DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2022

Food and Drug Administration

Justification of
Estimates for
Appropriations Committees

Letter from the Acting Commissioner

I am pleased to present the fiscal year (FY) 2022 Food and Drug Administration (FDA) Budget.

The FDA protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The Agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products to protect public health and to reduce tobacco use by minors.

Our mission impacts the life of every American, every day. FDA's public health mission encompasses an ever-widening array of foods, additives, cosmetics, medicines and medical devices as FDA regulates approximately 20 cents of every dollar spent annually by American consumers[1]. FDA's mission has steadily grown at a pace that far exceeds the growth in funding as innovative medical products and new foods are brought to market. FDA's scope has broadened alongside continuing critical activities such as ensuring that food products are wholesome, and the medical product supply is adequate to meet patient needs.

The FY 2022 Budget provides FDA necessary investments in critical public health infrastructure, core food safety and medical product safety programs, and vital public health programs. FDA requests a total of $6.5 billion, an overall increase of $477 million compared to the FY 2021 Enacted Level. This includes an increase of $322 million in budget authority.

The Budget includes the following budget authority increases:

- **+$185 million investment in FDA's Critical Public Health Infrastructure.** FDA's Budget includes funding to support critical public health infrastructure needs including enterprise-wide data modernization, improvements to our federal buildings and facilities, expanded laboratory safety efforts, and increased internal capacity to support our growing workforce of over 18,000. This funding will provide vitally needed investments to modernize FDA's outdated data infrastructure, ensure labs and facilities are safe, functional and integrated with program needs, and support fundamental FDA operations to keep pace with new requirements, legislation, and regulatory responsibilities.

- **+$97 million investment in Core FDA Safety Programs.** The Budget provides increases to core food and medical product safety programs that require significant investments to address unmet public health funding needs, as well as emerging issues of concern. Some of the food safety investments include: bolstering the funding provided to programs which are responsible for maternal and infant nutrition; providing much needed additional funds to address numerous emerging food-related chemical and toxicological issues; and strengthening animal food safety oversight. Medical product safety

[1] https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance

investments include: providing dedicated programmatic funding to strengthen and monitor the supply chain; increasing drug safety surveillance and oversight; and improving animal drug safety and predictive technologies.

- **+$61 million in additional investments in Public Health Issues Confronting the US.** The Budget provides increases to address public health needs and key investments to tackle complex challenges facing the country. Investments include increasing safe and secure inspections, promoting health equity, and addressing the opioids crisis by supporting development of new therapies and smarter enforcement.

The investments outlined in this Budget will advance the Agency's immediate priorities and funding needs and will allow us to carry out our vital public health mission.

Sincerely,

Janet Woodcock, M.D.
Acting Commissioner of Food and Drugs

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Department of Health and Human Services
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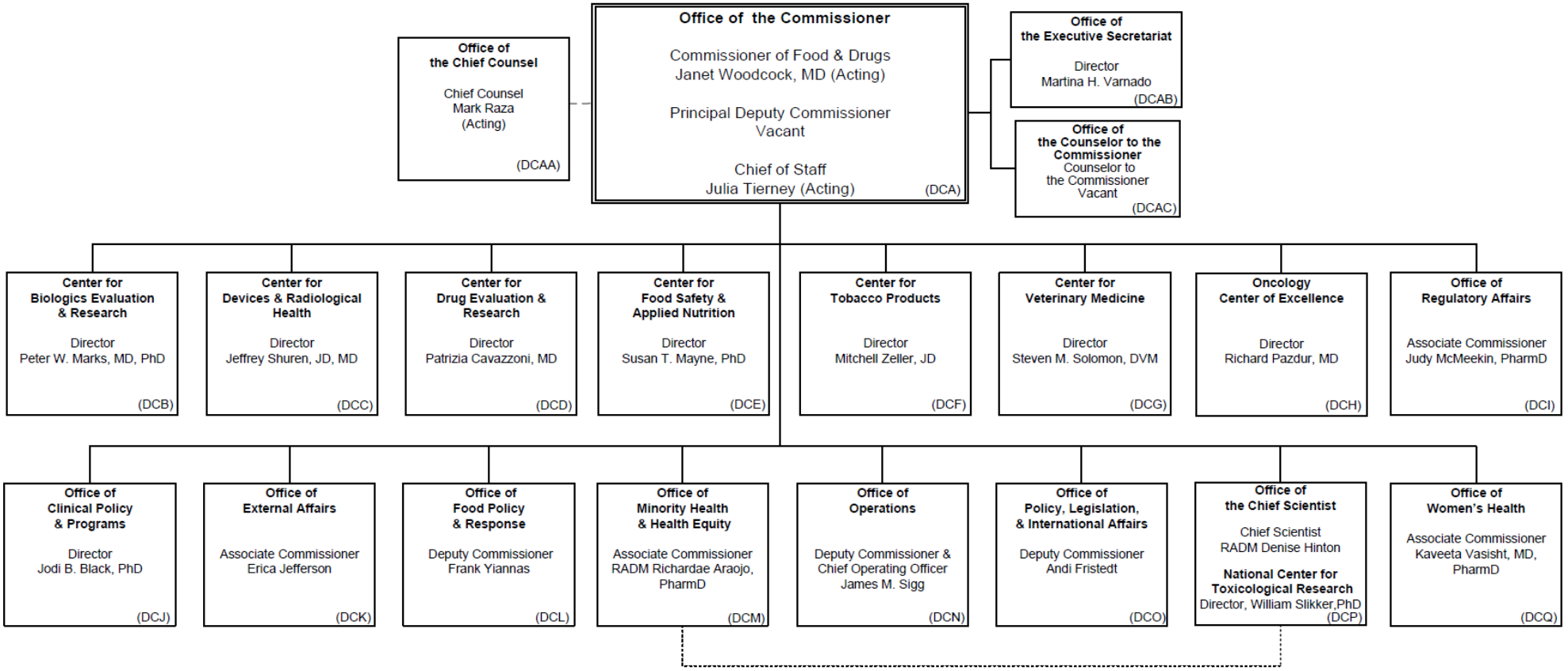
April 2021



Legend:

— — Direct report to DHHS General Counsel

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

FY 2022 EXECUTIVE SUMMARY

PERFORMANCE BUDGET OVERVIEW

EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2022 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 human and animal food, cosmetics, and radiation-emitting products; and regulating tobacco products. FDA's customers and key stakeholders include American patients and consumers; healthcare professionals; veterinarians; 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.

Response to National Opioid Crisis
In FY 2020, FDA reviewed over 50,000 products at the International Mail Facilities (IMF) and identified 215 opioids, with 97% being either destroyed, refused, or referred to FDA's Office of Criminal Inspections and the U.S. Customs and Border Protection (CBP). Additionally, the Chicago IMF Satellite Laboratory was added in partnership with CBP to address the opioid crisis, which increased package screenings for the presence of opioids. This builds upon the work FDA has done to set up inspection stations at the IMFs in 2018 and FDA will continue our efforts to address the national opioids crisis in FY 2022 and beyond.

Novel Human and Animal Drug Approvals, Emergency Use Authorizations for Medical Products, Supporting COVID-19 Vaccine and Therapeutic Development
Since early 2020, FDA's medical product centers have been especially focused on addressing the challenges of the Coronavirus Disease 2019 (COVID-19) public health emergency while continuing to fulfill our normal essential responsibilities. FDA made unparalleled contributions to public health in 2020.

To help facilitate clinical trials during COVID-19, FDA issued a new guidance to protect participant safety and maintain data integrity. The Center for Drug Evaluation and Research (CDER), in collaboration with the Center for Biologics Evaluation and Research (CBER) formed the Coronavirus Treatment Acceleration Program, designed to help bring new COVID-19 therapies to market as soon as possible. As of April 30, 2021 there are more than 600 COVID-19 drug development programs in the planning stages, more than 400 trials that have been reviewed by the FDA, and eight treatments authorized for use during the COVID-19 pandemic through Emergency Use Authorizations (EUAs) in collaboration with the Office of the Chief Scientist (OCS). FDA approved the first drug to treat certain patients with COVID-19. FDA also issued three EUAs for COVID-19 vaccines, and other COVID-19 vaccines are in development.

In 2020, CDER approved 53 novel drugs and many new uses for already FDA-approved drugs to treat a wide range of medical conditions, including infectious, neurological, cardiovascular, endocrine, and autoimmune diseases, rare diseases, and cancers. Thirty-one (58%) of these novel approvals will help patients with rare diseases – many for which no previous treatment had been FDA-approved. In 2020, CBER approved five novel biologics including a CAR-T cell immunotherapy product to treat refractory mantle cell lymphoma (MCL), a new vaccine for the prevention of invasive meningococcal disease, a coagulation factor VIIa to treat and control bleeding episodes in hemophilia patients, an adjuvanted Influenza A H5N1 vaccine, and an oral immunotherapy to mitigate allergic reactions to exposure to peanuts.

Of the many novel drugs and biologics approved over the past year, 16 are intended for treatment of cancer or related conditions, including 9 that were reviewed under the Oncology Center of Excellence's Project Orbis. In February 2021, CBER approved the first Regenerative Medicine Advanced Therapy (RMAT)-designated product for the treatment of certain types of large B-cell lymphoma in adult patients. The RMAT program was established by section 3033 of the 21st Century Cures Act.

FDA has continued its important work to ensure access to cost saving drugs and needed medications. In 2020, the FDA has approved or tentatively approved more than 900 generic drugs, including 72 first generics, such as a new approval for the treatment of severe hypoglycemia (very low blood sugar), one for a widely used albuterol inhaler to treat breathing conditions, and another to treat a parasitic infection. FDA has also worked to help improve patient access to insulin, issuing draft guidance that describes our recommendations regarding a streamlined approach to demonstrating bio similarity and interchangeability for certain insulin products.

CDER also took action to remove from the market a variety of drugs containing potentially cancer-causing nitrosamines. FDA announced the results of research concerning sunscreen safety, took steps to implement a new law that modernizes the way over-the-counter (OTC) drugs are regulated, required benzodiazepines to have stronger risk warnings, required new safety warnings for nonsteroidal anti-inflammatory drugs, and issued guidance to industry to further help those who compound medications identify and prevent insanitary conditions at their facilities.

CDER also made numerous decisions to address and reduce risks related to drug shortages. For example, FDA facilitated manufacturers' extensions of expiration dates, prioritized review and approval of many generic drugs to help ease shortages and issued guidance on the production of alcohol-based hand sanitizer to help boost supply.

The COVID-19 pandemic has driven a need for medical devices, including tests, that has far exceeded what FDA experienced in prior public health emergencies (PHE). The Center for Devices and Radiological Health (CDRH) has utilized Emergency Use Authorization (EUA) authorities to facilitate availability of tests for all six-prior declared PHEs, starting with H1N1 in 2009. The agency authorized a record number of novel medical devices in 2020[1] and has issued 10 times more EUAs during COVID-19 than all other previous PHEs combined. As the pandemic has evolved, CDRH has worked to reduce risk and strategically optimize resources, policies, and processes under the oversight of Center leadership to best serve public health.

[1] https://www.fda.gov/news-events/fda-voices/reflections-record-year-novel-device-innovation-despite-covid-19-challenges

In 2020, CDRH not only experienced an increase in "conventional" premarket submission types (510(k)s[2], De Novos[3], Premarket Approvals (PMAs)[4], and Q-Submissions (Q-Subs)[5]) of over 17,000 files, but also received over 5,500 pre-EUA and EUA submissions. This resulted in an overall increase in premarket submissions of 38%. FDA facilitated the development and availability of a historic number[6] of EUAs for COVID-19 tests and collection kits and personal protective equipment (PPE) to help control the spread of the disease. Many of the EUA requests included device types for which CDRH has never received requests previously, such as ventilators and personal protective equipment (PPE) and, in some cases, novel devices such as decontamination systems. Since the start of the pandemic, CDRH has issued EUAs or granted full marketing authorization to almost 1,300 medical devices for COVID-19.

As of March 2021, FDA has received over 6,000 EUA requests and pre-EUA submissions for medical devices intended to diagnose, treat, or prevent COVID-19. To help address the urgent need for critical devices, the Devices Program developed a novel "umbrella EUA" approach to help streamline authorization for some devices, such as respirators and ventilators. CDRH worked closely with manufacturers through interactive reviews for EUA requests and pre-EUA submissions, including many who were not familiar with FDA or the manufacturing of medical devices. In addition, CDRH reviewed data on a rolling basis to speed the process of reviews. One year since the pandemic hit the U.S., the Devices Program has authorized emergency use for more than 745 medical products, including rapid-at home tests for COVID-19, multi-analyte tests that detect both flu and COVID-19, molecular tests and antigen tests, respirators, ventilators, and remote monitoring systems, as well as granted full marketing authorization to more than 600 additional devices for COVID-19 through the traditional premarket programs. Moreover, CDRH conducted timely review of more than 2 million medical device adverse event reports and completed other pivotal work activities to reduce risk and better address supply chain shortages and counterfeit products related to COVID-19.

The COVID-19 pandemic exposed significant weaknesses in the domestic medical device supply chain resulting from dependence on foreign medical products. In FY 2020 and FY 2021, FDA used current statutory authorities and funding wherever possible to mitigate and prevent device shortages without an existing medical device supply chain and shortages program. Under the new 506J authority provided to the FDA through the CARES Act Section 3121, which allows FDA to collect information during or in advance of public emergencies, CDRH produced guidance to help industry understand the critical supply chain data FDA needs to identify significant disruptions and reduce risk associated with them.

CDRH continues to work towards achieving its goal of ensuring that patients in the U.S. have first-in-the-world access to high-quality, safe, and effective medical devices of public health importance, even while responding to the COVID-19 pandemic. For example, in 2020, CDRH authorized more than 130 novel devices, including the first game-based digital therapeutic to

[2] https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k

[3] https://www.fda.gov/medical-devices/premarket-submissions/de-novo-classification-request

[4] https://www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma

[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program

[6] https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/covid-19-tests-and-collection-kits-authorized-fda-2020-infographic

improve attention function in children with attention deficit hyperactivity disorder and the first cardiac ultrasound software that uses artificial intelligence to guide the user to capture high-quality diagnostic images. CDRH also launched the Digital Health Center of Excellence, an important step in furthering the agency's overarching dedication to the advancement of digital health technology, including mobile health devices, Software as a Medical Device (SaMD), wearables when they are a medical device, and technologies used to study medical products.

CBER worked collaboratively with industry, researchers, federal, domestic, and international partners to accelerate efforts to develop safe and effective vaccines for COVID-19. As part of this effort, CBER issued two guidances for industry on the development of COVID-19 vaccines which have been updated as needed to provide vaccine developers with the most current information. The first provided recommendations regarding the scientific data and information needed to support the development and licensure of safe and effective vaccines to prevent COVID-19. The second provided recommendations regarding the scientific data and information that would support the issuance of an EUA for an investigational vaccine intended to prevent COVID-19, including chemistry, manufacturing and controls information, nonclinical and clinical data, and regulatory and administrative information.

CBER authorized the COVID-19 vaccines in an expedited timeframe while adhering to FDA's rigorous standards for safety, effectiveness, and manufacturing quality needed to support emergency use authorization. FDA held three meetings of the Vaccines and Related Biological Products Advisory Committee (VRBPAC)[7] to seek input from independent scientific and public health experts on each of the vaccine candidates, underscoring our commitment to being as open and transparent as possible about the data and information needed to support authorization of these vaccines. This input, along with the careful and thorough evaluation by CBER's career scientists, is giving the public and medical community trust and confidence that these vaccines meet the FDA's rigorous standards for safety and effectiveness.

The Center for Veterinary Medicine (CVM) made history in FY 2020 with the approval of the first animal biotechnology product for both food and potential biomedical use, a tremendous milestone for scientific innovation. The FDA is committed to continuing its close work with developers to facilitate safe advancements of animal biotechnology. This is also the first approval of an animal biotechnology product from a sponsor participating in our new Veterinary Innovation Program, which focuses on providing greater certainty in the regulatory process, encouraging development and research of innovative public health products, as well as supporting an efficient and predictable pathway to the approval of Intentional Genomic Alterations – or IGAs – in animals.

Among the other 28 pioneer and generic animal drug approvals issued in FY 2020 by CVM are several products to treat, manage or prevent serious diseases in animals, including certain mast cell tumors in dogs, weight loss in cats suffering from chronic kidney failure, and severe asthma in horses. FDA has also provided important guidance to animal drug sponsors by issuing four key guidances to help facilitate the development of new animal drugs.

FDA is incorporating a One Health approach to help solve the complex health problems facing our world today. Approximately 75 percent of recently emerging infectious diseases affecting humans, including HIV, Ebola, and influenza, are zoonotic (i.e., spread from animals to

[7] https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines#meetings

humans).[8] It is also becoming increasingly clear that humans are also transmitting diseases to animals in what is often referred to as "reverse zoonoses." The health of humans, animals and the environment are intrinsically linked, and FDA is incorporating this approach to address complex regulatory and scientific challenges.

Since the epidemic began, the National Center for Toxicological Research (NCTR) has taken many actions to support FDA's regulatory role. Numerous research projects have been initiated at NCTR including a project to develop an approach to rapidly indicate effectiveness of COVID-19 therapeutic treatments, a project in coordination with OCS using computational drug-repositioning principles; and an AI-powered network pharmacology approach to comprehensively explore the opportunity of existing drugs for their potential to treat COVID-19.

COVID-19 Pandemic Response and Supplemental Funding

The COVID-19 pandemic has significantly impacted and dominated FDA's work and focus since early 2020. FDA has proactively issued policies and guidance to provide regulatory flexibility to respond to the pandemic as well as emergency use authorizations and worked to address supply chain vulnerabilities. FDA has made available safe and effective medical devices, therapeutics, vaccines, and human and animal drug approvals to fulfill our responsibilities to ensure that safe and reliable medical products are available to the American public.

FDA continues to actively assess the impact of new strains on authorized products and continues to evaluate the impact each variant may have on the effectiveness or utility of authorized medical products. FDA has adapted current operations as a result of COVID-19 and the emerging SARS-CoV-2 variants and will continue to address the challenges of this unprecedented public health emergency.

Since March 2020, FDA received $718 million in appropriations or directed transfers from Coronavirus Preparedness and Response Supplemental (P.L. 116-123), the Coronavirus Aid, Relief, and Economic Security Act or CARES Act (P.L. 116-136), the Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139), the Consolidated Appropriations Act, 2021 (P.L. 116-260), and the American Rescue Plan (P.L. 117-2). The COVID-19 emergency supplemental resources have supported FDA's ability to address the COVID-19 pandemic. The funds support FDA's ability to facilitate the development and availability of medical countermeasures, therapies and vaccines to diagnose, treat, and prevent COVID-19; surveille the supply chains for potential shortages or disruptions and fraudulent products; and help to mitigate risks related to such impacts, as necessary to protect the public health. The funds supported critical research to provide essential data and new tools using AI that will offer FDA a way to systematically survey and prioritize approved or investigational drugs for their potential use to treat COVID-19. The funds also supported configuration of FDA's foundational surveillance systems to monitor postmarket safety and effectiveness for preventative vaccines to allow near real-time surveillance through coordination with several partners, including government, academic and large non-government healthcare data systems.

FDA has also identified several legislative proposals that could aid in the Agency's pandemic response. The proposals include authorities to require more accurate supply chain information,

[8] World Organization for Animal Health (the OIE) (2018). – One Health "at a glance". Available at: http://www.oie.int/en/for-the-media/onehealth/ (accessed 28 Sep 2018).

enhance authorities related to potential shortages for foods and medical devices, enhance the use of records in advance or in lieu of inspections, expand information sharing with the states, and extend enforcement authority and penalties for counterfeit devices.

Over the past year, FDA initiated cross-agency efforts and achievements that both support the response to and apply lessons learned from COVID-19 to adapt and strengthen our work, as well as to increase coordination of scientific leadership, agency operations, communications, risk management, and programming. The Agency gained valuable insight from our experience during the pandemic, which has helped improve our response to the current crisis and will help us prepare for future public health emergencies.

New Era of Smarter Food Safety

In July 2020, FDA released the New Era of Smarter Food Safety Blueprint, which outlines the steps the FDA will take over the next decade to create a more digital, traceable and safer human and animal food system.[9] 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 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. The blueprint outlines the work FDA plans to undertake over the next decade to modernize its food safety approaches to bend the curve of foodborne illness and protect consumers from unsafe food. In 2020, the on-going COVID-19 pandemic has accelerated the need for many of the goals in the blueprint, such as enhancing traceability to better understand supply chain vulnerabilities, exploring the use of remote and virtual food inspections, addressing safety vulnerabilities for foods ordered online, and supporting strong food safety cultures that support prevention. Selected accomplishments towards the goals of the New Era of Smarter Food Safety are identified in the four items listed below.

Imported Seafood Artificial Intelligence/Machine Learning Pilot

As part of efforts to better leverage predictive analytics, FDA implemented a pilot program to understand the abilities of artificial intelligence (AI), specifically machine learning (ML), to rapidly analyze data for screening foods imported into the United States. Machine learning is a type of AI that makes it possible to rapidly analyze data, automatically identifying connections and patterns in data that people or even our current rules-based screening system cannot see. In August 2020, the FDA announced the results of the proof-of-concept for imported seafood, which demonstrated that machine learning could almost triple the likelihood of identifying a shipment containing potentially contaminated products. This is especially important since the United States imports upwards of 94 percent of its seafood supply. In February 2021, FDA launched the second phase of the AI imported seafood pilot, an in-field pilot, which is designed to enhance and improve the agency's ability to quickly and efficiently identify imported seafood products that may pose a threat to public health.

[9] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint

Tracking and Tracing of Food

In September 2020, FDA issued the *Proposed Rule for Food Traceability* as the first step toward enhanced traceability through harmonization of proposed key data elements and critical tracking events. Food traceability is the ability to follow the movement of a food product and its ingredients through all steps in the supply chain, both backward and forward. Traceability involves documenting and linking the production, processing, and distribution chain of food products and ingredients. In the case of a foodborne illness outbreak or contamination event, efficient product tracing helps government agencies and those who produce and sell food to rapidly find the source of the product and where contamination may have occurred. This enables faster removal of the affected product from the marketplace, reducing incidences of foodborne illnesses. Following the release of the proposed rule, FDA conducted three public meetings to discuss the rule and accepted public comments through the Federal Register. The proposed rule, when finalized, would establish a standardized approach to traceability recordkeeping, paving the way for industry to adopt, harmonize, and leverage more digital traceability systems in the future, as part of the goals of FDA's New Era of Smarter Food Safety.

FDA-Mexico Food Safety Partnership

In October 2020, the United States and Mexico officially launched the FDA-Mexico Food Safety Partnership (FSP), broadening and strengthening the scope of our existing partnership to include the safety of all human food regulated by the FDA. The earlier Produce Safety Partnership, signed in 2014, had created a framework for Mexico and the U.S. to work together to contain potentially serious outbreaks related to produce and to lessen consumer exposure to foodborne disease. In addition to produce, the new FSP includes all human food regulated by the FDA, as Mexico exports seafood, processed fruits and vegetables, and snack foods to the U.S. — totaling about $25 billion in 2019, according to the Office of the U.S. Trade Representative and the National Oceanic and Atmospheric Administration. The FSP also embraces the use of new and emerging technologies, including elements of the FDA's New Era of Smarter Food Safety initiative, to solve complex public health challenges. Further, it strengthens collaboration with academia, consumer groups, and other governmental offices in the U.S. and Mexico.

Food Supply Chain Continuity and COVID-19 Vaccine Distribution to Food and Agriculture Workers

To help ensure the continuity and resiliency of the food and agriculture sector, FDA developed a new data analysis tool called 21 *Forward* to provide a comprehensive, data-backed understanding of how COVID-19 is currently impacting all nodes in the food supply chain, from producers and growers to grocery stores. The unprecedented scale and pace at which the COVID-19 pandemic has spread presents unique challenges to the food supply chain. Utilizing a combination of FDA and and U.S. Department of Agriculture (USDA) data and the Centers for Disease Control and Prevention (CDC) forecasting for COVID-19, the 21 *Forward* platform is used to help FDA identify where there may be risks for interruptions in the food supply chain and conduct targeted outreach to the food industry to offer additional resources and technical assistance in addressing challenges. In collaboration with HHS, CDC, and USDA, data from *21 Forward* are also being made available to assist states with their planning efforts for vaccine distribution to workers in the food and agriculture sectors.

Produce Safety

In March 2020, FDA released the Leafy Greens STEC Action Plan[10] to foster a more urgent and collaborative approach to preventing leafy greens outbreaks caused by STEC. While millions of servings are consumed safely every day, fresh leafy greens have been implicated in outbreaks of foodborne illness caused by Shiga toxin-producing *E. coli*. While most strains of *E. coli* are harmless, Shiga toxin-producing *E. coli*, or STEC, can be life-threatening. Between 2009 and 2018, the FDA and the CDC identified 40 foodborne outbreaks of STEC infections with a confirmed or suspected link to leafy greens in the United States.

In 2020, FDA made significant progress on the Leafy Greens STEC Action Plan by enhancing prevention strategies, improving response activities by the agency and other entities, and identifying and addressing the knowledge gaps that exist around STEC contamination of leafy greens. FDA launched the California Longitudinal Study, developed an efficacy protocol for the development and registration of antimicrobial treatments for pre-harvest agricultural water and took critical steps to advance traceability of leafy greens. FDA has also conducted several focused inspections, follow-up investigations and sampling assignments.

In April 2021, FDA took additional steps to advance the safety of leafy greens. FDA released a report on the investigation into the Fall 2020 outbreak of E. coli O157:H7 illnesses[11] linked to the consumption of leafy greens. The report describes findings from the investigation, as well as trends key to understanding leafy greens outbreaks linked to the California Central Coast growing region (encompassing the Salinas Valley and Santa Maria growing areas) that have occurred every fall since 2017. Based on this investigation, FDA recommends that growers of leafy greens in the California Central Coast Growing Region consider this reoccurring E. coli strain a reasonably foreseeable hazard, and specifically of concern in the South Monterey County area of the Salinas Valley.

FDA also released an updated version of the Leafy Green STEC Action Plan[12], reaffirming the need for collaborative action to improve the safety of leafy greens, and building on the work accomplished in 2020. The updates for 2021 include a renewed emphasis on actions to help prevent contamination from adjacent land, to include new actions that build on the accomplishments and learnings from the 2020 plan, and to renew our commitment to actions that were difficult to accomplish in 2020 due to challenges presented by the COVID-19 pandemic.

Increasing the Safety of Foods for Babies and Young Children

In March 2021, FDA issued a letter to baby and toddler food manufacturers and processors covered by the preventive control provisions of the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food rule. The letter reminds them of their existing responsibility to consider risks from chemical hazards—including toxic elements—when conducting a hazard analysis.[13]

In April 2021, FDA announced a comprehensive plan to further reduce levels of toxic elements such as lead cadmium, mercury and arsenic in foods for babies and young children. The "Closer

[10] https://www.fda.gov/food/foodborne-pathogens/2020-leafy-greens-stec-action-plan

[11] https://www.fda.gov/food/outbreaks-foodborne-illness/factors-potentially-contributing-contamination-leafy-greens-implicated-fall-2020-outbreak-e-coli

[12] https://www.fda.gov/food/foodborne-pathogens/leafy-greens-stec-action-plan

[13] https://www.fda.gov/media/146423/download

to Zero: Action Plan for Baby Foods[14]" identifies actions the agency will take to reduce exposure to toxic elements from foods eaten by babies and young children to as low as possible. FDA has prioritized babies and young children because their smaller body sizes and metabolism make them more vulnerable to the harmful effects of these contaminants.

Consumer Nutrition Education Initiatives

The Center for Food Safety and Applied Nutrition (CFSAN) launched two new consumer education campaigns in 2020, one involving the New Nutrition Facts[15] label to help consumers use the updated Nutrition Facts label on food packages to make healthier food choices, and another called Feed Your Mind[16], in partnership with the U.S. Department of Agriculture and the U.S. Environmental Protection Agency (EPA), to provide science-based information on genetically engineered foods, commonly called GMOs.

In March 2020, FDA launched the "Feed Your Mind"[17] initiative which features a wide range of resources designed specifically for consumers, health care professionals and students. These materials feature new web content, fact-sheets and videos, engaging graphics and stories to provide information about genetically engineered foods. This initiative is an on-going effort, with additional materials planned for release later in 2021.

In June 2020, FDA also announced "The New Nutrition Facts Label: What's in it for You?" education campaign, which was developed to raise awareness about the changes to the Nutrition Facts label, increase its use, and help consumers, health care professionals, and educators learn how to use it as a tool for maintaining healthy dietary practices. The education campaign includes outreach through many channels including social media, indoor/outdoor advertising, videos, and consumer-friendly downloadable educational materials.[18]

Inspections and Investigations, Operation Quack Hack, and Lab Safety During the Era of COVID-19

To respond to new pandemic-related complexities to normal operations and sustain performance, FDA prioritizes work and incorporates mechanisms that optimize the agency's inspection operations. These include alternative inspectional approaches and novel assessment technologies that provide us with useful information to help ensure the safety and quality of the products consumers need. FDA also implemented the COVID-19 Advisory Rating system using real-time data to inform investigators when and where it is safest to conduct prioritized domestic inspections.

FDA continues to make important strides in preventing the distribution of fraudulent products, including disrupting many new efforts to exploit consumers through the sale of unproven

[14] https://www.fda.gov/food/metals-and-your-food/closer-zero-action-plan-baby-foods

[15] https://www.fda.gov/food/nutrition-education-resources-materials/new-nutrition-facts-label

[16] https://www.fda.gov/food/consumers/agricultural-biotechnology

[17] https://www.fda.gov/food/cfsan-constituent-updates/fda-launches-feed-your-mind-help-consumers-better-understand-science-behind-foods-derived-genetic

[18] https://www.fda.gov/food/nutrition-education-resources-materials/new-nutrition-facts-label

medical products, illegitimate test kits, and substandard or counterfeit respirators being offered for sale on the internet.

To proactively identify and neutralize these threats to consumers, and particularly to protect consumers from fraudulent FDA-regulated products during the COVID-19 pandemic, the FDA launched Operation Quack Hack in March 2020.

To date, the FDA has identified more than 1,300 fraudulent and unproven human medical products related to COVID-19, and Operation Quack Hack initiatives have led domain registrars and online marketplaces to review and take down hundreds of websites or listings illegally selling unproven FDA-regulated products. This is in addition to normal enforcement efforts by Office of Criminal Investigations, which last year initiated more than 600 criminal investigations targeting violations related to FDA-regulated products.

FDA's Office of Regulatory Affairs (ORA) continued to work together this year with states and the Centers for Disease Control and Prevention (CDC) to investigate the outbreak involving thousands of lung injuries and multiple deaths associated with vaping.

A cornerstone of the FDA's scientific work is to ensure that FDA laboratories operate in a safe and secure manner. For example, FDA continued a multi-year lab revitalization effort with the relocation of the Kansas City Laboratory to a new state-of-the-art facility to continue its own independent scientific testing to support both risk assessment and regulatory programs for the foreseeable future. FDA's work in this area depends on the collaborative efforts of the FDA's centers, ORA, our Employee Safety and Occupational Health, and the Office of Laboratory Safety to protect FDA staff.

In 2020, FDA biosafety and biosecurity professionals were integral to addressing the conditions for FDA staff to return to work safely, including laboratory staff doing SARS-CoV-2 research, given the new challenges and constraints posed by the transmission characteristics of SARS-CoV-2. They also played an important role in ensuring public safety. For example, ORA investigators and ORA laboratories worked together with the Center for Drug Evaluation and Research (CDER) to collect and analyze hundreds of hand sanitizer samples associated with an outbreak of illnesses and multiple deaths. While ORA adjusted inspections during the pandemic to protect employees, FDA has made considerable progress in other priority areas.

FDA expanded its working relationship with the U.S. Customs and Border Protection (CBP), and the U.S. Immigration and Customs Enforcement - Homeland Security Investigations with a new memorandum of understanding that identifies specific roles and responsibilities for DHS, CBP, ICE-HSI, and FDA when responding to controlled substances, unapproved drug imports including counterfeits, medical devices, and combination products interdicted at International Mail Facilities (IMFs). It also includes the establishment of satellite laboratories at selected IMFs, bringing FDA and CBP scientists with special training and advanced tools together for rapid testing. The first of these laboratories is in operation at the IMF in Chicago.

FDA consumer safety officers at ports of entry have continued to examine imported products. Working with CBP, investigators discovered shipments of sub-potent and dangerous methanol-

containing hand sanitizers from Mexico. Due to the massive increase in the number of new hand sanitizer manufacturers and importers, ORA initiated "Operation Dirty Hands" to increase screening of potentially adulterated import shipments of sanitizers. Additionally, in Fiscal Year 2020, FDA examined 20% more international mail parcels than in FY 2019. The mail parcels referred to FDA from CBP were unapproved prescription drugs, unapproved prescription opioid drug products, dietary supplements containing active pharmaceutical ingredients, medical devices such as contaminated decorative contact lenses and fraudulent covid-19 test kits, to name a few examples.

In support of the nation's COVID-19 response, ORA implemented strategies to facilitate the importation of COVID-related PPE and diagnostic tests to address shortages of these products, while denying entry to unauthorized or fraudulent products. ORA expedited over 3 million entry lines of PPE by adjusting import screening and issuing instructions to importers and FDA staff streamlining the entry process. ORA established a helpdesk for importers which has answered over 17,000 inquiries to date. FDA also protected consumers from unauthorized COVID-19 diagnostic tests by implementing an enforcement process with CBP, resulting in more than 800 FDA refusals and CBP seizures, and developed a-sampling program with CDC/National Institute for Occupational Safety and Health (NIOSH) to ensure filtering facepiece respirators meet standards; these efforts supported inclusion of more than 150 compliant foreign producers in EUAs and identified more than 200 unacceptable foreign producers.

In addition, ORA inspected seven cargo flights of medical products donated to the U.S. by six foreign governments. Before each flight, ORA coordinated with the U.S. Department of State, Federal Emergency Management Agency (FEMA), CBP, EPA, and other FDA headquarters and Center staff to resolve diplomatic and logistical issues and determine an inspection strategy. When the flights arrived, ORA inspected the cargo to ensure that the quantities and products matched what was declared and that all cargo complied with applicable regulations. FEMA distributed most of these medical products to hospitals, nursing homes, and long-term care facilities throughout the country.

Data and Technology Modernization Action Plans

In March 2021, FDA announced a Data Modernization Action Plan (DMAP). The DMAP builds on FDA's Technology Modernization Action Plan (TMAP), published in September 2019, which laid out a foundation for modernizing the FDA's technical infrastructure and signaled the development of the FDA's ongoing strategy concerning data management and data itself. FDA's Data Strategy focuses on the stewardship, security, quality control, analysis, and real-time use of data to accelerate the path to better therapeutic and diagnostic options for people and animals, better secure the food supply chain, and provide state-of-the-art tools to enhance and promote public health.

The DMAP proposes a framework and actionable recommendations for FDA's Data Strategy. It consists of 3 key components:

1. Identify and execute high value driver projects for individual centers and for the Agency;
2. Develop consistent and repeatable data practices across the Agency; and,

3. Create and sustain a strong talent network combining internal strengths with key external partnerships.

Data have always formed the basis of the FDA's science-based regulatory decision-making. With this Plan, FDA will continue to make advancements to protect the public health by ensuring safety, efficacy and security of medical & veterinary products, devices, food and cosmetics, regulate the manufacturing, marketing and distribution of tobacco products, speed innovations that make products more effective, safer and more affordable, and ensure the security of the food and medical supply chain by responding to deliberate and naturally emerging public health threats.

Tobacco Regulation

On April 29, 2021, FDA announced that it is committing to advancing two tobacco product standards to significantly reduce disease and death from using combusted tobacco products, the leading cause of preventable death in the U.S. The FDA is working toward issuing proposed product standards within the next year to ban menthol as a characterizing flavor in cigarettes and ban all characterizing flavors (including menthol) in cigars. This decision is based on clear science and evidence establishing the addictiveness and harm of these products and builds on important, previous actions that banned other flavored cigarettes in 2009.

In March 2020, CTP issued a final rule to require new health warnings on cigarette packages and in cigarette advertisements. Once implemented, these warnings will be the most significant changes to cigarette labels in more than 35 years and will considerably increase public awareness of lesser-known, but serious negative health consequences of cigarette smoking. FDA has issued guidance to assist small businesses and to provide recommendations for industry regarding the submission of plans for cigarette packages and advertisements.

The FDA is continuing to address the alarming increase in the use of e-cigarettes among our youth, and the significant health implications of nicotine addiction and tobacco use more broadly. FDA marked a milestone last September to protect public health, including the Agency's effort to combat youth e-cigarette use: the premarket review submission deadline for certain deemed new tobacco products, including e-cigarettes, was September 9, 2020. Applications are now undergoing a robust scientific evaluation to determine if products are appropriate for the protection of public health, the statutory standard for receiving FDA authorization. FDA is taking compliance and enforcement action against products that were not the subject of timely submitted applications.

Also in fall 2020, the FDA, in partnership with the CDC, released the results of the 2020 National Youth Tobacco Survey, which shows 1.8 million fewer U.S. youth currently using e-cigarettes compared to 2019, as well as reductions in youth current use of cigarettes, cigars, smokeless tobacco, and tobacco products overall. This is good news, but the FDA remains concerned about the 3.6 million U.S. youth who currently use e-cigarettes and the nearly 5 million youth who currently use any tobacco product. The data also shows a surge in youth use of disposable e-cigarettes and that more than 8 out of 10 youth e-cigarette users report use of flavored products. CTP's compliance actions against products targeted to young people continued throughout the year.

Maternal and Perinatal Health

NCTR's Virtual Center of Excellence for Perinatal and Maternal Pharmacology and Toxicology —also known as the FDA Perinatal Health Center of Excellence (PHCE) — focuses on the perinatal period (the period-of-time including pregnancy, child birth, and infant/child development) which is a vastly understudied population. PHCE works to fill knowledge gaps about safety, efficacy, or potential toxicity that currently exist during the perinatal period, with the goal to strengthen the scientific basis of decision-making for FDA-regulated products used during pregnancy and in premature infants, newborns, and children. Significant strides are being made through the PHCE projects, which have primary investigators representing CDER, CBER, CFSAN, CVM, and NCTR. A recently completed PHCE-funded study examined polyfluorinated alkyl substance (PFAS)-based compounds that are used in intravenous tubing on neonates in intensive care. It is important to better understand this substance and how it may affect the neonate population. Additionally, in FY 2021, PHCE scientists will provide preliminary results on the perinatal developmental toxicity and neurotoxicity of inorganic arsenic, which is an environmental contaminant that is taken up by growing plants, and so is present in low levels in some food.

BUDGET STRUCTURE AND PRIORITIES

FDA's 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, and medical devices 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.

- **Infrastructure: Facilities Investments and Rent** – ensures FDA staff have modern, safe, and reliable infrastructure and facilities, including labs, across the country to execute the agency's vital public health mission.

- **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, including youth, about tobacco products and the dangers their use poses.

ENTERPRISE RISK MANAGEMENT

To support the FDA core mission, operations, and functions, FDA employs Enterprise Risk Management (ERM), a method for assessing and prioritizing risks. ERM helps to ensure FDA's top risks are understood and examined to mitigate the risks to accomplishing the Agency's public health mission. This program supports the OMB A-123 and A-11 guidance that emphasizes the importance of alignment of Internal Controls, Enterprise Risk Management, and Agency strategic goals to budgetary requests. The application of ERM methodology and tools empower FDA to elevate the right enterprise risks to FDA leaders and governance bodies at the right time, improving FDA mission performance. The FY 2022 Budget identifies investments that address enterprise risks as part of the alignment of budget and enterprise risk management activities.

FY 2022 BUDGET

FDA's responsibilities are ever growing and more complex due to advances in food and medical product technology, global supply chains, and emerging scientific approaches, such as artificial intelligence. The FY 2022 Budget will support FDA's mission to ensure the safety and efficacy of medical products, protect and promote public health, and assure the safety of new food products and dietary supplements.

The Budget Authority Crosswalk in the suite of numbers tables provides a breakout of the proposed initiatives. New initiatives are summarized in the following sections by major activity with increases identified in parentheses. These initiatives balance long-term goals that help FDA to achieve its strategic and budget priorities with shorter-term activities needed to respond to urgent public health needs related to COVID-19.

FY 2022 REQUEST

The FY 2022 Budget is $6.5 billion, an overall increase of 7.9 percent or $477 million above the FY 2021 Enacted level. The request includes $3.6 billion in budget authority – an increase of $322 million or eight percent compared to FY 2021 Enacted – and $2.9 billion in user fees – an increase of $155.3 million or six percent compared to FY 2021 Enacted.

The Budget reflects investments to advance FDA's budget priorities. The Budget requests funding for initiatives that are agency-wide and cross-cutting in nature, advance Food Safety and Medical Product Safety efforts, and address critical Infrastructure, Buildings and Facility needs. These are significant investments in critical public health infrastructure, core food safety and medical product safety programs, and vital public health programs:

- **Critical Public Health Infrastructure** – FDA's Budget includes funding to support critical public health infrastructure needs including enterprise-wide data modernization, improvements to our federal buildings and facilities, expanded laboratory safety efforts, and increased internal capacity to support our growing workforce of over 18,000. This funding will provide vitally needed investments to modernize FDA's outdated data infrastructure, ensure labs and facilities are safe, functional and integrated with program needs, and support fundamental FDA operations to keep pace with new requirements, legislation, and regulatory responsibilities.

- **Core FDA Safety Programs** – The Budget provides increases to core food and medical product safety programs that require significant investments to address unmet public health funding needs, as well as emerging issues of concern. Some of the food safety investments include: bolstering the funding provided to programs which are responsible for maternal and infant nutrition; providing much needed additional funds to address numerous emerging food-related chemical and toxicological issues; and strengthening oversight of animal foods. Medical product safety investments include: providing dedicated programmatic funding to strengthen and monitor the supply chain; increased drug safety surveillance and oversight; and, improving animal drug safety and predictive technologies.

- **Additional Investment in Public Health Issues Confronting Americans today** – The Budget also provides resources to address public health needs and investments to tackle these complex challenges. Investments include increasing safe and secure inspections, promoting minority health and health equity and addressing the opioids crisis by supporting development of new therapies and smarter enforcement.

CROSS-CUTTING

The FY 2022 Budget includes $200.5 million, an increase of $170.8 million, to support agency-wide cross-cutting initiatives that support both Food Safety and Medical Product Safety. These initiatives include an Agency-wide Data Modernization and Enhanced Technologies effort, increased funding for inspections conducted by the Office of Regulatory Affairs (ORA), funding to address pay increases, funding for the Office of Minority Health and Health Equity, and crosscutting FDA Capacity Building activities. The Capacity Building efforts fund the Office of Laboratory Safety, Office of Chief Counsel, and FDA Essential Services such as Cybersecurity, IT Equipment Replacement, and business functions within the Office of Operations.

FDA's responsibilities are ever growing and more complex due to advances in food and medical product technology, global supply chains, and artificial intelligence. FDA needs agency-wide investments to address its public health infrastructure and support through these crosscutting initiatives.

DATA MODERNIZATION AND ENHANCED TECHNOLOGIES (+$75.9 MILLION / 72 FTE)

The FY 2022 Budget includes an increase of $75.9 million, for a total of $82.9 million, to support FDA data modernization by building core programs and infrastructure aligned to the specific needs in both the Foods and Medical Product programs as well as the critical enterprise technology capabilities. The Budget supports FDA's coordinated data modernization agenda that includes centralized resources and capabilities plus program-specific customization.

Technology, broadly defined, is revolutionizing human and animal health and generating exponential amounts of data. Scientific breakthroughs have enabled the development of new, more personalized therapeutic options and treatments, advanced manufacturing and information technologies, and state-of-the-art solutions such as blockchain, genomics, and real-time analytics. As a byproduct, the amount and variety of data that FDA generates, need and use is rapidly increasing. FDA is entering an era in which the data that is collected during the routine care of patients, coupled with traditional clinical trial evidence, will be used to generate steady improvements in patient care and FDA decision making.

FDA is a science-based agency that uses data to conduct our tasks in service of public health. Operational data power our financial systems and management of personnel within the Agency. Other data types, such as genomics, toxicology data, and output from medical devices, are a part of the evolving data ecosystem. Data-informed capabilities, such as artificial intelligence (AI) and distributed ledger solutions like blockchain, will be critical to support FDA's – and therefore our nation's – priorities. However, FDA utilizes antiquated methods such as inspecting large

volumes of PDFs, often "by hand," in order to identify critical safety signals such as human and animal drug safety concerns or emerging foodborne outbreaks.

In response, the FY 2022 Budget provides a significant investment to modernize the Agency's data infrastructure and put data to work. The FY 2022 request builds specific expertise and capabilities across FDA, while also taking an overall view of FDA and how the elements come together to advance the Administration's priorities.

The initiative includes two components: Enterprise Technology and Data ($44.5 million) and complementary program-specific investments ($31.4 million). The program-specific projects include: New Era of Smarter Food Safety ($17.4 million), Modernizing Data Enterprise and Infrastructure at CVM ($10.3 million), Digital Transformation at CDRH ($2.8 million), and Regulatory Information Management Modernization at CBER ($0.9 million). These resources are also captured in the Food Safety and Medical Product Safety totals noted on pages 22 and 25.

Enterprise Technology and Data (+$44.5 million / 49 FTE)
The FY 2022 Budget includes a total of $44.5 million for an Agency-wide centralized enterprise data modernization effort to strengthen the common data infrastructure established through the Technology Modernization Action Plan (TMAP) and Data Modernization Action Plan (DMAP). To fulfill its mission, FDA requires the ability to continuously access, aggregate, visualize and analyze multiple sources of information. The COVID-19 pandemic has highlighted, at a national and international level, the need to modernize FDA's IT infrastructure, analytic services, talent, and tools. IT is not only a core utility, but also the key infrastructure that facilitates seamless yet secure networking, data exchange and collaboration. FDA shares data both internally and externally and requires the ability to quickly and reliably extrapolate this information to inform emergency response as well as standard oversight activities.

FDA will focus on technical and data infrastructure in early years and gradually shift our financial investments toward programs and projects that utilize our data capabilities over time. To accomplish this, we will leverage our Agency-wide data and technology governance model, centralized financial decision-making and a culture that promotes sharing lessons learned across the Agency to accelerate the development and deployment of new data-rich capabilities like AI. The COVID-19 public health emergency accelerated the timing of our focus on enterprise data strategy with several investments to hire critical personnel and build a central data function. The FY 2022 Budget builds on these initial steps, incorporates lessons learned, and progresses FDA on a path for the modern era.

Program-Specific Investments (+$31.4 million / 23 FTE)
In addition to the $44.5 million for centralized enterprise technology and data activities, the FY 2022 Budget includes an increase of $31.4 million, for a total of $38.4 million, for four complimentary program-specific investments. Of the $31.4 million identified for the program-specific investments, $22.8 million is included for Food Safety and $8.6 million is for Medical Product Safety totals referenced on pages 22 and 25. Through the Agency-wide data and technology governance process, FDA Centers and Offices will build on the centralized data investments and strategy explained above to support customization and specific applications to support the following programs and projects.

New Era of Smarter Food Safety (+$17.0 million / 15 FTE)
This section of the FY 2022 Budget provides an increase of $17.0 million, a total of $20.6 million, for the New Era of Smarter Food Safety. This investment will provide for specific applications for food safety that align to FDA's Blueprint for a New Era of Smarter Food Safety[19], as well as the agency's cross-cutting Technology and Modernization Act Plans. The goal of the Smarter Food Safety initiative, as outlined in this Blueprint, is to bend the curve of foodborne illness in this country by reducing the number of illnesses attributed to FDA-regulated foods and to protect consumers from other unsafe foods. The New Era builds on the modernized food safety regulatory framework created by the FDA Food Safety Modernization Act (FSMA) by leveraging the use of new and emerging technologies and approaches to strengthen our predictive capabilities, accelerate prevention, and speed outbreak response.

