Department of Defense
DOX	Doxorubicin
DPA	Division of Pharmaceutical Analysis
DQSA	Drug Quality and Security Act
DRMS	Document Retrieval and Management Service
DSCSA	Drug Supply Chain Security Act
DSHEA	Dietary Supplement Health and Education Act of 1994
DTRA	Defense Threat Reduction Agency
DUNS	Dun & Bradstreet Number
EADB	Estrogenic Activity Database
EAFUS	Everything Added to Food in the U. S.
EDKB	Endocrine Disruptor Knowledge Base
EHR	Electronic Health Records
EMA	European Medicines Agency
ENDS	Electronic Nicotine Delivery Systems
EQUIP	Enhancing Quality Using the Inspection Program
ETT	Emerging Technology Team
EUA	Emergency Use Authorization
FACA	Federal Advisory Committee Act
FAP	Food Additive Petitions
FAQ	Frequently Asked Questions
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
FDATT	FDA Technology Transfer Program
FDCA	Federal Food, Drug and Cosmetic Act
FEMA	Federal Emergency Management Agency
FERN	Food Emergency Response Network

FMT	Fecal Microbial Transplantation
FOA	Funding Opportunity Announcement
FSMA	Food Safety Modernization Act
FSVP	Foreign Supplier Verification Program
FTC	Federal Trade Commission
FVM	Foods and Veterinary Medicine
GAO	Government Accountability Office
GDUFA	Generic Drug User Fee Amendments
GIS	Geographic Information System
GMP	Good Manufacturing Practices
GRAS	Generally Recognized as Safe
GSA	General Services Administration
GUDID	Global UDI Database
HACCP	Hazard Analysis and Critical Control Point
HCA	Hospital Corporation of America
HDAC	Histone Deactylase
HDE	Humanitarian Device Exemption
HHS	Health and Human Services
HICPAC	Healthcare Infection Control Practices Advisory Committee
HITU	High Intensity Therapeutic Ultrasound
HPV	Human Papillomavirus
HUS	Hemolytic Uremic Syndrome
IAA	Interagency Agreement
IAEA	International Atomic Energy Agency
IAS	International Accreditation Service
ICH	International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IFSAC	Interagency Food Safety Analytics Collaboration
IFSS	Integrated Food Safety System
IGA	Intergovernmental Affairs
IICA	Institute for Cooperation on Agriculture
IMDRF	International Medical Device Regulators Forum
IMEDS	Innovation in Medical Evidence and Development Surveillance
IMF	Opioids International Mail Facilities
IMS	Ion Mobility Spectroscopy
INTERACT	Initial Targeted Engagement for Regulatory Advice on CBER products
IOP	Import Operations Program
IQA	Integrated Quality Assessment
IRB	Guidance Institutional Review Board
ISO	International Organization for Standardization
ITACS	Industry Trade Auxiliary System
IVD	In Vitro Diagnostic
JLC	Alabama Jefferson Labs Complex
JMEDICC	Joint Mobile Emerging Disease Intervention Clinical Capability
KASA	Knowledge-Aided Assessment & Structured Application

LACF	Low- Acid Canned Foods
LGBT	Lesbian, Gay, Bisexual and Transgender
LOI	Letter of Intent
LPAD	Limited Population Pathway for Antibacterial and Antifungal Drugs
LSBC	Life Sciences - Biodefense Laboratory Complex
LUC	Learning UDI Community
MDDT	Medical Device Development Tools
MDIC	Medical Device Innovation Consortium
MDSAP	Medical Device Single Audit Program
MFRPS	Manufactured Food Regulatory Program Standards
MLDP	Management and Leadership Development Program
MMWR	Morbidity and Mortality Weekly Report
MOU	Memorandum of Understanding
MPL	Medical Products Laboratories
MQSA	Mammography Quality Standards Act
MRA	Mutual Recognition Agreement
MRC	Muirkirk Road Complex
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
MRTP	modified risk tobacco product
MRTPA	Modified Risk Tobacco Product Application
MUMS	Minor Use and Minor Species
NARMS	National Antimicrobial Resistance Monitoring System
NAS	National Academy of Sciences
NASDA	National Association of State Departments of Agriculture
NASEM	National Academies of Science, Engineering and Medicines
NCAPIP	National Council of Asian Pacific Islander Physicians
NCBI	National Center for Biotechnology Information
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NCTR	The Center for Toxicological Research
NDC	National Drug Code
NECC	New England Compounding Center
NEF	Non-Recurring Expenses Fund
NEST	National Evaluation System for health Technology
NEXT	Nationwide Evaluation of X-ray Trends
NFSDX	National Food Safety Data Exchange
NGS	Next Generation Sequencing
NHFT	New Hire Fundamentals Training
NHGRI	National Human Genome Research Institute
NHMA	National Hispanic Medical Association
NIH	National Institutes of Health
NIPP	New Inspection Protocol Project
NIST	National Institute of Standards and Technology
NLEA	Nutrition Labeling and Education Act
NLP	Natural language processing