To achieve the goals of the New Era of Smarter Food Safety, FDA will invest in enhanced technologies and data analytics to strengthen prevention of human and animal foodborne illnesses, enable food contamination to be rapidly traced to its source, and better understand food safety challenges. FDA will promote and support industry adoption of new traceability technologies and incrementally invest in predictive analytics to ensure that FDA can receive, efficiently process, and share new data streams, particularly in emergency response and outbreak scenarios. Improved traceability will help FDA respond more quickly to outbreaks, as well as expedite recalls, by reducing the time it takes to trace the origin of contaminated human and animal foods. Beyond outbreaks, the current lack of traceability is also a barrier to the transparency needed to create a more resilient and interoperable food system that can nimbly adjust supply chains during crises, such as the COVID-19 pandemic.

FDA will also further develop new predictive analytical capabilities to integrate rules-based and machine learning (ML) systems to work in tandem to target violative shipments of FDA-regulated products coming across our borders. Machine learning is a type of artificial intelligence (AI) that makes it possible to rapidly analyze data, automatically identifying connections and patterns in data that people or even our current rules-based screening system cannot see. In 2020, FDA completed a proof of concept for imported seafood that demonstrated AI/ML could almost triple the likelihood of identifying a shipment containing products of public health concern, while also expediting the clearance of lower risk seafood shipments. The FY 2022 request will support FDA's cross-cutting efforts to leverage use of AI-based technologies as part of both the New Era of Smarter Food Safety and Data Modernization and Enhanced Technologies initiative.

Modernizing Data Enterprise and Infrastructure (+$10.7 million / 8 FTE)
In FY 2022, FDA requests an increase of $10.7 million for CVM to modernize outdated and disparate IT systems and business processes to increase efficiency and effectiveness, reduce overall costs and provide the flexibility needed to meet the challenges of an

[19] https://www.fda.gov/media/139868/download

evolving regulatory landscape. The American public and regulated industry rely on CVM to evaluate the safety and effectiveness of animal drugs and to review animal food ingredients to help keep animals healthy, while also ensuring that the meat, milk, and eggs from food-producing animals are safe for people to eat. The health of humans and animals are intrinsically linked and updates are critical to position CVM to actively monitor animal food and drug products marketed in the U.S. for potential safety issues, and to quickly identify, analyze and mitigate any serious issues that may result in harm to humans or animals. CVM currently lags behind the industries it regulates and its information technology infrastructure is currently founded on the digitalization of paper-based processes and antiquated systems that are significantly outdated. For example, this request will increase CVM's capacity for data warehousing, analytics and reporting to keep pace with advances in bioanalytical evaluation for human and animal food contaminants, as well as advances in DNA editing and sequencing. Of the $10.7 million, $5.8 million is aligned to food safety and $4.9 million is aligned to medical product safety.

Recognizing the interconnectedness between humans, animals, and the environment plays a fundamental role in strategically evaluating, preparing for and responding to the nation's most complex and emerging public health threats. To solve the complex health problems facing our world today, collaboration is critical.

Digital Transformation (+$2.8 million)
In FY 2022, FDA requests an additional $2.8 million, for a total of $40.8 million, to support the Devices Program's Digital Transformation initiative. FDA needs modern systems to support patients and the ecosystem. Timely patient and consumer access to new, safe, innovative devices and continued safeguards depend on FDA having modernized IT systems. CDRH'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.

Regulatory Information Management Modernization (+$0.9 million)
In FY 2022, FDA requests an increase of $0.9 million to support CBER's regulatory capabilities through improved information management and data infrastructure, which are critical to managing and reviewing the increased number of novel and scientifically complex biologics, including those to prevent and treat emerging and changing infectious diseases such as COVID-19.

When FDA applies more advanced technologies to its work, the Agency can help support innovative development of FDA-regulated products and new methods of generating data to assure those products meet FDA's standards and have the assurances that patients depend upon. To do this, FDA must also invest in its regulatory programs to keep pace

with the tremendous changes taking place in how human and animal medical products are being produced so that we can adequately ensure safety of these innovative products and industries, and their responsible development. FDA's ongoing strategy around data itself will accelerate the path to better therapeutic and diagnostic options for patients and clinical care providers.

Inspections (+$18.8 million / 65 FTE)
The FY 2022 Budget requests an increase of $18.8 million for ORA to address inspections delayed by the pandemic and to increase the level of response for COVID-19 medical countermeasures, food facilities, and counterfeit and misbranded products. The COVID-19 pandemic has placed additional emphasis on the interconnected and complicated nature of global food and medical product supply chains. Additionally, ORA anticipates continuing growth in the medical product industry following the COVID-19 public health emergency. ORA is committed to further enhancing the surveillance of the pharmaceutical supply chain for essential medicines and biological products used in the treatment of COVID-19.

Without this increase, ORA cannot fully support our medical products programs which regulate the industry ensuring safe and effective products for American consumers. Without additional resources, there is a risk of needing to lessen frequency of inspections at domestic and foreign manufacturers that supply their products to US consumers. Further, the proposed increase will support FDA's ability to keep pace with the continued growth in the medical product industry and increase our responsiveness to foodborne outbreaks.

Pay Costs ($17.9 million)
The FY 2022 Budget includes $17.9 million to support approximately half of the anticipated cost of the pay costs requested in FY 2022. This funding is critical to avoid continued program erosion by funding increases in FDA public health employee pay costs.

When program funding remains flat, but the cost of payroll increases, FDA must either reduce the number of staff hired or reduce its programmatic efforts that allow the Agency to carry out its mission. These are costs that FDA has absorbed for years, which impacts the Agency's ability to regulate the food supply and medical products available in the country. The Budget will support FDA's ability to maintain current staffing levels and to meet program demands and statutory requirements so that FDA can continue to deliver high-impact results that help Americans every day.

Office of Minority Health and Health Equity (+$4.7 million / 3 FTE)
The FY 2022 Budget includes an increase of $4.7 million, for a total of $8.1 million, to enhance FDA's ability to support and expand health equity and health disparity efforts. This funding will allow FDA to expand culturally and linguistically tailored communication and outreach efforts, establish new scientific initiatives, support novel health disparity and health equity focused intramural and extramural research, advance activities that enhance meaningful inclusion of minority populations in clinical trials, understand and address health disparities (including, but not limited to, gender, ethnicity, race, age, geography, and disability), increase engagement with Historically Black Colleges and Universities, Minority Serving Institutions, and other collaborators to address gaps and needs of diverse communities, and develop FDA-wide training

programs that focus on the reduction of health disparities and advancement of health equity. OMHHE will utilize additional FTEs, contracts, and grants to support these activities.

CAPACITY BUILDING ($53.5 million, 57 FTE)
The FY 2022 Budget includes an increase of $53.5 million, for a total of $73.0 million, to fund crosscutting Capacity Building efforts including increases for the Office of Laboratory Safety ($6.6 million), Office of Chief Counsel ($6.6 million), and FDA's Essential Services ($40.3 million). The Essential Services funding will support improvements and investments fundamental to FDA's operations, including Cybersecurity, IT Equipment Replacement, eDiscovery, and business services and support. The Capacity Building investments included in the Budget support FDA's ability to ensure the safety of human and animal food and drugs, medical devices, biologics, cosmetics, and many other consumer goods, as well as foods and drugs for animals.

Office of Laboratory Safety (+$6.6 million / 11 FTE)
The FY 2022 Budget includes an increase of $6.6 million to support the Office of Laboratory Safety (OLS). OLS serves as the agency coordinator and lead for cross-cutting activities associated with laboratory security, environmental compliance, laboratory quality management, and occupational safety and health programs across the FDA. These activities focus on the safety and health of the FDA workforce and the generation of high-quality data to support regulatory decision-making. These activities also include independent inspections of FDA's laboratories and implementing agency-wide initiatives to ensure full compliance of occupational safety and health standards. The additional resources will enable FDA to reduce risk from laboratory work, enhance laboratory security and data quality, increase efficiencies across the Centers and ORA, and strengthen the culture of responsibility and safety. Additionally, this investment will sustain the development of new agency-wide standards and policies; training, tools, and resources associated with implementing standards and policies; quality and safety assessment and improvement strategies; and other activities that emphasize the benefits of a safety-oriented culture.

Office of the Chief Counsel (+$6.6 million / 25 FTE)
The FY 2022 Budget includes an increase of $6.6 million, for a total of $23.7 million, for the Office of Chief Counsel (OCC) and for accompanying administrative support. OCC has a critical need for increased funds for legal services to support crucial pandemic-related matters, as well as many other ongoing FDA regulatory activities such as medical product reviews, food safety assessments, enforcement cases, defense of agency decisions, and other high-profile matters involving multiple motivated stakeholders. This funding will allow FDA to effectively analyze legal risks and opportunities and to counsel and litigate to support FDA's public health mission. This request builds on activities currently being supported with COVID-19 supplemental appropriations.

Essential Services ($40.3 million / 21 FTE)
The FY 2022 Budget includes an increase of $40.3 million for Essential Services. The funds support FDA's operations and FDA's ability to keep pace with new requirements, legislation, and regulatory responsibilities.

The Budget will allow FDA to more efficiently recruit and hire staff, as well as properly award, manage, and monitor grants and contracts. The funding will help to ensure proper budget planning and control, and help FDA effectively manage and address Enterprise Risks. These funds will support FDA's security and project management of over 360 FDA-owned, GSA-owned, and GSA-leased buildings, and allow FDA to conduct an agency-wide comprehensive security vulnerability assessment. The funds will also address workload challenges to ensure compliance with ethics and equal opportunity requirements.

The Budget includes investments in eDiscovery which are critical to building and expanding the infrastructure needed to respond to growing demand and for future pandemic or public health crises. eDiscovery – the process of identifying, collecting, processing, reviewing, and producing electronic information relevant to civil, criminal, or regulatory matters – is critically needed to support litigation, third party subpoenas, FOIA requests, and criminal investigations.

The Budget will support critically needed equipment replacement, including replacing end-of-life servers, updating network devices, and upgrading storage solutions. The Budget also includes funding for Cybersecurity to address real, critical threats to FDA's underlying cybersecurity infrastructure with outdated solutions.

These capacity building investments are critical to supporting FDA's ability to operate sufficiently and effectively and support the expansive range of responsibilities.

FOOD SAFETY (BA $1.6 BILLION; UF $16.7 MILLION)

The FY 2022 Budget provides $1.6 billion for food safety, an increase of $134.3 million compared to the FY 2021 Enacted level. The request includes $1.6 billion in budget authority – an increase of $134 million compared to the FY 2021 Enacted level – and $16.7 million for user fees – an increase of $324,000 compared to the FY 2021 Enacted level. The Budget provides funding for FDA priorities for food safety across human and animal products.

In total, the Budget requests an increase of $134.3 million for food safety activities. Of that amount, $44.8 million is for efforts to support initiatives to advance the New Era of Smarter Food Safety, including $22.8 million for Food Safety as requested as part of FDA's Data Modernization and Enhanced Technologies initiative. The remaining $37.7 million will support additional critical food safety initiatives including $18.0 million for Maternal and Infant Health and Nutrition and $19.7 million for Emerging Chemical and Toxicology Issues. The Budget also includes funding aligned with Food Safety associated with the requests for Data Modernization and Enhanced Technologies, Capacity Building, the Pay Costs, Inspections, and Infrastructure, Buildings, and Facilities. The total for food safety also includes $42.8 million in crosscutting activities described above on page 16.

Additional funds are needed now to bolster FDA's Food Safety program so that FDA can better keep pace with the latest advances in science and technology and to address issues of concern,

such as maternal and infant health and nutrition and emerging chemical and toxicology issues. Likewise, without new resources for the New Era of Smarter Food Safety, FDA's ability to maintain appropriate safeguards in food safety will significantly lag behind rapid, sweeping changes occurring in the marketplace, potentially putting consumers at risk.

New Era of Smarter Food Safety (+$44.8 million / 46 FTE)
The FY 2022 Budget requests an increase of $44.8 million, for a total of $51.9 million across CFSAN, CVM, OFPR, NCTR, and ORA in budget authority, to initiate essential work towards the mission critical goals of the New Era of Smarter Food Safety Blueprint[20] that address important Food Safety efforts. The Blueprint outlines achievable goals to enhance traceability, improve predictive analytics, expand collaboration with our regulatory and public health partners, respond more rapidly to outbreaks and other food safety problems, address new business models (such as online ordering and direct delivery of foods that has accelerated due to the COVID-19 pandemic), advance the safety of foods sold in traditional retail establishments, and foster strong food safety cultures. This approach builds on the modernized food safety regulatory framework created by the FDA Food Safety Modernization Act (FSMA) and is also closely connected with FDA's response to the unprecedented challenges of the on-going COVID-19 pandemic by fortifying our public health infrastructure to help ensure that consumers have access to safe food when public health emergencies arise in the future. In FY 2022, FDA's request for New Era funding includes the $22.8 million food safety component of the Data Modernization and Enhanced Technologies initiative detailed above, as well as dedicated funding to improve Animal Food Safety Oversight.

New Era of Smarter Food Safety (+$5.7 million / 16 FTE)
The FY 2022 Budget includes an increase of $5.7 million in funding complimentary to the New Era of Smarter Food Safety component of FDA's cross-cutting Data Modernization and Enhanced Technologies initiative. Our world is evolving at a breakneck pace and many believe we are in the midst of a food revolution. Foods are being reformulated, new foods and new food production methods are being realized, and the food system is becoming increasingly digitized. With this evolution comes new technologies, ranging from new digital tools to new business models that change the way some foods are produced (e.g., animal cell culture technologies) and sold to consumers (e.g., the rapid rise in e-commerce). These advances provide opportunities and challenges for FDA in its mission to give consumers confidence in the safety of the global food supply.

Coupled with the Data Modernization and Enhanced Technologies initiative, the FY 2022 request for New Era of Smarter Food Safety funding will enable CFSAN and CVM to leverage the use of new and emerging technologies and data-driven approaches to strengthen our predictive capabilities, accelerate prevention, and speed traceback when contaminated foods are identified. This investment also includes resources for NCTR to focus research activities on the development of data-driven tools to increase access to data and information to better understand foodborne pathogens. In sum, the New Era of

[20] https://www.fda.gov/media/139868/download

Smarter Food Safety supports the Administration's vision of a strong, reliable food safety system.

Animal Food Safety Oversight (+$16.4 million / 13 FTE)
The FY 2022 Budget requests an increase of $16.4 million, for a total of $20 million across CVM and ORA in budget authority, to initiate critical work in FY 2022 towards the goals of Domestic Mutual Reliance as part of the New Era of Smarter Food Safety. Domestic mutual reliance is a critical component of the New Era of Smarter Food Safety as it strengthens partnerships with states to ensure optimal use of resources and maximize food safety reach. With this increase, FDA will provide funding to states to expand efforts to modernize, harmonize, and transform the U.S. animal food inspection system into one that is comprehensive and prevention oriented utilizing FSMA authorities, including the Preventive Controls for Animal Food framework. FDA will also update inspection and enforcement programs, develop outreach and training initiatives, and devote resources to the analysis of controls for expected and understanding unknown animal food hazards. Animals have died and humans have been sickened because animal food has been contaminated by preventable hazards. FDA has historically relied on states to conduct 80% of animal food safety inspections. In FY 2020, FDA received $3.2M as an initial investment in cooperative agreements with just 13 states. FDA and its state partners need these resources to help address the risk-based oversight needed of the existing inventory of approximately 34,000 animal food facilities subject to FDA's food safety regulations, including FSMA.

Maternal and Infant Health and Nutrition (+$18.0 million / 26 FTE)
The FY 2022 Budget requests an increase of $18.0 million, for a total of $22 million, for CFSAN to take regulatory and other actions to address emerging issues of concern, such as toxic elements in baby food, limited staff review capacity for premarket review of infant formula submissions to evaluate the safety and nutritional adequacy of infant formula, and nutrition work specific to infants, toddlers, and pregnant and lactating women. The health and well-being of mothers, infants, and children is critical, FDA is best positioned to make progress in this important area. FDA plans to establish reference levels for exposure to toxic elements from foods, set expectations to strive for continual improvement, and provide action levels with the expectation that they will decrease over time for lead, arsenic, cadmium, and mercury for different categories of foods consumed by babies and very young children. FDA will partner with USDA, the Health and Human Services Office of Disease Prevention and Health Promotion, and others to explore opportunities to better help consumers understand the new Dietary Guidelines for pregnant and lactating women and early childhood while also reducing dietary exposure to toxic elements.

With additional resources, CFSAN will recruit risk analysts, consumer safety officers, data analysts, public health information specialists, toxicologists, and chemists among others. Increased staffing in these areas will allow the Center to expand research on co-occurrence of toxic elements in baby foods and impacts on neurodevelopment, and evaluate how changes to laboratory procedures and minor adjustments to existing analytical methods, for certain foods, would improve industry's ability to detect levels of concern. Increased resources will also allow the Center to create risk communication and education materials for consumers on the risks from

toxic elements in foods, and the importance of healthy dietary patterns and variety as a strategy for reducing toxicants in the diet. FDA will also develop education and outreach materials for industry which outline requirements for managing and minimizing the presence of toxic elements in their products. CFSAN also seeks additional resources to expand agency capacity to review the increasing number, size, and complexity of infant formula submissions.

Emerging Chemical and Toxicology Issues, Food (+$19.7 million / 40 FTE)
The FY 2022 Budget requests a total of $19.7 million for CFSAN to support food safety programs that fall mostly outside of FSMA's purview to support FDA's ability to keep pace with innovation by industry. These resources will modernize and streamline approaches for products that in certain cases pose significant, chronic risks to human health. With new resources, CFSAN will enhance and update the Foods program's approach to chemicals—both those directly added as food ingredients and those that come into the food supply through food contact. Hiring additional experts will build capacity to utilize science and information technology advances in order to make CFSAN-regulated products safer and make these determinations more quickly. CFSAN will also acquire new tools that leverage new and evolving data sources to support pre-market safety evaluations and to prioritize our efforts in a scientific and risk-based way. Additionally, the Budget includes $150,000 for NCTR to develop research activities focused on the detection of novel sources, such as micro/nanoplastics found in foods.

Requested resources will also focus on reducing Per- and Polyfluoroalkyl Substances (PFAS) in the food supply based on safety data. PFAS, sometimes called "forever chemicals," are a family of human-made chemicals found in a range of products used by consumers and industry, which are now widespread in the environment. Bioaccumulation of certain PFAS may cause serious health conditions. New resources would make it possible for the agency to recruit additional experts such as toxicologists and environmental scientists to conduct this work. FDA will also expand scientific review capacity to assess the public health importance of allergens other than the major food allergens. Expanded resources will also allow FDA to support state health agencies and continue coordination with partners such as Department of Defense (DoD), Environmental Protection Agency (EPA), and USDA to respond to contamination events, which may arise as DoD continues to test water sources near their sites, and other states and municipalities test drinking water. Finally, new funding would provide modest increases to FDA's programs for cosmetics and dietary supplements.

MEDICAL PRODUCT SAFETY (BA $2 BILLION; UF $2.1 BILLION)

The FY 2022 Budget reflects $4 billion for medical product safety and availability, an increase of $223.4 million above FY 2021 Enacted. The request includes $2 billion for budget authority – an increase of $169 million compared to FY 2021 Enacted – and $2.1 billion for user fees – an increase of $55 million compared to the FY 2021 Enacted.

In total, the Budget requests an increase of $223.4 million for medical product safety activities. Of that amount, $8.6 million will support initiatives that advance medical product safety efforts including $38 million to Advance the Goal of Ending the Opioid Crisis, $21.6 million for Device Shortages and Supply Chain, $7.5 million is for Predictive Toxicology Roadmap – Guideline

Studies, $5.6 million is for Drug Safety Surveillance and Oversight, and $2.3 million for CVM Medical Product Safety. The budget also includes funding to support critical crosscutting efforts associated with FDA's Data Modernization and Enhanced Technology Initiative, Capacity Building, the Pay Costs, Inspections, and infrastructure, buildings, and facilities. The medical product safety activities level also reflects the scheduled adjustments of -$20 million, for a total of $50 million, to display the scheduled authorized level for 21st Century CURES Act funding in FY 2022. The total for medical product safety also includes $96.6 million in crosscutting activities described above on page 16.

The Budget funds FDA priorities for medical product safety and availability. FDA cannot underscore the significant underlying changes to FDA's current and future operations as a result of COVID-19 and the emerging SARS-CoV-2 variants. FDA continues to work with sponsors and review life-saving diagnostics, therapeutics and vaccines, but the Agency's work now also needs to shift to ensure FDA is appropriately monitoring and evaluating the continued performance, safety, and effectiveness of the products already on the market and support vital public health programs such as those to combat the opioid epidemic. The U.S. faces significant challenges including drug development, medical product shortages, and barriers to innovation.

Advancing the Goal of Ending the Opioid Crisis (+$38.0 million / 40 FTE)
The FY 2022 Budget FDA requests $38 million above FY 2021 Enacted to support activities in the Center for Drug Evaluation and Research (CDER), the Office of Regulatory Affairs (ORA), and the Center for Devices and Radiological Health (CDRH). This funding supports HHS's Department-wide initiative to Advance the Goal of Ending the Opioids Crisis.

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 is taking steps to address four priority areas of the epidemic: (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; (4) improving enforcement and assessing benefit-risk.

Within CDER, $26 million will support development of opioid overdose reversal treatments and treatments for Opioid Use Disorder (OUD). CDER will, among other things, validate clinical endpoints for drug development and identify new drug targets; assess feasibility to integrate the opioid Risk Evaluation and Mitigation Strategies (REMS) education into IT health systems/Electronic Health Records and explore use of health IT systems to support goals of REMS, such as prescriber education; and continue to support opioid research efforts.

Within ORA, $10 million will allow FDA to establish satellite laboratories at the International Mail Facilities (IMFs) to include permanent staffing by scientists along with expanding ORA's use of analytical tools for screening entries, expand the current IMF initiative to interdict shipments of opioids, unapproved foreign drugs, counterfeit pharmaceuticals and health fraud related shipments, and support Pharmacy Compounding (under section 503A of the FD&C Act) and Outsourcing Facility (under section 503B of the FD&C Act) inspections, which include an inspectional assessment for compounding or repackaging of opioid products.

Within CDRH, $2 million will be invested in efforts that will allow FDA to advance the development, evaluation, and market authorization of digital health medical devices that help address Opioid Use Disorder (OUD). These efforts will help FDA address unmet needs in our health care system. Funds will be used to establish a streamlined framework for FDA market authorization of these devices while assuring they meet FDA's standards. This mechanism will foster development of innovative new safe, effective, high-quality devices to address OUD that are based on evolving science and technology. The initiative will help enable infrastructure for systematic evaluation of these devices, increasing analytic capabilities to leverage real world data to support OUD digital technology evaluation, and incentivize the development of new digital risk assessments, diagnostics, and therapeutics, such as through a design-a-thon and other crowdsourcing measures.

Device Shortages and Supply Chain (+$21.6 million / 18 FTE)
The FY 2022 Budget requests $21.6 million for the new Resilient Supply Chain and Shortages Program (RSCSP). This funding will provide resources that will enable establishment of a permanent program for U.S. supply chain resilience for medical devices for the first time. The establishment of a permanent device shortages program will help ensure U.S. patients and health care providers have access to the critical devices they need and help reduce U.S. dependence on devices from other nations by enhancing CDRH's capacity to enable rapid intervention to prevent and mitigate supply chain interruptions through proactive regulatory measures and partnerships with industry, health care providers, patients, and others, develop and apply state of the art supply chain intelligence for predictive modeling, early signal detection and continuous surveillance, and foster a more resilient domestic supply chain through investments in preventive measures that help to avert shortages before they occur. Funding for a permanent device shortages program at FDA is critical to support resiliency in the medical device supply chain for devices to decrease or eliminate the risk of medical device supply chain shortages.

Predictive Toxicology Roadmap – Guideline Studies ($7.5 million)
The FY 2022 Budget requests $7.5 million for National Center for Toxicological Research (NCTR) predictive toxicology roadmap – guideline studies. This funding will allow FDA to address important questions of validation and regulatory trust-building for the new alternative paradigms, which are key to enable the implementation of the strategies articulated in the FDA Predictive Toxicology Roadmap. Working in close collaboration with the product centers on study selection and design, NCTR will conduct studies aimed at appraising side-by-side the value of guideline and alternative testing paradigms.

Drug Safety Surveillance and Oversight (+$5.6 million / 18 FTE)
The FY 2022 Budget requests $5.6 million for CDER Drug Safety Surveillance and Oversight. The funding will allow FDA to build the foundation to create and implement a *21st Century Roadmap* for modernizing FDA's safety surveillance and oversight program for marketed drug products. With additional resources, this initiative will modernize the regulatory framework for FDA's postmarket surveillance program to improve the program's efficiency and predictability to better ensure the safety of marketed drugs and develop and implement the organizational and process changes CDER will need to support efficient and effective postmarket safety for the 21st century.

CVM Medical Product Supply Chain (+$2.3 million / 7 FTE)
The FY 2022 Budget requests $2.3 million to enable CVM to strengthen its capacity to detect data gaps and mine data to help identify and anticipate the effects of the public health emergencies on the animal drug supply. Emerging diseases, such as COVID-19 and shifting trends in the marketplace result in vulnerabilities for unapproved fraudulent drugs products. While we are in the process of developing new systems funded by COVID-19 emergency supplemental appropriations, there is also an urgent need to hire additional staff who can help identify data gaps, and review and evaluate existing data to ensure sustained quality as we launch new data systems. The Center will also prioritize and review inspectional findings to address the workload anticipated from COVID-19 inspectional delays, while continuing to monitor for the presence of fraudulent and harmful products on the market.

INFRASTRUCTURE AND BUILDINGS & FACILITIES (+$37.5 MILLION)

The FY 2022 Budget provides a budget authority increase of +$37.5 million, for a total of $347.6 million, for Infrastructure, Buildings and Facilities. These funds will ensure that FDA's offices and labs across the country and its fully integrated headquarters campus are properly functioning to enable FDA to carry out its mission, evaluate food safety and medical products, and respond to emergencies.

The Infrastructure portion of the increase is $19.5 million, including $17.8 million for Other Rent and Rent Related (OR&RR) and $2.5 million for White Oak as well as a decrease of $0.8 million for GSA Rent. The requested budget for GSA Rent, including the decrease, considers new leases coming on line for which rent will begin, free-rent periods associated with some new leases, expected market rates for GSA-owned and leased locations, and that FDA will incur a double-rent period when it relocates a field lab as part of FDA's Lab Modernization effort, which is required to provide time to decommission the vacated lab. The OR&RR increase allows FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support the FDA mission. It also provides additional funding to address increased utility and maintenance costs associated with FDA's aging owned buildings. The White Oak increase provides the necessary resources for increased above-GSA-standard repairs and improvements as well as the most critical White Oak Campus infrastructure capacity and reliability improvements. It also addresses escalating costs for daily mission support services for the more than 11,000 employees, contractors, and visitors normally on the White Oak Campus, including, transportation services, labor and loading dock services, and a centralized safety program, as well as significantly increased support for teleworking personnel.

The Buildings & Facilities portion of this increase is $18.0 million. This increase will support additional repair and improvement projects to help reduce FDA's current backlog of maintenance and repairs (BMAR), which is greater than $220 million, to address facilities projects that support food safety and medical product program requirements and to improve the functionality and reliability of FDA's owned buildings and site infrastructure.

Maximizing the public health value of FDA funding is paramount. Therefore, FDA continues to prioritize crucial investments in real estate to ensure that facilities efficiently and cost-effectively meet the demands of FDA's scientific mission and expanding workforce. Additionally, the condition, configuration, and location of FDA-occupied facilities affect the Agency's ability to achieve its strategic goals and priorities.

TOBACCO REGULATION

Tobacco product regulation represents one of FDA's greatest opportunities to save lives. The Tobacco Control Act gave FDA immediate authority to regulate cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco. FDA finalized the Deeming rule in 2016, which extended FDA's tobacco regulatory authorities to all tobacco products, including electronic nicotine delivery systems (ENDS) - such as e-cigarettes, cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels. FDA regulates the manufacture, marketing, and distribution of tobacco products. Key areas of focus include policy and rulemaking, compliance and enforcement, premarket review, research support, and public education campaigns.

FDA's ongoing oversight of e-cigarettes and other ENDS products remains a high priority and is critical to the Agency's public health mission and, especially, to protecting kids from the dangers of nicotine addiction and other harmful health consequences. While certain ENDS products may hold some promise in helping addicted adult smokers who are over 21 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 youth. Years of progress to combat youth use of tobacco and to prevent lifetimes of addiction to nicotine is threatened by an epidemic of e-cigarette use by young people.

FDA's plan combines compliance and enforcement activities with high-profile, impactful public education efforts designed to reach nearly 10.7 million youth at risk of starting or continuing to use e-cigarettes. FDA has taken swift action aimed at the manufacturers of youth-appealing ENDS products and continues to take action to stop sales to minors. FDA has also taken a number of actions to remove tobacco products that lack FDA premarket authorization, including ENDS, from the market. From October 1, 2019 through February 28, 2021, these actions include:

- Conducting over 65,000 retail inspections at both brick-and-mortar and online retailers since October 1, 2019 and issuing more than 7,000 warning letters and civil money penalties to retailers for illegally selling tobacco products, including ENDS products, to minors
- Conducting inspections of over 140 tobacco manufacturing establishments and over 400 vape shops and conducting investigations involving thousands of websites
- Issuing hundreds of warning letters to manufacturers, importers, and vape shops for illegally marketing unauthorized ENDS products.

On January 2, 2020, FDA issued a final guidance for industry, revised in April 2020, entitled, "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and other Deemed Products on the Market Without Premarket Authorization."

FDA is prioritizing 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.

In light of the alarming uptick in youth use of disposable e-cigarettes revealed in the 2020 NYTS data, flavored disposable ENDS products have also become an enforcement priority for FDA.

In March 2020, FDA announced the temporary postponement of all routine domestic surveillance facility inspections due to health and safety concerns related to the COVID-19 pandemic. FDA also issued related partial stop work orders to the contractors engaged in tobacco retail compliance check inspections and vape retail inspections. The Agency subsequently extended the partial stop work orders through the end of FY 2020. Guided by health and safety considerations, FDA took appropriate actions, as outlined by its priorities. For example, certain enforcement efforts, such as monitoring the online marketing and sale of regulated tobacco products and issuing import alerts for unauthorized tobacco products, remained uninterrupted by COVID-19. In FY 2021, some tobacco manufacturer and retailer inspections resumed in certain areas where the spread of COVID-19 was less prevalent. FDA will continue taking appropriate actions that are guided by health and safety considerations and as outlined by the Agency's priorities.

Applications for premarket review for many e-cigarettes, cigars and other new tobacco products were required to be filed by Sept. 9, 2020. For companies that submitted timely applications, FDA may continue to exercise enforcement discretion, meaning their products would generally continue to be marketed without being subject to FDA enforcement actions, for up to one year from the deadline (up to Sept. 9, 2021), unless a negative action is taken by FDA on an application during that time.

In FY 2022, FDA will continue to invest in product review and evaluation, research, compliance and enforcement, public education campaigns, and policy development. FDA requests an additional $100 million in user fees and requests authority to include manufacturers and importers of all deemed products among the tobacco product classes for which FDA assesses tobacco user fees. These products represent an increasing share of the tobacco marketplace as well as FDA's tobacco regulatory activities. The additional funding will strengthen FDA actions to combat youth use of tobacco products, including e-cigarettes, through the Youth Tobacco Prevention Plan, which includes compliance and enforcement efforts for all tobacco products, 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 which will ensure that FDA has the resources to address all regulated tobacco products, including e-cigarettes, which currently have high rates of youth use, as well as new public health threats of tomorrow.

ALL-PURPOSE TABLE

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Foods	**3,863**	**1,098,470**	**3,816**	**1,087,215**	**3,882**	**1,110,471**	**3,990**	**1,194,161**	**108**	**83,690**
Budget Authority	***3,819***	***1,087,381***	***3,816***	***1,087,215***	***3,838***	***1,099,160***	***3,946***	***1,182,625***	***108***	***83,465***
User Fees	***44***	***11,089***	---	---	***44***	***11,311***	***44***	***11,536***	---	***225***
Center	1,144	335,815	1,125	334,966	1,157	344,655	1,242	399,985	85	55,330
Budget Authority	1,141	334,966	1,125	334,966	1,154	343,789	1,239	399,102	85	55,313
User Fees	3	849	---	---	3	866	3	883	---	17
Food and Feed Recall	1	248	---	---	1	253	1	258	---	5
Voluntary Qualified Importer Program	1	248	---	---	1	253	1	258	---	5
Third Party Auditor Program	1	353	---	---	1	360	1	367	---	7
Innovative Food Products (Proposed)	---	---	---	---	---	---	---	---	---	---
Field	2,719	762,655	2,691	752,249	2,725	765,816	2,748	794,176	23	28,360
Budget Authority	2,678	752,415	2,691	752,249	2,684	755,371	2,707	783,523	23	28,152
User Fees	41	10,240	---	---	41	10,445	41	10,653	---	208
Food and Feed Recall	4	1,020	---	---	4	1,040	4	1,061	---	21
Food Reinspection	19	4,667	---	---	19	4,760	19	4,855	---	95
Voluntary Qualified Importer Program	18	4,406	---	---	18	4,495	18	4,584	---	89
Third Party Auditor Program	---	147	---	---	---	150	---	153	---	3
Human Drugs	**6,649**	**1,973,122**	**6,478**	**1,995,820**	**6,737**	**1,997,174**	**6,856**	**2,121,242**	**119**	**124,068**
Budget Authority	***2,075***	***683,195***	***1,916***	***682,861***	***2,083***	***689,195***	***2,193***	***774,469***	***110***	***85,274***
User Fees	***4,574***	***1,289,927***	***4,562***	***1,312,959***	***4,654***	***1,307,979***	***4,663***	***1,346,773***	***9***	***38,794***
Center	5,612	1,734,133	5,399	1,756,076	5,700	1,753,685	5,765	1,854,233	65	100,548
Budget Authority	1,316	507,726	1,154	507,431	1,324	510,226	1,380	573,081	56	62,855
User Fees	4,296	1,226,407	4,245	1,248,646	4,376	1,243,459	4,385	1,281,152	9	37,693
Prescription Drug (PDUFA)	2,774	788,576	2,667	790,087	2,854	800,637	2,863	831,287	9	30,650
Generic Drug (GDUFA)	1,410	400,252	1,491	427,395	1,410	404,241	1,410	410,647	---	6,406
Biosimilars (BsUFA)	110	36,938	81	30,135	110	37,928	110	38,552	---	624
Outsourcing Facility	2	641	6	1,029	2	653	2	666	---	13
Field	1,037	238,989	1,079	239,743	1,037	243,489	1,091	267,009	54	23,520
Budget Authority	759	175,469	762	175,430	759	178,969	813	201,388	54	22,419
User Fees	278	63,520	317	64,313	278	64,520	278	65,621	---	1,101
Prescription Drug (PDUFA)	43	8,536	43	7,592	43	8,707	43	8,855	---	148
Generic Drug (GDUFA)	226	53,124	263	55,022	226	54,096	226	55,019	---	923
Biosimilars (BsUFA)	7	1,472	8	1,303	7	1,322	7	1,344	---	22
Outsourcing Facility	2	388	3	396	2	395	2	403	---	8

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Biologics	**1,439**	**419,302**	**1,441**	**426,027**	**1,438**	**437,071**	**1,462**	**457,889**	**24**	**20,818**
Budget Authority	***803***	***252,138***	***805***	***252,128***	***811***	***254,138***	***835***	***270,114***	***24***	***15,976***
User Fees	***636***	***167,164***	***636***	***173,899***	***627***	***182,933***	***627***	***187,775***	---	***4,842***
Center	1,211	375,583	1,213	382,468	1,210	393,322	1,217	408,118	7	14,796
Budget Authority	582	210,132	582	210,131	590	212,132	597	222,145	7	10,013
User Fees	629	165,451	631	172,337	620	181,190	620	185,972	---	4,782
Prescription Drug (PDUFA)	567	149,267	569	158,793	559	164,951	559	169,401	---	4,450
Medical Device (MDUFA)	55	14,578	61	13,366	56	14,981	56	15,203	---	222
Generic Drug (GDUFA)	4	960	1	132	4	983	4	1,088	---	105
Biosimilars (BsUFA)	3	646	---	46	1	275	1	280	---	5
Field	228	43,719	228	43,559	228	43,749	245	49,771	17	6,022
Budget Authority	221	42,006	223	41,997	221	42,006	238	47,969	17	5,963
User Fees	7	1,713	5	1,562	7	1,743	7	1,802	---	59
Prescription Drug (PDUFA)	6	1,485	5	1,340	6	1,514	6	1,569	---	55
Medical Device (MDUFA)	1	228	---	222	1	229	1	233	---	4
Animal Drugs and Foods	**1,006**	**238,678**	**1,011**	**234,507**	**1,042**	**245,307**	**1,086**	**285,541**	**44**	**40,234**
Budget Authority	***824***	***190,869***	***801***	***190,854***	***825***	***192,369***	***869***	***232,033***	***44***	***39,664***
User Fees	***182***	***47,809***	***210***	***43,653***	***217***	***52,938***	***217***	***53,508***	---	***570***
Center	690	168,474	697	165,361	726	175,083	760	198,200	34	23,117
Budget Authority	514	122,099	489	122,099	515	123,599	549	146,251	34	22,652
User Fees	176	46,375	208	43,262	211	51,484	211	51,949	---	465
Animal Drug (ADUFA)	115	27,670	132	28,024	138	30,117	138	30,454	---	337
Animal Generic Drug (AGDUFA)	61	18,591	76	15,216	73	21,250	73	21,376	---	126
Third Party Auditor Program	---	114	---	22	---	117	---	119	---	2
Field	316	70,204	314	69,146	316	70,224	326	87,341	10	17,117
Budget Authority	310	68,770	312	68,755	310	68,770	320	85,782	10	17,012
User Fees	6	1,434	2	391	6	1,454	6	1,559	---	105
Animal Drug (ADUFA)	2	383	2	391	2	390	2	426	---	36
Animal Generic Drug (AGDUFA)	1	228	---	---	1	224	1	277	---	53
Food Reinspection	3	823	---	---	3	840	3	856	---	16
Third Party Auditor Program	---	---	---	---	---	---	---	---	---	---

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Devices and Radiological Health	**2,302**	**599,940**	**2,172**	**587,305**	**2,345**	**627,664**	**2,382**	**676,547**	**37**	**48,883**
Budget Authority	***1,493***	***395,168***	***1,435***	***395,142***	***1,508***	***408,108***	***1,545***	***452,064***	***37***	***43,956***
User Fees	***809***	***204,772***	***737***	***192,163***	***837***	***219,556***	***837***	***224,483***	---	***4,927***
Center	1,796	501,296	1,665	488,115	1,839	528,784	1,864	571,124	25	42,340
Budget Authority	1,007	310,163	947	310,156	1,022	323,103	1,047	360,827	25	37,724
User Fees	789	191,133	718	177,959	817	205,681	817	210,297	---	4,616
Prescription Drug (PDUFA)	15	4,162	19	3,525	15	4,446	15	4,720	---	274
Medical Device (MDUFA)	746	180,073	674	168,730	774	194,199	774	198,400	---	4,201
Mammography Quality Standards Act (MQSA)	28	6,898	25	5,704	28	7,036	28	7,177	---	141
Field	506	98,644	507	99,190	506	98,880	518	105,424	12	6,544
Budget Authority	486	85,005	488	84,986	486	85,005	498	91,237	12	6,232
User Fees	20	13,639	19	14,204	20	13,875	20	14,186	---	311
Medical Device (MDUFA)	11	2,358	11	2,241	11	2,368	11	2,449	---	81
Mammography Quality Standards Act (MQSA)	9	11,281	8	11,963	9	11,507	9	11,737	---	230
National Center for Toxicological Research (BA Only)	**276**	**66,712**	**296**	**66,702**	**276**	**66,712**	**277**	**76,994**	1	10,282
Tobacco	**1,012**	**680,437**	**1,040**	**752,921**	**1,279**	**681,513**	**1,368**	**780,812**	**89**	**99,299**
Center	**940**	**664,168**	**965**	**732,476**	**1,190**	**658,906**	**1,279**	**754,159**	**89**	**95,253**
User Fees	940	664,168	965	732,476	1,190	658,906	1,279	754,159	89	95,253
Family Smoking Prevention and Tobacco Control Act	940	664,168	965	732,476	1,190	658,906	1,279	654,159	89	-4,747
Expand tobacco products (Proposed)	---	---	---	---	---	---	---	100,000	---	100,000
Field	**72**	**16,269**	**75**	**20,444**	**89**	**22,607**	**89**	**26,653**	---	**4,046**
Family Smoking Prevention and Tobacco Control Act	72	16,269	75	20,444	89	22,607	89	26,653	---	4,046
FDA Headquarters	**931**	**302,289**	**954**	**308,089**	**927**	**319,572**	**980**	**345,079**	**53**	**25,507**
Budget Authority	513	186,920	549	186,919	514	194,951	565	221,834	51	26,883
User Fees	***418***	***115,369***	***405***	***121,170***	***413***	***124,621***	***415***	***123,245***	***2***	***-1,376***
Prescription Drug (PDUFA)	215	56,756	194	60,918	215	60,354	215	58,773	---	-1,581
Medical Device (MDUFA)	36	9,219	29	8,306	36	10,459	36	11,185	---	726
Generic Drug (GDUFA)	100	32,834	124	37,214	100	34,575	100	34,517	---	-58
Biosimilars (BsUFA)	8	1,331	4	1,657	8	1,417	8	1,372	---	-45
Animal Drug (ADUFA)	4	914	4	724	4	1,172	4	1,279	---	107
Animal Generic Drug (AGDUFA)	3	756	3	594	3	740	3	895	---	155
Family Smoking Prevention and Tobacco Control Act	48	12,169	47	11,757	43	14,485	45	13,777	2	-708
Mammography Quality Standards Act (MQSA)	---	74	---	---	---	76	---	77	---	1
Food and Feed Recall	---	77	---	---	---	78	---	80	---	2
Food Reinspection	2	489	---	---	2	499	2	509	---	10
Voluntary Qualified Importer Program	1	283	---	---	1	288	1	294	---	6
Third Party Auditor Program	---	40	---	---	---	41	---	41	---	---
Outsourcing Facility	1	427	---	---	1	437	1	446	---	9
Innovative Food Products (Proposed)	---	---	---	---	---	---	---	---	---	---

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
FDA White Oak Complex	---	**53,913**	---	**59,744**	---	**52,944**	---	**55,892**	---	**2,948**
Budget Authority	---	45,914	---	45,913	---	45,914	---	48,414	---	2,500
User Fees	---	***7,999***	---	***13,831***	---	***7,030***	---	***7,478***	---	***448***
Prescription Drug (PDUFA)	---	3,848	---	11,082	---	3,886	---	3,925	---	39
Medical Device (MDUFA)	---	---	---	---	---	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	---	4,151	---	2,749	---	3,144	---	3,553	---	409
Other Rent and Rent Related	---	**132,970**	---	**119,877**	---	**136,257**	---	**155,096**	---	**18,839**
Budget Authority	---	80,173	---	80,172	---	84,262	---	102,095	---	17,833
User Fees	---	***52,797***	---	***39,705***	---	***51,995***	---	***53,001***	---	***1,006***
Prescription Drug (PDUFA)	---	26,389	---	17,796	---	26,652	---	26,919	---	267
Medical Device (MDUFA)	---	5,291	---	5,291	---	5,344	---	5,398	---	54
Generic Drug (GDUFA)	---	13,206	---	11,467	---	13,338	---	13,472	---	134
Biosimilars (BsUFA)	---	1,081	---	543	---	1,092	---	1,102	---	10
Animal Drug (ADUFA)	---	797	---	797	---	805	---	813	---	8
Animal Generic Drug (AGDUFA)	---	266	---	266	---	269	---	272	---	3
Family Smoking Prevention and Tobacco Control Act	---	5,283	---	3,506	---	4,001	---	4,522	---	521
Food and Feed Recall	---	44	---	---	---	45	---	46	---	1
Food Reinspection	---	208	---	---	---	212	---	216	---	4
Voluntary Qualified Importer Program	---	173	---	---	---	177	---	180	---	3
Third Party Auditor Program	---	24	---	5	---	25	---	25	---	---
Outsourcing Facility	---	35	---	34	---	35	---	36	---	1
GSA Rental Payments	---	**240,549**	---	**219,334**	---	**235,961**	---	**236,214**	---	**253**
Budget Authority	---	171,208	---	171,208	---	167,119	---	166,286	---	-833
User Fees	---	***69,341***	---	***48,126***	---	***68,842***	---	***69,928***	---	***1,086***
Prescription Drug (PDUFA)	---	35,695	---	24,354	---	36,052	---	36,412	---	360
Medical Device (MDUFA)	---	8,395	---	6,097	---	8,479	---	8,563	---	84
Generic Drug (GDUFA)	---	12,847	---	8,335	---	12,975	---	13,105	---	130
Biosimilars (BsUFA)	---	455	---	190	---	460	---	465	---	5
Animal Drug (ADUFA)	---	847	---	635	---	856	---	864	---	8
Animal Generic Drug (AGDUFA)	---	310	---	233	---	314	---	317	---	3
Family Smoking Prevention and Tobacco Control Act	---	9,960	---	8,277	---	8,857	---	9,336	---	479
Food and Feed Recall	---	74	---	---	---	76	---	77	---	1
Food Reinspection	---	355	---	---	---	362	---	369	---	7
Voluntary Qualified Importer Program	---	296	---	---	---	302	---	308	---	6
Third Party Auditor Program	---	48	---	5	---	49	---	50	---	1
Outsourcing Facility	---	59	---	---	---	60	---	62	---	2

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Color Certification	37	10,263	34	8,894	37	10,469	37	10,678	---	209
Export Certification	26	4,790	24	5,593	26	4,886	26	4,983	---	97
Export Certification (Proposed)	---	---	---	---	---	---	---	4,366	---	4,366
Priority Review Vouchers (PRV) Tropical Disease	---	2,506	---	---	---	2,556	---	2,608	---	52
Priority Review Vouchers (PRV) Pediatric Disease	11	7,840	49	11,156	11	7,997	11	8,156	---	159
Priority Review Vouchers (PRV) Medical Countermeasures	---	2,506	---	---	---	2,556	---	2,608	---	52
Over the Counter Monograph	---	---	---	---	---	28,400	---	28,968	---	568
Food and Drug Safety -- No Year (P.L. 113-6)	---	---	---	---	---	---	---	---	---	---
Food Safety	---	---	---	---	---	---			---	---
Drug Safety	---	---	---	---	---	---			---	---
21st Century Cures (BA Only)	136	75,000	187	64,592	187	70,000	187	50,000	---	-20,000
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	---	---	---	---	1,000	---	---	---	-1,000
MCMi - No Year	---	---	---	---	---	---	---	---	---	---
Opioids - No Year	---	---	33	48,257	---	---	---	---	---	---
Subtotal, Salaries and Expenses	**17,688**	**5,909,287**	**17,535**	**5,996,032**	**18,187**	**6,038,510**	**18,245**	**6,497,834**	**475**	**459,324**
Buildings and Facilities (Budget Authority)	**---**	**31,788**	**---**	**43,289**	**---**	**12,788**	**---**	**30,788**	---	18,000
Total Program Level	**17,688**	**5,941,075**	**17,535**	**6,039,321**	**18,187**	**6,051,298**	**18,662**	**6,528,622**	**475**	**477,324**
Non-Field Activities	*12,674*	*4,176,375*	*12,421*	*4,259,897*	*13,099*	*4,297,583*	*13,458*	*4,670,258*	*359*	*372,675*
Field Activities	*4,878*	*1,230,480*	*4,894*	*1,224,332*	*4,901*	*1,244,765*	*5,017*	*1,330,373*	*116*	*85,608*
White Oak, Rent Activities, and B&F	---	*459,220*	---	*442,243*	---	*437,950*	---	*477,990*	---	*40,040*
Opioids - No Year	---	---	*33*	*48,257*	---	---				
21st Century Cures	*136*	*75,000*	*187*	*64,592*	*187*	*70,000*	*187*	*50,000*	---	*-20,000*
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	---	---	---	---	*1,000*	---	---	---	*-1,000*
User Fees:										
Current Law										
Prescription Drug (PDUFA)	*3,620*	*1,074,714*	*3,497*	*1,075,487*	*3,692*	*1,107,199*	*3,701*	*1,141,861*	*9*	*34,662*
Medical Device (MDUFA)	*849*	*220,142*	*775*	*204,253*	*878*	*236,059*	*878*	*241,431*	---	*5,372*
Generic Drug (GDUFA)	*1,740*	*513,223*	*1,879*	*539,565*	*1,740*	*520,208*	*1,740*	*527,848*	---	*7,640*
Biosimilars (BsUFA)	*128*	*41,923*	*93*	*33,873*	*126*	*42,494*	*126*	*43,116*	---	*622*
Animal Drug (ADUFA)	*121*	*30,611*	*138*	*30,571*	*144*	*33,340*	*144*	*33,836*	---	*496*
Animal Generic Drug (AGDUFA)	*65*	*20,151*	*79*	*16,309*	*77*	*22,797*	*77*	*23,137*	---	*340*
Family Smoking Prevention and Tobacco Control Act	*1,060*	*712,000*	*1,087*	*779,211*	*1,322*	*712,000*	*1,413*	*712,000*	*91*	---
Over the Counter Monograph	---	---	---	---	---	*28,400*	---	*28,968*	---	*568*
Subtotal, Current Law	**7,583**	**2,612,764**	**7,548**	**2,679,269**	**7,979**	**2,702,497**	**8,079**	**2,752,197**	**100**	**49,700**

(Dollars in Thousands)	FY 2020 Final		FY 2020 Actuals		FY 2021 Enacted		FY 2022			
							FY 2022 President's Budget		FY 2022 PB +/- FY 2021 Enacted	
Indefinite										
Mammography Quality Standards Act (MQSA)	*37*	*18,253*	*33*	*17,667*	*37*	*18,619*	*37*	*18,991*	---	*372*
Color Certification	*37*	*10,263*	*34*	*8,894*	*37*	*10,469*	*37*	*10,678*	---	*209*
Export Certification	*26*	*4,790*	*24*	*5,593*	*26*	*4,886*	*26*	*4,983*	---	*97*
Priority Review Vouchers (PRV) Tropical Disease	---	*2,506*	---	---	---	*2,556*	---	*2,608*	---	*52*
Priority Review Vouchers (PRV) Pediatric Disease	---	*7,840*	*49*	*11,156*	*11*	*7,997*	*11*	*8,156*	---	*159*
Priority Review Vouchers (PRV) Medical Countermeasures	---	*2,506*	---	---	---	*2,556*	---	*2,608*	---	*52*
Food and Feed Recall	*5*	*1,463*	---	---	*5*	*1,492*	*5*	*1,522*	---	*30*
Food Reinspection	*24*	*6,542*	---	---	*24*	*6,673*	*24*	*6,805*	---	*132*
Voluntary Qualified Importer Program	*20*	*5,406*	---	---	*20*	*5,515*	*20*	*5,624*	---	*109*
Third Party Auditor Program	*1*	*726*	---	*31*	*1*	*742*	*1*	*755*	---	*13*
Outsourcing Facility	*5*	*1,550*	*9*	*1,459*	*5*	*1,580*	*5*	*1,613*	---	*33*
Subtotal, Indefinite	**155**	**61,845**	**149**	**44,800**	**166**	**63,085**	**166**	**64,343**	---	**1,258**
Proposed										
Export Certification (Proposed)	---	---	---	---	---	---	---	*4,366*	---	*4,366*
Expand tobacco products (Proposed)	---	---	---	---	---	---	---	*100,000*	---	*100,000*
Subtotal, Proposed	---	---	---	---	---	---	---	***104,366***	---	***104,366***
Total User Fees	**7,738**	**2,674,609**	**7,697**	**2,724,069**	**8,145**	**2,765,582**	**8,245**	**2,920,906**	**100**	**155,324**
Total Budget Authority, Pre-Transfer	**9,939**	**3,266,466**	**9,838**	**3,315,252**	**10,042**	**3,285,716**	**10,417**	**3,607,716**	**375**	**322,000**
BA, S&E	*9,803*	*3,159,678*	*9,618*	*3,159,114*	*9,855*	*3,201,928*	*10,230*	*3,526,928*	*375*	*325,000*
BA, B&F	---	*31,788*	---	*43,289*	---	*12,788*	---	*30,788*	---	*18,000*
21st Century Cures	*136*	*75,000*	*187*	*64,592*	*187*	*70,000*	*187*	*50,000*	---	*-20,000*
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	---	---	---	---	*1,000*	---	---	---	*-1,000*
MCMi - No Year	---	---	---	---	---	---				
Opioids - No Year	---	---	*33*	*48,257*	---	---				
Total Program Level, Pre-Transfer	**17,677**	**5,941,075**	**17,535**	**6,039,321**	**18,187**	**6,051,298**	**18,662**	**6,528,622**	**475**	**477,324**
HHS OIG transfer (BA Only)	---	**-1,500**	---	**-1,500**	---	**-1,500**	---	**-1,500**	---	---
Total Budget Authority, Post-Transfer	**9,939**	**3,264,966**	**9,838**	**3,313,752**	**10,042**	**3,284,216**	**10,417**	**3,606,216**	**375**	**322,000**
Total User Fees	**7,738**	**2,674,609**	**7,697**	**2,724,069**	**8,145**	**2,765,582**	***8,245***	***2,920,906***	***100***	***155,324***
Total Program Level, Post-Transfer	**17,677**	**5,939,575**	**17,535**	**6,037,821**	**18,187**	**6,049,798**	**18,662**	**6,527,122**	**475**	**477,324**
NEF	---	**59,300**			---	**8,000**	---	---	---	---

*FY 2020 Actuals do not include $26.625M User Fee Refunds and $3K de-obligation in emerging health no year funds (MCMi no-year).

**FTE figures do not include an estimated 80 reimbursable, 1 FOIA, 37 PEPFAR, and 7 COVID Supplemental.

***FDA Headquarters Budget Authority shown is not inclusive of the $1.5M OIG transfer amount, which when reflected will be $220 million

****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.

******Tropical Disease Priority Review Vouchers collection reflect estimates for FY 2021 and FY 2022.

*******The OTC Monograph User Fee Act was authorized in FY 2020 under the CARES Act PL 116-136.

BUDGET AUTHORITY CROSSWALK

Food and Drug Administration
FY 2022 Congressional Justification Crosswalk

(Dollars in Thousands)	FY 2021 Enacted		FY 2022 CJ															
			Infrastructure and B & F		Food Safety								Maternal and Infant Health and Nutrition		Emerging Chemical and Toxicological Issues		Total Food Safety	
					New Era of Smarter Food Safety													
					DMET Smarter Food Safety		Smarter Food Safety		Animal Food Safety Oversight		Subtotal New Era of Smarter Food Safety							
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:																		
Foods	**3,838**	**1,099,160**	---	---	**10**	**13,900**	**4**	**1,300**	---	---	**14**	**15,200**	**26**	**18,000**	**40**	**19,500**	**80**	**52,700**
Center	1,154	343,789	---	---	10	7,300	4	1,300	---		14	8,600	26	18,000	40	19,500	80	46,100
Field	2,684	755,371	---	---	---	6,600	---	---	---	---	---	6,600	---	---	---	---	---	6,600
Human Drugs	**2,083**	**689,195**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Center	1,324	510,226	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Field	759	178,969	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Biologics	**811**	**254,138**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Center	590	212,132	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Field	221	42,006	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Animal Drugs and Foods	**825**	**192,369**	---	---	**2**	**6,387**	**12**	**3,600**	**13**	**16,400**	**27**	**26,387**	---	---	---	---	**27**	**26,387**
Center	515	123,599	---	---	2	5,787	12	3,600	5	2,300	19	11,687	---		---		19	11,687
Field	310	68,770	---	---	---	600	---		8	14,100	8	14,700	---	---	---	---	8	14,700
Devices and Radiological Health	**1,508**	**408,108**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Center	1,022	323,103	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Field	486	85,005	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
National Center for Toxicological Research	**276**	**66,712**	---	---	---	---	---	**750**	---		---	**750**	---	---	---	**150**	---	**900**
FDA Headquarters	**514**	**194,951**	---	---	**5**	**2,500**	---	---	---	---	**5**	**2,500**	---	---	---	---	**5**	**2,500**
FDA White Oak Complex	---	**45,914**	---	**2,500**	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Other Rent and Rent Related	---	**84,262**	---	**17,833**	---	---	---	---	---	---	---	---	---	---	---	---	---	---
GSA Rental Payments	---	**167,119**	---	**-833**	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Subtotal, Salaries and Expenses Account	**9,855**	**3,201,928**	---	**19,500**	**17**	**22,787**	**16**	**5,650**	**13**	**16,400**	**46**	**44,837**	**26**	**18,000**	**40**	**19,650**	**112**	**82,487**
Buildings and Facilities Account	---	**12,788**		**18,000**	---	---	---	---	---	---	---	---					---	---
Total Budget Authority, Pre-Transfer	**9,855**	**3,214,716**	---	**37,500**	**17**	**22,787**	**16**	**5,650**	**13**	**16,400**	**46**	**44,837**	**26**	**18,000**	**40**	**19,650**	**112**	**82,487**
Non-Field Activities	**5,395**	**1,774,512**	---	---	**17**	**15,587**	**16**	**5,650**	**5**	**2,300**	**38**	**23,537**	**26**	**18,000**	**40**	**19,650**	**104**	**61,187**
Field Activities	**4,460**	**1,130,121**	---	---	---	**7,200**	---	---	**8**	**14,100**	**8**	**21,300**	---	---	---	---	**8**	**21,300**
Rent Activities, B&F, and White Oak	---	**310,083**	---	**37,500**	---	---	---	---	---	---	---	---	---	---	---	---	---	---
21st Century Cures	**187**	**70,000**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	**1,000**															---	**-1,000**
Total Budget Authority with 21st Century Cures	**10,042**	**3,285,716**	---	**37,500**	**17**	**22,787**	**16**	**5,650**	**13**	**16,400**	**46**	**44,837**	**26**	**18,000**	**40**	**19,650**	**112**	**81,487**
HHS OIG transfer	---	**-1,500**																

Food and Drug Administration
FY 2022 Congressional Justification Crosswalk

(Dollars in Thousands)	FY 2022 CJ													
	Medical Product Safety													
	Shortages & Supply Chain		CVM Medical Product Supply Chain		Drug Safety Surveillance and Oversight		Advancing the Goal of Ending the Opioid Crisis		Predictive Toxicology Roadmap		DMET Medical Product Safety		Total Medical Product Safety	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:														
Foods	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Center	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Field	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Human Drugs	---	---	---	---	**18**	**5,600**	**40**	**36,000**	---	---	---	---	**58**	**41,600**
Center	---	---	---		18	5,600	15	26,000	---	---	---		33	31,600
Field	---	---	---	---	---	---	25	10,000	---	---	---	---	25	10,000
Biologics	---	---	---	---	---	---	---	---	---	---	---	**900**	---	**900**
Center	---	---	---		---	---	---	---	---	---	---	900	---	900
Field	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Animal Drugs and Foods	---	---	**7**	**2,300**	---	---	---	---	---	---	**6**	**4,913**	**13**	**7,213**
Center	---	---	7	2,300	---	---	---	---	---	---	6	4,913	13	7,213
Field	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Devices and Radiological Health	**18**	**21,600**	---	---	---	---	---	**2,000**	---	---	---	**2,800**	**18**	**26,400**
Center	18	21,600	---	---	---	---	---	2,000	---	---	---	2,800	18	26,400
Field	---	---	---		---	---	---	---	---	---	---	---	---	---
National Center for Toxicological Research	---	---	---	---	---	---	---		---	**7,500**	---	---	---	**7,500**
FDA Headquarters	---	---	---		---		---	---	---	---	---	---	---	---
FDA White Oak Complex	---	---	---	---	---	---	---	---		---	---	---	---	---
Other Rent and Rent Related	---	---	---	---	---	---	---	---	---	---	---	---	---	---
GSA Rental Payments	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Subtotal, Salaries and Expenses Account	**18**	**21,600**	**7**	**2,300**	**18**	**5,600**	**40**	**38,000**	---	**7,500**	**6**	**8,613**	**89**	**83,613**
Buildings and Facilities Account												---	---	---
Total Budget Authority, Pre-Transfer	**18**	**21,600**	**7**	**2,300**	**18**	**5,600**	**40**	**38,000**	---	**7,500**	**6**	**8,613**	**89**	**83,613**
Non-Field Activities	**18**	**21,600**	**7**	**2,300**	**18**	**5,600**	**15**	**28,000**	---	**7,500**	**6**	**8,613**	**64**	**73,613**
Field Activities	---	---	---	---	---	---	**25**	**10,000**	---	---	---	---	**25**	**10,000**
Rent Activities, B&F, and White Oak	---	---	---	---	---	---	---	---	---	---	---	---	---	---
21st Century Cures	---	---	---	---	---	---	---	---	---	---	---	---	---	**-20,000**
Seafood Safety Studies-GP Sec. 763 (No-Year)													---	---
Total Budget Authority with 21st Century Cures	**18**	**21,600**	**7**	**2,300**	**18**	**5,600**	**40**	**38,000**	---	**7,500**	**6**	**8,613**	**89**	**63,613**
HHS OIG transfer														
Total Budget Authority, Post-Transfer	**18**	**21,600**	**7**	**2,300**	**18**	**5,600**	**40**	**38,000**	---	**7,500**	**6**	**8,613**	**89**	**63,613**

Food and Drug Administration
FY 2022 Congressional Justification Crosswalk

(Dollars in Thousands)	FY 2022 CJ																		FY 2022 President's Budget	
	Crosscutting																Total Changes			
	DMET Enterprise Wide		Inspections		Pay Cost		Office of Minority Health and Health Equity		Capacity Building						Total Crosscutting					
									Laboratory Safety		Office of the Chief Counsel		Essential Services							
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:																				
Foods	**10**	**9,374**	**12**	**3,500**	---	**7,049**	---	---	---	---	---	---	**6**	**10,302**	**28**	**30,225**	**108**	**82,925**	**3,946**	**1,182,085**
Center	3	2,992	---	---	---	2,731	---	---	---	---	---	---	2	3,294	5	9,017	85	55,117	1,239	398,906
Field	7	6,382	12	3,500	---	4,318	---	---	---	---	---	---	4	7,008	23	21,208	23	27,808	2,707	783,179
Human Drugs	**17**	**15,848**	**26**	**7,500**	---	**3,941**	---	---	---	---	---	---	**9**	**16,385**	**52**	**43,674**	**110**	**85,274**	**2,193**	**774,469**
Center	15	14,043	---	---	---	2,808	---	---	---	---	---	---	8	14,404	23	31,255	56	62,855	1,380	573,081
Field	2	1,805	26	7,500	---	1,133	---	---	---	---	---	---	1	1,981	29	12,419	54	22,419	813	201,388
Biologics	**6**	**4,644**	**16**	**4,500**	---	**1,470**	---	---	---	---	---	---	**2**	**4,462**	**24**	**15,076**	**24**	**15,976**	**835**	**270,114**
Center	5	4,119	---	---	---	1,109	---	---	---	---	---	---	2	3,885	7	9,113	7	10,013	597	222,145
Field	1	525	16	4,500	---	361	---	---	---	---	---	---	---	577	17	5,963	17	5,963	238	47,969
Animal Drugs and Foods	**2**	**1,968**	**1**	**300**	---	**1,332**	---	---	---	---	---	---	**1**	**2,377**	**4**	**5,977**	**44**	**39,577**	**869**	**231,946**
Center	1	1,231	---	---	---	906	---	---	---	---	---	---	1	1,568	2	3,705	34	22,605	549	146,204
Field	1	737	1	300	---	426	---	---	---	---	---	---	---	809	2	2,272	10	16,972	320	85,742
Devices and Radiological Health	**6**	**5,975**	**10**	**3,000**	---	**2,714**	---	---	---	---	---	---	**3**	**5,849**	**19**	**17,538**	**37**	**43,938**	**1,545**	**452,046**
Center	5	4,820	---	---	---	1,924	---	---	---	---	---	---	2	4,580	7	11,324	25	37,724	1,047	360,827
Field	1	1,155	10	3,000	---	790	---	---	---	---	---	---	1	1,269	12	6,214	12	6,214	498	91,219
National Center for Toxicological Research	**1**	**515**	---	---	---	**402**	---	---	---	---	---	---	---	**916**	**1**	**1,833**	**1**	**10,233**	**277**	**76,945**
FDA Headquarters	**7**	**6,176**	---	---	---	**992**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	---	**9**	**46**	**25,077**	**51**	**27,577**	**565**	**222,528**
FDA White Oak Complex	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**2,500**	---	**48,414**
Other Rent and Rent Related	---	---	---	---	---		---	---	---	---	---		---	---	---	---	---	**17,833**	---	**102,095**
GSA Rental Payments	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-833**	---	**166,286**
Subtotal, Salaries and Expenses Account	**49**	**44,500**	**65**	**18,800**	---	**17,900**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	**21**	**40,300**	**174**	**139,400**	**375**	**325,000**	**10,230**	**3,526,928**
Buildings and Facilities Account	---	---			---	---	---	---			---	---	---	---	---	---	---	**18,000**	---	**30,788**
Total Budget Authority, Pre-Transfer	**49**	**44,500**	**65**	**18,800**	---	**17,900**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	**21**	**40,300**	**174**	**139,400**	**375**	**343,000**	**10,230**	**3,557,716**
Non-Field Activities	**37**	**33,896**	---	---	---	**10,873**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	**15**	**28,656**	**91**	**91,325**	**259**	**226,125**	**5,654**	**2,000,637**
Field Activities	**12**	**10,604**	**65**	**18,800**	---	**7,027**	---	---	---	---	---	---	**6**	**11,644**	**83**	**48,075**	**116**	**79,375**	**4,576**	**1,209,496**
Rent Activities, B&F, and White Oak	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**37,500**	---	**347,583**
21st Century Cures	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-20,000**	**187**	**50,000**
Seafood Safety Studies-GP Sec. 763 (No-Year)															---	---	---	**-1,000**	---	---
Total Budget Authority with 21st Century Cures	**49**	**44,500**	**65**	**18,800**	---	**17,900**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	**21**	**40,300**	**174**	**139,400**	**375**	**322,000**	**10,417**	**3,607,716**
HHS OIG transfer																		---	---	**-1,500**
Total Budget Authority, Post-Transfer	**49**	**44,500**	**65**	**18,800**	---	**17,900**	**3**	**4,700**	**11**	**6,600**	**25**	**6,600**	**21**	**40,300**	**174**	**139,400**	**375**	**322,000**	**10,417**	**3,606,216**

MAJOR ACTIVITIES TABLE

(Dollars in Thousands)	FY 2020 Final						FY 2021 Enacted						FY 2022 President's Budget						FY 2022 President's Budget +/- FY 2021 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		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	**3,819**	**1,087,381**	---	---	**3,819**	**1,087,381**	**3,838**	**1,099,160**	---	---	**3,838**	**1,099,160**	**3,946**	**1,182,085**	---	---	**3,946**	**1,182,085**	**108**	**82,925**	---	---	**108**	**82,925**
Center	1,141	334,966	---	---	1,141	334,966	1,154	343,789	---	---	1,154	343,789	1,239	398,906	---	---	1,239	398,906	85	55,117	---	---	85	55,117
Field	2,678	752,415	---	---	2,678	752,415	2,684	755,371	---	---	2,684	755,371	2,707	783,179	---	---	2,707	783,179	23	27,808	---	---	23	27,808
Human Drugs	---	---	**2,075**	**683,195**	**2,075**	**683,195**	---	---	**2,083**	**689,195**	**2,083**	**689,195**	---	---	**2,193**	**774,469**	**2,193**	**774,469**	---	---	**110**	**85,274**	**110**	**85,274**
Center	---	---	1,316	507,726	1,316	507,726	---	---	1,324	510,226	1,324	510,226	---	---	1,380	573,081	1,380	573,081	---	---	56	62,855	56	62,855
Field	---	---	759	175,469	759	175,469	---	---	759	178,969	759	178,969	---	---	813	201,388	813	201,388	---	---	54	22,419	54	22,419
Biologics	---	---	**803**	**252,138**	**803**	**252,138**	---	---	**811**	**254,138**	**811**	**254,138**	---	---	**835**	**270,114**	**835**	**270,114**	---	---	**24**	**15,976**	**24**	**15,976**
Center	---	---	582	210,132	582	210,132	---	---	590	212,132	590	212,132	---	---	597	222,145	597	222,145	---	---	7	10,013	7	10,013
Field	---	---	221	42,006	221	42,006	---	---	221	42,006	221	42,006	---	---	238	47,969	238	47,969	---	---	17	5,963	17	5,963
Animal Drugs and Foods	**617**	**139,503**	**207**	**51,366**	**824**	**190,869**	**618**	**140,003**	**207**	**52,366**	**825**	**192,369**	**649**	**170,860**	**220**	**61,086**	**869**	**231,946**	**31**	**30,857**	**13**	**8,720**	**44**	**39,577**
Center	321	73,646	193	48,453	514	122,099	322	74,146	193	49,453	515	123,599	343	88,112	206	58,092	549	146,204	21	13,966	13	8,639	34	22,605
Field	296	65,857	14	2,913	310	68,770	296	65,857	14	2,913	310	68,770	306	82,748	14	2,994	320	85,742	10	16,891	---	81	10	16,972
Devices and Radiological Health	---	---	**1,493**	**395,168**	**1,493**	**395,168**	---	---	**1,508**	**408,108**	**1,508**	**408,108**	---	---	**1,545**	**452,046**	**1,545**	**452,046**	---	---	**37**	**43,938**	**37**	**43,938**
Center	---	---	1,007	310,163	1,007	310,163	---	---	1,022	323,103	1,022	323,103	---	---	1,047	360,827	1,047	360,827	---	---	25	37,724	25	37,724
Field	---	---	486	85,005	486	85,005	---	---	486	85,005	486	85,005	---	---	498	91,219	498	91,219	---	---	12	6,214	12	6,214
National Center for Toxicological Research	**45**	**10,317**	**231**	**56,395**	**276**	**66,712**	**21**	**5,087**	**255**	**61,625**	**276**	**66,712**	**21**	**6,088**	**256**	**70,857**	**277**	**76,945**	---	**1,001**	**1**	**9,232**	**1**	**10,233**
FDA Headquarters	**178**	**54,739**	**335**	**113,181**	**513**	**186,920**	**179**	**56,239**	**335**	**119,712**	**514**	**194,951**	**199**	**66,776**	**366**	**136,752**	**565**	**222,528**	**20**	**10,537**	**31**	**17,040**	**51**	**27,577**
FDA White Oak Complex	---	---	---	---	---	**45,914**	---	---	---	---	---	**45,914**	---	---	---	---	---	**48,414**	---	---	---	---	---	**2,500**
Other Rent and Rent Related	---	**40,450**	---	**39,723**	---	**80,173**	---	**42,513**	---	**41,749**	---	**84,262**	---	**51,510**	---	**50,585**	---	**102,095**	---	**8,997**	---	**8,836**	---	**17,833**
GSA Rental Payments	---	**79,947**	---	**91,261**	---	**171,208**	---	**78,038**	---	**89,081**	---	**167,119**	---	**77,649**	---	**88,637**	---	**166,286**	---	**-389**	---	**-444**	---	**-833**
SUBTOTAL, BA Salaries and Expenses	**4,659**	**1,412,337**	**5,144**	**1,682,427**	**9,803**	**3,159,678**	**4,656**	**1,421,040**	**5,199**	**1,715,974**	**9,855**	**3,201,928**	**4,815**	**1,554,968**	**5,415**	**1,904,546**	**10,230**	**3,526,928**	**159**	**133,928**	**216**	**188,572**	**375**	**325,000**
Building and Facilities	---	---	---	---	---	**31,788**	---	---	---	---	---	**12,788**	---	---	---	---	---	**30,788**	---	---	---	---	---	**18,000**
Non-Field Activities	**1,685**	**473,668**	**3,664**	**1,246,050**	**5,349**	**1,738,718**	**1,676**	**479,261**	**3,719**	**1,276,251**	**5,395**	**1,774,512**	**1,802**	**559,882**	**3,852**	**1,421,754**	**5,654**	**2,000,636**	**126**	**80,621**	**133**	**145,503**	**259**	**226,124**
Field Activities	**2,974**	**818,272**	**1,480**	**305,393**	**4,454**	**1,123,665**	**2,980**	**821,228**	**1,480**	**308,893**	**4,460**	**1,130,121**	**3,013**	**865,927**	**1,563**	**343,570**	**4,576**	**1,209,497**	**33**	**44,699**	**83**	**34,677**	**116**	**79,376**
White Oak, Rent Activities, and B&F	---	**120,397**	---	**130,984**	---	**329,083**	---	**120,551**	---	**130,830**	---	**310,083**	---	**129,159**	---	**139,222**	---	**347,583**	---	**8,608**	---	**8,392**	---	**37,500**
21st Century Cures	---	---	**136**	**75,000**	**136**	**75,000**	---	---	**187**	**70,000**	**187**	**70,000**	---	---	**187**	**50,000**	**187**	**50,000**	---	---	---	**-20,000**	---	**-20,000**
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	---	---	---	---	---	---	**1,000**	---	---	---	**1,000**	---	---	---	---	---	---	---	**-1,000**	---	---	---	**-1,000**
Total BA	**4,659**	**1,412,337**	**5,280**	**1,757,427**	**9,939**	**3,266,466**	**4,656**	**1,422,040**	**5,386**	**1,785,974**	**10,042**	**3,285,716**	**4,815**	**1,554,968**	**5,602**	**1,954,546**	**10,417**	**3,607,716**	**159**	**132,928**	**216**	**168,572**	**375**	**322,000**
Total BA, Pre-Transfer	**4,659**	**1,412,337**	**5,280**	**1,757,427**	**9,939**	**3,266,466**	**4,656**	**1,422,040**	**5,386**	**1,785,974**	**10,042**	**3,285,716**	**4,815**	**1,554,968**	**5,602**	**1,954,546**	**10,417**	**3,607,716**	**159**	**132,928**	**216**	**168,572**	**375**	**322,000**

(Dollars in Thousands)	FY 2020 Final						FY 2021 Enacted						FY 2022 President's Budget						FY 2022 President's Budget +/- FY 2021 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		Product Safety and Availability		Total	
Programs	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**
Total User Fees	**50**	**16,140**	**6,591**	**1,936,206**	**7,738**	**2,674,609**	**50**	**16,425**	**6,736**	**2,026,688**	**8,145**	**2,765,582**	**50**	**16,749**	**6,745**	**2,081,479**	**8,245**	**2,920,906**	**---**	**324**	**9**	**54,791**	**100**	**155,324**
Current Law																								
Prescription Drug (PDUFA)	---	---	3,620	1,074,714	3,620	1,074,714	---	---	3,692	1,107,199	3,692	1,107,199	---	---	3,701	1,141,861	3,701	1,141,861	---	---	9	34,662	**9**	**34,662**
Medical Device (MDUFA)	---	---	849	220,142	849	220,142	---	---	878	236,059	878	236,059	---	---	878	241,431	878	241,431	---	---	---	5,372	**---**	**5,372**
Generic Drug (GDUFA)	---	---	1,740	513,223	1,740	513,223	---	---	1,740	520,208	1,740	520,208	---	---	1,740	527,848	1,740	527,848	---	---	---	7,640	**---**	**7,640**
Biosimilars (BsUFA)	---	---	128	41,923	128	41,923	---	---	126	42,494	126	42,494	---	---	126	43,116	126	43,116	---	---	---	622	**---**	**622**
Animal Drug (ADUFA)	---	---	121	30,611	121	30,611	---	---	144	33,340	144	33,340	---	---	144	33,836	144	33,836	---	---	---	496	**---**	**496**
Animal Generic Drug (AGDUFA)	---	---	65	20,151	65	20,151	---	---	77	22,797	77	22,797	---	---	77	23,137	77	23,137	---	---	---	340	**---**	**340**
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	1,060	712,000	---	---	---	---	1,322	712,000	---	---	---	---	1,413	712,000	---	---	---	---	**91**	**---**
Mammography Quality Standards Act (MQSA)	---	---	37	18,253	37	18,253	---	---	37	18,619	37	18,619	---	---	37	18,991	37	18,991	---	---	---	372	**---**	**372**
Color Certification	---	---	---	---	37	10,263	---	---	---	---	37	10,469	---	---	---	---	37	10,678	---	---	---	---	**---**	**209**
Export Certification	---	2,003	26	2,787	26	4,790	---	2,003	26	2,883	26	4,886	---	2,043	26	2,940	26	4,983	---	40	---	57	**---**	**97**
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	2,506	---	2,506	---	---	---	2,556	---	2,556	---	---	---	2,608	---	2,608	---	---	---	52	**---**	**52**
Priority Review Vouchers (PRV) Pediatric Disease	---	---	---	7,840	---	7,840	---	---	11	7,997	11	7,997	---	---	11	8,156	11	8,156	---	---	---	159	**---**	**159**
Priority Review Vouchers (PRV) Medical Countermeasures			---	2,506	---	2,506			---	2,556	---	2,556			---	2,608	---	2,608	---	---	---	52	**---**	**52**
Food and Feed Recall	5	1,463	---	---	5	1,463	5	1,492	---	---	5	1,492	5	1,522	---	---	5	1,522	---	30	---	---	**---**	**30**
Food Reinspection	24	6,542	---	---	24	6,542	24	6,673	---	---	24	6,673	24	6,805	---	---	24	6,805	---	132	---	---	**---**	**132**
Voluntary Qualified Importer Program	20	5,406	---	---	20	5,406	20	5,515	---	---	20	5,515	20	5,624	---	---	20	5,624	---	109	---	---	**---**	**109**
Third Party Auditor Program	1	726	---	---	1	726	1	742	---	---	1	742	1	755	---	---	1	755	---	13	---	---	**---**	**13**
Outsourcing Facility	---	---	5	1,550	5	1,550	---	---	5	1,580	5	1,580			5	1,613	5	1,613	---	---	---	33	**---**	**33**
Over the Counter Monograph	---	---	---	---	---	---	---	---	---	28,400	---	28,400	---	---	---	28,968	---	28,968	---	---	---	568	**---**	**568**
Proposed											---	---					---	---	---	---	---	---	**---**	**---**
Export Certification (Proposed)	---	---	---	---	---		---	---	---	---	---	---	---	---	---	4,366	---	4,366	---	---	---	4,366	**---**	**4,366**
Expand Tobacco Products (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	100,000	---	---	---	---	**---**	**100,000**
Food and Feed additive user fee (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**---**	**---**
Cosmetics (Proposed)	---	---	---		---		---	---	---		---		---	---	---		---	---	---	---	---	---	**---**	**---**
Total Program Level, Pre-Transfer	**4,709**	**1,428,477**	**11,871**	**3,693,633**	**17,677**	**5,941,075**	**4,706**	**1,438,465**	**12,122**	**3,812,662**	**18,187**	**6,051,298**	**4,865**	**1,571,717**	**12,347**	**4,036,025**	**18,662**	**6,528,622**	**159**	**133,252**	**225**	**223,363**	**475**	**477,324**
HHS OIG transfer	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**---**
Total BA, Post-Transfer	**4,659**	**1,412,337**	**5,280**	**1,757,427**	**9,939**	**3,264,966**	**4,656**	**1,422,040**	**5,386**	**1,785,974**	**10,042**	**3,284,216**	**4,815**	**1,554,968**	**5,602**	**1,954,546**	**10,417**	**3,606,216**	**159**	**132,928**	**216**	**168,572**	**375**	**322,000**
Total Program Level, Post-Transfer	**4,709**	**1,428,477**	**11,871**	**3,693,633**	**17,677**	**5,939,575**	**4,706**	**1,438,465**	**12,122**	**3,812,662**	**18,187**	**6,049,798**	**4,865**	**1,571,717**	**12,347**	**4,036,025**	**18,662**	**6,527,122**	**159**	**133,252**	**225**	**223,363**	**475**	**477,324**

*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.

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

***Funding and FTE levels for FY 2020 and FY 2021 are shown without a comparability adjustment to reflect the updated realignment of the FDA HQ organizations

****FY 2021 reflects a correction to the Joint Explanatory Statement, shifting $1M for NARM from FS to MPS for Animal Drugs and Foods

TECHNICAL NOTES

	FTE	$000
Foods	---	**541**
Budget Authority	---	***541***
Center	---	196
Field	---	344
Human Drugs	---	**672**
User Fees	---	***672***
Center	---	534
User Fees	---	534
Prescription Drug (PDUFA)	---	201
Generic Drug (GDUFA)	---	330
Biosimilars (BsUFA)	---	3
Field	---	138
Budget Authority	---	---
User Fees	---	138
Generic Drug (GDUFA)	---	138
Biologics	---	**199**
User Fees	---	***199***
Center	---	169
User Fees	---	169
Prescription Drug (PDUFA)	---	79
Generic Drug (GDUFA)	---	90
Field	---	29
Prescription Drug (PDUFA)	---	29
Animal Drugs and Foods	---	**107**
Budget Authority	---	***87***
User Fees	---	***20***
Center	---	67
Budget Authority	---	47
User Fees	---	20
Animal Drug (ADUFA)	---	1
Animal Generic Drug (AGDUFA)	---	19
Field	---	40
Budget Authority	---	40
Devices and Radiological Health	---	**248**
Budget Authority	---	***18***
User Fees	---	***230***
Center	---	184
Prescription Drug (PDUFA)	---	184
Field	---	65
Budget Authority	---	18
User Fees	---	46
Medical Device (MDUFA)	---	46
National Center for Toxicological Research (BA Only)	---	**49**
Tobacco	---	**160**
Center	---	**160**
Family Smoking Prevention and Tobacco Control Act	---	160
FDA Headquarters	---	**-1,975**
Budget Authority	---	-695
User Fees	---	***-1,281***
Prescription Drug (PDUFA)	---	-493
Medical Device (MDUFA)	---	-46
Generic Drug (GDUFA)	---	-558
Biosimilars (BsUFA)	---	-4
Animal Drug (ADUFA)	---	-1
Animal Generic Drug (AGDUFA)	---	-19
Family Smoking Prevention and Tobacco Control Act	---	-160
Subtotal, Salaries and Expenses	---	-
Buildings and Facilities (Budget Authority)	---	---
Total Program Level	---	-
Non-Field Activities	---	*-616*
Field Activities	---	*616*

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; [$5,876,025,000] *$6,250,157,000*: Provided, That of the amount provided under this heading, [$1,107,199,000] *$1,141,861,000* 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; [$236,059,000] *$241,431,000* 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; [$520,208,000] *$527,848,000* 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; [$42,494,000] *$43,116,000* 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; [$33,340,000] *$33,836,000* 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; [$22,797,000] *$23,137,000* 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] *$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 [2021] *2022* 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 [2021] *2022*, including any such fees collected prior to fiscal year [2021] *2022* but credited for fiscal year [2021] *2022*, shall be subject to the fiscal year [2021] *2022* limitations: Provided further, That the Secretary may accept payment during fiscal year [2021] *2022* of user fees specified under this heading and authorized for fiscal year [2022] *2023*, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year [2022] *2023* for which the Secretary accepts payment in fiscal year [2021] *2022* 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) $1,099,160,000 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) $1,996,126,000 shall be for the Center for Drug Evaluation and Research and related field activities in the Office of Regulatory Affairs; (3) $437,071,000 shall be for the Center for Biologics Evaluation and Research and for related field activities in the Office of Regulatory Affairs; (4) $244,350,000 shall be for the Center for Veterinary Medicine and for related field activities in the Office of Regulatory Affairs; (5) $609,121,000 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) $681,513,000 shall be for the Center for Tobacco Products and for related field activities in the Office of Regulatory Affairs; (8) $188,707,000 shall be for Rent and Related activities, of which $52,944,000 is for White Oak Consolidation, other than the amounts paid to the General Services Administration for rent; (9) $235,112,000 shall be for payments to the General Services Administration for rent; and (10) $318,153,000 shall be for other activities, including the Office of the Commissioner of Food and Drugs, the Office of Food Policy and Response, 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, [$12,788,000] *$30,788,000*, to remain available until expended.

FDA Innovation Account, Cures Act (Including Transfer of Funds)

For necessary expenses to carry out the purposes described under section 1002(b)(4) of the 21st Century Cures Act, in addition to amounts available for such purposes under the heading ``Salaries and Expenses'', [$70,000,000] *$50,000,000*, to remain available until expended: Provided, That amounts appropriated in this paragraph are appropriated pursuant to section 1002(b)(3) of the 21st Century Cures Act, are to be derived from amounts transferred under section 1002(b)(2)(A) of such Act, and may be transferred by the Commissioner of Food and Drugs to the appropriation for ``Department of Health and Human Services Food and Drug Administration Salaries and Expenses'' solely for the purposes provided in such Act: Provided further, That upon a determination by the Commissioner that funds transferred pursuant to the previous proviso are not necessary for the purposes provided, such amounts may be transferred back to the account: Provided further, That such transfer authority is in addition to any other transfer authority provided by law.

Salaries and Expenses (Legislative Proposal, not subject to PAYGO)

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, 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.

Note:

The Salaries and Expenses Appropriation Language shown above differs slightly from the language included within the President’s Budget Appendix, which will be corrected accordingly.

FY 2022 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 [2021] *2022*; 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
Tobacco Control Act Fee Increase	The Administration proposes legislation to increase the fees collected under the Tobacco Control Act. 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 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
General Fund Discretionary Appropriation:			
Appropriation	3,264,966	3,284,216	3,606,216
Coronavirus Preparedness and Responses Supplemental Appropriations Act (P.L. 116-123)	61,000	---	---
Coronavirus Aid, Relief, and Economic Security Act (P.L. 116-136)	80,000	---	---
Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139)	22,000	---	---
Consolidated Appropriations Act (P.L. 116-260)	---	55,000	---
Total Discretionary Appropriation	**3,427,966**	**3,339,216**	**3,606,216**
Mandatory Appropriation:			
CRADA	2,000	2,000	2,000
American Rescue Plan Act of 2021 (P.L. 117-2)	---	500,000	---
Total Mandatory Appropriation	**2,000**	**502,000**	**2,000**
Offsetting Collections:			
Non-Federal Sources:	2,674,609	2,765,582	2,920,906
Total Offsetting Collections	**2,674,609**	**2,765,582**	**2,920,906**
Total Obligations	**6,104,575**	**6,606,798**	**6,529,122**

*FY 2020, FY 2021 and FY 2022 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.

SUMMARY OF CHANGES

FY 2021 Enacted	
Total estimated budget authority	$3,284.200
(Obligations)	
FY 2022 President's Budget	
Total estimated budget authority	$3,606.200
(Obligations)	
Net Change	+$322.000

	FY 2021 Enacted		FY 2022 President's Budget 1/		FY 2022 +/- FY 2021	
	FTE	BA	FTE	BA	FTE	BA
Increases:						
Built-in:						
Annualization of 2020 commissioned corps pay increase	--	$2.157	--	$3.367	--	+$1.210
Annualization of 2020 civilian pay increase	--	$63.455	--	$80.145	--	+$16.690
Subtotal, Built-in Increases	--	**$65.612**	--	**$83.512**	--	**+$17.900**
Infrastructure and Buildings & Facilities	--	$310.083	--	$347.583	--	+$37.500
Food Safety					--	--
Infant and Maternal Health and Nutrition	--	--	26	$18.000	+26	+$18.000
Emerging Chemical and Toxicology Issues	--	--	40	$19.650	+40	+$19.650
New Era					--	--
DMET Smarter Food Safety	--	--	17	$22.787	+17	+$22.787
Smarter Food Safety	--	--	16	$5.650	+16	+$5.650
Animal Food Safety Oversight	--	--	13	$16.400	+13	+$16.400
Medical Product Safety					--	--
Shortages & Supply Chain	--	--	18	$21.600	+18	+$21.600
CVM Medical Product Supply Chain	--	--	7	$2.300	+7	+$2.300
Drug Safety Surveillance and Oversight	--	--	18	$5.600	+18	+$5.600
Opioids 2/	14	$75.011	54	$113.011	+40	+$38.000
Predictive Toxicology Roadmap	--	--	--	$7.500	--	+$7.500
DMET Medical Product Safety	--	--	6	$8.613	+6	+$8.613
Crosscutting					--	--
DMET Enterprise Technology and Data	--	--	49	$44.500	+49	+$44.500
Inspections	--	--	65	$18.800	+65	+$18.800
Capacity Building:					--	--
Office of Minority Health and Health Equity	--	--	3	$4.700	+3	+$4.700
Lab Safety	--	--	11	$6.600	+11	+$6.600
Office of the Chief Counsel	--	--	25	$6.600	+25	+$6.600
Essential Services	--	--	21	$40.300	+21	+$40.300
Subtotal, Program Increases	**14**	**$385.094**	**389**	**$710.194**	**+375**	**+$325.100**
Total Increases	**14**	**$450.706**	**389**	**$793.706**	**+375**	**+$343.000**
Decreases:						
21 Century Cures	187	$70.000	187	$50.000	--	-$20.000
Seafood Safety GP Sec.763 (No year)	--	$1.000	--	--	--	-$1.000
Subtotal, Program Decreases	**187**	**$71.000**	**187**	**$50.000**	**--**	**-$21.000**
Total Decreases	**187**	**$71.000**	**187**	**$50.000**	**--**	**-$21.000**
Net Change	**201**	**$521.706**	**576**	**$843.706**	**+375**	**+$322.000**

1/ The FY 2022 President's Budget also includes $155.324 million in user fee increases. Within this amount, $100.000 million is requested for an increase for the Tobacco Control Act to collect fees on all deemed products including e-cigarettes/other ENDS products and other deemed products. The remaining amount reflects statutorily authorized inflationary increases to user fees.
2/ The Opioids funding includes the $64.5M dedicated base funding consistent with the Operating Plan.

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
Salaries and Expenses Account:			
Foods	**1,087,381**	**1,099,160**	**1,182,625**
Center	334,966	343,789	399,102
Field	752,415	755,371	783,523
Human Drugs	**683,195**	**689,195**	**774,469**
Center	507,726	510,226	573,081
Field	175,469	178,969	201,388
Biologics	**252,138**	**254,138**	**270,114**
Center	210,132	212,132	222,145
Field	42,006	42,006	47,969
Animal Drugs and Feeds	**190,869**	**192,369**	**232,033**
Center	122,099	123,599	146,251
Field	68,770	68,770	85,782
Devices and Radiological Health	**395,168**	**408,108**	**452,064**
Center	310,163	323,103	360,827
Field	85,005	85,005	91,237
National Center for Toxicological Research	**66,712**	**66,712**	**76,994**
FDA Headquarters	**186,920**	**194,951**	**221,834**
FDA White Oak Consolidation	**45,914**	**45,914**	**48,414**
Other Rent and Rent Related	**80,173**	**84,262**	**102,095**
GSA Rental Payments	**171,208**	**167,119**	**166,286**
Subtotal, Salaries and Expenses Account	**3,159,678**	**3,201,928**	**3,526,928**
21st Century Cures	**75,000**	**70,000**	**50,000**
Seafood Safety Studies-GP Sec. 763 (No Year)	**---**	**1,000**	**---**
Buildings and Facilities Account	**31,788**	**12,788**	**30,788**
Total Budget Authority	**3,266,466**	**3,285,716**	**3,607,716**
HHS OIG Transfer	**-1,500**	**-1,500**	**-1,500**
Total Budget Authority, Post-Transfer	**3,264,966**	**3,284,216**	**3,606,216**
FTE	**9,939**	**10,042**	**10,417**

* FTE figures do not include an estimated 80 reimbursable, 1 FOIA and 37 PEPFAR.

APPROPRIATIONS HISTORY

Salaries and Expenses

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation*:				
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				
Base	5,990,342,000	5,866,703,000	5,781,442,000	5,772,442,000
Supplemental #1 (P.L. 116-123)	---	---	---	61,000,000
Supplemental #3 (P.L. 116-136)	---	---	---	80,000,000
Supplemental #4 (P.L. 116-139)	---	---	---	22,000,000
FY 2021				
Base	6,058,065,000	5,925,641,000	5,916,811,000	5,904,425,000
Supplemental #5 (P.L. 116-260)	---	---	---	55,000,000
Supplemental #6 (P.L. 117-2)	---	---	---	500,000,000
FY 2022	6,279,125,000			

* 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.

3/ 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, $75 million for FY 2020, $70 million for FY 2021, and $50 million for FY

4/ Totals do not include $1 million for Seafood Safety Studies-GP Sec. 765 received in FY 2021 Appropriation

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	11,788,000	13,788,000	12,788,000
FY 2022	30,788,000			

*FY 2020 Appropriation excludes one-time $20 million provided in P.L. 116-94, section 780.

LEGISLATIVE PROPOSALS FOR FY 2022 CONGRESSIONAL JUSTIFICATION

MEDICAL DEVICE SHORTAGES

Even after passage of the CARES Act, FDA authorities for device shortages are more limited than those available with regard to drug shortages. While the new authority has been helpful, the temporal limitation and tie to Public Health Emergency (PHE) declarations puts FDA behind in terms of responding to any early signs of supply constraints or a potential shortage situation. The COVID-19 pandemic demonstrated that by the time there is an emergency, it is often too late to prevent shortages. Supply chain disruptions were already beginning to occur even before COVID-19 cases were identified in the U.S., as other nations had outbreaks and needed personal protective equipment (PPE), testing supplies, and other equipment in excess of supply. Moreover, there are situations such as hurricanes and other natural disasters that may not ever rise to the level of a PHE, but for which device shortages could significantly impact patient care. To assure a more resilient domestic supply chain and help reduce dependence on foreign production, FDA needs additional authorities including (but not limited to) specifying that notifications should be made to FDA any time there is the potential for a shortage, and should include production volume information; providing fuller oversight of supply chain disruptions, including requiring manufacturers to perform risk assessments, implement risk management plans, and identify alternate suppliers and manufacturing sites; enabling FDA to request records in advance or in lieu of an inspection; permitting FDA to allow temporary importation of unapproved devices, with appropriate scientific and regulatory controls, when in the interest of the public health; clarifying which entities should notify FDA, including contract terminal sterilizers of medical devices; and permitting FDA to allow devices to be distributed past their labeled shelf life, with appropriate, supportive scientific data, when needed to prevent or mitigate a shortage.

PREVENTING FOOD SHORTAGES, INCLUDING INFANT FORMULA AND CERTAIN MEDICAL FOODS

No law requires manufacturers of infant formulas or medical foods to notify FDA when they become aware of a circumstance that could lead to a shortage of these products. FDA is seeking authority to require any manufacturer of infant formula, essential medical food for patients with certain inborn errors of metabolism (e.g., phenylketonuria, medium chain acyl-coenzyme A dehydrogenase deficiency), or other designated category of food to provide shortage notifications, at a reasonable time and manner during a declared public health emergency. This proposal would ensure FDA routinely receives timely and accurate information about likely or confirmed shortages in the U.S. of infant formulas and essential medical foods for patients with certain inborn errors of metabolism to enable FDA to take steps to promote the continued availability of these infant formulas and essential medical foods of public health importance. The recent COVID-19 pandemic has demonstrated the need to help ensure the continuity of the food supply so that consumers have access to a safe and adequate food supply during public health crises. The proposal also would provide for reporting shortages of other categories of food, as designated by FDA.