NMA	National Medical Association
NME	New Molecular Entity
NPRM	Notice of Proposed Rulemaking
NRT	Nicotine replacement therapy
NSE	Not Substantially Equivalent
NTSO	No-Tobacco-Sale Orders
NYTS	National Youth Tobacco Survey
OARSA	Office of Applied Research Assessment
OCI	Office of Criminal Investigations
OECD	Organization for Economic Co-Operation and Development
OFBA	Office of Finance, Budget and Acquisitions
OFPR	Office of Food Policy and Response
OFRR	On-Farm Readiness Review
OGPS	Office of Global Policy and Strategy
OLSS	Office of Laboratory Science and Safety
OMHHE	Office of Minority Health and Health Equity
OOPD	Office of Orphan products and development
OPEQ	the Office of Product Evaluation and Quality
OPQ	Office of Pharmaceutical Quality
OPSC	Opioids Policy Steering Committee
ORA	Office of Regulatory Affairs
ORCA	Office of Regional and Country Affairs
OSAR	Online Search and Retrieval
OSBA	Office of Small Business Assistance
OSEL	Office of Science and Engineering Labs
OTC	Over-The-Counter
OTED	Office of Training Education and Development
OTS	Office of Translational Sciences
OWH	Office of Women's Health
PAC	Pediatric Advisory Committee
PAD	Program Activity Data
PAHO	Pan American Health Organization
PAHPRA	Preparedness Reauthorization Act of 2013
PAS	Prior Approval Supplement
PATH	Population Assessment of Tobacco and Health
PCAC	Pharmacy Compounding Advisory Committee
PCHF	Preventive Controls for Human Food
PDMA	Prescription Drug Marketing Act
PDUFA	Prescription Drug User Fee Act
PEAC	Patient Engagement Advisory Committee
PFAS	perfluoroalkyl substances
PFDD	Patient-focused drug development
PFIPC	Permanent Forum of international Pharmaceutical Crime
PHCE	Perinatal Health Center of Excellence
PHEIC	Public Health Emergency of International Concern
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise

PKU	Phenylketonuria
PMA	Premarket Approval
PMTA	Premarket Tobacco Product Applications
PPI	Patient Preference Initiative
PRA	Paperwork Reduction Act
PRAMS	Pregnancy Risk Assessment Monitoring System
PREA	Pediatric Research Equity Act
PRGLAC	Pregnant Women and Lactating Women
PRV	Priority Review Voucher
PSA	Public Service Announcement
PSN	Produce Safety Network
PSP	Produce Safety Partnership
PSR	Produce Safety Rule
QSAR	Quantitative Structure Activity Relationship
RASFF	Rapid Alert System for Food and Feed
RCA	Research Collaboration Agreements
RCCS	Rotary Cell Culture System
REMS	Risk Evaluation and mitigation strategies
RFA	Request for Applications
RHR	RadHealth Representatives
RIO	Research Impact and Outcomes
RMAT	Regenerative Medicine Advance Therapy
RWA	Reimbursable Work Authorization
RWE	Real-World Evidence
SAMHSA	Substance Abuse and Mental Health Services Administration
SECG	Small Entity Compliance Guide
SERIO	System for Entry Review and Import Operations
SERNAPESCA	Chile's National Director of Fisheries and Aquaculture Service
SLEP	Shelf Life Extension Program
SLTT	State, Local, Tribal and Territorial
SMA	Spinal Muscular Atrophy
SMG	Staff Manual Guide
SNS	Strategic National Stockpile
STEC	Shiga toxin producing E. Coli
SUI	Stress urinary incontinence
SUPPORT	Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment
TAN	Technical Assistance Network
TCE	Trichloroethylene
TCORS	Tobacco Centers of Regulatory Science
TNBC	Triple-Negative Breast Cancer
TPLC	Total Product Lifecycle
TPP	Third-Party Program
TPSAC	Tobacco Products Scientific Advisory Committee
TRS	Tobacco Regulatory Science
TRSP	Tobacco Regulatory Science Program

TTIMS	Transmissible Infections Monitoring System
TTX	Table Top Exercise
UALR	University of Arkansas at Little Rock
UAMS	University of Arkansas for Medical Sciences
UDI	Unique Device Identification
UESC	Utility Energy Service Contract
USACE	U.S. Army Corps of Engineers
USCIITG	United States Critical Illness and Injury Trials Group
USDA	U. S. Department of Agriculture
USDHHS	U. S. Department of Health and human Services
USPS	United States Postal Service
VAI	voluntary action indicated
VNRFRPS	Voluntary National Retail Food Regulatory Program Standards
VQIP	Voluntary Qualified importer Program
WCF	Working Capital Fund
WCFC	Working Capital Fund Council
WEAC	Rico Winchester Engineering & Analytical Center
WGS	Whole Genome Sequencers
WHO	World Health Organization
WONDER	Wide-ranging online data for epidemiologic research

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