IMPROVING CRITICAL INFRASTRUCTURE THROUGH IMPROVED DATA SHARING: REQUIRING MORE ACCURATE PHARMACEUTICAL SUPPLY CHAIN INFORMATION

This proposal would further clarify FDA's authority to require information that would improve FDA's ability to assess pharmaceutical critical infrastructure as well as manufacturing quality

and capacity. For example, FDA is seeking to require detailed drug listings on a quarterly basis for finished drug product or in-process material, regardless of whether they were directly or indirectly imported into the U.S. This proposal would cover both human and animal pharmaceutical products and would create new requirements for manufacturers of animal drugs to notify FDA about product discontinuances and manufacturing interruptions.

Lengthen Expiration Dates to Mitigate Critical Drug Shortages
Shortage 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 authorities 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.

Records in Advance of or in Lieu of Inspections
FDA currently has limited authority to request records and other information in advance of or in lieu of drug inspections. This proposal would expand FDA's authority to include other FDA-regulated products by revising section 704(a)(4) of the FD&C Act to explicitly include the authority to request records or other information in advance of or in lieu of inspections of device, food, and tobacco product establishments, and to clarify applicability for biomedical research monitoring inspections. This expanded authority would help ensure the Agency is able to continue to protect the public health, including during a public health emergency like the COVID-19 pandemic, and help ensure the availability of emerging and medically necessary products that mitigate, diagnose treat, prevent, or cure disease when travel to or inspection of an establishment is inadvisable. Further, this authority would help optimize Agency resources for oversight of some foreign facilities; help FDA determine if a facility is still in business, thereby allowing the Agency to avoid unnecessary travel; and improve efficiency of any subsequent inspections by helping to identify in advance specific products or manufacturing processes on which to focus on-site inspectional time. The Agency anticipates this authority will similarly benefit FDA partners conducting inspections, and benefit regulated industry by reducing the burden related to on-site inspectional time.

Expanding Information Disclosure Authorities with States
State, local, and territorial governments play an important role in the protection of public health, particularly as FDA partners in the regulation of products, helping to ensure the safety and integrity of supply chains, and assisting in enforcement against products that are being unlawfully sold. FDA works closely with our state partners to employ complementary authorities to achieve fast and effective action to protect the public health during national public health emergencies such as the COVID-19 crisis, other state/local disaster declarations, outbreaks or other public health events, and for routine regulatory oversight. FDA proposes to amend the FD&C Act, to allow for disclosure of non-public information to state, local, and U.S. territorial government agencies with counterpart functions related to FDA regulated products by preempting any and all related state, local, or territorial disclosure laws. This proposal would advance an integrated food safety system and more effectively leverage the oversight capabilities and resources of FDA's state regulatory partners to allow for expanded mutual reliance related activities and other partnerships. The limitations on sharing all regulated commodity information seamlessly and in real time with states prevents FDA from taking swift action to ensure a robust supply and protect the integrity of supply chains. The Agency anticipates this authority will also

benefit FDA partners conducting inspections and regulated industry by reducing the burden related to duplicative inspectional activities.

Enforcement Authority and Penalties for Counterfeit Devices

The Safeguarding Therapeutics Act (Pub. L. 116-304), signed into law on January 5, 2021, which provided a definition for "counterfeit device," included only limited enforcement provisions (*e.g.*, authority to administratively destroy medical devices that are refused entry at the time of import and that are valued at $2500 or less). FDA proposes to extend the provisions that currently apply to counterfeit drugs in sections 301 (prohibited acts), 303 (penalties), and 304 (seizure) of the FD&C Act and Title 18 of the U.S. Code to also cover counterfeit devices. Without these statutory revisions, FDA's enforcement authority for counterfeit devices, including counterfeit medical devices that are being imported to diagnose, prevent, or treat COVID-19, such as test kits, respirators, and face masks, is incomplete and there will be limited deterrence for the selling of counterfeit devices, especially domestically. The revisions proposed will help keep counterfeit devices like these out of the United States and facilitate enforcement actions against those that find their way into interstate commerce.

FOODS

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Foods	**1,098,470**	**1,087,215**	**1,110,471**	**1,194,161**	**83,690**
Budget Authority	***1,087,381***	***1,087,215***	***1,099,160***	***1,182,625***	***83,465***
User Fees	***11,089***	---	***11,311***	***11,536***	***225***
Center	335,815	334,966	344,655	399,985	55,330
Budget Authority	334,966	334,966	343,789	399,102	55,313
User Fees	849	---	866	883	17
Food and Feed Recall	*248*	---	*253*	*258*	5
Voluntary Qualified Importer Program	*248*	---	*253*	*258*	5
Third Party Auditor Program	*353*	---	*360*	*367*	7
Innovative Food Products (Proposed)	---	---	---	---	---
Field	762,655	752,249	765,816	794,176	28,360
Budget Authority	752,415	752,249	755,371	783,523	28,152
User Fees	10,240	---	10,445	10,653	208
Food and Feed Recall	*1,020*	---	*1,040*	*1,061*	21
Food Reinspection	*4,667*	---	*4,760*	*4,855*	95
Voluntary Qualified Importer Program	*4,406*	---	*4,495*	*4,584*	89
Third Party Auditor Program	*147*	---	*150*	*153*	3
FTE	**3,863**	**3,816**	**3,882**	**3,990**	***108***

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.

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[21]
- 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[22]

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.[23]

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.

[21] 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.

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

[23] 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

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.[24]

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. As of July 2020, FDA has awarded 47 states and 1 territory a total of $133 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.

Launched 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 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.[25]

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

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

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.

Provided Flexibility to Farms Regarding Eligibility for the Qualified Exemption Under the Produce Safety Rule

In May 2020, FDA announced that it will provide flexibility regarding eligibility criteria for the qualified exemption under the Produce Safety Rule during the COVID-19 public health emergency.[26]

Under the FSMA Produce Safety Rule, farms are eligible for a qualified exemption and associated modified requirements if they meet certain criteria:

- The farm's food sales averaged less than $500,000 (adjusted for inflation) per year during the previous three years, and,

- The average value of the farm's sales to qualified end-users exceeded the average value of the farm's sales to all others during the previous three years

Because of COVID-19, state and local governments across the United States have instituted public health orders that have resulted in many restaurants and retail food establishments either closing or significantly limiting their operations, leaving many farmers without their usual buyers. The guidance is intended to allow affected farmers to shift their sales away from qualified end-users while still being considered eligible for the qualified exemption.

Specifically, under the temporary policy announced in the guidance, farms that are currently eligible for the qualified exemption and associated modified requirements will still be considered eligible, even if they shift sales away from qualified end-users, so long as they continue to meet the requirement that their average food sales during the previous three years total less than $500,000 – adjusted for inflation.

FDA recognizes that providing flexibility to farms to allow them to shift food sales to available buyers during the COVID-19 public health emergency can help reduce food waste and food

[26] https://www.fda.gov/food/cfsan-constituent-updates/fda-provides-flexibility-farms-regarding-eligibility-qualified-exemption-under-produce-safety-rule

shortages. This temporary policy is intended to remain in effect only for the duration of the public health emergency, after which FDA intends to issue additional guidance.

Provided Additional Temporary Flexibilities and Policies During the COVID-19 Pandemic
In March and April 2020, FDA issued several guidances to industry to provide temporary flexibility, aid and policy in light of the COVID-19 pandemic. The guidances issued include:

- Temporary policy regarding enforcement of 21 CFR Part 118 (the Egg Safety Rule) to provide producers of shell eggs that normally would be sent to facilities for further processing the flexibility to sell eggs for distribution to retail locations[27]

- Temporary policy regarding certain requirements under the FSMA Accredited Third-Party Certification Program for foreign food entities and their products[28]

- Communicated FDA's intention to temporarily not enforce supplier verification onsite audit requirements for receiving facilities and importers under FSMA in response to the global pandemic of COVID-19[29]

- Issuance of the temporary policy regarding nutrition labeling of certain packaged food which is designed to provide restaurants and food manufacturers with flexibility regarding labeling[30]

- Temporary policy regarding nutrition labeling of standard menu items in chain restaurants and similar retail food establishments, to provide temporary flexibility to the current requirements in providing nutrition information[31]

Announced the New Era of Smarter Food Safety Blueprint
In July 2020, FDA released the New Era of Smarter Food Safety blueprint.[32]The New Era of Smarter Food Safety represents a new approach to food safety, leveraging technology and other tools to create a safer and more digital, traceable food system.

The blueprint outlines the work FDA plans to undertake over the next decade to modernize its food safety approaches and bend the curve of foodborne illness. It includes work to enhance traceability, improve predictive analytics, respond more rapidly to outbreaks, address new business models, reduce contamination of food, and foster the development of stronger food safety cultures.

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[27] https://www.govinfo.gov/content/pkg/FR-2009-07-09/pdf/E9-16119.pdf

[28] https://www.fda.gov/food/cfsan-constituent-updates/fda-issues-temporary-policy-certain-requirements-under-accredited-third-party-certification-program

[29] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-regarding-preventive-controls-and-fsvp-food-supplier-verification-onsite-audit

[30] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-regarding-nutrition-labeling-certain-packaged-food-during-covid-19-public-health

[31] https://www.fda.gov/food/cfsan-constituent-updates/fda-provides-flexibility-regarding-menu-labeling-requirements-chain-restaurants-and-similar-retail

[32] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint

In September 2020, FDA announced a proposed rule to establish additional traceability recordkeeping requirements for certain foods.[33] FDA also published a draft Food Traceability List which describes the foods that would be subject to the proposed requirements. The list includes leafy greens, fresh cut fruits and vegetables, some types of fish, shell eggs, and more. The proposed rule and draft Food Traceability List are available for public comment. FDA also held three public meetings during the public comment period.

The proposed rule, "Requirements for Additional Traceability Records for Certain Foods" (Food Traceability Proposed Rule) is a key component of FDA's New Era of Smarter Food Safety Blueprint and would implement Section 204(d) of FSMA.[34]If finalized, the proposal would standardize the data elements and information firms must establish and maintain, and the information they would need to send to the next entity in the supply chain to facilitate rapid and accurate traceability. While limited to only certain foods, this proposal lays the foundation for a standardized approach to traceability recordkeeping, paving the way for industry to adopt, harmonize, and leverage more digital traceability systems in the future.

Additionally, in October 2020, FDA began launching a voluntary pilot program to evaluate alignment of private third-party food safety audit standards with the food safety requirements in two regulations under the FSMA - the Preventive Controls for Human Food (PC Human Food)[35] and the Produce Safety rules.[36] This pilot program will help both FDA and industry better understand how to determine whether these standards align with FDA regulations, a goal that is consistent with the New Era of Smarter Food Safety Blueprint.[37]

Developed 2020 Leafy Greens STEC Action Plan

Between 2009 and 2018, FDA and the Centers for Disease Control and Prevention (CDC) identified 40 foodborne outbreaks of Shiga toxin-producing E. coli (STEC) infections in the U.S. with a confirmed or suspected link to leafy greens. While most strains of E. coli are harmless, STEC can cause bloody diarrhea, anemia, blood-clotting problems, and kidney failure – conditions that are potentially life-threatening. The most common STEC, E. coli O157:H7, is the type most often associated with outbreaks.

Most leafy greens are grown outdoors, where they are exposed to soil, animals, and water, all of which can be a source of pathogen contamination. In addition, leafy greens are mostly consumed raw, without cooking or other processing steps to eliminate microbial hazards. The Produce Safety Rule under FSMA sets science-based standards to help ensure that water, soil amendments (e.g., fertilizer or compost), food contact surfaces and other materials that touch produce during growing, harvesting, packing, and holding do not contribute to produce contamination. The Produce Safety Rule also addresses animal intrusion into fields and worker hygiene.

[33] https://www.fda.gov/food/food-safety-modernization-act-fsma/fsma-proposed-rule-food-traceability

[34] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint

[35] https://www.fda.gov/food/food-safety-modernization-act-fsma/fsma-final-rule-preventive-controls-human-food

[36] https://www.fda.gov/food/food-safety-modernization-act-fsma/fsma-final-rule-produce-safety

[37] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint

Due to the reoccurring nature of outbreaks associated with leafy greens, FDA has developed this commodity-specific action plan. The plan describes the actions FDA plans to take in 2020 to advance work in three areas: (1) prevention, (2) response, and (3) addressing knowledge gaps.

Despite challenges posed by the COVID-19 pandemic, FDA has made significant progress on the plan in 2020 and 2021. Because outbreaks have continued to occur, including a multistate outbreak of E. coli O157:H7 infections in 2020 linked to leafy greens, FDA understands that there is more work to be done to adapt its approach and strategies to address outbreaks.

Greater emphasis will be needed around such complex issues as adjacent land use, agricultural water, and understanding likely routes by which human pathogens may contaminate leafy greens. FDA has updated its approach to these issues and has outlined specific actions to address new findings and provide resources for mitigating risk.[38] For some of the most pressing issues around the broader agricultural environmental and animal activity, industry leadership will be critical to addressing potential hazards, and industry will need support from a variety of other partners.

With this in mind, FDA will continue to build on critical partnerships with other government entities, all parts of the leafy greens industry, consumer groups, retailers, and the broader agricultural community to achieve the public health impacts envisioned, recognizing that food safety is a shared responsibility.

Selected Guidances Issued in 2020

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.[39]

Date	#	Title	Description
Jun 2020	FDA-2020-D-1108	Temporary Policy Regarding Preventive Controls and FSVP Food Supplier Verification Onsite Audit Requirements During the COVID-19 Public Health Emergency	States FDA's intent, in certain circumstances related to the impact of the coronavirus outbreak (COVID-19), not to enforce requirements in three foods regulations to conduct onsite audits of food suppliers if other supplier verification methods are used instead.
May 2020	FDA-2020-D-1139	Reporting a Temporary Closure or Significantly Reduced Production by a Human Food Establishment and	Provides certain FDA-regulated food establishments with a convenient mechanism to voluntarily report to FDA if they have temporarily ceased or significantly reduced

[38] https://www.fda.gov/food/foodborne-pathogens/leafy-greens-stec-action-plan

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

Date	#	Title	Description
		Requesting FDA Assistance During the COVID-19 Public Health Emergency	production or if they are considering doing so.
May 2020	FDA-2020-D-1386	Temporary Policy During the COVID-19 Public Health Emergency Regarding the Qualified Exemption from the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption	Provides flexibility in the eligibility criteria for the qualified exemption from the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption (Produce Safety Rule) (21 CFR Part 112) due to disruptions to the supply chain for the duration of the COVID-19 public health emergency.

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 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.[40] 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 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. All investigations are tracked in FDA's CORE Investigation Table, issued in November 2020. This new tool allows FDA to give consumers early awareness of developing foodborne illness outbreaks in the United States and will also align with CDC efforts to provide information on the number of illness clusters they are investigating each week. 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.

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

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

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 eighth year and has collected more than 580,000 whole bacterial genome sequences (including more than 335,000 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 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 70 state, international, FDA, and federal partner (CDC and USDA-Food Safety and Inspection Service [FSIS]) laboratories.

In 2020, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions. To date, WGS has supported more than 730 cases of product adulteration and contaminated conditions investigated by the FDA. For example, in 2020 an outbreak of E. coli O157:H7was linked to leafy greens that affected 40 people in 19 states. Whole genome sequencing provided a strong linkage between the environmental samples and clinical cases, and helped identify the geographic region of origin.

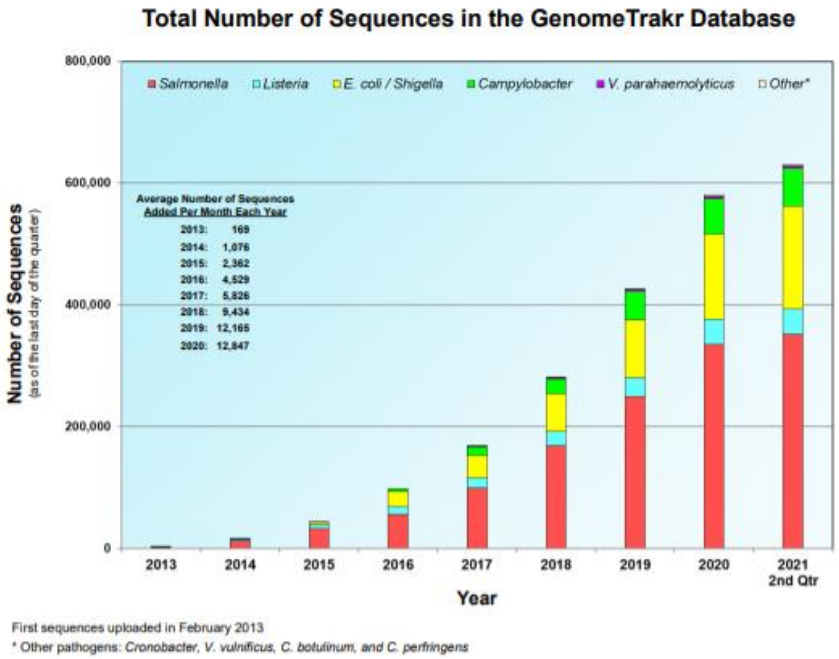


Figure 2 The Total Number of Sequences in the GenomeTrakr Database

Issued Best Practices on Safe Food Handling and Employee Health in Retail Food Settings During COVID-19 Pandemic

In April of 2020, FDA issued information and best practices for retail food stores, restaurants, and pick-up and delivery services during the pandemic to protect workers and customers.[41] Many of these are smart food safety practices that employers can consider at any time. This includes a factsheet on "Best Practices for Retail Food Stores, Restaurants, and Food Pick-Up and Delivery Services During the COVID 19 Pandemic." This information addresses key considerations for how foods offered at retail can be prepared safely and delivered to the public, as well as key best practices for employee health and personal hygiene, cleaning and sanitizing.

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 2020, FDA issued seven injunctions related to adulterated or misbranded food, dietary supplements, and cosmetics. 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.

[41] https://www.fda.gov/food/food-safety-during-emergencies/best-practices-retail-food-stores-restaurants-and-food-pick-updelivery-services-during-covid-19

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 2020, FDA issued 134 import alert notices for human food, cosmetic, and dietary supplement products.

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 2020, FDA ensured safe access to the food supply by reviewing 7 Food Additive or Color Additive Petitions, 64 GRAS notifications, and 81 premarket notifications for Food Contact Substances.

Announced Voluntary Phase-Out by Industry of Certain PFAS in Food Packaging

FDA scientists developed improved methods to detect the chemical per- and polyfluoroalkyl substances (PFAS) in foods and to better understand the impact of certain types of PFAS in the body. In July 2020, FDA announced a voluntary agreement with industry to phase-out sales of certain short-chain PFAS used as food contact substances in the U.S.[42]

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 different types of PFAS. Many PFAS are resistant to grease, oil, water, and heat. For this reason, PFAS have been used in a variety of applications including in stain- and water-resistant fabrics, cleaning products, and paints. Certain PFAS are also authorized by FDA for limited use in cookware, food packaging, and food processing equipment.

[42] https://www.fda.gov/food/cfsan-constituent-updates/fda-announces-voluntary-phase-out-industry-certain-pfas-used-food-packaging

FDA will continue working with other Department of Health and Human Services agencies, other federal agencies, and our state and local partners, to identify routes of PFAS exposure, understand associated health risks, and reduce the public's exposure to those health risks.[43]

FDA Works to Increase the Safety of Foods for Babies and Young Children

In March 2021, FDA issued a letter to baby and toddler food manufacturers and processors covered by the preventive control provisions of the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food rule. The letter reminds them of their existing responsibility to consider risks from chemical hazards—including toxic elements—when conducting a hazard analysis.[44] The preventive control provisions require industry to implement controls to significantly minimize or prevent any identified chemical hazards requiring a control.

In April 2021, FDA announced a comprehensive plan to further reduce levels of toxic elements such as lead cadmium, mercury and arsenic in foods for babies and young children. The "Closer to Zero: Action Plan for Baby Foods[45]" identifies actions the agency will take to reduce exposure to toxic elements from foods eaten by babies and young children—to as low as possible. FDA has prioritized babies and young children because their smaller body sizes and metabolism make them more vulnerable to the harmful effects of these contaminants.

FDA will set action level with respect to these toxic elements, with input from stakeholders. FDA will also encourage adoption of best practices by industry to lower levels of toxic elements in agricultural commodities and products, and increase targeted compliance and enforcement actions. Partnering with other federal agencies, academia and other stakeholders, FDA will continue its ongoing surveillance sampling of these products to monitor progress levels over time and to better understand the variability of toxic element levels in different foods and the potential impacts, if any, of low exposures on childhood development.

Inform 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 equipped 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.

Encouraged the Safe Production of Dietary Supplements

In FY 2020, FDA's operations and oversight, including inspection activities, were significantly impacted by the COVID-19 pandemic. As a result, fewer dietary supplement inspections were conducted in FY 2020 as compared with previous years. However, FDA's overall dietary supplement compliance activity continued and resulted in:

- 49 warning letters

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

[44] https://www.fda.gov/media/146423/download

[45] https://www.fda.gov/food/metals-and-your-food/closer-zero-action-plan-baby-foods

- 15 detentions
- 1 injunction (filed)

FDA continued to emphasize regulatory actions aimed at protecting consumers from dangerous or otherwise unlawful products – including fraudulent products that were, in some cases, marketed as dietary supplements. These included products making unlawful claims related to COVID-19 and products making unlawful claims about curing or preventing hangovers. In February 2020, FDA issued a public health alert warning consumers to avoid using dietary supplements containing cesium chloride or any other cesium salt.

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 2020, FDA responded to 43 NDI notifications. FDA acknowledged 16 of the notifications submitted with no objection. Of the remaining 27 notifications, nine were deemed incomplete or determined to not pertain to a dietary ingredient or dietary supplement, while FDA raised safety or identity concerns with 18.

In FY 2020, FDA received more than 3,112 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 November 2019, FDA formally convened the Botanical Safety Consortium (BSC), partnering with the National Institutes of Health's National Institute of Environmental Health Sciences and the Health and Environmental Sciences Institute. In May 2020, the BSC held its first annual public meeting.

Launched Initiative to Help Consumers Better Understand the Science Behind Foods Derived from Genetic Engineering

In March 2020, FDA launched a new education initiative called "Feed Your Mind" to help consumers better understand genetically engineered foods, commonly called GMOs or genetically modified organisms.[46]

The initiative was developed with the U.S. Department of Agriculture (USDA) and the Environmental Protection Agency (EPA) to provide consumers with science-based educational information to better understand how GMOs are made, learn more about the types of crops that have been modified, address questions they may have about the health and safety of GMOs as well as explain how GMOs are regulated in the U.S.

"Feed Your Mind" features a wide range of resources designed specifically for consumers, health care professionals and students. These materials feature new web content, fact-sheets and videos using common language, engaging graphics and stories to provide information about genetically engineered foods, including information about the history of genetic modifications in agriculture. This initiative is an on-going effort, with additional materials such as a professional learning

[46] https://www.fda.gov/food/cfsan-constituent-updates/fda-launches-feed-your-mind-help-consumers-better-understand-science-behind-foods-derived-genetic

series for dietitians and supplementary science curriculum for high schools planned for release later in 2021.

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.[47]

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.[48]

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

Provided Uniform Compliance Date and Resources for Nutrition Facts Labeling Rules

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

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

FDA announced that January 1, 2022, will be the uniform compliance date for final food labeling regulations that were 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.

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.[49] 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.[50]

Figure 3 Nutrition Facts Label

In June 2020, FDA also announced "*The New Nutrition Facts Label: What's in it for You?"* education campaign, which was developed to raise awareness about the changes to the Nutrition Facts label, increase its use, and help consumers, health care professionals, and educators learn how to use it as a tool for maintaining healthy dietary practices.

The education campaign includes outreach through many channels including social media, indoor/outdoor advertising, videos, and consumer-friendly downloadable educational materials.[51]

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

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

[51] https://www.fda.gov/food/nutrition-education-resources-materials/new-nutrition-facts-label

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2018 Actual	$1,059,291,000	$1,059,291,000	---
FY 2019 Actual	$1,059,926,000	$1,059,926,000	---
FY 2020 Actual	$1,087,215,000	$1,087,215,000	---
FY 2021 Enacted	$1,110,471,000	$1,099,160,000	$11,311,000
FY 2022 President's Budget	$1,194,161,000	$1,182,625,000	$11,536,000

BUDGET REQUEST

The FY 2022 Budget Request is $1,194,161,000, of which $1,182,625,000 is budget authority and $11,536,000 is user fees. The budget authority increases by $83,465,000 compared to FY 2021 Enacted, and user fees increase by $225,000. The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is $399,985,000. The Office of Regulatory Affairs amount is $794,176,000.

BUDGET AUTHORITY

Food Safety (+$82.9 million / 108 FTE)

New Era of Smarter Food Safety
(Center: +$8.6M / 14 FTE; Of this, $7.3M / 10 FTE under New Era/Data Modernization and Enhanced Technologies, $1.3M / 4 FTE under New Era of Smarter Food Safety)

The FY 2022 Budget includes an increase of $8.6 million for CFSAN to implement essential work outlined in the New Era of Smarter Food Safety Blueprint, which includes achievable goals to enhance traceability, improve predictive analytics, expand collaboration with our regulatory and public health partners, respond more rapidly to outbreaks and other food safety problems, address new business models (such as e-commerce), advance the safety of foods sold in traditional retail establishments, and foster strong food safety cultures. This approach builds on the modernized food safety regulatory framework created by FSMA. Of the $8.6 million requested by CFSAN in FY 2022 for New Era of Smarter Food Safety, the request includes $7.3 million of the food safety component of the Data Modernization and Enhanced Technologies initiative that will bolster many FDA priorities.

Coupled with the Data Modernization and Enhanced Technologies initiative, the FY 2022 request for New Era of Smarter Food Safety funding will enable CFSAN to leverage new and emerging technologies and data-driven approaches to strengthen our predictive capabilities, accelerate prevention, and speed traceback when contaminated foods are identified. With this funding, FDA will enhance preparations for implementation of the FSMA Food Traceability Final Rule, to be issued in late 2022, which establishes requirements for industry to keep additional records to reduce the time it takes to identify the recipients of certain commodities to prevent or mitigate foodborne illness. In addition, FDA will prepare for implementation of the final rule by developing an internal product tracing system to receive traceability information. As

required under FSMA 204(c), FDA will enhance existing information technology systems to receive traceback data directly from stakeholders in circumstances such as outbreaks in order to expand FDA's capacity to process data quickly. This effort will also support FDA's collaboration with federal, state, local, tribal and territorial partners on new ways of conducting accelerated tracebacks and trace forwards in a tech-enabled food traceability world to identify contaminated foods more quickly. FDA will also conduct outreach to the food industry, international partners, and non-traditional stakeholders (e.g. financial industry, technology firms, insurance companies) that can support and amplify FDA's efforts to extend tracing throughout the food supply.

With strengthened traceback capabilities, FDA's ability to conduct root-cause analyses will be greater, and findings from this work can be used to better inform the prevention-based framework that FSMA established and can provide more robust data for predictive analytics. FDA will establish a root cause analysis expert working group to enhance communication tools to quickly and transparently relay the outcomes of root cause analyses, both internally and externally, to help modify food safety practices to better avoid identified risks. FDA will also formalize root cause analysis procedures with federal, state, local, tribal, and territorial partners to broaden the use of rapid deployment tools as soon as an outbreak is traced to a specific site. As more data streams and tools for rapidly analyzing data become available, FDA will evaluate how we can best use predictive analytics tools to identify when and where contamination might be likely to occur, to prevent contaminated products from entering the food supply, and target efforts to remove potentially contaminated product from the market.

FDA will adapt our oversight framework to help ensure the safety of foods produced and distributed using new business models. FDA will conduct outreach with stakeholders and complete an evaluation of the regulatory landscape to assess needs for additional guidance documents, education and outreach efforts, and compliance activities to support new food business models. For more traditional business models, FDA will conduct an independent review of the traditional retail food safety program's effectiveness in preventing foodborne illness and communicating effectively across partners.

Without new resources for the New Era of Smarter Food Safety, FDA's ability to maintain appropriate safeguards will significantly lag behind changes occurring in the marketplace, potentially putting consumers at risk and adversely impacting industry. A lack of resources to address emerging food safety challenges will become increasingly obvious and impactful to stakeholders and may undermine the agency's ability to continually strengthen the food safety system.

Maternal and Infant Health and Nutrition: (+$18 million / 26 FTE)
Center (+18.0 million / 26 FTE)

The health and well-being of mothers, infants, and children is critical. Additional resources will make it possible for CFSAN to take regulatory and other actions to address emerging issues of concern, such as toxic elements in baby food, limited staff review capacity for premarket review of infant formula submissions to evaluate the safety and nutritional adequacy of infant formula, and nutrition work specific to infants, toddlers, and pregnant and lactating women. FDA is

uniquely positioned to address these critical areas but meaningful progress hinges upon a significant infusion of new resources to perform this work.

Toxic heavy metals such as lead, arsenic, mercury, and cadmium are naturally present in air, water, and soil so a certain amount of exposure through food is unavoidable, but exposure risk for infants and young children could be reduced from these toxic elements in foods. FDA has prioritized babies and young children because their smaller body sizes and metabolism make them more susceptible to these metals and because of the impact that these metals can have on children's neurological development. On April 8, 2021, FDA announced its Closer to Zero[52] action plan, which outlines action items and a proposed timeline, which would be bolstered with the new funding. FDA plans to establish reference levels for exposure to toxic elements from foods, set expectations to strive for continual improvement, and provide action levels with the expectation that they will decrease over time for lead, arsenic, cadmium, and mercury for different categories of foods consumed by babies and very young children. FDA will also provide guidance on best practices and engage with industry on initiatives to reduce amounts of toxic elements and increase accountability, e.g., through sampling and routine testing and compliance and enforcement-related to action levels.

With additional resources, CFSAN will recruit risk analysts, consumer safety officers, data analysts, public health information specialists, toxicologists, and chemists among others. Increased staffing in these areas will allow the Center to expand research on co-occurrence of toxic elements in baby foods and impacts on neurodevelopment, and work to develop more accessible and affordable laboratory detection methods necessary for ensuring industry compliance with interim action levels. Increased resources will also allow the Center to create risk communication and education materials for consumers on the risks from toxic elements in foods, and the importance of healthy dietary patterns and variety as a strategy for reducing toxicants in the diet. FDA will also develop education materials for industry which outline requirements for managing and minimizing the presence of toxic elements in their products. CFSAN will also partner with USDA and others to explore methods for mitigating the presence of toxic elements in the food supply and will issue any related guidance to industry on reducing exposure.

Infant formula is a significant or even sole source of nutrition for many infants during a critical period of growth and development. Approximately 75% of infants in the U.S. receive infant formula or other non-breastmilk nutrition by 6 months of age. The Infant Formula Act specifies that manufacturers make a submission to FDA for any new infant formula, and that the FDA complete premarket reviews for these submissions within 90 days. However, the current infant formula submission rate, along with the increasing complexity of submissions, exceeds the capacity for the small FDA staff of 9 to complete their review in a 90-day period, and we expect these trends to continue. If FDA misses the 90-day window, we have lost a critical opportunity to resolve serious issues and questions with manufacturers before they begin marketing products. CFSAN seeks additional resources to expand agency capacity to review the increasing number, size, and complexity of infant formula submissions, reflecting an increase in the number of manufacturers as well as innovation by manufacturers.

[52] https://www.fda.gov/food/metals-and-your-food/closer-zero-action-plan-baby-foods

Additionally, the U.S. has a high prevalence of obesity and nutrition-related chronic disease. Nutrition-related diseases such as heart disease and cancer are a leading cause of death and disability in the U.S. Among children and adolescents, almost one in five are obese. Evidence suggests dietary patterns are established early in life. Establishing patterns of healthy eating through investments in early childhood nutrition offer one of FDA's greatest opportunities to have a profound, generational impact on human health. FDA will partner with USDA, the Health and Human Services Office of Disease Prevention and Health Promotion and others to explore opportunities to better help consumers understand the new Dietary Guidelines for pregnant and lactating women and early childhood (released in December 2020) while also reducing dietary exposure to toxic elements.

Emerging Chemical and Toxicological Issues: (+$19.5 million / 40 FTE)
Center: +$19.5 million, 40 FTE

Over the last decade, CFSAN has placed a major emphasis on implementing the 2011 FDA Food Safety Modernization Act (FSMA), which transformed the nation's food safety laws for the first time since the 1930's. In that time, however, many food safety programs that fall mostly outside of FSMA's purview have been falling further behind in their ability to keep pace with increasing innovation by industry and advances in science. These programs have a critical need for resources to modernize and streamline regulatory frameworks for products or ingredients that in certain cases pose potential chronic risks to human health. Issues such as: food additives and substances added to food; chemicals used in food contact such as phthalates; allergens; dietary supplements; and contaminants in cosmetics—continue to receive major attention from the public as new potential health concerns emerge. However, without significant new resources to address these critical issues FDA will be unable to acquire and deploy emerging science risk-based assessments to evaluate product safety and protect public health.

With new resources, CFSAN will enhance and update the Foods program's approach to chemicals, both directly added as food ingredients and those that come into the food supply through food contact. Hiring additional experts will build capacity to utilize science and information technology advances in order to make CFSAN-regulated products safer and make these determinations more quickly. In the past five years, FDA's food ingredient safety program has reviewed a steady number of industry submissions for new ingredients and food contact substances, which are increasing in number and complexity. CFSAN will acquire new tools that leverage new and evolving data sources to support pre-market safety evaluations and to prioritize our post-market safety review efforts in a science-based, systematic way that will focus on the substances that have the greatest potential for public health impact. A modernized approach to data will allow FDA to monitor the food supply for a broad range of ingredients, including for emerging health concerns from food additives.

Included in this work is a specific resource need to reduce Per- and Polyfluoroalkyl Substances (PFAS) in the food supply based on safety data. PFAS, sometimes called "forever chemicals," are a family of human-made chemicals found in a range of products used by consumers and industry, which are now widespread in the environment. Bioaccumulation of certain PFAS may cause serious health conditions. FDA has initiated a comprehensive review of available toxicological data on PFAS to determine which information is applicable to the specific PFAS

chemicals found in food and to utilize this information to both assess exposures and determine if actions are needed to address safety concerns. New resources would make it possible for the agency to recruit additional experts such as toxicologists, chemists, environmental scientists, and regulatory policy experts to conduct this work, determine appropriate next steps, and communicate with the public about potential risks related to PFAS. Expanded resources will also allow FDA to support state health agencies and continue coordination with partners such as Department of Defense (DoD), Environmental Protection Agency (EPA), and USDA to respond to contamination events, which may arise as DoD continues to test water sources near their sites, and other states and municipalities test drinking water.

Allergens are another important food safety topic, and in April 2021, Congress passed the "Food Allergy Safety, Treatment, Education, and Research Act of 2021" or the "FASTER Act," which adds sesame to the list of major allergens and requires that FDA propose a process for evaluating additional candidate major allergens in the future. With new funding, FDA will enhance efforts to protect consumers in keeping with the latest science on allergens by hiring staff to develop and implement new allergen and gluten testing methods and conduct additional research necessary to inform FDA's regulatory work on allergens and gluten. Approximately 32 million consumers in the U.S. report having food allergies, with reactions ranging from mild to quite severe and even fatal in rare cases. Each year in the U.S., 200,000 people require emergency medical care for allergic reactions to food. Currently, food allergies cannot be cured, treatments to prevent allergic reactions are limited, and diagnostic methods to help people understand their risks for severe reaction are poor. As a result, avoidance of food allergens is critical to prevent serious health consequences. FDA will hire staff to develop new compliance policies and coordinate industry compliance and increased enforcement activities. FDA will also expand scientific review capacity to assess the public health importance of allergens other than the major food allergens for which additional controls may be needed, including manufacturing controls and labeling.

Finally, new funding would provide modest increases to FDA's programs for cosmetics and dietary supplements. FDA's regulatory authority for cosmetics comes from the 1938 Federal Food, Drug, and Cosmetic Act, which gives the Agency limited post-market authority over cosmetic safety. This new funding will provide FDA's cosmetics program with some additional resources, including personnel to begin to assess products in the post-market space that would focus on health equity issues, for example the safety of cosmetic products and ingredients that are disproportionately marketed to populations including women and girls of color. FDA will also update IT systems to increase oversight capacity in one of FDA's smallest programs. FDA will also increase scientific and regulatory capacity focused on dietary supplements. FDA will expand efforts related to guidance development, technical assistance and training for industry and FDA inspectors, and outreach to stakeholders, with an emphasis on vulnerable populations.

Increases in each of these programs would have outsized impacts on the progress that CFSAN can make toward improving health outcomes. Significant data gaps exist to monitor the thousands of chemicals that are contained in foods, dietary supplements, and cosmetics. FDA will direct these additional resources to identify, manage, and gather relevant toxicology data on the smaller subset of potentially dangerous chemicals that may present public health hazards.

Crosscutting: (+$30.2 million / 28 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data: (+$9.4 million / 10 FTE)
Center: (+$3.0 million/ 3 FTE)
Field: (+$6.4 million / 7 FTE)

FDA will strengthen the common data infrastructure established through the Technology Modernization Action Plan (TMAP) and COVID-19 investments as well as leverage Agency-wide data and technology governance model, accelerate the development and deployment of new data-rich capabilities like AI.

Inspections: (+$3.5 million)
Field (+$3.5 million / 12 FTE)

The FY 2022 Budget includes $18.8 million across FDA for inspections. ORA will increase site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID-19 related delays, and the Budget includes $3.5 million for the Field portion of the Foods Program.

Pay Costs: (+$7.0 million)
Center: (+$2.7 million)
Field: ($4.3 million)

The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

Capacity Building: (+$10.3 million / 6 FTE)
Center: (+$3.3 million / 2 FTE)
Field: (+$7.0 million / 4 FTE)

The FY 2022 Budget includes $40.3M to support the Essential Services component of the Capacity Building initiative. The FY 2022 Budget Request supports the Foods Program components of vital cross-agency services.

USER FEES

Current Law User Fees: +$225,000
Center: +$17,000 / Field: +$208,000

The Foods Program request includes an increase of $225,000 for user fees authorized, 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 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
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 2020: 863 enrolled Target: 867 enrolled (Target Not Met)	878	893	+15
212415: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired Shiga toxin-producing *Escherichia coli* (STEC) infections. *(Outcome)*	CY 2019: 5.0 cases/100,000 (New Measure Historical Actual)	4.4	4.3	-0.1
212416: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired *Listeria monocytogenes* infections. *(Outcome)*	CY 2019: 0.3 cases/100,000 (New Measure Historical Actual)	0.26	0.25	-0.01
212417: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired	CY 2019: 15.4 cases/100,000 (New Measure Historical Actual)	14.3	14.0	-0.3

Measure	Year and Most Recent Result /Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
Salmonella infections. *(Outcome)*				
214306: The average number of working days to serotype priority pathogens in food. (Screening Only) *(Output)*	FY 2020: 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 2020: 93.4% 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 2020: 76.2% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2020: 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 2020: 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 2019 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 foodservice operations. The voluntary use of the Retail Program Standards by a food inspection program reflects a commitment toward continuous improvement and the application of effective risk-based strategies for reducing foodborne illness. The FY 2020 actual enrollment number of State, local and tribal agencies in the Retail Program Standards reflects an annual increase of 11 enrollments from the year-end FY 2019 total enrollments (852). 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 achieving key milestones. Though FDA fell slightly short of meeting its target in FY 2020, it was largely due to the impacts of the global pandemic. It is reasonable to assume that FDA would have met this target in a normal year, and that future year targets will be met. The FY 2021 and FY 2022 targets reflect increases in the number of enrollees by 15 above the previous year's actual number of enrollees or target.

Key Pathogens
Measures 212404, 212405 and 212407 (reductions of *Campylobacter*, *E. coli* O157, and *Salmonella*) are being retired. They were based on Healthy People 2020 objectives. They have been replaced by measures 212415, 212416, and 212417, which are based on new Healthy People 2030 objectives. Although these objectives are similar, they were modified for Healthy People 2030, so the data are not comparable with the Healthy People 2020 versions. In general, the difference is the 2020 objectives tracked the incidence of culture-confirmed cases of these infections, while the 2030 objectives will track the incidence of domestically acquired infections only, but will include both culture-confirmed cases and those identified through culture-independent diagnostic tests (CIDTs). Also, measure 212405 was limited to *E. coli* O157, whereas measure 212415 includes all Shiga toxin-producing *E. coli* (STEC).
The *Campylobacter* measure is being retired as its illnesses are most often attributed to non-FDA-regulated products. Measures for STEC and *Salmonella* are being retained, and a measure for *Listeria monocytogenes* is being added. These organisms remain significant in terms of the number and severity of illnesses, and outbreaks are frequently attributed to FDA-regulated products. Therefore, there is a continued need to invest resources into prevention activities in order to reduce illness caused by these pathogens.

Pathogen Detection

FDA microbiologists are evaluating and integrating commercially available instrumentation into its microbiological testing workflow that is vastly improving the ability of FDA to more quickly and effectively detect and characterize foodborne pathogens such as *Salmonella* directly from the food supply. Improvements in sample throughput, along with the high degree of sensitivity and specificity built into new pathogen detection technologies, will dramatically improve FDA's foodborne response and traceback capabilities. When fully deployed, technologies such as next-generation whole-genome sequencing (WGS) and others will reduce the time to conduct these analyses from 14 days originally to just a few days. One updated technology which provides highly accurate and rapid *Salmonella* serotype results for FDA, known as the flow cytometry/fluorescence platform, has been validated extensively and is now deployed in nearly all FDA field laboratories, as well as in CFSAN and CVM laboratories. In FY 2020, FDA met the target of reducing the average number of days to serotype priority pathogens in foods to three days. The proposed targets for FY 2021 and FY 2022 are three days, maintaining the critically important downward progress in analytical return times achieved in prior years.

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. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA's ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

Foods Program Activity Data

CFSAN Workload and Outputs	FY 2019 Actuals	FY 2020 Actuals[7]	FY 2021 Estimate	FY 2022 Estimate
Food and Color Additive Petitions				
Petitions Filed [1]	5	7	10	10
Petitions Reviewed [2]	5	7	10	10
Premarket Notifications for Food Contact Substances				
Notifications Received	86	81	94	94
Notifications Reviewed [3]	86	81	94	94
Infant Formula Notifications				
Notifications Reviews Due to Be Completed [4]	24	38	45	45
Notification Reviews Completed Within 90 Days of Filing [5]	16	33	45	45
FDA Review Time	90 days	90 days	90 days	90 days
New Dietary Ingredient Notifications				
Notification Reviews Due to Be Completed	40	43	49	49
Notification Reviews Completed Within 75 Days of Filing [6]	36	43	49	49
FDA Review Time	75 days	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] Since mid-March 2020, FDA operations and FDA oversight of the U.S. food supply have been significantly impacted by the COVID-19 pandemic. The Agency's priorities during this time period have been the safety of our staff, conducting mission-critical activities, including inspections, responding to foodborne disease outbreaks, sampling and testing of imported food, and managing recalls. We have also worked to support continuity of the food supply chain, which includes keeping food and agricultural workers safe to allow continued production of food. Given these priorities, and state and local travel restrictions, FDA adjusted its approach to oversight activities.

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate[5]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	3941	***2,500***	***8,000***
Domestic Food Safety Program Inspections	2,312	**Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high**	**Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high**
Imported and Domestic Cheese Program Inspections	64		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	124		
Domestic Fish & Fishery Products (HACCP) Inspections	338		
Import (Seafood Program Including HACCP) Inspections	90		
Juice HACCP Inspection Program (HACCP)	93		
Interstate Travel Sanitation (ITS) Inspections	245		
Domestic Field Exams/Tests	805	*850*	2,500
Domestic Laboratory Samples Analyzed	11,238	*11,500*	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***641***	***50***	***1,400***
All Foreign Inspections	912	*50*	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***4,582***	***2,550***	***9,400***
IMPORTS			
Import Field Exams/Tests[2]	82,382	*82,500*	168,200
Import Laboratory Samples Analyzed	11,750	*12,000*	35,300
Import Physical Exam Subtotal	**94,132**	**94,500**	**203,500**
Import Line Decisions	16,983,686	17,000,000	17,850,000
Percent of Import Lines Physically Examined	0.55%	0.56%	1.14%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***5,476***	***2,500***	***2,078***
State Contract Food Safety (Non HACCP) Inspections	4,960	4,090	5,000
State Contract Domestic Seafood HACCP Inspections	365	327	400
State Contract Juice HACCP	34	29	35
State Contract LACF/Acidified Food Inspections	64	61	75
State Contract Foods Funding	$13,727,413	$13,756,200	$13,893,762
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***10,058***	***5,050***	***11,478***

[1] The FY 2020 actual unique count of foreign inspections includes 38 OGPS inspections (22 for China, 9 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.

[4] FERN State Laboratory funding has ended in FY20. It been removed from PAD.

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2020Actuals	FY 2021 Estimate[2]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***25***	***5***	***100***
		5	
Domestic Inspections	25	5	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***3***	***0***	***0***
Foreign Inspections	3	0	0
IMPORTS			
Import Field Exams/Tests[1]	3,210	3300	1,600
Import Laboratory Samples Analyzed	208	215	400
Import Physical Exam Subtotal	**3,418**	**3,500**	**2,000**
Import Line Decisions	2,350,216	2,375,673	2,494,457
Import Line Decisions	0.15%	0.15%	0.08%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***28***	***5***	***100***

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

[2] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

HUMAN DRUGS

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Human Drugs	**1,973,122**	**1,995,820**	**1,997,174**	**2,121,242**	**124,068**
Budget Authority	***683,195***	***682,861***	***689,195***	***774,469***	***85,274***
User Fees	***1,289,927***	***1,312,959***	***1,307,979***	***1,346,773***	***38,794***
Center	1,734,133	1,756,076	1,753,685	1,854,233	100,548
Budget Authority	507,726	507,431	510,226	573,081	62,855
User Fees	1,226,407	1,248,646	1,243,459	1,281,152	37,693
Prescription Drug (PDUFA)	*788,576*	*790,087*	*800,637*	*831,287*	*30,650*
Generic Drug (GDUFA)	*400,252*	*427,395*	*404,241*	*410,647*	*6,406*
Biosimilars (BsUFA)	*36,938*	*30,135*	*37,928*	*38,552*	*624*
Outsourcing Facility	*641*	*1,029*	*653*	*666*	*13*
Field	238,989	239,743	243,489	267,009	23,520
Budget Authority	175,469	175,430	178,969	201,388	22,419
User Fees	63,520	64,313	64,520	65,621	1,101
Prescription Drug (PDUFA)	*8,536*	*7,592*	*8,707*	*8,855*	*148*
Generic Drug (GDUFA)	*53,124*	*55,022*	*54,096*	*55,019*	*923*
Biosimilars (BsUFA)	*1,472*	*1,303*	*1,322*	*1,344*	*22*
Outsourcing Facility	*388*	*396*	*395*	*403*	*8*
FTE	**6,649**	**6,478**	**6,737**	**6,856**	***119***

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, generic, and over-the-counter (OTC) drug products; monitoring the safety of marketed drugs; and

overseeing drug quality to prevent and detect substandard or counterfeit drugs in the U.S. market. The Center for Drug Evaluation and Research (CDER) and Office of Regulatory Affairs (ORA) field drugs program comprise FDA's Human Drugs Program, which operates with funding from budget authority and user fees. CDER is advancing its mission across its large portfolio of human drugs. In FY 2020, CDER approved 61 novel drugs, of which 21 were first-in-class, which is one indicator of the drug's potential for strong positive impact on public health. In the same year, CDER continued support for grants to help encourage the establishment of high-tech manufacturing platforms in the United States, and issued final guidance that 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.

This list is only a sample of CDER's accomplishments, and a testament to CDER's strong programmatic foundation. The Center remains committed to continue building on that foundation to ensure patients have access to safe and effective drugs, and to support our public health partners, stakeholders, and industry. CDER is implementing ongoing, strategic efforts for success in the short- and long-term. Those efforts include incorporating patient focused drug development, ensuring access to data for regulatory actions, supporting drug development science, increasing efficiency through technology and process modernization, and issuing guidance to address the process of drug development and manufacturing.

Leveraging our strong programmatic foundation has enabled CDER to advance therapies for myriad diseases while also launching an aggressive and multi-pronged approach to address the unexpected challenge of COVID-19. CDER's role is integral to the government's COVID-19 response effort, including our Coronavirus Treatment Acceleration Program (CTAP), which is using every available method to move safe and effective treatments to COVID-19 patients as quickly as possible. CDER is also ensuring that such drugs are evaluated in diverse populations, monitoring the supply of medicines and acting to prevent or mitigate drug shortages, and protecting the American public from fraudulent products that claim to diagnose, prevent, treat, or cure COVID-19. In October 2020, FDA approved Veklury (remdesivir), the first drug approved for the treatment of COVID-19 in certain adults and pediatric patients requiring hospitalization.

Looking forward, CDER is identifying opportunities where these strategic efforts can build on our foundation and better support patients, industry, partners, and stakeholders and position the Center for success as we transition to a post-pandemic world.

CDER is also drawing upon lessons learned from the pandemic, including from disruptions to drug development and clinical trials caused by COVID-19, to launch trials during the pandemic. CDER continues to explore alternative approaches to inspections of clinical trials, including the use of remote assessments and access to electronic systems. Importantly, for prompt start-up of COVID-19 clinical trials, the use of digital technologies has allowed for electronic informed consent in situations where face-to-face contact is not possible or practical due to COVID-19 control measures. For example, FDA invested in the COVID MyStudies App to provide a free platform to obtain informed consent securely from patients for eligible clinical trials when face-to-face contact is not possible or practical. Since launch, MyStudies has received more than 200 email inquiries, 25 CBER study requests (22 COVID/3 non-COVID) and 91 CDER study requests (51 COVID/40 non-COVID). There are currently 9 INDs with 33 studies configured for immediate use. Further, technology has enabled sponsors and clinical research organizations to conduct elements of clinical trial monitoring remotely. Remote review of trial activities and data during COVID-19 is essential for the safety of trial participants, personnel, and data reliability.

Decentralized clinical trials may make use of local health care services, telemedicine tools such as videoconferencing and electronic patient-reported outcomes, and when appropriate, direct shipping of investigational products to patients. These features are intended to improve convenience for patients and to reduce the risks of exposure to the coronavirus for trial participants and trial personnel.

It is important to note that FDA's ability to make meaningful progress and build a strong programmatic foundation has historically relied on receiving dedicated funding. For example, since 2018, Congress has provided additional resources for the under-funded compounding program. As a result, FDA has been able to build a compounding program from the ground up to carry out its responsibilities under the Drug Quality and Security Act (DQSA), with the acknowledgement that there is still significant work ahead. This program's buildout has included hiring needed experts to staff the program, establishing the Compounding Quality Center of Excellence, and implementing education and training for outsourcing facilities and other stakeholders, in addition to many other critical activities CDER has undertaken to advance the authorities outlined in the DQSA.

CDER's ability to advance its mission while addressing the challenges of the COVID-19 pandemic can be traced back to its programmatic foundation. Looking ahead to FY 2022, CDER is implementing strategic efforts to further strengthen that foundation. Ultimately, these efforts, accompanied by the necessary funding, will allow the Center to further our goals of helping to ensure that human drugs are safe and effective for their intended use, that they meet established quality standards, and that they are available to patients. The narrative provides greater detail about CDER programs and activities and our recent accomplishments.

Harnessing Real-World Evidence

FDA has a long history of using real-world evidence (RWE) to monitor and evaluate postmarket safety of drug products, whereas the use of RWE to support effectiveness has been more often limited to the settings of oncology and rare diseases. The 21st Century Cures Act requires FDA to evaluate the potential use of RWE to support the approval of new indications of approved medical products, or to satisfy post-approval study requirements for marketed products. FDA is committed to realizing the full potential of fit-for-purpose real-world data (RWD), such as electronic health records, registries, and medical claims data, to generate evidence that will advance the development of therapeutic products and strengthen the regulatory oversight of medical products across their life-cycle.

In 2019, CDER and CBER issued guidance[53] to encourage sponsors and applicants who propose to use RWD to generate RWE as part of a regulatory submission to identify for FDA certain information about their proposed use of RWE in those submissions.[54]

To better understand how RWD can generate RWE that meets regulatory requirements, CDER announced a funding opportunity in April 2020 to solicit research exploring the use of RWD to generate RWE for regulatory decision-making.[55] FDA received 31 proposals, and awarded 3-year grants after scientific review. In addition, FDA established an Intra-Departmental Delegation of Authority with the National Institutes of Health (NIH) to better understand how

[53] https://www.fda.gov/media/124795/download

[54] FDA will use this information for internal tracking purposes only.

[55] https://grants.nih.gov/grants/guide/notice-files/NOT-FD-20-025.html

current ethical and human subject protection frameworks can be applied to the use of RWD; two supplements to existing NIH-funded trials were funded via this mechanism in FY 2020.

Additional RWE-related activities involved FDA's cooperative agreement with the Duke-Margolis Center for Health Policy, with FDA hosting two public workshops in FY20. In October 2019, FDA brought the stakeholder community together to discuss considerations when leveraging RWD from diverse sources, as well as insights into methodological approaches and analytic and regulatory considerations. In July 2020, FDA expanded on that first meeting to learn from stakeholders' practices, challenges, and considerations when establishing a high-quality RWD ecosystem.

Sentinel

The FDA Amendments Act of 2007 established FDA's Sentinel System and has given rise to one of the world's premier RWE platforms. In September 2019, a new 5-year Sentinel contract was awarded to 2 consortiums led by Harvard Pilgrim Health Care and Deloitte Consulting, which established 3 distinct coordinating centers: the Sentinel Operations Center, Innovation Center, and Community Building and Outreach Center. This was the third 5-year contract awarded since Sentinel was established. The new Sentinel structure widens participation to a broader array of scientific expertise, seeks to translate new technologies from data science and big data, creates laboratories to develop new approaches to using electronic health records, and cultivates a robust scientific community to uncover novel ways to leverage the system's core capabilities beyond drug safety.

The new contract retains and builds upon the core innovations that were responsible for many of the achievements in the prior decade: the participation of data partners who bring their knowledge and expertise to the Sentinel network, the re-useable analytic tools that use data formatted in the Sentinel Common Data Model, the multifaceted data quality and curation process, and the ability to trace important clinical information back to the medical record. Sentinel remains one of the world's largest multi-site, privacy-preserving, medical product safety surveillance systems with highly-curated data with more than 70 million patients actively accruing new data.

The year 2020 marked 5 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. For example, the Sentinel System has evaluated the risk of stroke after using antipsychotics,[56] the risk of seizures after using ranolazine,[57] and the risk of venous thromboembolism after using extended or continuous cycle oral contraceptives.[58] The Sentinel system has been leveraged to address public health crises, such as the opioid crisis and currently is being used in FDA's efforts to understand COVID-19.

In addition, through the Sentinel system, the Catalyst program was launched to leverage the Sentinel infrastructure and supplement it with data from interventions or interactions with health

[56] https://www.sentinelinitiative.org/sites/default/files/Communications/Publications/Sentinel-ICPE-2017-Symposium-Snapshot-of-the-First-Year_Antipsychotic_stroke.pdf

[57] https://www.sentinelinitiative.org/sites/default/files/Communications/Publications/Sentinel-ICPE-2017-Symposium-Snapshot-of-the-First-Year_Ranexa-Seizures.pdf

[58] https://www.sentinelinitiative.org/sites/default/files/Communications/Publications/Sentinel-ICPE-2017-Symposium-Snapshot-of-the-First-Year_Lybrel.pdf

plan members and/or providers. FDA is currently supporting a randomized trial that uses data that are part of the Sentinel System to test whether a patient and provider educational intervention can increase anticoagulant use for individuals who, according to the data within the Sentinel System, have atrial fibrillation and are at increased risk of stroke. The Catalyst program was also critical to the development of the FDA My Studies app that sponsors can use to collect data directly from patients.

Featured below are notable achievements in FY 2020:

- Drug safety analyses conducted in Sentinel informed updates to the labels for IV iron products, hydrochlorothiazide-containing products, and montelukast
- Descriptive analyses of ranitidine utilization provided context for CDER's Nitrosamine Impurities Task Force to understand use patterns in the United States
- Redesigned, updated and successfully launched the Sentinel Initiative website on July 17, 2020, to better serve FDA and industry users. Staying up to date with Sentinel assessments, tools, and news is now easier.
- Activated Sentinel to help FDA's response to the COVID-19 pandemic, launching new studies, including:
    - A study to validate several COVID-19 algorithms using lab results and select the most accurate algorithm to identify COVID-19 cases in administrative claims data
    - Near real-time monitoring of up to 120 critical drugs for the care of patients with COVID-19 to assess changing patterns of use and help identify drug shortages
    - A study to assess the feasibility of evaluating the natural history of coagulopathy among hospitalized COVID-19 patients
    - A study to use electronic healthcare data to describe COVID-19 clinical characteristics and identify patient factors related to disease progression/prognosis
- Participated in the Reagan-Udall Foundation COVID-19 Evidence Accelerator initiative to share insights, compare results, and answer key questions about COVID-19 treatment

IT Roadmap

To advance CDER's public health mission and keep up with innovation in the environment, the Center continues to execute its IT strategic roadmap, which includes planned investments in workflow management, data and analytics, and administrative work processes and cloud infrastructure. Priority actions include:

- Expanding Workflow Management: CDER is using a common workflow platform to enable drug lifecycle management across the Center, and process automation to be more efficient in service of our mission.
    - CDER has already implemented multiple applications supporting key processes for new drug review, drug safety and Bioresearch monitoring.
    - CDER's strategy includes a roadmap and plan for prioritized major drug lifecycle workflows to migrate to its common workflow platform in a staged approach beginning with its new drug review workflows.
- Prioritize Data and Analytics Portfolio: CDER has focused on consolidating its analytics portfolio by creating a data and analytics service that funnels all its analytics needs

through one intake mechanism to enable prioritization while investing in an enterprise cloud analytics platform including a data lake.

- Modernize Financial and Administrative Capabilities: CDER is automating key financial and administrative workflows with investments to build solutions leveraging enterprise capabilities. CDER has deployed solutions supporting administrative functions such as tracking personnel-related work process.
- Transition to a Cloud Infrastructure: CDER is leveraging cloud infrastructure for its core technologies, allowing for quick scale-up of new capabilities and flexible, cost-effective management of core computing needs.

Opioids

Opioids are effective medications that, when prescribed and used in accordance with FDA-approved labeling, can help treat pain, cough, diarrhea, or opioid use disorder. The Agency recognizes that the nation is currently facing a public health crisis of opioid misuse, abuse, and addiction, which increase the consequent risks of opioid overdose and death. Ensuring the safe use of opioids and doing its part to ameliorate the opioid crisis are among FDA's highest priorities. FDA is working to improve the transparency of our benefit-risk approval paradigm for opioids, and to ensure that it continues to consider appropriately the wider public health effects of prescription opioids. The Agency is engaged in many ongoing activities aimed at furthering this goal, including:

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

Further, the Agency continuously examines its policies in the regulation of drugs (including opioids) and devices used in the treatment of pain, opioid use disorder, as well as those drugs (e.g., naloxone) used to treat opioid overdose.

FDA continues to accomplish its goals as 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 explained in the HHS Opioid Strategy, FDA is committed to examining all facets of the crisis: opioid use, misuse and abuse, and their potential clinical consequences, addiction, overdose and death. FDA has identified four priority areas and has taken the following steps to reduce the scope of the opioid addiction and overdose crisis:

1) Decrease Exposure and Prevent New Addiction:

- Evaluated the public comments submitted to the docket and gathered additional stakeholder input to determine next steps on requiring fixed-quantity blister packaging for certain opioid pain medicines to help decrease unnecessary exposure to opioids

- In September 2019, approved new packaging for brand-name over-the-counter loperamide products to help curb abuse and misuse
- Advanced the development of evidence-based guidelines for appropriate opioid analgesic prescribing through the National Academies of Sciences, Engineering, and Medicine, who released a consensus report, commissioned by FDA, on framing opioid prescribing guidelines for acute pain by indication in December 2019
- In June 2020, submitted a report to Congress on how the agency will utilize evidence-based opioid analgesic prescribing guidelines to protect the public health and a description of the public health need with respect to each such indication-specific treatment guideline
- In August 2020, awarded a grant to University of Pittsburgh/American Dental Association to develop, disseminate, implement, and evaluate, an evidence-based Clinical Practice Guideline for the treatment of acute dental pain (surgical and non-surgical)

2) Support Treatment of Those with Opioid Use Disorder:

- In September 2019, clarified that all forms of naloxone are appropriate for community use, issuing a statement on the FDA's continued efforts to increase availability of all forms of naloxone to help reduce opioid overdose deaths
- In July 2020, issued a Drug Safety Communication and Safety Labeling Change announcing that the agency is requiring the drug manufacturers for all opioid pain relievers and medicines to treat OUD to add new recommendations about naloxone to the prescribing information
- In August 2020, approved supplement for extension of shelf life for NARCAN Nasal Spray from the current 2-year shelf-life to 3 years and updates to the labeling
- In October 2020, issued final guidance "Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Treatment Guidance for Industry" intended to assist sponsors in developing drugs for medication-assisted treatment of opioid use disorder and addresses clinical endpoints acceptable to demonstrate effectiveness of such drugs

3) Foster Development of Novel Pain Treatment Therapies:

- In September 2019, held a public hearing, "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
- In October 2019, hosted a public meeting, "Strategies to Improve Health Equity Amidst the Opioid Crisis," to discuss the current opioid crisis and how it specifically affects minority populations across the country, approaches to prevent and treat opioid use disorder, and emerging research as it relates to improving care for racial and ethnic minority, underrepresented, and underserved populations

- In September 2020, held an advisory committee meeting to discuss the results of required postmarketing studies that evaluated the effect of the ADF reformulation of OXYCONTIN on abuse, misuse, and fatal and non-fatal overdose as well as the broader public health impact of OXYCONTIN's ADF reformulation

4) Improve Enforcement and Assess Benefit/Risk:

- In September 2019, issued first FDA and DEA joint warning letters to website operators illegally marketing unapproved and misbranded versions of opioids.
- In June 2020, launched a 120-day pilot with the National Telecommunications and Information Administration (NTIA) to help reduce the availability of unapproved opioids illegally offered for sale online.

In addition, FDA launched the Opioid Data Warehouse (ODW) with the goal of making the FDA's work more efficient by bringing in and refreshing multiple data sources as part of one central internal resource. Bringing these separate data sources into the ODW will help to streamline the FDA's work and help the Agency determine how best to respond.

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. Addressing opioid misuse and abuse remains one of FDA's highest priorities. It will take carefully developed, coordinated, and sustained action by multiple stakeholders to reduce the incidence of opioid addiction, overdose, and death, while preserving appropriate access to these drugs for patients who need them.

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. PFDD is motivated by the recognition that patients have direct experience living with a disease. They have firsthand knowledge of the impact of the disease on their life and on how they feel and function. They bring a unique and valuable perspective to drug development, one that cannot be provided by the clinical, scientific, legal and other experts.

Throughout the drug development process there are opportunities to increase the quality of the development program through effective inclusion of the patient's perspective. These opportunities include but are not limited to: understanding the clinical context for drug development and evaluation; incorporating product design features including formulation and delivery modes that minimize burden and support adherence; development of endpoints which reflect benefits that matter most to patients; designing trials that support better enrollment and retention; and informing regulatory decision-making including patient acceptability of benefits versus risks, and effective risk management.

FDA has advanced patient-focused drug development (PFDD) through implementation of provisions of the 21st Century Cures Act and implementation of related commitments made under the FDA Reauthorization Act of 2017 Title I (PDUFA VI). Work on these initiatives since 2019 has included, but is not limited to, the following accomplishments that were in accordance with the 21stCentury Cures Act, Section 3002 and PDUFA VI:

- Issued final draft guidance addressing sampling methods for collecting representative information on patient experience to inform the development and evaluation of medical products throughout the medical product lifecycle[59]
- Issued draft guidance on methods to identify patient priorities regarding the burden of disease, as well as the benefits and risks of treatment when managing a patient's disease[60]
- Convened a December 2019 public workshop to inform development of guidance about incorporating clinical outcome assessments (COAs) into endpoints for regulatory decision making[61]

In September 2019, FDA issued three new grant awards to support the development of publicly available core set(s) of COAs and their related endpoints. In June 2020, FDA issued a Funding Opportunity Announcement to fund the development of three additional core sets.

Strengthening the Compounding Program

The Drug Quality and Security Act (DQSA), enacted in 2013, provided FDA with additional responsibilities to oversee compounding and created a new category of compounders known as outsourcing facilities. Following the enactment of DQSA, FDA acted quickly to increase its drug compounding oversight through inspections and enforcement, developing policies regarding the compounding provisions of Federal law, convening and obtaining advisory committee input, collaborating and coordinating with state regulators, and conducting stakeholder outreach. FDA has taken the following actions to respond to adverse events associated with compounded drugs and identify poor drug production practices that could cause widespread patient harm:

- Conducted over 784 inspections of compounders since the passage of QSA, including 54 inspections conducted in FY2020.
- Issued over 265 warning letters to compounders Issued over 183 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 250 recall events regarding compounded drug products.
- Worked with the Department of Justice on civil and criminal enforcement actions, including 12 that resulted in injunctive relief

FDA has issued more than 40 draft, final, and revised draft guidance documents[62] regarding compounding and related activities, 5 proposed rules, 3 of which have been finalized, and 3 Federal Register notices related to the development of the 503B bulk drug substances list. In FY2020, FDA issued a revised draft guidance concerning current good manufacturing practices for outsourcing facilities and five temporary policies to respond to the COVID-19 public health emergency. FDA continued to develop a list of bulk drug substances (active pharmaceutical

[59] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input

[60] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-methods-identify-what-important-patients-guidance-industry-food-and

[61] https://www.fda.gov/drugs/development-approval-process-drugs/public-workshop-patient-focused-drug-development-guidance-4-incorporating-clinical-outcome

[62] https://www.fda.gov/drugs/human-drug-compounding/regulatory-policy-information

ingredients) for which there is a clinical need (the 503B Bulks List) and identified certain bulk drug substances that FDA has considered and proposes to include on the 503B Bulks List.[63] FDA also made available a final standard memorandum of understanding between the FDA and the states, marking a significant milestone in FDA's regulation of human drug compounding and reflecting years of collaborative dialogue and stakeholder input. In addition, FDA requested nominations for voting members for the Pharmacy Compounding Advisory Committee, which provides advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[64]

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. In FY2020, FDA held virtual listening sessions with more than 75 stakeholder organizations and an intergovernmental working meeting with representatives of the state boards of pharmacy.

Through the Compounding Quality Center of Excellence, FDA delivered 2 in-person and 8 virtual interactive training sessions with more than 250 total attendees, for outsourcing facilities on topics related to Current Good Manufacturing Practices (CGMP) and developed and launched 6 self-guided web-based trainings on compounding policy and CGMP. FDA held *The Compounding Quality Center of Excellence Virtual Conference: Working Together for Patient Safety*[65] with more than 350 participants, to engage outsourcing facilities and other stakeholders on key topics and best practices.

Research at CDER

Research is critical for creating and validating the tools and standards needed to accelerate development. Such tools increase quality while reducing inefficiency and costs, leading to approval of innovative therapies. In view of the dramatic rise in the costs associated with modern drug development, the prediction of treatment outcomes is becoming increasingly important for efficient development of novel therapeutics. Additionally, based on CDER's experience, establishment and expansion of clinical trial networks are needed to expedite clinical studies and increase efficiency while also increasing the quality of evidence captured during the trials.

New Drug Review

With PDUFA V, FDA created a new review program (the Program) for Enhanced Review Transparency and Communication for new molecular entity new drug applications (NDAs) and original biologics license 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

[63] https://www.federalregister.gov/documents/2020/07/31/2020-16649/list-of-bulk-drug-substances-for-which-there-is-a-clinical-need-under-section-503b-of-the-federal

[64] https://www.federalregister.gov/documents/2020/06/17/2020-13042/request-for-nominations-for-voting-members-on-a-public-advisory-committee-pharmacy-compounding

[65] https://www.fda.gov/drugs/news-events-human-drugs/compounding-quality-center-excellence-virtual-conference-working-together-patient-safety-09212020

the FDA review team, as well as a 60-day review clock for FDA to meet with the applicant and address review activities for these highly complex applications.

PDUFA VI contained many enhancements designed to build on the achievements of earlier agreements. The Program is one of the key programs continuing under PDUFA VI. As of October 1, 2020, FDA has received 407 applications through this Program since its October 1, 2012 inception, with more communication between the applicant and the FDA review team during review of marketing applications.

FDA dedicates PDUFA resources to support early and meaningful communication with drug sponsors, including through the resource-intensive breakthrough therapy designation program. Of the 61 novel drugs approved in FY 2020, 47 (77 percent) were approved in the United States before any other country. Of the novel drugs approved in FY 2020, 21 (34 percent) were first-in-class, which is one indicator of the drug's potential for a strong positive impact on the health of the American people. Additionally, 39 (64 percent) of the FY 2020 novel drug approvals were designated in one or more of the following expedited programs: fast track, breakthrough therapy, priority review, and/or accelerated approval.

During FY 2020, CDER's, Office of New Drugs (OND) published 32 guidance documents. Sixteen of these guidance documents were considered clinical/medical in nature and included guidance on notable topics such as developing drugs and biologics for treatment and prevention of COVID-19 as well as bridging for drug-device and biologic-device combination drugs. In FY 2020, FDA also conducted ten 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 goals letter include:

- Resources for implementing the breakthrough therapy designation program
- Commitments regarding FDA's ongoing patient-focused drug development initiative
- Enhanced use of RWE in regulatory decision-making
- Additional postmarket funding for FDA's Sentinel system
- Process improvement work related to combination product review

Drug Development Tools

In accordance with the Cures Act, FDA established an updated qualification process for drug development tools (DDTs) including biomarkers, clinical outcome assessments (COAs), and animal models for proposed contexts of use for drugs, including biological products. In November 2020, FDA published guidance, "Qualification Process for Drug Development Tools Guidance for Industry and FDA Staff."[66] The DDT Qualification Programs also executed a new, user-friendly IT support system to enable more efficient and timely review of submissions and facilitate mandated bi-annual reporting. In addition, to make the transparency provisions' public posting of information more user friendly, the qualification programs will be launching a searchable web-based tool.

[66] https://www.fda.gov/media/133511/download

Biomarker Qualification Program

In 2019 and 2020, FDA worked with external stakeholders to develop biomarkers as DDTs. The Biomarker Qualification Program (BQP) has over 60 independent biomarker projects under development. As part of the new DDT grants program, FDA has provided financial support to ten projects to assist them with their ongoing development efforts. Qualified biomarkers have the potential to advance public health by encouraging efficiencies and innovation in drug development.

Clinical Outcome Assessment Qualification Program

The CDER Clinical Outcome Assessment Qualification Program (COAQP) manages the qualification process for COAs intended to address unmet public health needs. Since January 2020, COAQP received 53 new COA development project submissions and qualified one COA. In total there are 65 independent COA projects under development. FDA also awarded 6 grants to further the development of COAs.

International Harmonization

FDA believes that the pursuit of common global pharmaceutical standards is critical to realizing the benefits of safe, effective, and high-quality medicines. FDA is a founding member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), an international venue bringing together regulatory authorities and drug developers to develop and implement consistent global standards for drug quality, safety and efficacy utilizing common elements of applications to file for review and approval in multiple markets.

In FY 2020, FDA is continuing to advance several harmonization projects under ICH. This includes leading efforts to revise the ICH E6(R2) Guideline on Good Clinical Practices to address the increasing diversity of study types and data sources, and the use of innovative technologies. This will facilitate therapeutic product development and will help provide robust evidence that supports regulatory and other health policy decisions. The guideline also seeks to incorporate lessons and examples from public health emergencies, including leveraging existing healthcare infrastructure; remote assessment; remote monitoring; identifying and prioritizing critical processes; leveraging technological tools and innovations to ensure trial integrity; and effective communication.

As another example, FDA is leading international efforts to revise the ICH Q5A Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin guideline. Efforts are focusing on updating guidance on technologies for virus detection and quantification, validation approaches for virus clearance, and including new biotechnology products such as viral-like particles and viral-vectored particles.

Although many existing ICH guidelines are applicable to generic drugs, historically ICH has focused on standards for new drugs. FDA is leading efforts to identify and recommend areas for harmonization of scientific and technical standards for generic drugs.[67] Harmonization of these requirements could allow manufacturers to use the data submitted in support of a generic drug

[67] https://admin.ich.org/sites/default/files/2019-04/ICH_ReflectionPaper_GenericDrugs_Final_2019_0130.pdf

marketing application to meet other regions' regulatory requirements for approval thereby resulting in more efficient development and increased patient access.

FDA continues to collaborate with regulatory authorities and the pharmaceutical industry under ICH to identify new areas for regulatory harmonization and improve the quality and efficiency of global drug development, manufacturing, and postmarket safety oversight. ICH has over 30 active working groups many of which are led by FDA's scientific and medical experts. FDA will continue to pursue other ways to harmonize international standards for 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.

Advanced Manufacturing

Advanced manufacturing is a high priority for CDER because it will greatly help address significant challenges or issues related to drug development, supply chain, quality, emerging public health issues, and manufacturing. Not the least of these challenges is COVID-19. Challenges like this arise quickly and require a rapid response. Current manufacturing technologies and facilities do not provide sufficient flexibility and agility to respond to these urgent health issues.

To support this, CDER focuses on the following strategic objectives:

- Establishing a regulatory program and framework to accelerate the development and implementation of advanced manufacturing of pharmaceuticals;
- Engaging with stakeholders through strategic partnerships and proactive communication to promote the implementation of advanced manufacturing, perform technology forecasting activities, and reduce barriers to entry;
- Advancing drug development science to support technology implementation, science- and risk-based regulatory evaluation, and workforce development in advanced manufacturing; and
- Leading the global effort to establish international regulatory convergence for development, implementation, operation, and lifecycle management of advanced manufacturing.

The 21st Century Cures Act authorized FDA to issue grants to study continuous manufacturing (CM) – an advanced manufacturing technology. Continuous manufacturing provides a faster, more reliable way to make drugs, including biological products, and can help reduce drug shortages and recalls related to problems with product or facility quality. In 2020, FDA continued support for these ongoing grants.
Examples of other key accomplishments include:

- CDER published the FDA draft guidance on CM of solid oral products and, in partnership with CBER, is leading the development of ICH Q13 guideline on CM of drug substances and drug products.[68]
- CDER held over 100 FDA-industry meetings on advanced manufacturing technologies to facilitate regulatory approaches to adoption. As part of the outcome of this effort, CDER

[68] https://www.fda.gov/media/121314/download

approved 6 applications utilizing CM for finished dosage form manufacturing, 1 application utilizing CM for a top-selling active pharmaceutical ingredient, 1 application utilizing semi-CM technologies for dialysis solution, 1 application using CM for a biological product, and 1 using 3-D printing technology. For example, Vertex, Janssen, and Lilly use CM to make their cystic fibrosis, HIV/AIDS, and oncology drugs, respectively.[69] Companies, like Vertex and Sanofi, have built modern manufacturing facilities incorporating advanced manufacturing technologies in the United States.[70]

Drug Pricing and Access – Biosimilars

In July 2018, FDA released the Biosimilars Action Plan[71] (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 biological 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; and
- Supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition.

The Biosimilar User Fee Amendments (BsUFA) supports the review process for biosimilar 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 October 1, 2020, 84 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 39 different reference products. As of December, 2020, FDA has licensed 29 biosimilar products. These accomplishments increase treatment options for patients.

In February 2020:

- FDA and the Federal Trade Commission signed a joint statement[72] regarding enhanced collaboration in support of a robust marketplace for biological products.
- FDA issued guidance, *Promotional Labeling and Advertising Considerations for Prescription Biological Reference and Biosimilar Products--Questions and Answers*.[73] FDA issued this guidance to provide manufacturers, packers, distributors, and their

[69] https://ispe.org/pharmaceutical-engineering/ispeak/continuous-osd-manufacturing-product-patient-perspective. Accessed February 25, 2020.

[70] https://optimal-ltd.co.uk/vertex-manufacturing; https://www.multivu.com/players/English/8627651-sanofi-new-digital-manufacturing-facility/. Accessed February 25, 2020.

[71] https://www.fda.gov/media/114574/download

[72] https://www.ftc.gov/system/files/documents/public_statements/1565273/v190003fdaftcbiologicsstatement.pdf

[73] https://www.fda.gov/media/134862/download

representatives (firms) with information to consider when developing FDA-regulated promotional labeling and advertisements (promotional materials) for prescription reference and biosimilar products licensed under the PHS Act. The guidance does not discuss considerations unique to promotional materials for interchangeable products.

- FDA issued guidance, *Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed*.[74] This guidance provides recommendations to applicants seeking licensure under section 351(k) of the PHS Act of a proposed biosimilar product or proposed interchangeable product for fewer than all of the reference product's licensed conditions of use. This guidance also provides recommendations on the submission of a supplement to a licensed 351(k) biologics license application seeking to add a condition of use that previously has been licensed for the reference product to the labeling of a licensed biosimilar or interchangeable product, including considerations related to the timing of such submissions.
- FDA issued a final rule to amend its regulation that defines "biological product" to incorporate changes made by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) and the Further Consolidated Appropriations Act, 2020 (FCA Act), and to provide FDA's interpretation of the statutory term "protein."[75] Under this final rule, the term protein means any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size. This final rule is intended to clarify the statutory framework under which such products are regulated.

In March 2020, FDA issued a final guidance, *The 'Deemed to Be a License' Provision of the BPCI Act: Questions and Answers*.[76] This guidance is intended to provide answers to common questions about FDA's implementation of the statutory provision under which an application for a biological product approved under the FD&C Act is deemed to be a license for the biological product under the Public Health Service Act (PHS Act) on March 23, 2020.
In addition, FDA completed the phased release of the enhanced *Purple Book: Database of FDA-Licensed Biological Products* in August 2020.[77] The Purple Book provides the public with an accessible, easy-to-use online search engine with information about FDA-licensed biological products, including biosimilar and interchangeable products. The updated Purple Book was released in three phases to allow for modifications based on public comment and user testing. The searchable database contains information about all FDA-licensed biological products regulated by CDER, including licensed biosimilar and interchangeable products, and their reference products and includes allergenic, cellular and gene therapy, hematologic, and vaccine products regulated by CBER.

[74] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/biosimilars-and-interchangeable-biosimilars-licensure-fewer-all-conditions-use-which-reference

[75] https://www.federalregister.gov/documents/2020/02/21/2020-03505/definition-of-the-term-biological-product

[76] https://www.fda.gov/media/119274/download

[77] https://purplebooksearch.fda.gov/

Drug Pricing and Access – Generic Drug Review

Many Americans face challenges with access to 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:

- Brought greater transparency to the generic drug review and approval process and supported prospective generic drug developers by issuing guidances for industry intended to help support the development of generic drugs and submission of complete, high quality abbreviated new drug applications (ANDAs).
- Encouraged development of generic versions of brand name drugs that have limited competition by updating FDA's List of Off-patent, Off-Exclusivity Drugs without an Approved Generic (described further below).
- Improved the speed and predictability of the generic drug review process by enhancing the efficiency of FDA's review process.
- Maximized scientific and regulatory clarity with respect to complex generic drugs to help reduce the time, uncertainty, and cost of complex generic drug development by issuing guidances for industry, launching informational web pages, and holding workshops.
- Communicated with and assisted generic drug applicants early in the product development phase by establishing the pre-abbreviated new drug application (pre-ANDA) program that is composed of research, product-specific guidances, pre-ANDA meetings, and controlled correspondences (described further below).
- Taken steps to make FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) even more accessible and useful by publishing a draft guidance and opening two public dockets on the use of the Orange Book and patent-listing information (described further below).

The 2017 reauthorization of the Generic Drug User Fee Amendments (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-ANDA program, noted above, designed to support development of complex generic drug products. The pre-ANDA program features meetings between FDA and applicants at various stages of drug development to help clarify regulatory expectations early in product development and during application assessment.

FDA has also taken 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 and FY 2020, FDA established policies and took actions under the DCAP to promote generic drug development in areas where there is inadequate competition. As of September 30, 2020, FDA published 510 new, revised, and final product-specific drug development guidance documents. Of these, 265 address the development of generic versions of complex, difficult-to-copy, drugs.

FDA supported prospective generic drug developers by issuing guidances for industry in FY2020 intended to increase transparency into the generic drug review and approval process, thereby supporting the development of generic drugs and ANDAs, including the following:

- A draft guidance for industry, *Failure to Respond to an ANDA Complete Response Letter Within the Regulatory Timeframe*, intended to assist ANDA applicants in requesting extensions to respond to complete response letters from FDA
- A final guidance for industry, *ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs*, which provides recommendations on the timing and content of amendments to tentatively approved ANDAs to facilitate submission in a timely fashion that can result in final approval on the earliest lawful approval date

Furthermore, FDA launched a new website[78] with information about FDA's plans for issuing 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 2020, FDA also published two updates to the List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic. This list is comprised of approved 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 March 2020, FDA took another step to encourage generic entry for drugs that face inadequate competition by publishing a final guidance[79] entitled *Competitive Generic Therapies*. 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. FDA posts a public list online of all approved abbreviated new drug application for drug products that received a Competitive Generic Therapy (CGT) designation.[80]

[78] https://www.fda.gov/drugs/guidances-drugs/upcoming-product-specific-guidances-complex-generic-drug-product-development

[79] https://www.fda.gov/media/136063/download

[80] https://www.fda.gov/drugs/generic-drugs/competitive-generic-therapy-approvals

As part of FDA's continued efforts to improve transparency and provide helpful information to regulated industry and the public, in addition to the guidances and other initiatives described above, in FY2020, FDA published the following:

- A draft guidance for industry,[81] *Orange Book Questions and Answers*, which provides answers to commonly asked questions FDA has received from interested parties regarding the Orange Book. Topics covered include the content and format of the Orange Book, petitioned ANDAs, the movement of drug products between the Active and Discontinued Sections in the Orange Book, and drug product and patent listings.
- A Federal Register notice opening a public docket[82] to solicit comments on how stakeholders and the public use the Orange Book and whether and how it can be improved.
- A Federal Register notice opening a public docket[83] to solicit comments from stakeholders on the types of patent information that should be included in the Orange Book.
- A final guidance for industry, *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act*, identifies the content for the marketing status notifications required by the FDA Reauthorization Act of 2017, the recommended format for submitting these notifications to FDA, and the timelines for submission.

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.

Drug Pricing and Access – Center-Wide Efforts

In addition to its program-specific efforts to facilitate access to low cost drug and biological products, the FDA has also worked to increase access to low-cost products through efforts that span multiple program areas.

CREATES Implementation

Among these is FDA's work to implement the recently-passed law widely known as CREATES, which provides a pathway for follow-on product developers (including those interested in developing generic, 505(b)(2), and biosimilar products) to obtain access to the product samples they need to develop these products. In addition to developing internal processes to ensure that requests for covered product authorizations under the new law are received, reviewed, and responded to within statutory timeframes across CDER, FDA launched an informational web page on how product developers can obtain access to samples under the new law.[84]

Drug Shortages

FDA's access-related work also includes addressing drug shortages, which can delay or prevent patients from getting needed care. Shortages can worsen patients' health outcomes by causing

[81] https://www.fda.gov/media/138389/download

[82] https://www.regulations.gov/document?D=FDA-2020-N-1069-0001

[83] https://www.regulations.gov/document?D=FDA-2020-N-1127-0001

[84] https://www.fda.gov/drugs/guidance-compliance-regulatory-information/access-product-samples-creates-act

delays in treatment or changes in treatment regimens, such as substituting less effective alternative therapies when a drug of choice is not available. Even when alternatives to the preferred drug are available, a patient's care may be compromised.

The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) and the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), enacted in March 2020, amended the FD&C Act to impose certain requirements and grant certain authorities that have enabled FDA to coordinate with manufacturers to help prevent or mitigate drug shortages. The FD&C Act (as amended) requires manufacturers to provide early notification of permanent discontinuances of certain prescription drugs or interruptions in manufacturing of such drugs that are likely to lead to a meaningful disruption in supply of those drugs in the United States. These requirements have helped ensure that FDA is able to work with industry early on to address problems before shortages occur and have resulted in decreasing numbers of new shortages in recent years.

FDA continues to make significant progress in reducing the number of drug shortages, from 251 new shortages in 2011 to 51 new shortages in 2019. FDA also helped to prevent 160 additional shortages in 2018 and 154 during 2019; FDA continued these important prevention efforts in to 2020. However, challenges persist. The COVID-19 public health emergency has exacerbated the problem and strained the medical supply chain. Moreover, a couple of major drug manufacturers have closed manufacturing facilities for remediation purposes, and these closures resulted in the loss of manufacturing capacity needed for supplies of drug products. FDA has been working with manufacturers to resume production and has expedited review of new submissions, helping to increase supplies.

In October 2019, the inter-agency Drug Shortage Task Force, led by FDA, released a report, *Drug Shortages: Root Causes and Potential Solutions*,[85] identifying three root causes of drug shortages and recommending three enduring solutions; the report was updated in February 2020. As part of this work, FDA invited public participation through a public meeting and a docket to receive comments, invited stakeholders to a series of listening sessions, and commissioned a team of FDA economists and other scientists to analyze drugs that went into shortage between calendar years 2013-2017 with a view to understanding the underlying forces that were driving them.

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. Developing antibacterial products for the treatment of serious infections is challenging for several reasons. For instance, patients with serious infections are likely to be acutely ill and in need of urgent empiric therapy, which results in challenges in completing trial enrollment procedures in a timely manner. There is often diagnostic uncertainty regarding the infecting pathogens, thereby necessitating use of concomitant therapies. Additionally, 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 drug development.

[85] https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

Despite these considerable challenges in developing antibacterial drugs, since 2012 after the passage of the Generating Antibiotic Incentives Now (GAIN) provisions under FDASIA, FDA has approved 26 antibacterial and antifungal new drug applications that 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 are intended to facilitate the development and informed use of antibacterial drugs.

CDER has funded research to aid in developing new antibacterial drugs. Examples include the following:

- Animal model studies to assist the development of new antibacterial drugs targeting high-priority resistant pathogens;
- Research to advance the science of antibacterial susceptibility testing to ensure that up-to-date susceptibility testing criteria (breakpoints) are available for patient care and antimicrobial stewardship;
- Development of a novel patient-reported outcome tool for use in clinical trials to measure symptoms in patients with non-cystic fibrosis bronchiectasis with and without non-tuberculous mycobacterial lung infections; and
- Developmental work on natural language processing of electronic health records to acquire RWE to advance understanding of antimicrobial resistance.

In addition, CDER has Interagency Agreements to work with other Federal agencies to support the development of antibacterial drugs. For example, FDA funded:

- Assistant Secretary for Planning and Evaluation studies to understand the market for antibacterial drugs, incentives for developing new antibacterial drugs, and social value of developing new antibacterial drugs;
- National Institutes of Health studies to explore the feasibility of assessing the relationship between minimum inhibitory concentrations and clinical outcome (mortality) for various drug-bacteria combinations using RWE from electronic health records; and
- Centers for Disease Control and Prevention studies to understand the impact of antibacterial drugs on the cystic fibrosis (CF) lung microbiome.

CDER also funded research fellowships through the Oak Ridge Institute for Science and Education (ORISE) to perform research, including establishment of a database of antimicrobial drugs in development and assessment of trends; evaluation of the current state of animal models of serious bacterial infections; and research analyses regarding key characteristics of clinical trials in hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia and endpoints in community-acquired bacterial pneumonia clinical trials with the goal of seeking alignment with other regulatory authorities such as EMA and PMDA. These projects resulted in publications in peer-reviewed journals and provide an important resource to various stakeholders.

CDER's coordinated activities address some important gaps in facilitating antibacterial drug development. Continued funding will support high-priority regulatory science research to facilitate the development of new antimicrobial drugs that are active against multi-drug resistant organisms.

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

CDER recognizes that efficient regulatory processes, informed by up-to-date science, can support the development of treatments that target the underlying causes of diseases. Drug applicants can use in silico (i.e., computational) approaches — such as modeling and simulation — to apply predictive models early in drug development. These same modeling and simulation tools help CDER conduct pre-market analyses, including addressing a variety of drug development, regulatory, and therapeutic questions. Additionally, these tools can help promote a safe and adequate drug supply.

Modeling and simulation play a role in integrating diverse data sets and exploring alternative study designs, which enable safe and effective new therapeutics to advance efficiently through the stages of clinical trials. CDER employs these tools in the following ways: predicting clinical outcomes, informing clinical trial designs and efficiency, supporting evidence of effectiveness, optimizing drug dosing/therapeutic individualization, predicting product safety and evaluating potential adverse event mechanisms, optimizing clinical development programs and increasing the probability of regulatory success, and developing new policies.

Specific examples include:

- CDER uses these strategies in the review of investigational new drug applications and new drug applications. These approaches help assess the combined effect of drug interactions, renal impairment, and hepatic insufficiency in patients in the absence of dedicated trials and help inform clinical management strategies to be included in drug labeling where appropriate.
- CDER uses modeling and simulation to support the creation of natural history databases for model-based drug development. FDA is collaborating with scientists to develop natural history models in Alzheimer's disease and muscular dystrophy to better evaluate the behavior of new treatments in settings that are inherently hard to study. Many of these modeling and simulation efforts are published or presented at public meetings.
- CDER also uses modeling and simulation in the premarket setting for predictive safety assessments. Approaches such as quantitative structure activity relationship (QSAR) are used to make predictions of whether a drug or drug impurity is likely to have mutagenic (cancer-causing) effects based on the chemical structure. Another example in CDER is the use of a cardiac physiology/pharmacology model to predict the risk of a drug to cause abnormal heart rhythms and thus alleviating the need for certain cardiac safety clinical trials.
- Pre-clinical in silico modeling is important to support drug repurposing to explore potential new uses of FDA-approved drugs. NCTR and CDER are collaborating to identify drugs in silico that may be promising for use in novel indications or diseases where there are serious unmet clinical needs.
- Modeling and simulation of drug supply chain information can be used to facilitate prompt, proactive actions to address potential disruptions of drug availability to further assure a safe and adequate drug supply. For example, drug supply chain risk signaling information within the CDEROne data analytics platform, including from CDER's Portal

for U.S. Hospitals, has been utilized during the COVID-19 pandemic to predict disruptions in the drug commercial supply chain.

Drug Supply Chain Security

FDA continues to establish the regulatory framework authorized under the Drug Supply Chain Security Act (DSCSA) that will enhance our ability to protect consumers from exposure to potentially harmful drugs through improved detection and removal of such products from the supply chain. Critical areas of DSCSA implementation are product tracing, identification and verification, as well as licensing.

Product Tracing, Identification and Verification: 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; and
- Transparency and accountability in the pharmaceutical distribution supply chain.

Trading partners have implemented lot-level product tracing and verification, and since November 27, 2018, manufacturers and repackagers have been encoding unique product identifiers on prescription drug packages and homogenous cases. To establish an electronic, interoperable system for enhanced drug distribution security by 2023, trading partners and other supply chain stakeholders are developing and testing new processes and systems. FDA has operationalized several requirements related to the receipt and processing of drug notifications of illegitimate products from trading partners and determining the appropriate response to protect the public health, in addition to industry requests for a waiver, exception or exemption of certain DSCSA requirements. FDA is also working to develop the electronic interoperable system that will integrate FDA with system(s) of members of the pharmaceutical distribution supply chain.

Licensing: FDA established a database specifically for wholesale drug distributors and third-party logistics providers to comply with annual reporting requirements. 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. Since enactment of the DSCSA, FDA has worked to develop regulations, standards, policies, and programs to implement the law.[86] FDA has issued 10 draft guidance documents and 9 final guidances. These efforts included one final guidance, issued in April 2020, supporting our response efforts to the COVID-19 pandemic by clarifying an exemption and exclusion from certain supply chain security requirements during the COVID-19 public health emergency. FDA also recently issued a final guidance describing our compliance policy related to wholesale distributor requirements for saleable returns and certain dispenser verification requirements, providing additional time to comply with these requirements until 2023. FDA continues stakeholder engagement and outreach through activities such as public

[86] https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/default.htm

meetings and conference participation to increase awareness of the upcoming DSCSA requirements.

As of June 2020, FDA completed the 20 pilot projects selected for our DSCSA Pilot Project Program. 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. The DSCSA Pilot Project Program provided a means for FDA and stakeholders to share information obtained from the pilots in an open way to further inform the enhanced system that goes into effect in 2023.

FDA continues to refine the long-term schedule for implementing the DSCSA's statutory requirements. New DSCSA requirements will go into effect over the next three 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.

COVID-19 Pandemic Response Activities

This year, leveraging our strong programmatic foundation has enabled CDER to advance therapies for myriad diseases while also launching an aggressive and multi-pronged approach to address the unexpected challenge of COVID-19. In January 2020, at the earliest sign of the impending worldwide impact of COVID, CDER established a novel response infrastructure that leveraged expertise of Center staff and built unique collaborations across FDA, HHS, and other USG agencies. CDER's multidisciplinary teams are addressing complex issues, sparking innovations that are generating treatments, protecting trial participants, and closely monitoring the drug supply chain to prevent and mitigate shortages.

CDER's role is integral to the whole-of-government COVID-19 response effort and includes evaluating multiple therapeutic approaches such as using antivirals that act directly on the coronavirus to keep it from multiplying, and providing immune inhibitors that tamp down the body's over-reaction to the virus and resulting detrimental inflammation.. As of December 31, 2020, CDER has reviewed more than 400 trials of potential therapies for COVID-19 and there are more than 590 drug development programs in planning stages. CDER's response efforts also include:

- Authorizing first drugs to treat COVID-19, including novel antiviral and monoclonal antibodies unique in their ability to target and boost innate immune response to COVID-19. Increasing transparency by disclosing scientific rationales supporting authorizations.
- Approving Veklury (remdesivir), the first drug approved to treat certain adults and pediatric patients with COVID-19 requiring hospitalization.
- Establishing the Coronavirus Treatment Acceleration Program (CTAP),[87] using every available method to move safe and effective treatments to COVID patients as quickly as possible. Ensuring that such treatments are evaluated in diverse populations, including those most vulnerable to COVID-19.
- Preventing/mitigating drug shortages by expanding supply chain surveillance; modeling to predict demand of critical drugs and visualize trouble spots; working with

[87] https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap

manufacturers of critical COVID-19 therapeutics to increase production/supply; and consolidating information for stakeholders about development and manufacturing to help get safe, effective, high-quality products for preventing or treating COVID-19 to market quickly. Per Executive Order, developed list of 227 "essential medicines" for the United States, setting the stage for onshoring pharmaceutical manufacturing, increasing supply chain resiliency, and reducing shortages.

- Collaborating across USG to: advise on drug product acquisition; guide clinical trial design/conduct; consult on treatment guidelines; establish new data source partnerships; ensure consistent USG communications to stakeholders.
- Protecting the American public from fraudulent products that claim to diagnose, prevent, treat, or cure COVID-19. This includes taking action against firms marketing hand sanitizer products in the United States that contain dangerous ingredients by broadly disseminating information about the associated dangers and requesting that manufacturers recall such products. Guiding stakeholders that continue clinical trials during COVID-19 while ensuring the safety of participants, maintaining compliance with good clinical practices, and minimizing risks to trial integrity.

In 2020, Congress passed the Coronavirus Preparedness and Response Supplemental Appropriations Act (P.L. 116-123), Coronavirus Aid, Relief, and Economic Security (CARES) Act (P.L. 116-136) and the Consolidated Appropriations Act (P.L. 116-260), which provided the FDA with supplemental resources to support the response effort to the COVID-19 pandemic. These additional resources support critical activities at FDA, including to help:

- Establish an advanced manufacturing center of excellence.
- Enhance the coordination of drug supply chain initiatives, develop IT requirements and acquire data, conduct research and develop analytic methodologies to identify products at risk of a drug shortage, and assess other supply chain vulnerabilities.
- Support review of complex scientific data and provide expedited feedback and advice to sponsors, government, and international partners regarding plans for the early phase development of antiviral therapeutics for coronaviruses.
- Address the most critical COVID response activities, and support operating costs, including a contract for a predictive modeling tool that incorporates multiple sources of data to analyze the drug supply chain and predict human drug shortages in the future.
- Continue to support activities to help produce critical care drugs in severe shortage. Funding will support advanced manufacturing grants and contracts to enable scientific study and advances, train a new workforce, and research and testing facilities to support acceleration of drug development and manufacturing in the U.S.

In March 2021, Congress passed the American Rescue Plan Act of 2021 (P.L. 117-2), which provided FDA with additional supplemental resources to support the response effort, including to:

- Conduct surveillance of the pharmaceutical supply chain for essential medicines used in the treatment of COVID-19 and novel COVID-19 therapeutics, and support mitigation of shortages of essential medical products.

- Establish a surveillance system for the monitoring of COVID-19 therapeutics for safety issues and emergent loss of utility due to COVID-19 variants, and support development of novel therapies to combat COVID-19.
- Support additional capacity and modernization efforts by CDER to accelerate recovery from the pandemic's effect on inspections.

Additional Information

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.[88]

Product Category	Approved	Product Name	FDA-Approved Use as of Approval Date
Autoimmune Disease	August 2020	Enspryng	Treatment of neuromyelitis optica spectrum disorder
Cancer	September 2020	Gavreto	Treatment of non-small cell lung cancer
Cardiovascular Disease	February 2020	Nexletol	Treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C
Infectious Diseases	August 2020	Lampit	Treatment of Chagas disease in certain pediatric patients
Genetic Disorders	August 2020	Viltepso	Treatment of Duchenne muscular dystrophy

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.[89]

Product Category	Approved	Product Name	FDA - Approved Use as of Approval Date
Anticoagulant	Dec 2019	Apixaban Tablets (generic of Eliquis)	Reduce risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; prophylaxis of deep vein thrombosis

[88] http://www.fda.gov/NewsEvents/ProductsApprovals/

[89] http://www.fda.gov/NewsEvents/ProductsApprovals/

Product Category	Approved	Product Name	FDA - Approved Use as of Approval Date
			(DVT) in patients who have undergone hip or knee replacement surgery; treatment of DVT and pulmonary embolism (PE), and reducing the risk of recurrent DVT and PE following initial therapy
Asthma/ Chronic obstructive pulmonary disease (COPD)	Mar 2020	Dabigatran Etexilate Capsules (generic of Pradaxa)	Reduce risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation; treatment and prophylaxis of DVT and PE
Asthma/ Chronic obstructive pulmonary disease (COPD)	Apr 2020	Albuterol Sulfate Inhalation Aerosol (generic of Proventil HFA)	For the treatment or prevention of bronchospasm with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in adults and children 4 years of age and older
Multiple Sclerosis	Dec 2019	Fingolimod Capsules (generic of Gilenya)	For the treatment of relapsing forms of multiple sclerosis in patients 18 years of age and older
Toxoplasmosis	Feb 2020	Pyrimethamine Tablets (generic of Daraprim)	For the treatment of toxoplasmosis when used conjointly with a sulfonamide

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$1,995,820,000	$682,861,000	$1,312,959,000
FY 2021 Enacted	$1,997,174,000	$689,195,000	$1,307,979,000
FY 2022 President's Budget	$2,121,242,000	$774,469,000	$1,346,773,000

BUDGET REQUEST

The FY 2022 Budget Request for the Human Drugs Program is $2,121,242,000 of which $774,469,000 is budget authority and $1,346,773,000 is user fees. The budget authority is increased by $85,274,000 compared to the FY 2021 Enacted and user fees increased by $38,794,000. The Center for Drug Evaluation and Research (CDER) amount in the request is $1,854,233,000. The Office of Regulatory Affairs amount is $267,009,000.

The Human Drugs Program will continue activities to uphold its public health mission of ensuring the safety and efficacy of new, generic, biosimilar, and OTC drug products.

The FY 2022 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. The Agency will continue to promote patient and health professional awareness of drug benefits and risks through effective communication of drug information.

FDA under the FY 2022 Budget 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 carry forward the Agency's support of 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 2022 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 2022 Budget will support efforts to strengthen FDA's drug safety surveillance and oversight of marketed drug products. Investments will be used to modernize FDA's regulatory framework and create and implement organizational and procedural changes to support efficient and effective postmarket safety for the 21st century. Continuous enhancements to FDA's drug surveillance and safety oversight program will help the Agency better leverage the advances in drug safety science to protect the health of the American public.

The FY 2022 Budget will also support one of FDA's highest priorities – the goal of ending the opioids crisis. As opioid-related deaths continue to increase in the U.S., further research is needed to address this crisis, including the impact of COVID-19 on patients with Opioid Use Disorder (OUD). The FY 2022 Budget will provide FDA with additional resources for opioids research, development of opioid reversal treatments, treatments for OUD and related activities to combat this public health crisis.

BUDGET AUTHORITY

Medical Product Safety (+$41.6 million / 58 FTE)

Drug Safety Surveillance and Oversight: (+$5.6 million / 18 FTE)
Center: +$5.6 million / 18 FTE

The FY 2022 Budget request will help CDER build the foundation for implementing a 21st Century Roadmap for modernizing FDA's safety surveillance and oversight program for marketed drug products. Additional funds will allow FDA to bolster activities to modernize the regulatory framework for FDA's postmarket surveillance program and implement foundational organizational and process changes. CDER will need to support efficient and effective postmarket safety surveillance and oversight for the 21st century—activities that cannot be supported with the current base funding.

As part of its mission to protect public health and safety, FDA's postmarket surveillance program continuously monitors the safety of all drug products while they are being marketed. When information that may change the benefit-risk profile of a product is uncovered, FDA investigates the issue and takes appropriate action. These actions may include requesting or requiring labeling changes, issuing drug safety communications, requiring postmarket studies, requiring or modifying risk evaluation and mitigation strategies (REMS), or withdrawing approval of a product. The Agency maintains a wide-ranging postmarket surveillance and risk evaluation program to identify and evaluate new adverse events and medication errors—those that did not appear during the drug development and approval process. Although clinical trials provide important information on a drug's efficacy and safety, it is impossible to have complete information about the safety of a drug at the time of its approval. The true picture of a medical product's safety can evolve over the months, and years of the product's lifetime in the marketplace. Protecting the health of the American public requires FDA to continuously enhance its drug safety surveillance and oversight program, consistent with advances in the science of drug safety.

FDA currently faces significant challenges to its ability to maintain an efficient and effective postmarket safety surveillance program. Staffing levels have not kept pace with the increasing amount of postmarket work from the growing number and complexities of recent approvals, and the increasing amount of data needing review. In order to leverage the rapid advances in the science of drug safety, FDA needs to update its scientific standards and modernize its assessment tools, approaches, organizational structure, and processes to enable FDA scientists to effectively and efficiently aggregate and analyze important drug safety data to protect the American public.

FDA is currently engaged in efforts to strengthen postmarket safety surveillance and risk assessment; and create a system that efficiently and cost-effectively improves drug safety and public health outcomes. As part of the New Drugs Regulatory Program (NDRP) modernization initiative[90], FDA is building the foundation for implementing a 21st Century Roadmap for modernizing surveillance under the Postmarket Safety Workstream. For these efforts to be successful, the FDA requires funding to expand its existing postmarket safety pilot programs and establish a permanent and dedicated postmarket safety policy team. The activities below describe

[90] https://www.fda.gov/drugs/regulatory-science-research-and-education/modernizing-fdas-new-drugs-regulatory-program

how the additional resources will help to advance the foundational work initiated under the NDRP modernization initiative to promote public health.

Modernize the regulatory framework

Funding will be used to develop a modernized regulatory framework for FDA's postmarket safety surveillance program. This modernized approach will include:

- a surveillance system that is able to adapt to the ever-changing science of drug development
- the application of new technologies that can inform our understanding of safety in the postmarket setting.

The FDA will assemble a multidisciplinary team of regulatory counsels, project managers, and scientists to craft a risk-based approach to determining what types of scientifically valid information the Agency requires industry to submit, and how that information will be used. This approach—which will be dynamic—may factor in differential risks including those associated with active pharmaceutical ingredients, excipients, or delivery mechanisms. FDA's goal with these efforts is to determine which set of information we can both require of industry and utilize internally to maximize the value of data that we receive, while considering the legal, financial, and economic burdens imposed on all stakeholders. This team will evolve into a permanent, cross-discipline function dedicated to post-market safety policy.

Develop and implement organizational and process changes to support efficient and effective postmarket safety

Modernizing the postmarket drug safety system will contribute to advancing CDER's overall vision for integrated, multi-disciplinary benefit risk monitoring across the product lifecycle. It will require staff whose primary responsibilities include integrating and synthesizing scientific reviews from a broad array of disciplines (e.g., clinicians, pharmacists, epidemiologists, regulatory specialists, informaticists, project managers) to coordinate with other parts of the Center and enable a thorough understanding of the portfolio of ongoing and completed drug safety work. Additional resources will help support the development of proactive postmarket safety strategies and the assessment of information across multiple disciplines. These activities will advance the foundational work initiated under the New Drugs Regulatory Program including the establishment of work streams to support Drug Safety Teams, Pharmaco-vigilance Strategy, Periodic Safety Reports and the Integrated Safety Assessment.

Advancing the Goal of Ending the Opioid Crisis: (+$36 million / 40 FTE)
Center: +$26 million / 15 FTE

Field: + $10 million / 25 FTE

FDA requests $26 million to advance the goal of ending the opioids crisis and to support the substantial work that is needed to implement the SUPPORT Act, enacted in October 2018. The SUPPORT Act gave FDA new authorities to continue current opioid-related efforts and new directives to implement policy actions to help patients in need while also reducing the use, misuse, and abuse of opioid medicines. FDA will use the funding to further develop and advance strategies to confront the opioid crisis through the Agency's four priority areas:

- Decrease Exposure & Prevent New Addiction
- Support Treatment of Those with Opioid Use Disorder
- Foster Development of Novel Pain Treatment Therapies
- Improve Enforcement & Assess Benefit-Risk

Critical areas related to appropriate pain management as well as the use, misuse, and abuse of opioid analgesics demand science-based study and analysis. Research will include collecting, generating, and analyzing pre-clinical, clinical, and real-world data needed to validate clinical endpoints for drug development and help identify new drug targets. Studies will inform better pain management as well as the development of novel treatments for opioid overdose reversal and for opioid use disorder. Findings from these studies will support the Agency's ongoing opioid initiatives, which include industry guidance clarifying FDA's thinking on clinical trial designs and help sponsors bring novel treatments to market for acute pain, chronic pain, opioid overdose reversal, and OUD.

The requested funding will advance the development of evidence-based clinical practice guidelines for acute pain. Implementing Sec. 3002 of the SUPPORT Act, FDA will work collaboratively with relevant professional organizations to support the development and adoption of evidence-based clinical practice guidelines.

Funding will also support FDA's implementation of Sec. 3032 of the SUPPORT Act, which provided FDA with new authority to mandate safety-enhancing packaging and disposal technologies for opioids and other drug products that carry serious risks of abuse or overdose.

FDA's use of modern approaches and IT solutions, including the expansion of using social media data to analyze real-world patterns of opioid use, misuse, and abuse will be supported by this funding. FDA also plans to transition and maintain the Opioid Data Warehouse to the CDEROne platform – a cloud-based enterprise data lake and augmented analytical platform – to support opioid data analysis including an expansion to capture all transactional information not currently available in CDEROne. Together, these efforts are critical to foster the safe use of opioids and detect new potential emerging threats. Furthermore, funding will help FDA explore strategies and IT solutions to improve and promote prescriber education. For example, FDA will assess the feasibility of integrating the Opioid Analgesic Risk Evaluation and Mitigation Strategies (REMS) education into IT health systems and Electronic Health Records. Such efforts may help our work to expand and promote prescriber education, improve pain management, and broaden patient access to OUD treatment.

Funding will also provide staffing to support FDA's opioid policy programs. The opioid crisis is rapidly evolving and is further complicated by the impact of the COVID-19 pandemic. As the number of drug overdose deaths are projected to exceed past reports, additional staff are needed – now more than ever – to sustain FDA's critical work in this area.

ORA requests funding to expand the current International Mail Facilities (IMF) initiative to interdict shipments of opioids, unapproved foreign drugs, counterfeit pharmaceuticals and health fraud related shipments. FDA reviews in the IMF have increased from just under 14,000 to more than 50,000 in FY2020, with a commensurate increase in destructions of non-compliant drugs.

Under the current IMF initiative, ORA has multiple laboratory subcomponents that support drug testing efforts including illegal, unapproved, counterfeit and opioid testing. Laboratory resources

will be used to establish IMF satellite laboratories, develop field deployable toolkits, train and deploy laboratory personnel, and analyze additional samples associated with regulatory and criminal investigations. As the program matures, additional resources are required to meet the increased volume and complexity of the samples as well as for management and support of new or existing analytical tools deployed for field use; development of new analytical methods or strategies; development and support of laboratory reachback capabilities, accreditation/proficiency requirements; and expansion of the safety program for the geographically diverse locations.

Compounding and outsourcer inspections have added an investigational assessment for compounding of opioids and opioid products. This expanded investigation involves tracking and tracing supply chains along with production activities at the compounding facilities. Additional resources are needed as the outsourcer inventory has grown and the products produced, and supply chains have become more complex.

Crosscutting: (+$43.7 million / 52 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data: (+$15.8 million / 17 FTE)
Center: +$14 million / 15 FTE

Field: + $1.8 million / 2 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in the Medical Product programs as well as FDA's enterprise technology capabilities. Within this amount, CDER requests $14

million, and ORA requests $1.8 million to support the Enterprise Technology and Data crosscutting efforts.

Inspections: (+$7.5 million / 26 FTE)
Field: +$7.5 million / 26 FTE

The FY 2022 Budget includes $18.8 million for inspections. ORA will increase site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID-19 related delays, and the Budget includes $7.5 million for the Field portion of Human Drugs.

Pay Costs: (+$3.9 million)
Center: +$2.8 million

Field: +$1.1 million

The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

Capacity Building: (+$16.4 million / 9 FTE)
Center: +$14.4 million / 8 FTE

Field: +$2 million / 1 FTE

The FY 2022 Budget includes $40.3 million to support centrally administered services to support critical, high-priority Capacity Building activities. Within this, CDER requests $14.4 million, and ORA requests $2 million for these efforts.

USER FEES

Current Law User Fees: +38.8 million

Center: +$37.7 million / Field: $1.1 million

The Human Drugs Program request includes an increase of $38,794,000 for user fees authorized, 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.

PROGRAM ACTIVITY DATA

CDER Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	151	171	201
Efficacy Supplements	267	322	294
Manufacturing Supplements	2,231	2,187	2,418
Commercial INDs (Drugs and Biologics) with Activity	8,045	8,565	9,121
Sponsor Requests: IND-Phase Formal Meetings	3,701	3,701	3,701
Sponsor Requests: Review of Special Study Protocols	148	148	148
Submissions of Promotional Materials	131,301	136,000	140,000
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	59	59	59
Reviews: Standard NDA/BLA	149	149	149
Approvals: Priority NDA/BLA	48	48	48
Approvals: Standard NDA/BLA	91	91	91
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	7.9	7.9	7.9
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	20.8	20.8	20.8
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	6.9	6.9	6.9
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	12	12	12
Reviews: NDA Supplementals	3186	3186	3186
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	7937	8493	9087
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	224	224	224
Receipts: IND/IDE Amendments (Biologics Only)	27,202	27,202	27,202
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	22	22	22
Approvals: PLA/BLA	20	20	20
Reviews: License Supplement (PLA/ELA/BLA)	626	626	626
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	865	1,000	1,000
Outputs – Reviews/Approvals			
Actions – ANDA	3,212	3,000	3,000
Approval Actions - ANDA (both Tentative and Full Approvals)	909	850	850
Median Review Time from ANDA Receipt to Approval (months)	22.44	24	24
Actions - ANDA Supplementals (Labeling and Manufacturing)	10,922	10,000	10,000
Over-the-Counter Drug Review			
OTC Monographs Under Development*	25	25	25
OTC Monographs Published*	0	5	5
** On March 27, 2020, the President signed the Coronavirus Aid, Relief, and Economic Security Act (CARES Act). The CARES Act includes statutory provisions that reform and modernize the way OTC monograph drugs are regulated in the United States. The CARES Act replaces the rulemaking process with an administrative order process for issuing and revising OTC monographs. The figures beginning in FY 2021 reflect this change.*			
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information	20	21	19
New Written Requests Issued	15	20	21
Pediatric Exclusivity Determinations made	7	11	12
Post Exclusivity Safety Report	5	7	8
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	2,194,361	2,221,607	2,249,191
Electronic Submissions: % of Total Adverse Drug Reaction Reports	96%	96%	96%
Electronic Submissions: % of Serious/Unexpected Adverse Drug Reaction Reports	100%	100%	100%
Submissions: Drug Quality Reports	25,270	26,000	28,000
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,070	7,211	7,355
Number of drugs with Risk Communications	185	235	250
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	19	33	33
Number of FOI Requests	2,501	2,800	2,800
Number of FOI Requests Processed	2,478	2,825	2,825
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	93	95	95
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	176	180	180
Number of Citizen Petitions Completed [1] (excluding suitability petitions and OTC monograph-related petitions)	105	110	110

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

Field Human Drugs Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate[4]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***882***	***150***	***1,695***
Pre-Approval Inspections (NDA)	55	10	100
Pre-Approval Inspections (ANDA)	41	6	90
Bioresearch Monitoring Program Inspections	411	66	600
Drug Processing (GMP) Program Inspections	315	52	650
Compressed Medical Gas Manufacturers Inspections	13	2	50
Adverse Drug Events Project Inspections	25	4	88
OTC Monograph Project and Health Fraud Project Inspections	6	1	70
Compounding Inspections[1]	54	9	127
Domestic Laboratory Samples Analyzed	818	701	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***516***	***40***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	58	11	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	89	16	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	139	24	255
Foreign Drug Processing (GMP) Program Inspections	251	44	900
Foreign Adverse Drug Events Project Inspections	4	1	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,398***	***190***	***3,055***
IMPORTS			
Import Field Exams/Tests	7,096	7,100	10,000
Import Laboratory Samples Analyzed	841	850	620
Import Physical Exam Subtotal	**7,937**	**7,950**	**10,620**
Import Line Decisions	959,585	967,604	967,604
Percent of Import Lines Physically Examined	0.83%	0.82%	1.10%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,398***	***190***	***3,055***

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

[2] The FY 2019 actual unique count of foreign inspections includes 36 OGPS inspections (16 for China, 16 for India, and 0 for Latin America).

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

[4] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 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	42	*3*

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[91]

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

Over 760 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 2020, OOPD received 47 clinical trial applications and funded 6 new grants from those applications, including studies to

[91] FY 2020 includes $1.2 million of OOPD program funds to support Orphan Product Grants

treat Stargardt Disease, cystic fibrosis patients colonized with nontuberculosis mycobacterium, peripheral T-cell Lymphoma and pancreatic cancer. OOPD provided funding or continued support for approximately 70 other ongoing clinical study projects, including several Phase 3 trials. In addition, in FY 2020, due to the challenges and increased costs for clinical trials due to the COVID-19 pandemic, OOPD provided existing grantees with additional funding. These new resources allow ongoing studies to implement necessary steps to allow their research to continue and assure the safety of study participants, to maintain compliance with good clinical practice, and to minimize risks to trial integrity.

OOPD's RFA for FY 2021 and 2022 is focusing on efficiency, innovation, and impact, with an added focus on leveraging patient input, infrastructure, and financial resources. It also includes new optional innovative demonstration projects that can be used as models for future drug development in rare diseases in one of the following areas: 1) innovative collaborations; 2) innovative patient recruitment/retention strategies; or 3) innovative methods using data simulation/modeling. OOPD received 45 applications in October 2020 for the FY 2021 applications cycle and these applications are currently under review.

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. These grants continue to be a way to de-risk rare disease products for marketing development and are an important source of funding for rare disease research.

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 and conditions, identification of genotypic and phenotypic subpopulations, and development and validation of clinical outcome measures, biomarkers and companion diagnostics. OOPD funded 6 applications from that initial cycle and due to the overwhelming need and support for this program, OOPD published a new Request for Applications (RFA) in FY 2019. Two new grants from those applications including studies to follow medullary thyroid cancer patients and cardiac disease in Duchenne muscular dystrophy patients were funded. These studies will add important data to help develop targeted therapies and lead to more efficient and better designed clinical trials. FDA continues to fund these two awards along with six previous awards that have served to move the fields along in these rare diseases, including beginning design of clinical trials, forming collaborations with industry and others, and publishing several articles on the outcomes reached thus far.

A new RFA is planned for FY 2022 and FY 2024 for these critical rare disease natural history studies that provide essential information to design efficient clinical trials for rate diseases.

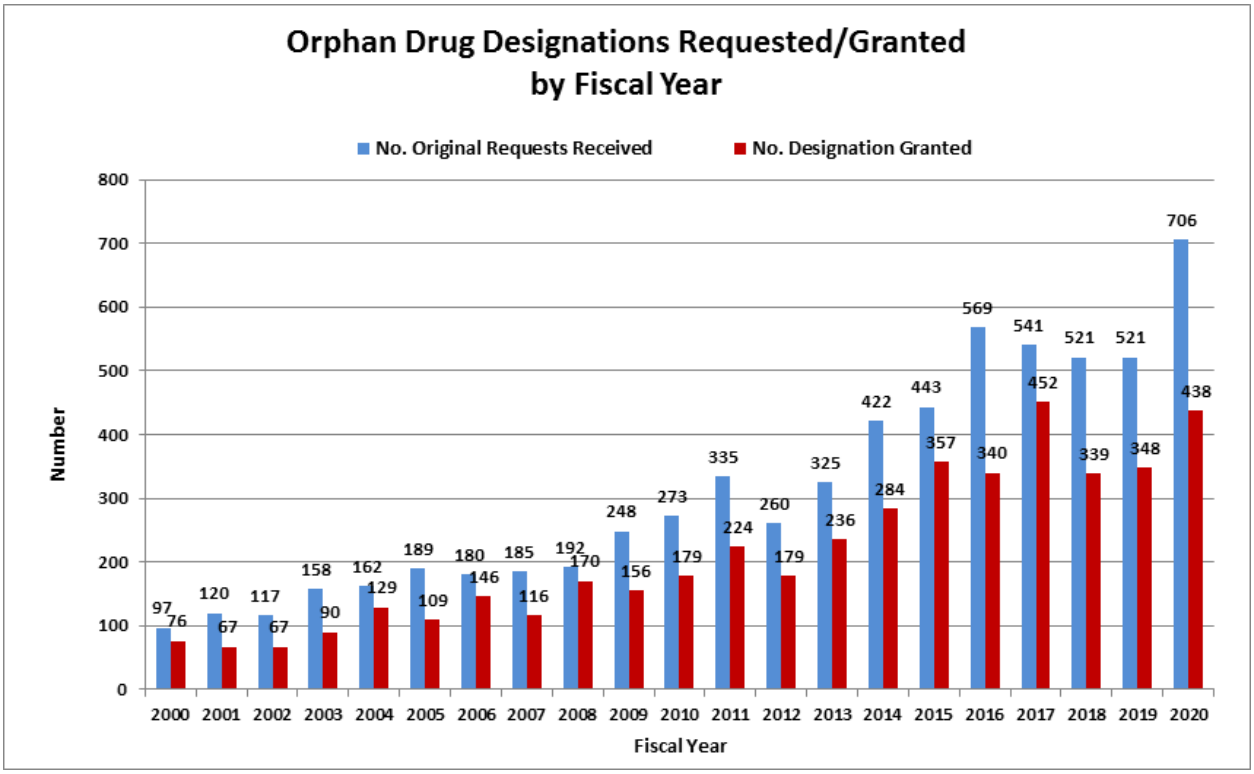


Figure 5 Orphan Drug Designations Requested/Granted by Fiscal Year

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

Over 5,600 orphan drug designations issued by OOPD issued since 1983 have resulted in over 900 marketing approvals, the majority having been awarded orphan exclusivity. In contrast, the decade prior to 1983 saw fewer than 10 such products developed by industry make it into the market. In FY 2020, OOPD received 753 new applications and designated 476 orphan drugs. These included potential treatments for many kinds of rare diseases, such as rare cancers, sickle cell disease, and cystic fibrosis. FDA approved 91 orphan designated drugs for marketing indications during that time.

The number of requests for orphan designation has had a six-fold increase 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. Then number of orphan drug designation requests received in FY 2020, as compared to FY 2019, have increased 36%.

Product Designations
Below are examples of Orphan Product designations that occurred in 2020.[92]

Date	Product	Purpose or Benefit
April 2020	Selumetinib	Neurofibromatosis type 1
May 2020	Pomalidomide	Kaposi sarcoma

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 an optional "rare pediatric disease" designation through OOPD, which 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 2020, OOPD received 272 new rare pediatric disease designation and consult requests. OOPD determined that 235 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 2020, a total of five rare pediatric disease priority review vouchers were issued.

On December 13, 2016, Congress extended the designation aspect of the program to September 30, 2020. As of October 1, 2020, the designation aspect of the program is set to sunset on December 11, 2020. OOPD has seen the number of requests for rare pediatric disease designation quintupled in FY 2020, as compared FY 2019.

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 may be 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

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

restrictions set forth in Section 520(m) of the FD&C Act. Since 1990, 77 HUD devices have been approved for marketing through the HDE pathway.

Except in certain circumstances, a HUD approved under an HDE cannot be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (for profit). Under Section 520(m)(6)(A)(i) of the FD&C Act, as amended by FDASIA, a HUD is eligible to be sold for profit after receiving HDE approval if the device meets certain criteria. As of FY 2020, 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 2020, OOPD received 14 new HUD applications and designated 12 devices.

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, 24 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. In FY 2020, FDA received $1 million of additional funding to support pediatric medical device development, of which the PDC grantees received $750,000 and CDRH received $250,000. The funds will be used to support innovative device solutions to address critical emerging public health needs for pediatric patients.

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 27 new devices are now available for use in pediatric patients as a result of advisory assistance received from the consortia, such as the bili-hut™ and the Minimally Invasive Deformity Correction (MID-C) System. The sponsor of bili-hut™ received 510(k) clearance from the FDA for this portable neonatal phototherapy system that leverages a bassinet-like design to treat hyperbilirubinemia, commonly known as neonatal jaundice. The consortia collectively have also raised more than $320 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 2020, OOPD participated in 43 individual industry outreach and 13 patient-oriented meetings. In addition, OOPD received 49 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 24 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 FY 2020 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. 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 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 Actual	$33,257,000	$29,099,000	$4,158,000
FY 2021 Enacted	$33,257,000	$29,099,000	$4,158,000
FY 2022 President's Budget	$33,257,000	$29,099,000	$4,158,000

BUDGET REQUEST

The FY 2022 Budget Request is $29,099,000. With this funding level, OOPD will fund approximately 4-8 new clinical trials grant awards and provide funding or continued support for approximately 70 other ongoing clinical study projects. In addition, OOPD plans to award 2-5 new natural history grants and continue to fund two ongoing grants for natural history studies targeted on expediting the development of products for these rare conditions.

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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
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 2019: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
223211: Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60-day filing date. (*Output*)	FY 2019: 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 2019: 99% Target: 90% (Target Exceeded)	90%	90%	Maintain
223213: Review and act on 90 percent of priority non-NME original NDA submissions within 6 months of receipt. *(Output)*	FY 2019: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
223215: Review and act on 90 percent of standard original Abbreviated New Drug Application (ANDA) submissions within 10 months of receipt. *(Output)*	FY 2019: 97% [93] 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 2019: 98%[93] Target: 90% (Target Exceeded)	90%	90%	Maintain
224221: Percentage of Human and Animal Drug significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2020: 77.7% Target: 80% (Target Not Met)	80%	80%	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 2020: 69.3% Target: 55% (Target Exceeded)	55%	55%	Maintain
292203: Number of medical product analyses conducted through FDA's Sentinel Initiative. *(Output)*[94]	FY 2020: 79 Target: 55 (Target Exceeded)	60	65	+5

[93] 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 99% (2% more than just applying the 10-month metric). This imminent approval performance number reflects FDA's decision to work through the goal date to achieve an approval or TA within 60 days of the goal date rather than issue a complete response or tentative approval letter by the goal date.

[94] The performance targets for the Sentinel Initiative performance measure remain consistent with those previously reported for the Sentinel Active Risk Identification and Analysis (ARIA). FDA will continue to assess the activities of this Sentinel Initiative and determine if these targets should be updated for future reporting years.

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

Review Goals

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

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

Sentinel

The Sentinel Initiative comprises multiple components including the Sentinel System, and its Active Risk Identification and Analysis (ARIA) program, FDA Catalyst, and the Biologics Effectiveness and Safety System. The Sentinel Initiative has continued to evolve rapidly in the last two years. In 2019, Congress required that FDA build on Sentinel's core successes by establishing a new Real-World Evidence Medical Data Enterprise with access to at least 10 million electronic medical records. The year 2021 marks six 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 informs regulatory decision-making and expands our knowledge of how medical products perform once they are widely used in medical practice. In 2020, FDA began to leverage Sentinel in novel ways as part of a multi-layered response to the COVID-19 pandemic. These activities range from developing the capability for near real-time drug monitoring to inform the potential for drug shortages, describing the course of illness among patients with COVID-19, and evaluating the impact of therapies being used in COVID-19 patients under real-world conditions.

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.

COVID Impact on ORA Field Performance Measures

Due to COVID-19, ORA faced many challenges in meeting the FY 2020 performance targets. FDA paused on-site surveillance inspections due to COVID-19, needing to balance our public health mission with investigator safety concerns, geographic and establishment restrictions, and increased work related to public health need during the pandemic. Despite these challenges, ORA continued conducting its mission critical work, and met all of the performance goals, except one. Given the 3-year rolling basis methodology of this performance goal and the continued prioritization of follow-up after regulatory actions, the inspections not conducted toward this goal in FY 2020 will be a responsibility in FY 2021. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA's ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

Program Workload and Outputs	**FY 2020 Actuals**	**FY 2021 Estimates (Actuals pending end of FY21)**	**FY 2022 Estimate**	**FY 2023 Estimate**
Grant Programs				
Total Orphan Product Grant (New and Continuations)	76	80	80	80
Total Pediatric Consortia Grants (New and Continuations)	5	5	5	5
Total Natural History Grants (New and Continuations)	7	7	10	10
Orphan Drug Designation Requests/Designations/Granted/Orphan Drug Approvals				
New Orphan Drug Designation Requests	706	600	600	600
Drug Designations Granted	438	400	400	400
FDA Orphan Drug Marketing Approvals	86	90	90	90
HUD Requests and Designations				
New HUD Designation Requests	14	18	20	20
HUD Designations Granted	12	14	15	15
Rare Pediatric Disease Priority Review Vouchers Requests and Designations				
New RPD Requests	272	TBD (program due to sunset (12/11/20)	TBD	TBD
RPD Designations	235	TBD	TBD	TBD

BIOLOGICS

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Biologics	**419,302**	**426,027**	**437,071**	**457,889**	**20,818**
Budget Authority	***252,138***	***252,128***	***254,138***	***270,114***	***15,976***
User Fees	***167,164***	***173,899***	***182,933***	***187,775***	***4,842***
Center	375,583	382,468	393,322	408,118	14,796
Budget Authority	210,132	210,131	212,132	222,145	10,013
User Fees	165,451	172,337	181,190	185,972	4,782
Prescription Drug (PDUFA)	*149,267*	*158,793*	*164,951*	*169,401*	*4,450*
Medical Device (MDUFA)	*14,578*	*13,366*	*14,981*	*15,203*	*222*
Generic Drug (GDUFA)	*960*	*132*	*983*	*1,088*	*105*
Biosimilars (BsUFA)	*646*	*46*	*275*	*280*	*5*
Field	43,719	43,559	43,749	49,771	6,022
Budget Authority	42,006	41,997	42,006	47,969	5,963
User Fees	1,713	1,562	1,743	1,802	59
Prescription Drug (PDUFA)	*1,485*	*1,340*	*1,514*	*1,569*	*55*
Medical Device (MDUFA)	*228*	*222*	*229*	*233*	*4*
FTE	**1,439**	**1,441**	**1,438**	**1,462**	***24***

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; and Further Consolidated Appropriations Act, 2020.

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 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, approval of, and access to safe and effective products and promising new technologies; and
- Strengthen CBER as a preeminent regulatory organization for biologics.

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.[95] These accomplishments align with the Department of Health and Human Services and CBER's strategic plan[96], and reflect implementation of legislative mandates.

Fostering Competition And Innovation

FDA's Biologics Program is committed to helping to set the stage for the continued advancement of novel products by providing guidance to industry and, when appropriate, expediting the development and evaluation of new biological products for emerging infectious diseases and a broad range of complex, life-threatening and rare diseases. CBER also encourages the development and adoption of advanced technologies and manufacturing to support processes with fewer interruptions in production, fewer product failures, and greater assurance that products manufactured will provide the expected clinical performance. This work aligns with the HHS Strategic Plan FY 2018-2022 to "Protect the Health of Americans Where They Live, Learn, Work, and Play." It further aligns with CBER's strategic goal to "Facilitate the development and availability of safe and effective medical products through the integration of advances in science and technology."

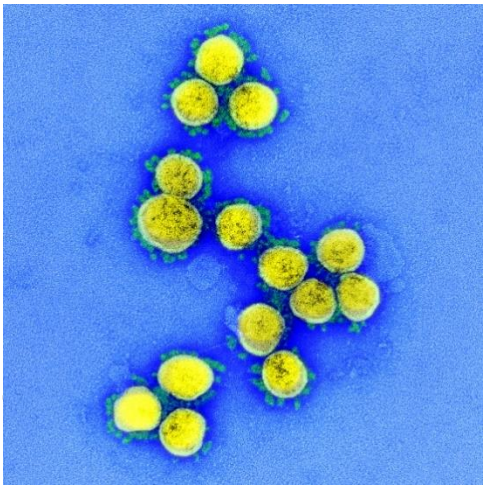
Addressing COVID-19

COVID-19 presented as a novel viral infection that could not be addressed with existing vaccines or therapeutics. Protecting public health by ensuring the development of safe and effective

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

[96] Center for Biologics Evaluation and Research 2021 - 2025 Strategic Plan https://www.fda.gov/media/81152/download

COVID-19 therapeutics, vaccines, and other medical products is currently one of the highest priorities at the FDA. This will help reduce incidence rates, mortality, and pandemic-related disruptions. CBER is using every tool available to help patients access promising biological products while facilitating applied scientific research to evaluate their safety, effectiveness and manufacturing.



FDA recognizes the urgent need to develop safe and effective vaccines and therapeutics for COVID-19 and continues to work collaboratively with industry, researchers, federal, domestic, and international partners to accelerate these efforts. To help move these important products forward in development and availability FDA published the following final guidance documents: "Investigational COVID-19 Convalescent Plasma" (April 2020, updated May, September, and November 2020 and January and February 2021), "Development and Licensure of Vaccines to Prevent COVID-19" (June 2020), and "Emergency Use Authorization for Vaccines to Prevent COVID-19" (October 2020, updated February 2021).

Based on available safety and effectiveness data, CBER issued the first emergency use authorization (EUA) for a vaccine to prevent COVID-19 in December 2020. This emergency use authorization allows the Pfizer-BioNTech COVID-19 vaccine to be distributed in the U.S. A week later, CBER issued an EUA for the second vaccine to prevent COVID-19 to allow the Moderna vaccine to be distributed in the U.S. The Pfizer and Moderna vaccines both contain a synthetic, small piece of the SARS-CoV-2 genetic material (mRNA) that instructs cells in the body to make the virus's distinctive "spike" protein. When vaccinated, the body produces copies of the spike protein and the immune system learns to react defensively, producing an immune response against SARS-CoV-2. In February 2021, FDA issued an EUA for the third vaccine for the prevention of COVID-19. The EUA allows the Janssen COVID-19 vaccine to be distributed in the U.S. The vaccine used a specific type of virus called adenovirus type 26 (Ad26) to deliver a piece of the spike protein DNA to trigger an immune response to protect individuals from COVID-19.

Through an open and transparent scientific review process, CBER authorized the COVID-19 vaccines in expedited timeframe while adhering to its rigorous standards for safety, effectiveness, and manufacturing quality needed to support emergency use authorization. The vaccine evaluation process included public and independent review from members of the Vaccines and Related Biological Products Advisory Committee (VRBPAC). VRBPAC reviews and evaluates data concerning the safety, effectiveness, and appropriate use of vaccines and related biological products which are intended for use in the prevention, treatment, or diagnosis of human diseases, and, as required, any other products for which the FDA has regulatory responsibility. Due to early interaction with the sponsor and receipt of chemistry, manufacturing, and controls information prior to the EUA submission, FDA was able to grant authorization of the EUA's within days of receiving recommendations from the VRBPAC.

CBER's configuration of foundational surveillance systems builds upon existing postmarket safety and effectiveness surveillance systems for preventative vaccines and therapeutics. CBER

is monitoring the safety of authorized COVID-19 vaccines through surveillance systems in collaboration and coordination with several different partners, including government, academic and large non-government healthcare data systems. FDA is using the Vaccine Adverse Event Reporting System (VAERS) to monitor the occurrence of adverse events reported by health providers, consumers and manufacturers. FDA is also conducting near real time surveillance using the Sentinel BEST (Biologics Effectiveness and Safety) System and the surveillance system using the CMS Medicare Claims Database. CBER is using BEST to monitor about 15 adverse events that have been seen with the deployment of previous vaccines but have not been associated with a safety concern for an authorized COVID-19 vaccine at this time.

CBER is working to help ensure a safe and adequate blood supply during a time of reduced blood donations due to social distancing and cancelled blood drives due to COVID-19. FDA issued five final guidance documents to improve the availability of blood and blood components during the pandemic. CBER also serves as a member 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 collaborated with the Biomedical Advanced Research and Development Authority (BARDA) to help facilitate a Mayo Clinic-led Expanded Access Program for convalescent plasma from April to August 2020 to fill an urgent need to provide access to convalescent plasma to approximately 100,000 patients. In August 2020, FDA issued an emergency use authorization (EUA) for investigational convalescent plasma for the treatment of COVID-19 in hospitalized patients. In February 2021, FDA revised the EUA to limit the authorization to the use of high titer convalescent plasma only for the treatment of hospitalized patients with COVID-19 early in the disease course and to those hospitalized patients who have impaired humoral immunity based on new data.

CBER scientists have initiated research studies to facilitate evaluation of vaccines, treatments, and diagnostics in response to the COVID-19 pandemic. CBER scientists are developing assays that may be useful in evaluating vaccines, studying the immune response to inform vaccine development, and evaluating small animal models for their feasibility to study vaccines and therapeutics. Using animal models to better understand the various antibody responses triggered by spike-protein-based vaccines, FDA scientists identified and evaluated the quality of antibody responses triggered by various SARS-CoV-2 spike antigens. CBER also worked with the Center for Devices and Radiological Health to develop a SARS-CoV-2 reference panel to aid in the evaluation of diagnostic tests for SARS-CoV-2 to help ensure trustworthy diagnostic tests.

FDA is working with industry and government partners to accelerate the development and availability of SARS-Cov-2 Immune Globulin (human) for investigation for potential COVID-19 treatments. As a part of this effort, FDA provided technical assistance to help establish the Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC) study, that began in

October and is conducted by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health.

CBER is protecting the American public from potentially unsafe, unapproved products during the COVID-19 pandemic. CBER issued the guidance "Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products During COVID-19 Public Health Emergency" (January 2021) to provide manufacturers with risk-based recommendations to minimize the potential transmission of SARS-CoV-2. FDA released an update for human cell, tissue, or cellular or tissue-based product (HCT/Ps) in January 2021, though to date there have been no reported cases of transmission of COVID-19 via these products. FDA continues to monitor the situation. FDA also issued a Safety Alert pertaining to SARS-CoV-2 and COVID-19 for Fecal Microbiota for Transplantation (FMT), as SARS-CoV-2 may be transmitted by FMT (March 2020).

Since the beginning of FY 2020 through March 1, 2021, FDA:

- Issued six Warning Letters for unapproved COVID-19 products, four of which were issued jointly with the United States Federal Trade Commission.
- Issued four Untitled Letters for unapproved COVID-19 products, including exosome, adipose, and umbilical cord products.

Beyond products for COVID-19, the pandemic has impacted the conduct of clinical trials, including challenges from quarantines, site closures, travel limitations, and safety of participants, that may lead to difficulties in meeting protocol-specified procedures. The guidance "Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency" (March 2020, updated April, May, June, July, and September 2020and January 2021) provides general considerations to assist sponsors in assuring safety of clinical trial participants, maintain compliance with good clinical practice, and minimize risks to trial integrity.

To help develop assays, animal models, and clinical trials, CBER participated in international efforts to address the COVID-19 pandemic, including in meetings sponsored by Coalition for Epidemic Preparedness Innovations, and WHO Working Groups. This includes the R&D blueprint to improve coordination between scientists and global health professionals, accelerate the research and development process, and develop new norms and standards to learn from and improve upon the global response. FDA has been actively assessing the impact of new strains on authorized products and continues to work with its international partners to evaluate the impact that each variant may have on effectiveness or utility of authorized medical products.

Modernizing the Regulatory Process to Improve Innovation

To help ensure that the regulatory process is predictable and transparent, even when dealing with innovative products that incorporate state-of-the-art science, 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. FDA meets with prospective

innovators and developers of advanced manufacturing technologies and innovative investigational products at early stages to provide informal consultation. Mechanisms for these interactions include the CBER INitial Targeted Engagement for Regulatory Advice on CBER producTs (INTERACT) program and the CBER Advanced Technologies Team (CATT) meeting program.

FDA uses existing programs to expedite the development and evaluation of innovative products to treat or prevent serious conditions, when appropriate. As of FY2020, CBER granted 58 Breakthrough Therapy designations, with 30 of the products being for rare diseases (Orphan designated). FDA granted 59 RMAT Designations since program inception in December 2016 with 30 being for rare diseases.[97] In February 2021, CBER approved the first RMAT-designated product Breyanzi (lisocabtagene maraleucel), a chimeric antigen receptor (CAR) T cell therapy, for the treatment of certain types of large B-cell lymphoma in adult patients.

Gene therapy developers face unique challenges for rare diseases, especially the commercial viability of products that are going to have markets of fewer than 100 patients per year. To help address these challenges and streamline production of these products CBER:

- Held a public workshop, "Facilitating End-to-End Development of Individualized Therapeutics" to discuss partnerships and collaborations, nonclinical and clinical development, and manufacturing;
- Established an Individualized Therapeutics Council;
- Developed a public-private partnership with NIH's National Center for Advancing Translational Sciences (NCATS) and the Foundation for the National Institutes of Health.

Modernizing manufacturing processes improves the agility, flexibility, cost, and reliability of product manufacturing, including vaccines and cell and gene therapies. FDA continues its work to support improved manufacturing technologies intramurally and through extramural awards. In FY 2020, a grant was awarded for the project "Identification of critical quality attributes of cell therapy products by multi-omics analyses and predictive modeling for vaccines." As part of its continued implementation of the 21st Century Cures Act, FDA renewed grants awarded in FY 2018 and awarded a new grant to enhance innovations in the manufacture of Adeno-associated virus vectors to help advance the development of gene therapies for diseases affecting very small populations.

Strengthen Science And Efficient Risk-Based Decision Making

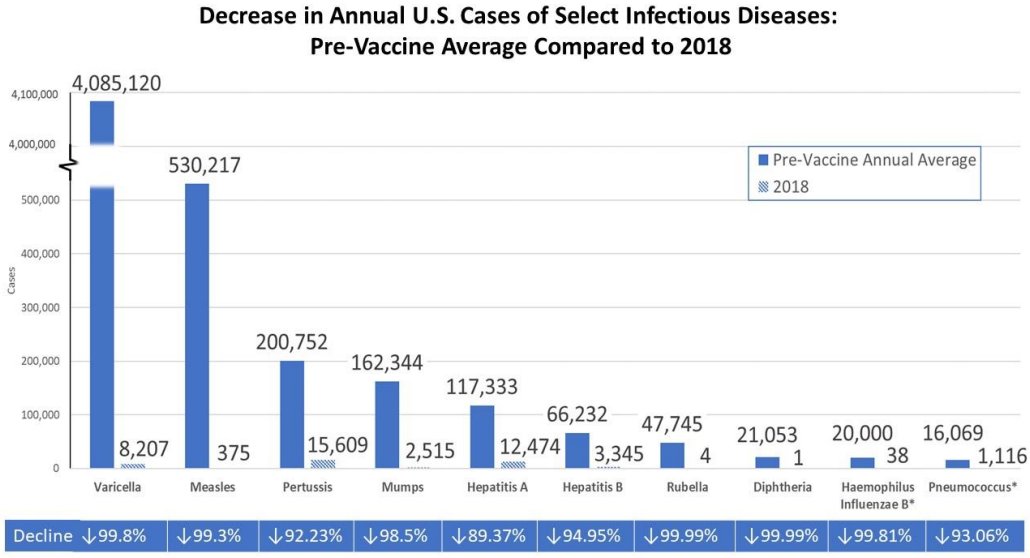
To continually modernize its regulatory toolbox, FDA incorporates scientific advancements into its regulatory and scientific work and implements policies to expedite availability of beneficial innovations to consumers. This is important for improving accessibility, safety, and effectiveness of products for consumers to treat or reduce incidence of infectious disease. Using tools such as real-world evidence to monitor safety and enforcement tools helps keeps protect and improve the public health.

[97] As of December 31, 2020

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. The following accomplishments 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." These accomplishments also align with CBER's strategic goals to "Conduct Research to address challenges in the development and regulatory evaluation of medical products" and "Increase preparedness for emerging threats and promote global public health."

Reducing Incidence of Infectious Disease

The World Health Organization (WHO) recognized vaccine hesitancy one of the top 10 threats to global health. In the United States, vaccine hesitancy has led to recent outbreaks, such as the outbreak of measles in 2019. FDA joined colleagues at HHS, CDC, and NIH to continue to promote vaccinations against preventable diseases. 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. The following graphic provides a comparison between the pre-vaccine average cases and the 2018 cases of several select infectious diseases.



2018: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, 2018 Annual Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance, 2019. Available at: https://www.cdc.gov/nndss/infectious-tables.html.[98]

Annual vaccination remains the best way to prevent influenza disease and its complications and inhibit its transmission to others. Influenza vaccination can help avoid influenza-associated

[98] Pre-Vaccine: Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation. Appendix E (Errata 2019).

healthcare visits and hospitalizations, which would help preserve healthcare resources for patients with other diseases and medical conditions, including COVID-19.

To select strains for the annual influenza vaccines, FDA, the World Health Organization, the Centers for Disease Control and Prevention and other public health experts collaborate to review of influenza disease surveillance and laboratory data collected from around the world to identify strains that may cause the most illness. Based on that information and recommendations of the VRBPAC, the FDA selects the influenza strains that manufacturers should include in their vaccines for the U.S. population. In March 2020, VRBPAC recommended the strains for inclusion in the influenza vaccines for the 2020-2021 U.S influenza season. VRBPAC met again in October 2020 to recommend the strains 2021-2022 southern hemisphere influenza season.

Many of the products FDA regulates address infectious disease threats that are not unique to the U.S., and international engagements are a critical component of how FDA carries out its regulatory responsibilities. Over the past year, FDA 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 where regulator and industry representatives work to improve the efficiency of new drug development process, promote public health, prevent duplication of clinical trials in humans, and minimize the use of animal testing without compromising safety and effectiveness.

FDA participated in WHO's Global Advisory Committee for Vaccine Safety meeting to provide advice on vaccine safety issues of global or regional concern that may affect short or long-term national immunization programs (May 2020). CBER collaborated with WHO and other national regulatory authorities to revise a WHO guideline on quality, safety and efficacy of DNA vaccines. FDA also participated in Coalition for Epidemic Preparedness Innovation meetings on well characterized biologics and assays, Nipah virus vaccine development, and maternal immunization with Lassa and Ebola vaccines.

FDA facilitates the design of better methods to predict and evaluate the safety, purity, potency and effectiveness of biological products early in their lifecycle by adopting the most advanced science and risk management tools to inform policy. FDA's applied research program supports development of new tools, models, standards, and methods, harnessing new technologies to expedite product development and provide effective scientific and regulatory responses for public health emergencies.

Blood products are critical to public health and offer potentially life-saving benefits for a variety of acute and chronic conditions. Pathogen reduction technologies can address the infectious risk from viral and bacterial pathogens, which currently address more than 95 percent of the existing and emerging pathogens that are of concern for the blood supply. CBER awarded a contract for the development of next-generation compounds to optimize pathogen reduction treatment of whole blood to reduce the risk of transfusion-transmitted infections.

Compliance and Oversight

FDA conducts compliance and surveillance activities to ensure the quality of products through their entire lifecycle. These activities include pre-market application inspections, monitoring the

safety, purity, and potency of biological products through review of product deviation reports, investigations into transfusion and donation related fatalities and adverse events. FDA also initiates regulatory action to address non-compliance with relevant statutes and FDA regulations, monitors research on biological products, and assesses the protection of the rights, safety, and welfare of human research subjects.

Inspections of marketed products are conducted after products are approved and help to ensure the safety and effectiveness of CBER-regulated products on the U.S. market. These inspections are performed to ensure that products are manufactured in compliance with Current Good Manufacturing Practice (CGMP) and other applicable requirements.

FDA works with manufacturers to ensure the availability of CBER-regulated products. For FY 2020, CBER documented one new product shortage, 19 prevented shortages, seven ongoing shortages, and 33 notifications from 23 different manufacturers. CBER uses regulatory flexibility and expedited reviews to prevent or mitigate shortages when appropriate. To help mitigate an ongoing Immune Globulin (IG) product shortage, FDA is working closely with industry to improve the manufacturing yield and availability of IG products.

FDA continued its oversight and enforcement to protect people from dishonest manufacturers, clinics, and health care providers offering illegal and potentially harmful HCT/Ps. FDA's regenerative medicine framework clarifies how it interprets existing regulatory definitions and describes FDA's compliance and enforcement policy. FDA has been exercising enforcement discretion in order to give developers time to come into compliance for certain products that do not raise reported or potential safety concerns, and extended the period of enforcement discretion in the"Regulatory Considerations for Human Cells, Tissues and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use" guidance (July 2020) until May 31, 2021. FDA's temporary program to help manufacturers of HCT/Ps come into compliance, the Tissue Reference Group Rapid Inquiry Program (TRIP), has also been extended through March 31, 2021.

Since the beginning of FY 2020 through March 1, 2021, FDA sent 248 letters to manufacturers, clinics or health care providers across the country who may be offering unapproved regenerative medicine products, reiterating FDA's compliance and enforcement policy. Compliance actions on HCT/P taken by FDA include:

- Issued four Warning Letters for unapproved and/or adulterated regenerative medicine products, including umbilical cord blood, umbilical cord, amniotic membrane, amniotic fluid, and exosome products.
- Issued 15 Untitled Letters for marketing of unapproved regenerative medicine products for numerous diseases or conditions, including some that are serious or life threatening.

FDA also issued an Untitled Letter for marketing of unapproved allergenic extracts.

Real-World Evidence to Evaluate Effectiveness and Safety

Real-world evidence (RWE) is the clinical evidence for the usage and potential benefits or risks of a medical product derived from analysis of Real-World Data (RWD). CBER is expanding the role of RWD and RWE to inform the discovery, development, and delivery of new therapies for patients, provide high-quality evidence about risks and benefits in practice, and inform which therapies are best for which patients. RWD can come from a variety of sources including electronic health records (EHRs), claims and billing activities, product and disease registries, and other patient-generated data.

CBER's Biologics Effectiveness and Safety (BEST) Program continues to expand and enhance 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 EHRs for over 50 million persons and access to over with 100 million claims to conduct robust, rapid safety and effectiveness studies of blood, advanced therapeutics and vaccines.

BEST 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 to improve FDA's ability to identify cases of serious, life-threatening adverse effects. Recent studies include Transfusion-Associated Circulatory Overload and Post-transfusion Sepsis and pregnancy outcomes related to immunizations. BEST is currently conducting a study to delineate utilization in patterns and doses of immunoglobulins for licensed and unlicensed indications to support potential regulatory actions. In addition to the BEST system, CBER continued to leverage other data partners and systems such as Centers for Medicare & Medicaid Services, Veterans Affairs, and the Vaccine Adverse Event Reporting System to build postmarket safety and effectiveness surveillance systems for vaccines and therapeutics.

RWD is being used to inform FDA policies, such as blood donor eligibility, by actively monitoring over 60 percent of the U.S. blood supply. 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. FDA published four articles in peer-reviewed journals concerning the data and preliminary analyses of trends in human immunodeficiency virus (HIV) incidence and risk over time for the first 42 months of data collected by TTIMS. To inform the use of RWD in vaccine development and licensure, CBER convened a symposium in September 2020 to exchange information with industry, academia, and government stakeholders about the scientific, clinical and regulatory challenges and opportunities in using RWE to assess the effectiveness of preventive vaccines.

Select Guidance Documents to Support Mission and Priority Areas

FDA guidance documents are non-binding documents that explain its 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.

Below are other selected guidance documents recently issued by CBER, not discussed elsewhere in the Biologics Program Description and Accomplishments.[1]

Date	#	Title	Description
Jan 2021	FDA-2020-D-2101	Draft Guidance for Industry: Human Gene Therapy for Neurodegenerative Diseases	Provides recommendations to sponsors developing human gene therapy products for neurodegenerative diseases affecting adult and pediatric patients.
Aug 2020	FDA-2015-D-1211	Final Guidance for Industry: Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus by Blood and Blood Products	Provides blood establishments with FDA's revised donor deferral recommendations for individuals with increased risk for transmitting human immunodeficiency virus infection.
Jan 2020	FDA-2019-D-5392	Draft Guidance for Industry: Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations	Provides FDA's thinking on determining sameness of human gene therapy products under FDA's orphan drug regulations for purposes of orphan-drug designation and orphan drug exclusivity.
Jan 2020	FDA 2018-D-2238 FDA-2018-D-2236 FDA-2018-D-2258 FDA-2008-D-0205 FDA-1999-D-0081 FDA-2018-D-2173	Final Guidances for Industry: Human Gene Therapy for Hemophilia, Retinal Disorders, Rare Diseases Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs) Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus During Product Manufacture and Patient Follow-up Long Term Follow-up After Administration of Human Gene Therapy Products	Six guidances on gene therapy manufacturing and clinical development of products help shape the modern structure for the development and manufacture of gene therapies.
Dec 2019	FDA-2018-D-1216	Final Guidance for Industry: Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review	Provides sponsors detailed information and specifications for the content of datasets submitted to aid reviewers in the review of vaccine applications.

Select Biologics Product Approvals

Below are select recent Biological product approvals not discussed elsewhere in the Biologics Program Description and Accomplishments.

Approved	Trade Name/Proper Name	Purpose or Benefit
Jul 2020	Tecartus/ *Brexucabtagene autoleucel*	CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory Mantle Cell Lymphoma.
Apr 2020	Sevenfact/*Coagulation Factor VIIa (Recombinant)*	Coagulation Factor VIIa to treat and control bleeding episodes occurring in adults and adolescents with hemophilia A or B with inhibitors.
Apr 2020	MenQuadfi /*Meningococcal (Groups A, C, Y, W) Conjugate Vaccine*	Vaccine to prevent invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, W, and Y in individuals 2 years of age and older.
Jan 2020	AUDENZ/*Influenza A (H5N1) Monovalent Vaccine, Adjuvanted*	Pandemic influenza vaccine indicated for active immunization to prevent disease caused by the influenza A H5N1 subtype.
Jan 2020	Palforzia/ Peanut (Arachis hypogaea) Allergen Powder-dnfp	Oral immunotherapy for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut.

[1] 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

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$426,027,000	$252,128,000	$173,899,000
FY 2021 Enacted	$437,071,000	$254,138,000	$182,933,000
FY 2022 President's Budget	$457,889,000	$270,114,000	$187,775,000

BUDGET REQUEST

The FY 2022 President's Budget Request for the Biologics Program is $457,899,000, of which $270,114,000 is budget authority and $187,775,000 is user fees. The budget authority increases by $15,976,000 compared to the FY 2021 Enacted. User Fees increase by $4,842,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is $408,118,000. The Office of Regulatory Affairs amount is $49,771,000.

The FY 2022 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 including vaccines, allergenics, blood and blood products, and cell, tissues, and gene therapies to the American public. CBER aims to increase preparedness for emerging threats and promote global public health. CBER continues to work on multiple fronts to address the COVID-19 pandemic and will continue to prioritize the COVID-19 response in FY 2022 as necessary. CBER facilitates the development and availability of safe and effective medical products through the integration of advances and science and technology through a variety of mechanisms. CBER uses enhanced FDA-sponsor communications in its user fee programs, the continued use of its expedited programs, and streamlined regulatory pathways. RMAT designation, Fast Track, Breakthrough Therapy Designation, Accelerated Approval, and Priority Review all may be used, when appropriate, to accelerate the approval and availability of important products. Many innovative biological products address unmet medical needs in patients with rare, serious, or life-threatening diseases.

CBER provides an interactive mechanism for prospective innovators/developers of advanced manufacturing and testing technologies to discuss with CBER staff issues related to the implementation of these technologies in the development of CBER-regulated products. To further support advanced manufacturing, CBER will continue to conduct intramural research and make extramural awards to study and recommend improvements for the advanced manufacturing of biological products, including the investigation and development of innovative monitoring and control techniques.

CBER is developing a regulatory program for individualized (bespoke) therapies and fostering global regulatory convergence for cell and gene therapies. There is significant potential in the use of gene therapies for conditions that affect one or a small number of individuals (less than 100). FDA will continue to work with stakeholders to facilitate end-to-end solutions for key issues limiting the development and application of gene therapies, including manufacturing challenges that make these therapies cost-prohibitive and presently not commercially viable.

FDA will continue to initiate regulatory action to address non-compliance with relevant statutes and regulations. The Biologics program will continue its compliance actions to manufacturers, clinics or health care providers who may be offering unapproved regenerative medical products that have the potential to put patients at significant risk and reiterate compliance and enforcement policy. CBER's regenerative medicine framework clarifies how it interprets existing regulatory definitions and describes the Biologics program's compliance and enforcement policy. Regenerative medicine is a complex and rapidly evolving field. CBER will continue to reassess its application of the HCT/P regulatory framework as additional scientific evidence emerges in this field.

The regulatory science and research programs will continue to engage in forward-looking priority setting to allocate 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. CBER's cadre of scientific experts will conduct research to inform guidance and support development of new tools, models, standards, and methods, harnessing new technologies to expedite product development.

FDA will continue to protect the public against emerging infectious diseases and bioterrorism. CBER will protect 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. CBER monitors

the impact of emergencies or outbreaks of disease on the safety and availability of the blood supply. CBER aims advance pathogen reduction research to improve blood safety by reducing or eliminating infectious organisms, including bacteria, viruses, and parasites, from blood components intended for transfusion. In addition to protecting the blood supply from infectious disease, CBER aims to improve the availability of vaccines to immunize the public prior to EID exposure, decreasing the number of infections and contamination events. CBER will continue to advance vaccine manufacturing to support preparedness for potentially pandemic strains of influenza. CBER works with other federal agencies and industry, through the Public Health Emergency Medical Countermeasure Enterprise, on a broad array of products aimed at making the U.S. better prepared for chemical, biological, radiological, and nuclear (CBRN) threats and emerging disease through the development of new countermeasures.

To ensure that biologic products are safe and effective, FDA conducts compliance and surveillance activities to ensure the quality of products through their entire lifecycle. Real-world evidence (RWE) is the clinical evidence for the usage and potential benefits or risks of a medical product derived from analysis of Real-World Data (RWD). RWD has a wide variety of applications, from being used to inform blood donor eligibility to assessing the effectiveness of preventative vaccines. CBER will continue its work using RWD and RWE to monitor postmarket safety, life-threatening adverse events, and regulatory decisions. Specifically, for vaccines, CBER will engage in post-approval vaccine surveillance programs including data analysis from the Vaccine Adverse Event Reporting System (VAERS), FDA BEST, and the FDA-CMS partnership. FDA also strategizes to harmonize existing regulatory standards and works with international scientific efforts to establish and maintain reference materials and standards for biologics.

BUDGET AUTHORITY

Medical Product Safety (+$5.5 million / 6 FTE)

Data Modernization and Enhanced Technologies: (+$5.5 million / 6 FTE)
Center: +$5.0 million / 5 FTE

Field: +$543,000 / 1 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CBER, $4.1 million is requested to support the Enterprise Technology and Data crosscutting effort and $900,000 for CBER to accelerate efforts to modernize and streamline review of complex biologics.

A robust information management and data infrastructure that supports regulatory capabilities is critical to managing and reviewing the increased number of novel and scientifically complex biologics, including those to prevent and treat emerging and evolving infectious diseases. These capabilities, enabled by a modern regulatory information management system, can help to address challenging scientific, medical, and regulatory issues and facilitate getting safe and effective vaccines and therapeutics to the public. CBER will use these resources to accelerate efforts to modernize and streamline its review of complex biologics, including using new

capabilities and enhanced platforms to capture and share information from submissions and review, and will leverage other FDA capabilities where possible.

CBER has reached a critical juncture in the regulation of biological products, including novel and scientifically complex biologics such as cell and gene therapies, vaccines, and blood products. In recent years, CBER has dramatically increased the overall number of regulatory submissions reviewed. Many of these regulatory submissions to CBER are increasingly incorporating novel data sources including real world evidence, digital health technologies, adaptive clinical trial designs, and genomics and computational biology, which consist of large and varied data sets. This initiative will allow CBER to manage its increasingly complex portfolio of biologics, devices and combination products, facilitating improved development and review of novel and complex biologics.

Crosscutting: (+$15.1 million / 24 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data: (+$4.6 million / 6 FTE)
Center: +$4.1 million / 5 FTE

Field: +$525,000 / 1 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CBER, $4.1 million is requested to support the Enterprise Technology and Data crosscutting effort, and $525,000 is for ORA.

Capacity Building: (+$4.5 million/ 2 FTE)
Center: +$3.9 million / 2 FTE

Field: +$577,000

The FY 2022 Budget includes $40.3 million to support centrally-administered services to support critical, high-priority Capacity Building activities.

Inspections: (+$4.5 million / 16 FTE)
Field: +$4.5 million / 16 FTE

The FY 2022 Budget includes $18.8 million for inspections. ORA will increase site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID-19 related delays, and the Budget includes $4.5 million for the Field portion of Biologics Program.

Pay Costs: (+$1.5 million)
Center: +$1.1 million

Field: +$360,680

The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

USER FEES

Current Law User Fees: +$4.8 million
Center (+$4.8 million)

Field (+$59,216)

The Biologics Program request includes an increase of $4,842,000 for user fees authorized, 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
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 2019: 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	FY 2019:100% Target 90% (Target Exceeded)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
day filing date. *(Output)*				
233205: Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. *(Output)*	FY 2019: 100% Target 100%	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 2020: 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	Continue evaluation of new methods to produce more stable high-yield influenza vaccine reference	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
		improve current manufacturing processes	strains and improve current manufacturing processes	
231301: Percentage of Lot Distribution Reports that were entered into the Regulatory Management System - Biologics License Applications (RMS-BLA) within 7 Days.	FY 2020: 99% Target 85% (Target Exceeded)	85%	85%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2020: 70.0% Target: 70% (Target Met)	70%	70%	Maintain
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward	FY 2020: 77.8% Target: 65% (Target Exceeded)	65%	65%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
compliance. (Outcome)				

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

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 2020, FDA met the target to continue evaluation of new methods to produce high-yield influenza vaccine reference strains. Activities to meet this target included the following:

FDA continued efforts to develop new methods for determining influenza vaccine potency, an important component in the evaluation of high-yield influenza vaccine viruses. An international collaborative study comparing several alternative potency methods and alternative reference reagents was completed in FY 2020. This study assessed whether reference standard in the same hemagglutinin (HA) conformation as a vaccine sample can more accurately assess potency in alternative potency assays than whole inactivated virus (SRID) reference standard. The results suggested that alternative reference antigens might improve the current process that entails production of many different reference antigens. Additional follow-up studies are being planned for FY 2021 that will continue to evaluate and compare alternative potency methods.

The reassortant A/Shanghai/2/2013 (H7N9) candidate vaccine virus had a low protein yield in chicken eggs. To optimize the protein yield of this virus, FDA serially passaged the virus in eggs, and acquired an egg-adapted progeny that significantly overgrew the wild type with 3-fold increase in total viral protein yield. Analysis revealed increased influenza virus neuraminidase (NA) expression and higher NA/ HA ratio; neuraminidase activity assay demonstrated enhanced NA enzymatic activity. These data suggest that the increased NA function was responsible for the egg-adaptation of this strain.

Additional efforts related to the target goal included studies that modified the candidate vaccine virus backbone to produce inactivated virions that generate a more balanced HA and NA response, and a systematic evaluation of recombinant NAs to assess the impact of the design on immunogenicity.

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. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA's ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

CBER Workload and Outputs	FY 2020 Actual	FY 2021 Estimate	FY 2022 Estimate
Original Biologics License Applications (BLA)			
Workload [1]	9	9	9
Total Decisions [2]	26	26	26
Approved	10	10	10
BLA Efficacy Supplements			
Workload [1]	30	30	30
Total Decisions [2]	23	23	23
Approved	19	19	19
BLA Manufacturing Supplements			
Workload [1]	1,442	1,442	1,442
Total Decisions [2]	1,349	1,349	1,349
Approved	1,224	1,224	1,224
BLA Labeling Supplements			
Workload [1]	128	128	128
Total Decisions [2]	238	238	238
Approved	230	230	230
Original New Drug Application (NDA)			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
NDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
NDA Manufacturing Supplements			
Workload [1]	17	17	17
Total Decisions [2]	18	18	18
Approved	17	17	17
NDA Labeling Supplements			
Workload [1]	0	0	0
Total Decisions [2]	1	1	1
Approved	1	1	1
Original Abbreviated New Drug Application (ANDA)			
Workload [1]	1	1	1
Total Decisions [2]	0	0	0
Approved	0	0	0
ANDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0

ANDA Manufacturing Supplements			
Workload [1]	3	3	3
Total Decisions [2]	4	4	4
Approved	4	4	4
ANDA Labeling Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
Device 510Ks			
Workload [1]	50	50	50
Total Decisions [2]	71	71	71
Final Decision - SE	52	52	52
Device Premarket Applications (PMA)[6]			
Workload [1]	2	2	2
Total Decisions [2]	8	8	8
Approved	3	3	3
Device Premarket Applications (PMA) Supplements[7]			
Workload [1]	76	76	76
Total Decisions [2]	81	81	81
Approved	20	20	20
Investigational New Drugs (IND)			
Receipts: IND (new)	6,969	617	617
Receipts: IND Amendments	23,547	23,547	23,547
Total Active IND [3]	9,494	9,494	9,494
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	21	21	21
Receipts: IDE Amendments	329	329	329
Total Active IDE [3]	87	87	87
Patient Safety			
Adverse Event Reports Received [4]	108,119	150,000	150,000
Biological Deviation Reports Received	30,930	15,000	15,000
Sponsor Assistance Outreach			
Meetings	740	740	740
Final Guidance Documents [5]	51	40	40
Admin/Management Support			
Advisory Committee Meetings Held	5	10	10
FOI Requests Processed	280	400	400

[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 transfusions 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 Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***744***	***100***	***1,892***
Bioresearch Monitoring Program Inspections	69	8	100
Blood Bank Inspections	233	90	900
Source Plasma Inspections	106	12	190
Pre-License, Pre-Market Inspections	44	5	55
GMP Inspections	17	2	28
GMP (Device) Inspections	3	1	7
Human Tissue Inspections	283	30	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***29***	***5***	***47***
Bioresearch Monitoring Program Inspections	8	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	0	1	7
Pre-License, Pre-market Inspections	7	1	7
GMP Inspections (Biologics & Device)	0	1	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***773***	***105***	***1,939***
IMPORTS			
Import Field Exams/Tests	85	45	45
Import Line Decisions	152,158	155,000	197,462
Percent of Import Lines Physically Examined	0.06%	0.02%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***773***	***105***	***1,939***

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

[2] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

ANIMAL DRUGS AND FOODS

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Animal Drugs and Foods	**238,678**	**234,507**	**245,307**	**285,541**	**40,234**
Budget Authority	***190,869***	***190,854***	***192,369***	***232,033***	***39,664***
User Fees	***47,809***	***43,653***	***52,938***	***53,508***	***570***
Center	168,474	165,361	175,083	198,200	23,117
Budget Authority	122,099	122,099	123,599	146,251	22,652
User Fees	46,375	43,262	51,484	51,949	465
Animal Drug (ADUFA)	*27,670*	*28,024*	*30,117*	*30,454*	*337*
Animal Generic Drug (AGDUFA)	*18,591*	*15,216*	*21,250*	*21,376*	*126*
Third Party Auditor Program	*114*	*22*	*117*	*119*	*2*
Field	*70,204*	*69,146*	*70,224*	*87,341*	*17,117*
Budget Authority	68,770	68,755	68,770	85,782	17,012
User Fees	1,434	391	1,454	1,559	105
Animal Drug (ADUFA)	383	391	390	426	*36*
Animal Generic Drug (AGDUFA)	228	---	224	277	*53*
Food Reinspection	823	---	840	856	*16*
FTE	**1,006**	**1,011**	**1,042**	**1,086**	***44***

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 Foods 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 from a One Health perspective by helping ensure:

- 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, effectiveness and manufacturing quality
- Monitors animal drugs, animal foods, and animal devices and take appropriate action to mitigate violative products on the market
- Evaluates animal food additives for safety and utility
- Conducts applied research to further scientific understanding and support data-based decision making to protect human and animal health
- Works to prevent and respond to human and animal health emergencies
- Develops and implements policies to combat antimicrobial resistance

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 pheasants, and for minor uses (infrequent and limited) in the major species, such as cattle, pigs, chickens, dogs, cats, horses and turkeys.

The Animal Drugs and Foods 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. The Food Safety Modernization Act (FSMA) also directed FDA to establish a user fee program by which FDA assesses fees and requires reimbursement for the work FDA performs to establish and administer the accredited third-party certification program.

Responding to COVID-19 Public Health Emergency

The Center for Veterinary Medicine is facilitating the incorporation of a One Health approach to promote the health of humans, animals, and the environment using science, technology, and innovation. Approximately 75 percent of recently emerging infectious diseases affecting humans, including HIV, Ebola, and influenza, are zoonotic (i.e., spread from animals to humans)[99]. It is also becoming increasingly clear that humans are also transmitting diseases to animals in what is often referred to as "reverse zoonoses."

In response to the COVID-19 pandemic and disruptions of supply chains that are leading to shortages of animal drugs, in May 2020, FDA published *GFI #271 Reporting and Mitigating Animal Drug Shortages During COVID-19 Public Health Emergency* to assist animal drug sponsors in providing FDA timely, informative notifications about changes in the production of animal drugs that will, in turn, help the Agency in its efforts to prevent or mitigate shortages of these products. During the COVID-19 outbreak, FDA continues to monitor the animal drug supply chain and work closely with animal drug sponsors, to ascertain as early as possible, any

[99] World Organization for Animal Health (the OIE) (2018). – One Health "at a glance". Available at: http://www.oie.int/en/for-the-media/onehealth/ (accessed 28 Sep 2018).

shortage or potential shortage that is likely to lead to a disruption in the availability of animal drugs or their components in the United States. From February 2020 through February 2021, 44 potential or confirmed product shortages were reported. Excluding those for which confirmation is still pending, shortages were averted 86% of the time.

To better position FDA to quickly identify and address critical facilities and animal drugs impacted by emerging diseases or natural disasters and help to identify solutions to potential drug shortages, the Animal Drugs and Foods Program began developing the system requirements needed to create an Animal Drug and Manufacturing System to readily retrieve information on animal drug products, active pharmaceutical ingredients, and the status of manufacturing sites. The system will also include sales information that will aid in identifying new animal drug shortage situations and directing any subsequent regulatory response.

FDA's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) supported the response to the COVID-19 pandemic by facilitating an inter-laboratory comparison exercise to help veterinary diagnostic laboratories ensure that their tests for the novel SARS-CoV-2 virus are reliable for use in animals. As of March 15, 2021, there are 149 animals in the U.S. (cats, dogs, tigers, lions, gorillas, snow leopards, cougar and wild mink), identified as being infected with COVID-19. Additionally, 16 mink farms involving large numbers of mink have been identified as having COVID positive mink, and many have died.

During FY 2020, FDA helped ensure the continuity of the human and animal food supply by releasing recommendations, checklists, and factsheets to assist the human and animal food industries as they respond to the COVID-19 pandemic. Recommendations were developed to help address shortages of supplies, like disinfectants and personal protective equipment (PPE), that are critical for worker safety, food safety, and employee and consumer confidence. The constraints on these supplies were causing concerns about the potential for interruptions in the food supply chain. FDA partnered with the Occupational Safety and Health Administration (OSHA) to release a checklist for use when assessing human and animal food operations during the COVID-19 pandemic, especially when re-starting operations after a shut down. The Agency also released a factsheet "At a Glance: Safely Distributing Unused Human Food for use as Animal Food" to assist human food facilities with surplus food caused by the disruptions to supply chains during the COVID-19 pandemic.

Fostering Innovation in Biotechnology 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 provides an overview of priorities FDA is pursuing to advance the Agency's public health mission while supporting innovation 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 the FDA's approach to innovative plant and animal biotechnology

- Increasing engagement with domestic and international partners on biotechnology issues

As of February 2021, there are 25 animal drug sponsors participating in the Veterinary Innovation Program (VIP) pilot which offers technical assistance to developers of innovative veterinary products to provide greater regulatory predictability, reduce overall time to approval, and enable early, sustained interactions with innovators. Animal Drugs and Foods Program scientists have developed novel manufacturing processes that improve reliability and quality in the production of veterinary stem cells and provided critical review and advice to advance the approvals of novel veterinary protein therapeutics. In September 2020, FDA also announced a stakeholder outreach initiative for developers of animal biotechnology, including an informational, pre-recorded webinar to help developers understand data expectations for marketing a new biotechnology product. 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.

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.

FDA exceeded the Animal Drug User Fee Amendment (ADUFA) and Animal Generic Drug User Fee Amendment (AGDUFA) performance goals for FY 2019 and met performance goals for all FY 2020 cohort submissions reviewed by September 30, 2020. FDA completed reviews of more than 8,000 new and abbreviated new animal drug applications, supplements, and related investigational submissions in FY 2020. With some reviews still pending, FDA has the potential to exceed all performance goals for FY 2020.

As part of the ADUFA reauthorization in 2018, 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. Expanded conditional approval has the potential to incentivize drug development and provide veterinarians with legally marketed new animal drugs to fill treatment gaps for serious or life-threatening diseases or conditions. In September 2019, FDA released draft *GFI #261 Eligibility Criteria for Expanded Conditional Approval in New Animal Drugs* to assist animal drug sponsors interested in pursuing conditional approval.. FDA received 16 requests for expanded conditional approval eligibility. Eight products have been designated as eligible for the process with three products' eligibility currently under consideration. On January 14, 2021, FDA conditionally approved the first drug under the expanded conditional approval authority. KBroVet-CA1 (potassium bromide chewable tablets) is conditionally approved for the control of seizures associated with idiopathic epilepsy in dogs.

The agency also continues to enhance international harmonization and collaboration with international organizations, other countries' regulatory agencies and related industry. As of December 2020, FDA implemented 49 internationally harmonized guidelines for animal drugs with work currently ongoing to revise 14 guidelines and develop 4 new harmonized guidelines.

FDA also simultaneously reviewed and approved 13 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

Minor Use Minor Species

The Minor Use and Minor Species (MUMS) Animal Health Act creates incentives to help 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 legally available 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.

As of February 2021, the Index included a total of 14 animal drugs. 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 intended for non-food-producing animals. This process is beneficial in cases, like for zoo animals or ornamental fish, when 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.

As of December 2020, FDA has provided more than $5.4 million in grant funding in support of 61 MUMS studies. FDA granted 155 MUMS drug "designations" over the last 15 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.

FDA also collaborates with the United States Department of Agriculture's Minor Use Animal Drug Program to help support 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 full approval of 29 MUMS products.

Product Approvals

Below are some of the Animal Drugs and Foods Program's recent animal drug product approvals. This list does not represent any degree of importance or priority ranking of products.

Species	Date	Product Name	Purpose or Benefit

Dogs	Jan 2021	ThyroKare	For replacement therapy for diminished thyroid function
Dogs	Jan 2021	KBroVet-CA1 Chewable Tablets	For the control of seizures associated with idiopathic epilepsy (conditional approval for a major use in a major species)
Dogs	Jan 2021	LeverdiaLeverdiaLeverdiaLaverdia-CA1Leverdia	For the treatment of lymphoma (conditional approval for a minor use in a major species)
Pigs	Dec 2020	pPL657 rDNA Construct	Results in undetectable endogenous galactose-alpha-1,3-galactose sugar residues on biological derivatives of the homozygous GalSafe® lineage that are intended to be used as sources of food or human therapeutics, including excipients, devices, drugs, or biological products
Dogs	Nov 2020	Stelfonta	For the treatment of 1) non-metastatic cutaneous mast cell tumors and 2) non-metastatic subcutaneous mast cell tumors located at or distal to the elbow or the hock

Animal Food Safety

In FY 2020, FDA significantly increased its capacity to review complex and innovative new animal food ingredients. The Animal Drugs and Foods Program is now positioned to allow greater predictability and timeliness for animal ingredient reviews, thus bringing safe, innovative ingredients to the animal food market. 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 new nutritional ingredients to help keep animals healthy, while also ensuring that the meat, milk, and eggs from those animals are safe for people to eat. 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 necessary, 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
- Conducting safety evaluations of human food diverted to animal food during and after natural disasters to ensure animal and human food safety
- Conducting research to evaluate different treatments to control hazards in human and animal food

In December 2020, FDA published *draft GFI #262 Pre-Submission Consultation Process for Animal Food Additive Petitions or Generally Recognized as Safe (GRAS) Notices* describing the recommended types of information for stakeholders (industry, academia, other organizations, or an individual) to include in consultations with FDA. Pre-submission consultations are intended to help stakeholders comply with the applicable requirements for an FAP or a GRAS notice, making the submission process more efficient and effective, and facilitating the introduction of safe and innovative new products onto the market. In FY 2019, performance measure data on FAP reviews were made publicly available as part of the ADUFA and AGDUFA reauthorizations.

The animal food ingredient industry is evolving, and submissions of innovative new animal food ingredients are more complex and have more data in their submissions. For example, FDA evaluated a GRAS notice for a popular enzyme in livestock and poultry diets, phytase, that reduces the phosphorus excretion to the environment. Although available through other methods, this particular notice was for phytase produced within genetically engineered corn, a staple of many of these diets. 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 pigs, poultry and salmon.

Modernizing Animal Food Safety Oversight

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 production and supply chains. To keep pace with this evolution, FDA released the Blueprint for a New Era of Smarter Food Safety to build on the modernized food safety regulatory framework created via the FDA Food Safety Modernization Act (FSMA) by leveraging the use of new and emerging technologies to speed outbreak response and accelerate prevention.

FDA has developed a new approach to modernize animal food safety inspections that incorporates new regulations and traditional regulations into a single comprehensive inspection. This comprehensive inspection approach will help ensure a holistic, risk-based, and prevention-oriented approach to inspections and will better utilize resources of both FDA and state inspection partners, who FDA works with routinely to ensure greater inspectional oversight of the animal food industry.

Within the comprehensive inspection model, one of the foundational pieces is incorporating the foundations of hazard control in the FSMA Preventive Controls for Animal Food (PCAF)

regulation. In FY 2020, FDA received $3.2M to fund cooperative agreements to support 13 states in implementing the recommendations of the National Association of State Departments of Agriculture (NASDA) Preventative Control Animal Food Framework. The NASDA PCAF Framework outlines key considerations for states to evaluate and build infrastructure, update inspection and enforcement programs, develop outreach and training initiatives, and devote laboratory resources for the analysis of expected and unknown animal food hazards. The cooperative agreement funds are used to implement these pieces of the NASDA PCAF Framework and to begin to transition states into the modernized comprehensive inspection approach that FDA outlined in the February 2021 Compliance Program update.

In FY 2020, 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, with five additional guidance dedicated to complying with FSMA during the COVID-19 pandemic. FDA also continues to proactively engage with industry and regulatory partners through:

- Ongoing outreach efforts targeted to the animal food industry aimed at providing updated information, clarifying policy positions, and discussing emerging issues
- The FSMA Technical Assistance Network (TAN), a central source for providing responses to questions related to FSMA rules, programs, and implementation strategies,
- Delivering Current Good Manufacturing Practices (CGMP) and Preventive Controls (PC) regulator training on the PCAF regulation and identifying gaps in training needed to implement the comprehensive animal food inspection model

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.

Preventing and Responding to Human and Animal Food Emergencies

Comprehensive and risk-based oversight of the animal food supply is vital to protecting the health of pets and livestock. Animals generally eat a very defined diet over their lifetime. Exposure to improperly formulated, contaminated, mislabeled, or adulterated animal foods, whether intentional or not, can cause illness or death. Comprehensive and risk-based oversight of the animal food supply is also important for ensuring the safety of humans who consume meat, milk, and eggs from food-producing animals or who handle animal food, such as pet food that, if contaminated, can result in either the pet or the pet's food spreading pathogens to humans.

Animal food hazards can enter the food supply through a number of means, and FDA has to be prepared to quickly respond to ensure the protection of the food supply. In January 2021, FDA announced that it was collaborating with 10 states to investigate certain pet food products that may contain potentially fatal levels of aflatoxins. Aflatoxins are toxins produced by the mold Aspergillus flavus, which can grow on corn and other grains used as ingredients in pet food. Pets experiencing aflatoxin poisoning may have symptoms such as sluggishness, loss of appetite, vomiting, jaundice (yellowish tint to the eyes or gums due to liver damage), and/or

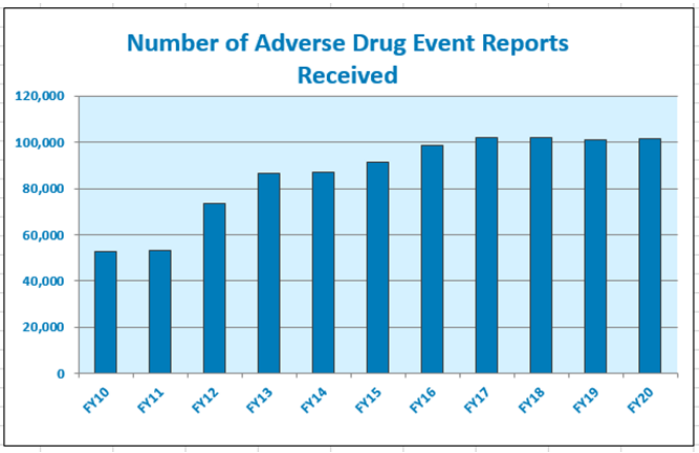
diarrhea. In severe cases, this toxicity can be fatal. As of February 2021, FDA has been notified of 130 deaths and more than 210 illnesses in pets potentially due to aflatoxin contaminated pet food. FDA is continuing to investigate the root cause of this contamination.

In FY 2020, FDA's Veterinary Laboratory and Response Network (Vet-LIRN) 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.* After inspections, sampling, recalls and public health advisories slowed the rate of human illness reports, FDA provided advice to industry on controlling hazards and managing supply chains to reduce the likelihood of future incidences. FDA's Vet-LIRN partners with 43 state and university veterinary diagnostic laboratories to help prevent and respond to animal food emergencies by carefully investigating the clinical aspects of reported illnesses.

The interdisciplinary use of science, technology, and innovation (a One Health approach) could also significantly enhance the FDA's emergency preparedness and response capabilities for natural disasters, like Tropical Storms, which impact humans, animals and their shared environment. Crops harvested from flooded fields are often unacceptable because of mold growth or contamination with sewage and rainwater. In FY 2020, FDA issued multiple advisories to help animal food producers prepare for and respond to the tropical storms and hurricanes hitting the Southeastern US and Gulf Coasts.

FDA's National Antimicrobial Resistance Monitoring System (NARMS) conducts ongoing surveillance of foodborne bacteria in raw poultry, meats and seafood. While a central part of combating antimicrobial resistance, this monthly testing has the added benefit of supporting outbreak investigations related to these sources, thereby benefitting the broader food safety initiatives of the Department, as well as state and local authorities. These data are shared online in near real-time for rapid detection and response to both human and animal foodborne illnesses.

Leveraging Real-World Adverse Event Data



The Animal Drugs and Foods 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 Program has the largest animal drug adverse event database in the world, containing real-world safety and effectiveness data from more than 1,000,000 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 90,000,000 food animals, and approximately 870,000 companion animals.

In FY 2020, 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 FY 2020, safety evaluators used data mining strategies to routinely screen and analyze adverse event reports received for more than 50% of all actively marketed approved animal drug products. The program also increased its efficiency by finalizing a mandatory electronic reporting rule for adverse events submitted by industry.

Compounded Animal Drugs

Animal drugs compounded from bulk drug substances are marketed and used in the United States to treat animals, even though many of these products have not met FDA's standards for safety and effectiveness and are of unknown quality or labeling. These compounded drugs have posed some safety issues to animals and potential safety issues to humans, especially when used in food-producing animals through the potential for drug residues.

In FY 2020, FDA led a number of for-cause compliance actions in the midst of the COVID-19 pandemic to reduce the risk of harm from these compounded animal drugs, including:

- Reviewed 28 inspections of compounders of animal drugs
- Oversaw 14 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.
- Generated 1 CVM compounding pharmacy warning letter for food producing animals

In June 2020, FDA extended the comment period through October 2020 for draft *GFI #256 Compounding Animal Drugs from Bulk Drug Substances* to solicit additional input 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 these situations, veterinarians may prescribe an animal drug compounded from bulk drug substances as an appropriate treatment option.

Guidances

Below are notable Animal Drugs and Foods Program guidances issued by FDA in 2020. This list does not represent any degree of importance or priority ranking among the guidances.

Issued	Docket #	Title	Description
Jul 2020	FDA-2020-D-1396	CVM GFI #265 Use of Data from Foreign Investigational Studies to Support Effectiveness of New Animal Drugs	To assist sponsors in incorporating data from foreign countries to support the demonstration of effectiveness of new animal drugs

Jul 2020	FDA-2020-D-1400	CVM GFI #266 Use of Real-World Data and Real-World Evidence to Support Effectiveness of New Animal Drugs	To assist sponsors in incorporating real-world evidence into proposed clinical investigation protocols and applications for new animal drugs
Jul 2020	FDA-2020-D-1402	CVM GFI #267 Biomarkers and Surrogate Endpoints in Clinical Studies to Support Effectives of New Animal Drugs	To describe how FDA intends to evaluate biomarkers to determine whether they may be used to support effectiveness of new animal drugs
Jul 2020	FDA-2020-D-1401	CVM GFI #268 Adaptive and Other Innovative Designs for Effectiveness Studies of New Animal Drugs	To describe how sponsors could use complex adaptive and other novel investigation designs to support the effectiveness of new animal drugs
Jul 2020	FDA-1997-D-0444	CVM GFI #61 Special Considerations, Incentives, and Programs to Support Approval of New Animal Drugs for Minor Uses and for Minor Species	To help researchers and animal drug sponsors navigate the pathway to approval for animal drugs for minor uses and minor species

Combating Antimicrobial Resistance

The Animal Drugs and Foods Program ensures the safety and effectiveness of animal drugs, including antimicrobials. Antimicrobial drugs have been successfully and widely used in medicine for more than 75 years to effectively fight bacterial infections in humans and animals. When bacteria develop resistance to an antimicrobial drug, that drug may be less effective in fighting infections caused by those bacteria.

In January 2021, FDA published a concept paper on a potential framework for how animal drug sponsors could voluntarily make changes to the approved conditions of use for certain medically approved antimicrobial drugs and establish defined durations of use; the public comment period is open until June 2021. One component to the development of antimicrobial resistance could be the administration of medically important antimicrobial drugs for undefined periods of time.

In December 2020, FDA announced the availability of additional performance measures to track the progress of its five-year action plan: "Supporting Antimicrobial Stewardship in Veterinary Settings: Goals for Fiscal Years 2019 - 2023." This plan builds on past successes and 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

In October 2020, FDA announced a potential revised process and criteria for ranking antimicrobial drugs based on their importance in human medicine. The Agency published a concept paper, and issued a Request for Comments in the *Federal Register*, to obtain early public feedback on the content of the paper; the public comment period is open until March 2021. FDA also held a virtual public meeting in November 2020 to present the details and receive additional comments. FDA is committed to ensuring that this ranking process be based on current and sound science, given the role that the ranking of antimicrobials plays in guiding FDA's activities related to managing antimicrobial resistance risks associated with antimicrobial use in animals.

Antimicrobial Drug Sales

In December 2020, FDA published the 2019 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, which reflects the third year of changes in the marketplace since all medically important antimicrobials used in the food and water of food-producing animals transitioned from OTC marketing status to veterinary oversight. The report indicated sales:

- Decreased by 25% from 2010 through 2019
- Decreased by 36% from 2015 (the year of peak sales) through 2019
- Increased by 3% from 2018 through 2019

While some sales increased slightly in 2019, there remains a substantial reduction in the quantity of these drugs sold or distributed in 2019 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

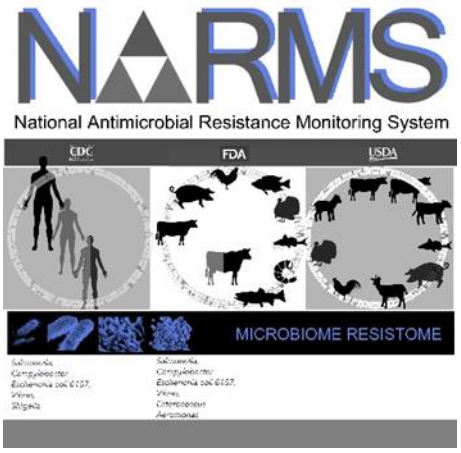
Although sales data provide insight regarding antimicrobial drugs entering the marketplace, it is also important to consider additional sources of information when assessing the progress of the Agency's efforts to combat antimicrobial resistance, including actual use data, animal demographic information, animal health data and data on resistance. The Agency continues to work with federal, academic, and industry partners to obtain more information about how, when, and why animal producers and veterinarians use medically important antimicrobial drugs in food-producing animals.

In November 2020, antimicrobial use information collected via FDA funded cooperative agreements was published for the first time in a special issue of Zoonoses and Public Health, a journal that brings together veterinary and human health researchers and policy makers. FDA has funded cooperative agreements with university researchers for the last five years to develop approaches for collecting data on antimicrobial use in cattle, swine, and poultry.

In August 2020, FDA also began funding two grants for the collection of data on antimicrobial use in dogs and cats. While FDA's focus in the past has been primarily on collecting data for food-producing animals, it is also important to collect data on the use of antimicrobial drugs in companion animals to help understand whether these use practices contribute to the development of antimicrobial resistant bacteria in pet owners and their pets.

The 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 December 2020, NARMS published the 2018 Integrated Summary along with 2019 and current 2020 results using updated online tools in NARMS Now. Data sharing is based on extensive use of next generation DNA sequencing and allows FDA to share NARMS findings in near real-time, greatly shortening the time for public health response. These data displays include enhanced animal pathogen monitoring from Vet-LIRN.

In October 2020, NARMS hosted a public meeting to review and discuss the recently published NARMS Strategic Plan: FY 2021 – FY 2025. FDA, the United States Department of Agriculture (USDA), Center for Disease Control and Prevention (CDC), and the Environmental Protection Agency (EPA) will each focus on different aspects of the plan according to their mission and expertise. The strategic plan established over-arching goals, including operating within a One Health paradigm and improving data sharing, communication and collaboration.

In FY 2020, NARMS began systemic testing of specific seafood products and continued a provisional program to test catfish, lamb, goats, and veal, and modified laboratory processes to explore the value of additional bacterial species. These data will improve understanding about the post-approval impact of antimicrobial use in these animals. In keeping with the One Health paradigm, NARMS also partnered with EPA to begin pilot studies examining antibiotic resistance in environmental waters across the country using both classical microbiology and new genomic sequencing technologies. Advances in Whole Genome Sequencing (WGS) are revolutionizing infectious disease diagnosis and surveillance by providing a complete picture of antibiotic resistance genes.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$234,507,000	$190,854,000	$43,653,000
FY 2021 Enacted	$245,307,000	$192,369,000	$52,938,000
FY 2022 President's Budget	$285,541,000	$232,033,000	$53,508,000

BUDGET REQUEST

The FY 2022 Budget Request for the Animal Drugs and Foods Program is $285,541,000 of which $232,033,000 is budget authority and $53,508,000 is user fees. The budget authority is increased by $39,664,000 compared to the FY 2021 Enacted and user fees increased by $570,000. The Center for Veterinary Medicine (CVM) amount in the request is $198,200,000. The Office of Regulatory Affairs amount is $87,341,000.

The Animal Drugs and Foods Program is responsible for protecting and promoting the health of humans and animals from a One Health perspective by helping ensure the safety of the American food supply, the safety of animal food and devices, and the safety and effectiveness of animal drugs. 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 Foods 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 Foods 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 Foods 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 Foods 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 Foods 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 Foods 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 2022 Budget Request support mission critical activities, and Presidential, HHS, and FDA human and animal health priorities.

BUDGET AUTHORITY

Food Safety: (+$26.4 million / 27 FTE)

Animal Food Safety Oversight: (+$16.4 million / 13 FTE)
Center: +$2.3 million / 5 FTE
Field: +$14.1 million / 8 FTE

With this increase, FDA will provide funding to states to expand efforts to modernize, harmonize, and transform the U.S. animal food inspection system into one that is comprehensive and prevention oriented utilizing FSMA authorities including the Preventive Control for Animal Food framework. FDA will also update inspection and enforcement programs, develop outreach and training initiatives, and devote resources to the analysis of controls for expected and understanding unknown animal food hazards. Animals have died and humans have been sickened because animal food has been contaminated by preventable hazards. FDA has historically relied on states to conduct 80% of animal food safety inspections. In FY 2020, FDA received $3.2M as an initial investment in cooperative agreements with just 13 states. FDA and its state partners need these resources to help address the risk-based oversight needed of the existing inventory of approximately 34,000 animal food facilities subject to FDA's food safety regulations, including FSMA.

Data Modernization and Enhanced Technologies – New Era of Smarter Food Safety: (+$6.4 million / 2 FTE)
Center: +$5.8 million / 2 FTE
Field: +$600,000 / 0 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CVM $10.7 million ($5.8 million in New Era of Smarter Food Safety) is requested to modernize outdated and disparate IT systems and business processes to increase efficiency and effectiveness, reduce overall costs and provide the flexibility needed to meet the challenges of an evolving regulatory landscape. CVM currently lags behind the industries it regulates and its information technology infrastructure is currently founded on the digitalization of paper-based processes and antiquated systems that are

significantly outdated. The American public and regulated industry rely on CVM to evaluate the safety and effectiveness of animal drugs and to review animal food ingredients to help keep animals healthy, while also ensuring that the meat, milk, and eggs from food-producing animals are safe for people to eat. The health of humans and animals are intrinsically linked and updates are critical to position CVM to actively monitor animal food and drug products marketed in the U.S. for potential safety issues, and to quickly identify, analyze and mitigate any serious issues that may result in harm to humans or animals. For example, this request will increase CVM's capacity for data warehousing, analytics and reporting to keep pace with advances in bioanalytical evaluation for human and animal food contaminants, as well as advances in DNA editing and sequencing. Within ORA, $0.8 million is requested to support the Enterprise Technology and Data crosscutting effort and $0.6 million is requested to support the New Era of Smarter Food Safety.

New Era of Smarter Food Safety: (+$3.6 million / 12 FTE)
Center: +$3.6 million / 12 FTE

With this increase, CVM will increase its traceback capabilities, while invigorating root cause analysis, predictive analytics, mutual reliance, new inspection tools development and outbreak response when contaminated animal food is identified. New tools and approaches will help FDA prevent and detect food safety problems efficiently by reducing the time it takes to trace the origin of contaminated human and animal food. Enhancing traceability will also provide greater supply chain visibility to help anticipate the kind of marketplace imbalances that have surfaced during the COVID-19 pandemic.

Medical Product Safety: (+$7.2 million / 13 FTE)

Data Modernization and Enhanced Technologies – Medical Product Safety (+$4.9 million / 6 FTE)
Center: +$4.9 million / 6 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CVM $10.7 million ($4.9 million in Medical Product Safety) is requested to modernize outdated and disparate IT systems and business processes to increase efficiency and effectiveness, reduce overall costs and provide the flexibility needed to meet the challenges of an evolving regulatory landscape. CVM currently lags behind the industries it regulates and its information technology infrastructure is currently founded on the digitalization of paper-based processes and antiquated systems that are significantly outdated. The American public and regulated industry rely on CVM to evaluate the safety and effectiveness of animal drugs and to review animal food ingredients to help keep animals healthy, while also ensuring that the meat, milk, and eggs from food-producing animals are safe for people to eat. The health of humans and animals are intrinsically linked and updates are critical to position CVM to actively monitor animal food and drug products marketed in the U.S. for potential safety issues, and to quickly identify, analyze and mitigate any serious issues that may result in harm to humans or animals. For example, this request will increase CVM's

capacity for data warehousing, analytics and reporting to keep pace with advances in bioanalytical evaluation for human and animal food contaminants, as well as advances in DNA editing and sequencing.

Medical Product Supply Chain: (+$2.3 million / 7 FTE)
Center: +$2.3 million / 7 FTE

With this increase, CVM will strengthen its capacity to detect data gaps and mine data to help identify and anticipate the effects of the COVID-19 public health emergency on the animal drug supply. Emerging diseases, such as COVID-19 and shifting trends in the marketplace result in vulnerabilities for unapproved fraudulent drugs products. While we are in the process of developing new systems funded by COVID supplements, there is also an urgent need to hire additional staff who can help identify data gaps, and review and evaluate existing data to ensure quality as we launch new data systems. The Center will also prioritize and review inspectional findings to address the workload anticipated from OVID-19 inspectional delays, while continuing to monitor for the presence of fraudulent and harmful products on the market.

Crosscutting (+$5.9 million / 4 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data (+$1.9 million / 2 FTE)
Center: +$1.2 million / 1 FTE
Field: +$737,000 / 1 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CVM $1.2 million is requested to support the Enterprise Technology and Data crosscutting effort, and $737,000 is requested for ORA.

This funding will allow ORA to expand our initial AI and data sharing efforts; incrementally improving and scaling our initial investments to build a broad network of AI capabilities and data sharing with our regulatory partners. Investing in FDA employees to retrain current staff and hire well-qualified new staff will expand our in-house expertise and enable smooth engagement with external AI and data sharing experts.

Inspections: (+$300,000 / 1 FTE)
Field: +$300,000 / 1 FTE

The FY 2022 Budget includes $18.8 million for inspections. ORA will increase site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID-19 related delays, and the Budget includes $300,000 for the Field portion of Animal Drugs and Foods.

Pay Costs: (+$1.3 million / 0 FTE)

Center: +$906,000 / 0 FTE
Field: +$426,000 / 0 FTE

The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

Capacity Building: (+$2.4 million / 1 FTE)
Center: +$1.6 million / 1 FTE
Field: +$809,000 / 0 FTE

The FY 2022 Budget includes $40.3 million to support centrally administered services to support critical, high-priority Capacity Building activities.

USER FEES

Current Law User Fees: +$570,000
Center: +$465,000 / Field: $105,000

The Animal Drugs and Foods Program request includes an inflation increase of $570,000 in 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 Foods 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
243201: Complete review and action on original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. (Output)	FY 2019[100]: 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	FY 2019: 100% w/in 240 day	90% w/in 240 days	90% w/in 240 days	Maintain

[100] Represents FDA's preliminary performance for FY 2019 cohort submissions. Final performance will be available via the FY 2020 ADUFA and AGDUFA performance reports

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
reactivations of such applications received during the fiscal year. (Output)	Target: 90% w/in 240 days (Target Exceeded)			
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 2020: 36% 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 2020: 95% Target: 90% w/in 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 2020: 93.4% 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 2020: 77.7% Target: 80% (Target Not Met)	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 2020: 76.2% 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	FY 2020: 69.3% Target: 55% (Target Exceeded)	55%	55%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
that moved toward compliance. (Outcome)				

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

New Animal Drug Application Review

In FY 2019, CVM completed review and action on 100 percent of original NADAs as well as other ADUFA sentinel submissions within the timeframes specified. CVM also completed review and action on 100 percent of original ANADAs as well as other AGDUFA sentinel submissions within the timeframes specified. FY 2019 saw a reduction in review goal timeframes for the AGDUFA program as part of the reauthorization of AGDUFA III, and CVM exceeded performance expectations in the first year of the reauthorization.

Warning Letters

FDA monitors marketed animal drugs to assure their safety and effectiveness as well as food additives and veterinary devices to assure their safety. 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 2020, CVM participated in an agency-wide coordinated effort through FDA's CBD Strike Force to issue a warning letter blitz to companies for illegally selling products containing cannabidiol (CBD). CVM was involved in 13 of the 15 warning letters produced by the CBD Strike Force. The warning letters involved extremely sensitive and novel legal and policy issues and required coordination and clearance across the agency (CDER, CFSAN, CVM, OCC, and FDA's CBD Policy Working Group led by the Commissioner's Office). This additional coordination and clearance resulted in these 13 warning letters being completed after the 25-day goal. This singular effort, along with fewer inspections performed due to the pandemic, caused the missed target in FY 2020. However, these issues shouldn't be a factor moving forward, and CVM is confident in meeting the current performance targets in FY 2021 and FY 2022.

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.

COVID Impact on ORA Field Performance Measures

Due to COVID-19, ORA faced many challenges in meeting the FY 2020 performance targets. FDA paused on-site surveillance inspections due to COVID-19, needing to balance our public health mission with investigator safety concerns, geographic and establishment restrictions, and increased work related to public health need during the pandemic. Despite these challenges, ORA continued conducting its mission critical work, and met all of the performance goals, except one. Given the 3-year rolling basis methodology of this performance goal and the continued prioritization of follow-up after regulatory actions, the inspections not conducted toward this goal in FY 2020 will be a responsibility in FY 2021. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA's ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

Center Animal Drugs & Foods Program Activity Data (PAD)				
CVM Workload and Outputs	**FY 2019 Actual**	**FY 2020 Actuals**	**FY 2021 Estimate**	**FY 2022 Estimate**
New Animal Drug Applications (NADAs) [1]				
Received	14	20	20	20
Completed	15	14	20	19
Approved	13	11	18	18
Pending [2]	14	20	20	21
New Animal Drug Application Supplements [1, 3]				
Received	685	694	670	700
Completed	648	659	680	675
Approved	569	602	550	600
Pending [2]	194	229	219	244
Abbreviated New Animal Drug Applications (ANADAs) [1]				
Received	40	34	25	25
Completed	36	37	20	20
Approved	31	30	16	16
Pending [2]	15	12	17	22
Abbreviated New Animal Drug Application Supplements [1, 3]				
Received	257	387	390	400
Completed	288	323	350	375
Approved	204	231	250	300
Pending [2]	120	184	224	249
Investigational New Animal Drug (INAD) Files [4]				
Received	2996	3423	3000	3000
Completed	3019	3439	3000	3000
Pending [2]	383	367	367	367
Generic Investigational New Animal Drug (JINAD) Files [4]				
Received	638	925	880	900
Completed	754	898	800	975
Pending [2]	105	132	212	137
Animal Food Additive Petition Reviews Completed	46	67	60	60
Investigational Food Additive File Reviews Completed	63	72	100	100
Adverse Drug Event (ADE) [5]				
ADE Reports Received	100,995	101,566	104,000	110,000
Post-Approval ADE Data Reviews	159	311	300	300

[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. Excluded from this count are Agency initiated actions (Q submissions) and amendments to INAD submissions.

[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 2020 Actuals			FY 2021 Estimate[5]			FY 2022 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	***598***	***78***	***520***	***105***	***5***	***100***	***1,696***	***298***	***1,398***
Pre-Approval /BIMO Inspections	3	3	0	1	1	0	79	79	0
Drug Process and New ADF Program Inspections	51	51	0	9	9	0	175	175	0
BSE Inspections	87	0	87	16	0	16	1,205	0	1,205
Feed Contaminant Inspections	0	0	0	0	0	0	25	0	25
Illegal Residue Program Inspections	120	0	120	20	0	20	450	0	450
Feed Manufacturing Program Inspections	54	0	54	10	0	10	200	0	200
Domestic Laboratory Samples Analyzed	463	1	462	421	17	404	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS[1]	***52***	***19***	***33***	***5***	0	5	***5***	***0***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	6	6	0	0	0	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	14	14	0	0	0	0	33	33	0
Foreign Feed Inspections	2	2	0	2	0	2	5	0	5
BSE Inspections	2	0	2	2	0	2	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***650***	***97***	***553***	***110***	***5***	***105***	***1,701***	***298***	***1,403***
IMPORTS									
Import Field Exams/Tests	1,467	491	976	1,500	500	1000	3,795	495	3,300
Import Laboratory Samples Analyzed	363	0	363	400	0	400	867	2	865
Import Physical Exam Subtotal	**1,830**	**491**	**1,339**	**1,900**	**500**	**1,400**	**4,662**	**497**	**4,165**
Import Line Decisions	493,192	68,371	424,821	479,518	68,500	425,000	503,494	71,925	446,250
Percent of Import Lines Physically Examined	0.37%	0.72%	0.32%	0.40%	0.73%	0.33%	0.93%	0.69%	0.93%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***1,543***	***0***	***1,543***	***1,000***	***0***	1,000	***1,600***	***0***	1,600
State Contract Inspections: BSE	637	0	637	403	0	403	650	0	650
State Contract Inspections: Feed Manufacturers	382	0	382	248	0	248	400	0	400
State Contract Inspections: Illegal Tissue Residue	0	0	0	0	0	0	0	0	0
State Contract Animal Feeds Funding	$3,123,039		$3,123,039	$3,200,000	0	$3,200,000	$3,296,000	0	$3,296,000
State Contract Tissue Residue Funding			$0	$0	0	$0	$0	0	$0
Total State Funding	**$3,123,039**	**$0**	**$3,123,039**	**$3,200,000**	**$0**	**$3,200,000**	**$3,296,000**	**$0**	**$3,296,000**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***2,193***	***97***	***2,096***	***1,110***	***5***	***1,105***	***3,301***	***298***	***3,003***

[1] The FY 2019 actual unique count of foreign inspections includes 1 OGPS inspections (1 for China).

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

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

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

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Devices and Radiological Health	**599,940**	**587,305**	**627,664**	**676,547**	**48,883**
Budget Authority	***395,168***	***395,142***	***408,108***	***452,064***	***43,956***
User Fees	***204,772***	***192,163***	***219,556***	***224,483***	***4,927***
Center	501,296	488,115	528,784	571,124	42,340
Budget Authority	310,163	310,156	323,103	360,827	37,724
User Fees	191,133	177,959	205,681	210,297	4,616
Prescription Drug (PDUFA)	*4,162*	*3,525*	*4,446*	*4,720*	*274*
Medical Device (MDUFA)	*180,073*	*168,730*	*194,199*	*198,400*	*4,201*
Mammography Quality Standards Act (MQSA)	*6,898*	*5,704*	*7,036*	*7,177*	*141*
Field	*98,644*	*99,190*	*98,880*	*105,424*	*6,544*
Budget Authority	85,005	84,986	85,005	91,237	6,232
User Fees	13,639	14,204	13,875	14,186	311
Medical Device (MDUFA)	2,358	2,241	2,368	2,449	*81*
Mammography Quality Standards Act (MQSA)	11,281	11,963	11,507	11,737	*230*
FTE	**2,302**	**2,172**	**2,345**	**2,382**	***37***

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.[101]

There are 230,000 different types of medical devices on the U.S. market, manufactured at 25,000 facilities worldwide. FDA's Center for Devices and Radiological Health (CDRH) has about 1,800 dedicated employees who oversee these devices, 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, and supports Agency efforts to assess industry compliance with applicable regulation and conducts inspections of domestic and foreign manufacturers. This is all while promoting access, enhancing safety, and advancing innovation. These efforts are critical for the U.S. supply chain, as well as the U.S. health care system as a whole.

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.

[101] 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.

Figure 3 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:

- Aimed 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 and 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.

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

- Reduced the median 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 2020.
- As of 2020, over 84 percent of novel technology device manufacturers contacted by FDA during device development indicated they intend to bring their device to the U.S. first or in parallel with another major market.
- The number of approved early feasibility studies in the U.S. where devices are evaluated early in development is projected to more than double – from 21 in FY 2014 to 54 in FY 2020.
- Approved, cleared, or authorized a record high of 132 novel medical devices in 2020, surpassing the 40-year high mark we set in 2018 and capping off 10 years of progress.

It is also important to understand that medical devices have been important to support the U.S. response to the COVID-19 pandemic. This public health emergency caused unprecedented demand for medical devices and, as a result, the Devices Program received thousands of Emergency Use Authorization (EUA) submissions for tests, personal protective equipment (PPE), ventilators, decontamination systems for PPE, remote monitoring systems, and other devices. The Devices Program has engaged in unprecedented levels of activity to review as many EUAs as possible to help ensure health care providers on the front lines of the US response had as much access to the critical medical devices needed as possible. The Devices Program did this unprecedented work while continuing its ongoing operations and commitments to US patients. The Devices Program's success in providing patients with new options for effective health care, is not coming at the expense of the robust non-clinical and clinical science on which we rely to make our regulatory decisions. In some cases, we are receiving clinical evidence more quickly and more efficiently and answering post-market questions we would not have been able to easily address in the past, due in part to our efforts to strengthen the clinical trial enterprise and leverage real world data.

As evidence of FDA's continued efforts to make the requirements for meeting U.S. 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 that meet FDA's standard. Ultimately, the Devices Program's efforts better serve the needs of patients, who are at the heart of everything the Devices Program does.

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 is intended to help patients have more timely access to breakthrough medical devices by expediting their development, assessment, and review, while preserving the statutory standards for marketing authorization, consistent with the FDA's mission to protect and promote public health.

Over the last year, FDA has seen a significant increase in the utilization of sprint discussions 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. So far in FY 2021, the total number of designated breakthrough devices exceed 355, increasing by 151 devices since FY 2019 and more than tripling since FY 2018.

Devices coming through the Breakthrough Devices Program represent a pipeline of innovations that will improve and extend patient lives in the years to come. For example, in FY 2020, through the Breakthrough Devices Program FDA approved a device intended to genetically identify non-small cell lung cancer patients who may benefit from treatment with a certain therapy. Using a routine blood draw, this companion diagnostic device can also be used for tumor mutation profiling by providing clinicians with a list of select genomic alterations specific to the patient's cancer, helping them to make more informed and personalized treatment plan decisions.

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.

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.

National Evaluation System for Health Technology (NEST)

The FDA continues its collaboration 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. The NEST data network is currently comprised of 14 collaborators with records on over 141 million individuals across 3,075 outpatient practices, 291 specialty clinics, and 162 Hospital or Medical Centers. The benefits of NEST for patients and the ecosystem include:

- Helping to improve the quality of real-world evidence that FDA can use to detect emerging safety signals quickly and take appropriate actions.
- Providing an expanded source of information for medical device manufacturers to assess the safety and effectiveness of their devices and continue to develop innovative improvements.
- Supporting healthcare providers and patients access to information about the evolving benefit-risk profile of devices on the market and enable them to make more informed decisions.
- Greatly enhancing 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.
- Providing real-time device safety information to enable 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 is set up for long-term success to advance public health. The Devices Program has established formal partnerships with health providers, payers, and professional registries, to collect, curate, and analyze evidence from clinical experience contained in electronic health records, claims, pharmacies, and other sources, including registries. 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. This 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. NEST continues to develop the infrastructure needed to establish an active surveillance system that can be utilized by FDA and other stakeholders.

Unique Device Identification (UDI)

FDA continues implementation of 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 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.

Case for Quality

The Devices Program has been advancing manufacturing and product quality through its Case for Quality Voluntary Improvement Program (CfQVIP) Pilot. The goal of the program and pilot is to improve the safety, quality, and access of medical devices for patients by driving quality and continuous improvement within the device industry. The CfQVIP appraisals assess the capability of the device manufacturer to meet business, quality, and safety objectives.

Appraisal results are then used to focus the continuous improvement activities, manufacturing investments, and quality system integration to increase success in meeting the objectives. This focus and integration have resulted in increased production and access to higher quality medical devices for patients, decreases in safety issues, and lower production costs, which increases value to industry, patients, providers, payors, and FDA.

The Devices Program has received more than 400 modified submissions for manufacturing changes as part of the program. The number of submissions received shows a higher rate of manufacturing improvements, new equipment investment, and process optimizations implemented by participating manufacturing sites. Along with the improved value, participating manufacturing sites have demonstrated product quality improvements in the safety and quality of devices for patients, such as 19 percent reduction in process defects, 76 percent reduction in medical device reports, and 48 percent reduction in recalls and field actions since enrollment in the VIP program.

In response to the COVID-19 pandemic and at the request of participants who wanted to sustain the improvements, the VIP program was able to quickly adjust, develop, and incorporate virtual assessments. This has allowed participating manufacturing sites to sustain and focus their improvements to reduce the impact of the pandemic on their operations.

The Devices Program has also taken learnings from the VIP program and initiated two additional pilot activities. These include 1) a broad improvement of the corrective and preventive action system across the medical device industry and 2) the Accelerate Sustainable Capability (ASC) pilot, which utilizes principles from the program to assist struggling manufacturers in improving their systems by focusing on quality and safety. Manufacturing sites piloting the Corrective and Preventive Actions (CAPA) improvement framework have reported up to 70 percent increase in early detection and resolution of issues, with savings of 10,900 man-hours of effort. This has enabled participants to increase improvement projects, process improvements, and enhance capacity.

Medical Device Development Tools (MDDT)

An MDDT is a method, material, or measurement used to assess the effectiveness, safety, or performance of a medical device. The intent of this voluntary program is to promote the development and use of tools to streamline device development and regulatory evaluation while

assuring devices meet FDA's standard. Qualification improves efficiency in the regulatory process because a qualified MDDT can be used by multiple sponsors across multiple medical device development programs.

CDRH developed an MDDT for the assessment of possible thermal damage after use of high intensity therapeutic ultrasound has been qualified. This new MDDT represents the first example of an internally developed MDDT and exemplifies the Devices Program's promotion of regulatory efficiency that maintains FDA's standard.

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.

Coronavirus (COVID-19)

The COVID-19 pandemic has created an unprecedented demand for new tests and created shortages of PPE, ventilators, testing supplies, and other medical devices at a level never before seen during any other Public Health Emergency (PHE). As a result, the Devices Program has received an unprecedented volume of Emergency Use Authorization (EUA) requests for medical devices, including devices that have been reviewed for premarket submission but have never been issued EUAs, such as ventilators, infusion pumps, remote monitoring devices, and blood purification devices. In addition, the Devices Program reviewed EUA requests for novel medical products that have never been reviewed under any circumstances, such as decontamination systems for N95 respirators and ventilator splitters enabling use of a single ventilator to support multiple patients.

As of March 2021, the Devices Program has received over 6,000 EUA requests and pre-EUA submissions for medical devices intended to diagnose, treat, or prevent COVID-19. To help address the urgent need for critical devices, the Devices Program developed for the first time during this PHE, a novel "umbrella EUA" approach to help streamline authorization for some devices, such as respirators and ventilators. In addition, FDA worked closely with manufacturers through interactive reviews for EUA requests and pre-EUA submissions, including many who were not familiar with FDA or the manufacturing of medical devices, and reviewed data on a rolling basis to speed the process of reviews. One year since the pandemic hit the US, the Devices Program has authorized emergency use of over 745 medical products, including rapid-at

home tests for COVID, molecular tests, respirators, ventilators, and remote monitoring systems. This is the highest number issued in any year of FDA's history. While the Devices Program has worked to meet the unprecedented demand caused by this pandemic, our regular work has continued. CDRH received more than 16,000 non-COVID submissions in 2020, including premarket submissions and pre-submissions.

Despite our experience with six other PHEs, CDRH has never faced a PHE of this scale. The level of unmet clinical needs confronting the healthcare system has required new levels of engagement. During this time, the Devices Program has supported the development, distribution, and use of other devices by issuing many guidances, publishing and regularly updating several sets of frequently asked questions (FAQs), developing templates with recommendations for validating different types COVID-19 tests, and streamlining the submission of EUA requests for these tests. FDA has continued to update and reissue EUAs and guidance, when appropriate, based on new information and changing circumstances during the evolving pandemic. In addition, the Devices Program provided support to product developers and others since March 2020 by holding weekly webinars, sharing information and guidance on our website, and managing a 24/7 hotline to answer questions on a range of pandemic-related issues.

The Devices Program has also initiated a new research program to both strengthen the regulatory science gaps identified during the PHE and to better prepare the Center to contribute to future efforts including, the 3D printing of PPE.

Device Shortages and Advanced Manufacturing

FDA consistently works to prevent shortages of medical devices; however, it is challenging for the Devices Program to support an optimally resilient supply chain, as the FDA does not have the same authorities for device shortages it has for drugs and has overall limited statutory authority to get the information it needs to intervene before shortages and other disruptions occur. Despite limits in its authority, FDA is proactive, reaching out to companies to get the information we need, though it is always a time-consuming and challenging process because medical device companies are not required to notify FDA about potential supply chain disruption or to respond to requests for information from FDA except for under limited circumstances.

In FY 2020 and FY 2021, FDA responded to the outbreak of COVID-19 with Agency-wide efforts in the area of Device Shortages, including:

- Producing guidance in response to the new 506J authorities provided to the FDA under the CARES Act Section 3121 which allows FDA to collect information during or in advance of public emergencies. This guidance helped industry to understand the critical data FDA needed about the supply chain and as well as learn about meaningful disruptions.

- Reached out to over 1,000 medical device manufacturing device facilities to help understand current inventory and the ability of the facilities to ramp up production during this critical time. This information helped direct efforts to secure alternate manufacturers and production capability where it was needed.

- Hired experts in supply chain management and fund positions to review and evaluate the multitude of EUA applications for personal protective equipment after publishing guidance on the requirements for the sale of PPE in this country.

FDA is also working with hospitals, physician societies, patient organizations and other groups to understand the extent of medical device shortages and take appropriate action. In order to mitigate the impact of medical device shortages, FDA is also analyzing other potential sources of shortages such as upcoming influenza and hurricane seasons. FDA aims to expand our shortage assessment capability to be even more forward-leaning and effective at reducing or eliminating shortages with future funding.

As part of the forward-leaning efforts, FDA has worked to establish programs that help manufactures drive internal improvements and the capability to proactively increase production capacity, production yield, and device access, such as the Case for Quality Voluntary Improvement Program (VIP). Participants in VIP have demonstrated 62% daily production increase in products that have been on shortage allocation in their efforts to improve quality and safety. This has resulted in investments in technology and equipment in participants' U.S. manufacturing sites, with one participant moving from one manufacturing line to four manufacturing lines, along with investments in statistical process control technology and multi-variate data analysis.

In addition, the Devices Program is developing an advanced manufacturing clearinghouse, which, over time, would enable the adoption of advanced methods and technologies in U.S. manufacturing to increase production capacity, improve quality, and reduce costs. FDA is collaborating with the Medical Device Innovation Consortium (MDIC) and other partners on establishing the clearinghouse and is in the process of awarding a contract to fund several advanced manufacturing technology implementation projects to improve digital capability throughout production.

Leveraging And Learning From Real World Evidence Collected During The COVID Pandemic

FDA announced participation in the COVID-19 Diagnostics Evidence Accelerator, a multi-stakeholder collaborative project to advance the development of diagnostics through the generation of real-world evidence.

The Evidence Accelerator is organized by the Reagan-Udall Foundation for the FDA in collaboration with Friends of Cancer Research to allow the community to analyze both diagnostic and clinical data in real time, which has the potential to contribute to the scientific evaluation of diagnostic tools and medical interventions for COVID-19. The Accelerator project will leverage FDA's SHIELD initiative, a multi-stakeholder collaboration to improve the quality, interoperability and portability of laboratory data within and between institutions so that diagnostic information can be drawn from different sources or shared between institutions. SHIELD harmonizes COVID-19 test data referenced in the HHS COVID-19 laboratory data reporting requirements, which can be used to evaluate the real-world performance of SARS-CoV-2 diagnostic tests and antibody tests.

Evidence generated by the Accelerator project is intended to be complementary to other studies that have been conducted or are underway as well as to provide actionable information about the prevalence of SARS-CoV-2 in specific populations and highlight individual risk factors for patients. This helps improve our understanding of the disease, tailor public health interventions and strategies to mitigate risks for individuals and communities and help stop the spread of SARS-CoV-2.

Mammography Quality Standards Act Program

According to the Centers for Disease Control and Prevention, breast cancer is the second most common cancer (after skin 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 and in plain language that they can understand.

As part of the mammography program, FDA and its state partners annually inspect more than 8,600 certified mammography facilities in the U.S. to ensure compliance with national quality standards for mammography. In FY 2020, over 87 percent of mammography facilities had no serious violations of the law and less than one percent of facilities were cited with the most serious violations. These MQSA-certified facilities provide more than 39 million mammography procedures annually in the U.S.

The promotion of clinical image quality is a primary goal of the Mammography Quality Standards Act (MQSA). Due to concerns with what was reported by the American College of Radiology related to image quality during the accreditation and reaccreditation processes, the MQSA program implemented the Enhancing Quality Using the Inspection Program (EQUIP) initiative, which adds inspection questions to the annual inspection process which emphasize the image quality and quality assurance regulations that have been in place since the MQSA Final Regulations were published. The initiative is intended to continue MQSA's emphasis on the significance of clinical image quality, which is one of the most important determinants of the accuracy of mammography. Since the introduction of EQUIP in the inspection process, the total compliance rate is near 98% which is due to a heavy focus on educating facilities about the EQUIP initiative. Additionally, since January 1, 2019, a total of 13 facilities were found to have repeat EQUIP violations which resulted in the FDA requesting Additional Mammography Reviews (AMRs) performed by the facilities' Accrediting Bodies (AB) to determine if the overall quality of mammography had been compromised due to the failure to operate in compliance with MQSA regulations. Four facilities passed their AMRs. Six facilities had AMRs that were found to be deficient and the facilities were required by their accreditation body to complete corrective action plans that addressed the noted clinical image quality deficiencies. Two facilities failed the AMRs and FDA deemed those two facilities to be a Serious Risk to Human Health, resulting in FDA ordered Patient and Provider Notifications (PPNs) in which a total of 3,618 patients were notified that the facility where the patient's mammogram was performed failed to meet the clinical image quality standards established by the facility's AB. One AMR case is ongoing and remains under review.

Radiological Health Program

The Radiological Health Program protects public health and safety by monitoring industry's compliance with regulatory performance standards in order to minimize the emissions of and the exposure of people to unnecessary electronic product radiation. The program reviews initial and periodic reports, inspects establishments that manufacture radiation-emitting electronic products, and prioritizes product types for sampling and testing at FDA's Winchester Engineering and Analytical Center to determine compliance. The program also engages with regulatory scientists to identify high-priority projects 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, public safety notices, and internal process improvements.

For example, 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. The public comments have been analyzed, and FDA is working to finalize the amendments. 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, coordinating with FDA's Office of Regulatory Affairs to enhance the success of inspections, and streamlining FDA's laser variance review process.

The Devices Program also continues to collaborate with the medical imaging industry and radiological professional societies to address the safety of all x-ray imaging modalities, promote the use of international consensus standards, and promote the use of alternative technologies when appropriate. The Devices Program actively seeks to address safety issues and incorporate internationally accepted performance requirements and testing methods to enhance product safety through standards. Recent accomplishments include incorporation of pediatric safety features in standards for computed tomography (CT), fluoroscopy, and general and dental radiography.

The Radiological Health Program partners with many other national and international organizations to identify, characterize, and reduce medical radiation exposures. Among other organizations, the Program works with the National Council on Radiation Protection and Measurements (NCRP), a Congressionally-chartered non-profit organization. In recent years, NCRP has published, with collaboration from the Devices Program, several key reports including the Radiation Protection in Dentistry and Oral & Maxillofacial Imaging (Report No. 177), Medical Radiation Exposure of Patients in the United States (Report No. 184), and Evaluating and Communicating Radiation Risks for Studies Involving Human Subjects: Guidance for Researchers and Institutional Review Boards (Report No. 185).

Likewise, the Devices Program also continues work to support the Conference of Radiation Control Program Directors (CRCPD), which facilitates collaboration among Federal and State agencies to address radiological health issues of mutual interest. With guidance from FDA liaisons, CRCPD organizes annual meetings and numerous subcommittee meetings to facilitate education and collaboration. FDA and CRCPD collaborations include radiation safety initiatives, inspector training programs, and collection of real-world evidence on the use of radiation for specific types of diagnostic imaging exams to improve patient safety and public health.

Patient Science & Engagement
The Patient Science and Engagement Program is committed to engaging with patients, understanding their experiences, and proactively integrating patient perspectives into medical device decisions and regulatory activities where appropriate. FDA has created forward-leaning mechanisms to facilitate patient involvement in regulatory activities as well as fostered innovative approaches to supporting the science of patient input. By collaborating with patients, the research community, and industry, FDA has fostered the creation of well-defined outcome measures and assessments of patient preference information that directly impact medical device decisions and assure that these devices have the assurances patients depend upon.

FDA is at the forefront in describing ways that structured collection of patient preference information can be used as scientific evidence in the evaluation of medical products. Since issuing the guidance on patient preference information in 2016, industry is increasingly including this information in medical device submissions, growing from initially none to 23 studies that are completed or in the pipeline. In addition, patient-reported outcomes are being collected consistently in more than 50 percent of medical device submissions with clinical studies.

Wearable digital health technologies are increasingly being used by patients to continuously capture elements of their daily life. In FY 2020, FDA worked with partners to understand ways that data can be analyzed, integrated, and used to understand how patients living with diverse medical conditions feel and function. These technological advances offer new opportunities for patients to harness data and integrate it as complementary scientific evidence to impact regulatory decision making. Through collaborative educational programs and outreach, FDA is clarifying the regulatory pathways for developers of digital health technologies, streamlining the timelines from concept to care.

FDA also established the first advisory committee comprised solely of patient and family caregiver representatives and is working hand-in-hand with patients to incorporate their values and perspectives into all aspects of the medical device total product life cycle. The Patient Engagement Advisory Committee (PEAC) is comprised solely of patients, caregivers and representatives of patient organizations to provide formal recommendations to FDA on general scientific matters related to medical devices. Since the inaugural meeting in October 2017, the PEAC has provided insightful recommendations on matters including patient involvement as advisors in medical device clinical investigations and patient-generated health data as evidence to monitor and promote medical device safety.

In September 2019, FDA integrated the PEAC recommendations into a draft guidance on the ways patients can engage as advisors in the design of clinical studies. The paper suggests important considerations for communicating cybersecurity vulnerabilities to patients. By including patient perspectives in the evaluation of medical devices, FDA is moving the needle to better meet the needs of patients. The committee helps the Agency to work on systematic approaches to include patient preference information in our decisions when it helps to establish that medical devices are safe and effective.

Digital Health
FDA is a world-leader in fostering development of safe 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 is 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 Devices 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 lower risk software that could be classified as a device.

As of September 2020, there are three major manufacturers of consumer wearables who are pioneers in providing ECG to individuals. These products are reaching millions and helping individuals engage in their heart health. Likewise, in the field of digital therapeutics, we are seeing an increased use of software that provides coaching and cognitive behavior therapy for many conditions with the FDA permitted marketing of a novel game-based therapy for children with ADHD.

Examples of lower 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 FDA's regulatory purview are safe and effective.

Digital Health Center of Excellence

FDA launched the Digital Health Center of Excellence to empower stakeholders to advance health care by fostering responsible and high-quality digital health innovation. This marks the next stage in applying a comprehensive approach to digital health technology to realize its full potential to empower consumers to make better-informed decisions about their own health and provide new options for facilitating prevention, early diagnosis of life-threatening diseases, and management of chronic conditions outside of traditional care settings.

The Digital Health Center of Excellence intends to provide centralized expertise and serve as a resource for digital health technologies and policy for digital health innovators, the public, and FDA staff. The Digital Health Center of Excellence is primarily focused on helping both internal and external stakeholders achieve their goals of getting high quality digital health technologies to patients by providing technological advice, coordinating and supporting work being done across the FDA, advancing best practices, and reimagining digital health device oversight.

Artificial Intelligence

Artificial intelligence (AI) and machine learning (ML) technologies that are incorporated in medical devices 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. The Devices Program has been the forefront of facilitating responsible adoption of AI technologies for the benefits of patients and our health care system as a whole.

FDA has authorized several AI/ML based software as a medical device. These authorizations include the first AI based diagnostic software as a medical device, designed to automatically detect the presence of more-than-mild diabetic retinopathy; software-only device that uses artificial intelligence to emulate the expertise of sonographers and provides real-time guidance to the users during acquisition of echocardiography to assist them in obtaining anatomically correct images.

Other authorizations include devices for the characterization and assessment of breast abnormalities from MRI data in patients with high-risk and a device that analyzes CT angiogram images of the brain in order to notify a neurovascular specialist when a suspected large vessel occlusion has been identified and is in need of expert review. In addition to these specific products, CDRH in January of 2020 issued a final order to reclassify certain radiological medical image analyzers, including computer-assisted detection (CADe) devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection devices from Class III to Class II devices, subject to premarket notification. The order provides special controls that, in addition to general controls, will provide a reasonable assurance of safety and effectiveness for CADe devices.

As seen from the current COVID-19 pandemic, patients and providers need to be able to access, read and interpret information provided by these devices and use them as they are intended. Moreover, they need to be able to facilitate care remotely – as this helps decrease the risk of exposure for patients and health care providers to COVID, if care can be delivered at a distance. Leveraging lessons learned from other industries will advance medical technology sector to be on par or be a leading sector within the envisioned industry of the future. Successful development of digital heath technologies powered by AI is poised to inform the physical, cognitive, and psychological characteristics on the design of medical devices including software as a medical device for human use.

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. Such adaptive algorithms are in development by a number of companies, and the publication of the discussion paper has initiated a constructive dialogue with manufacturers so that the technology introduction can occur in a responsible manner.

The goal of the framework is to ensure 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 include real-world monitoring of performance once the device is on the market to ensure safety and effectiveness are maintained. FDA is exploring this approach because the Agency

expects 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.

FDA received supportive feedback from stakeholders towards the concepts outlined in the proposed approach. Many stakeholders applauded FDA's pragmatic approach and recommended furthering the proposed approach which will advance science, transparency and use of these technologies and software that is powered by AI.

FDA is undertaking activities in the broad array of MedTech that are starting to adopt AI/ ML, such as digital pathology. The use of AI/ML to assist in or make diagnoses based on whole slide imaging systems is increasing rapidly. It is essential that FDA understands the technology being developed to help ensure the appropriate balance of benefit risk as these systems come to market.

On January 12, 2021, FDA released the agency's first Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. This action plan describes a multi-pronged approach to advance the Agency's oversight of AI/ML-based medical software. The AI/ML-Based Software as a Medical Device Action Plan outlines five actions that the FDA intends to take, including:

- Further developing the proposed regulatory framework, including through issuance of draft guidance on a predetermined change control plan (for software's learning over time);
- Supporting the development of good machine learning practices to evaluate and improve machine learning algorithms;
- Fostering a patient-centered approach, including device transparency to users;
- Developing methods to evaluate and improve machine learning algorithms; and
- Advancing real-world performance monitoring pilots.

The plan outlines a holistic approach based on total product lifecycle oversight to further the enormous potential that these technologies have to improve patient care while delivering safe and effective software functionality that improves the quality of care that patients receive. To stay current and address patient safety and improve access to these promising technologies, the Devices Program anticipate that this action plan will continue to evolve over time.

Digital Health Software Precertification (Pre-Cert) Program

Pre-Cert is a more holistic approach to evaluating a product's safety and effectiveness. The goal of the program is to build a least burdensome regulatory framework that will assist in the development of high quality software as a medical device (SaMD) products by using a tailored streamlined premarket review process and leveraging postmarket data to verify continued safety, effectiveness, and performance of SaMD products in the real world, throughout their total product lifecycle.

FDA's 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.
- 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.

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.
In September 2020, The FDA published a program update highlighting learnings to date from the building and testing of the Pre-Cert Pilot Program and how the pilot program is leveraging its learnings for the next iteration of testing. The update also highlighted that additional testing is needed to understand how health benefits may be observed in Real World Performance data.

Based on public comments and other information collected in support of program development, the FDA is working with pilot participants and test case companies to define structured data models for the information and objective evidence needed to make key decisions at each stage of the product lifecycle under the future Pre-Cert Program. As we learn and iterate, these data models will inform how components of the future Pre-Cert Program interact to support a determination that marketed products are safe and effective.

Advancing Consensus Standards
The use of voluntary consensus standards in device submissions contributes to a least-burdensome approach to device review that maintains FDA's standards, and is broadly supported by industry and FDA. The goal of CDRH's Standards and Conformity Assessment Program (S-CAP) is to promote the use of standards in device submissions to demonstrate that these submissions meet the criteria to be fully marketed. To that end, we have published two guidances, the Appropriate Use of Voluntary Consensus Standards and Recognition and Withdrawal of Voluntary Consensus Standards, while conducting robust outreach to educate and encourage manufacturers to cite FDA-recognized standards in submissions.

S-CAP leads a sophisticated standards recognition program in which over 400 Devices Program staff help evaluate standards for formal recognition. More than 1,400 standards are currently recognized and published in our public database. Our staff also contribute to the development of regulatory-ready consensus standards in which our experts participate in and often lead standards development organizations' Technical Committees. Under the Pilot, FDA will grant ASCA Accreditation to qualified testing laboratories, who will perform testing for manufacturers. A reduced need for documentation in ASCA submissions, coupled with FDA's enhanced confidence in ASCA-accredited laboratories' methods and results, should result in a more streamlined review process for those submissions.

Cybersecurity
The Devices Program's goal is to encourage a coordinated approach of vigilance, responsiveness, resilience, and recovery with respect to cybersecurity that fits FDA's culture of continuous quality improvement. This means taking a total product lifecycle approach, starting at the product design phase when FDA encourages manufacturers to build in security to help foil potential risks, followed by having a plan in place for managing any risks that might emerge, and planning for how to reduce the likelihood of future risks. One area of focus is the ability of 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 is taking steps to help build on the work that the Devices Program and FDA stakeholders have already achieved that include:

- Working with the Patient Sciences and Engagement program to develop a paper on updated, more effective, and more comprehensive strategies for communicating cybersecurity vulnerabilities to patients.
- Funding a series of threat modeling bootcamps, in addition to a threat modeling playbook, to both assist and train industry in how to perform threat modeling for cybersecurity threats in the medical device sector.
- Collaborating with the MITRE Corporation to develop a supplemental rubric for the Common Vulnerability Scoring System (CVSS) that may be used by industry to characterize and assess the severity of a cybersecurity vulnerabilities.
- Updating the 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.

In addition, FDA continues to coordinate its cybersecurity efforts with other agencies. FDA participates in the HHS Cybersecurity Working Group and works collaboratively with the Cybersecurity Infrastructure Security Agency (CISA) 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.

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.

Personalized Medicine

The Devices Program has a unique role in advancing precision medicine. Personalized, or 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 and other technologies that the Devices Program oversees used for risk assessment, diagnosis, and treatment must be accurate and reliable.

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.

In 2020, FDA's public human variant database recognition program was utilized for the first time to support clinical validity in a premarket submission. NIH's All of Us Research Program, which seeks to gather health and genomic data from a diverse group of one million research participants across the US to help speed the progress of precision medicine, used the ClinGen resource to support its premarket submission. The database recognition program continues to be expanded in the domains of hereditary diseases, pharmacogenetics, and oncology.

In February 25, 2020, FDA published the Table of Pharmacogenetic Associations as a resource to provide transparency into FDA's view of the state of scientific evidence in pharmacogenetic gene-drug associations, and where the evidence is sufficient to support therapeutic management recommendations. Pharmacogenetic tests are of increasing interest to practitioners in selecting therapeutic agents and avoiding toxicities. This resource is a living document which reflects continuous improvement in the evidence base for pharmacogenetic testing and takes into consideration scientific evidence reported by stakeholders through a public docket.

In addition, in April 2020 FDA published a guidance on the development and labeling of companion diagnostics to support the use of multiple targeted cancer therapies. This guidance will facilitate the development and use of more than one companion diagnostic test that is essential for the safe and effective use of a corresponding group of personalized medicine cancer therapies. Transparency into group labeling is now provided through FDA's List of Cleared or Approved Companion Diagnostic Devices [5].

The Devices Program also participates in several standardization and harmonization efforts across the FDA and with external stakeholders, including the Sustainable Predictive Oncology Therapeutics and Diagnostics Quality Pilot,[102] FNIH ctDNA Quality Control Materials

[102] https://www.jmdjournal.org/article/S1525-1578(16)30219-7/fulltext

Project,[103] and the Sequencing Quality Control Consortium.[104] For instance, the Devices Program actively contributes to the revision of Nucleic Acid Sequencing Methods in Diagnostic Laboratory Medicine and supporting International Organizations for Standardization (ISO) working groups to help bring safe and effective diagnostics and treatments that use personalized medicine to American patients.

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. [105] 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.

Date	Docket#	Title	Description
Feb 2021	FDA-2020-D-0987	Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests	FDA is issuing this guidance to provide a policy and recommendations on evaluating the potential impact of emerging and future viral mutations of SARS-CoV-2 on COVID-19 tests for the duration of the COVID-19 public health emergency.
Jan 2021	FDA-2019-D-4048	Safer Technologies Program for Medical Devices	The FDA is introducing a new, voluntary program for certain medical devices and device-led combination products that are reasonably expected to significantly improve the safety of currently available treatments or diagnostics.
Oct 2020	FDA-2019-D-1876	Testing for Biotin Interference in In Vitro Diagnostic Devices: Guidance for Industry	Recommendations on the testing for interference by biotin on the performance of in vitro diagnostic devices (IVDs).

[103] https://fnih.org/ctdna

[104] https://www.fda.gov/science-research/bioinformatics-tools/microarraysequencing-quality-control-maqcseqc

[5] https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools

[105] https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products

May 2020	FDA-2020-D-1138	Recommendations for Sponsors Requesting EUAs for Decontamination and Bioburden Reduction Systems for Face Masks and Respirators During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency	Guidance to provide recommendations for sponsors of decontamination and bioburden reduction systems about what information should be included in a pre-Emergency Use Authorization (pre-EUA) and/or EUA request to help facilitate FDA's efficient review of such request.
May 2020	FDA-2020-D-0987	Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency	Guidance to provide a policy to help accelerate the availability of novel coronavirus (COVID-19) tests developed by laboratories and commercial manufacturers for the duration of the public health emergency.

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
Apr 2021	TheraSpher	TheraSphere is a radiation treatment for people who have a specific type of liver cancer called unresectable hepatocellular carcinoma (HCC).
Jan 2021	Imagio Breast Imaging System	The Imagio Breast Imaging System uses both optoacoustic (OA) and ultrasound (US) to image breast tissues to help physicians examine breast lesions.
Sep 2020	Oncomin Dx Target Test	Oncomin Dx Target Test is a lab test designed to detect several specific genetic changes in tumors found in patients with non-small cell lung cancer and determine if certain medications may help treat the cancer.
Jul 2020	Quest SARS-CoV-2 rRT-PCR test	First COVID-19 diagnostic test to be authorized for use with pooled samples.
Jun 2020	EndeavorRx	The first game-based digital therapeutic device to improve attention function in children with attention deficit hyperactivity disorder (ADHD).

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$587,305,000	$395,142,000	$192,163,000
FY 2021 Enacted	$627,664,000	$408,108,000	$219,556,000
FY 2022 President's Budget	$676,547,000	$452,064,000	$224,483,000

BUDGET REQUEST

The FY 2022 President's Budget for the Devices Program is $676,547,000, of which $452,064,000 is budget authority and $224,483,000 is user fees. The budget authority increases by $43,956,000 compared to the FY 2021 Enacted and User Fees increase by $4,927,000. The CDRH amount in this request is $571,124,000 and the ORA amount is $105,424,000.

FDA's focus on both safety and innovation stems from FDA's historic mission to both protect and promote public health by assuring timely patient access to devices that are high-quality, safe and effective. Innovation in health tech does not simply mean new or novel. It has to provide value to patients and consumers. 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 2022 President's Budget 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 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 requirements to bring devices to the U.S. 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.

FDA's success in providing patients with new treatments and diagnostics, and more options for effective health care 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 efficiently answering postmarket questions FDA would not have been able to address in the past.

The FY 2022 funding enables 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: (+$26.4 million / 18 FTE)

Shortages & Supply Chain: (+21.6 million / 18 FTE)
Center: +$21.6 million / 18 FTE

The Budget includes funding to ensure the U.S. has a strong domestic supply chain for the medical devices our patients and health care providers rely upon every day and reduce reliance on products from China and other nations. This dedicated funding will strengthen the capability of the Devices Program to respond in everyday situations, as well as in emergencies. The importance of a robust supply chain has never been more evident than during the COVID-19 pandemic, where the nation's response relies upon the availability of devices such as personal protective equipment (PPE), ventilators, in vitro diagnostic tests and the components necessary to run them and other critical devices. Without the appropriate infrastructure and resources to rapidly assess, mitigate and communicate about shortages and other identified and potential supply chain disruptions, the Center will not be positioned to support a resilient domestic supply chain or reduce dependence on foreign countries for the critical devices our health care system depends upon.

In addition, the COVID-19 pandemic has shown the significance of advanced manufacturing to help accelerate manufacturing and authorization of innovative and emerging technologies in the U.S. This work is critical for the future of the domestic supply chain and to assure patients and health care providers have timely access to the devices they need during public health emergencies. Advanced manufacturing means devices are made efficiently and are safe, effective, and of high quality, preventing patients from being exposed to substandard devices.

The Devices Program will use the requested funding to strengthen the domestic supply chain through investments in preventive measures, continuing surveillance, and rapid intervention. It will establish a program to identify potential medical product supply short-falls, work with all parties in the ecosystem, including hospitals, distributors, and patients, to mitigate shortages wherever possible. This funding is necessary to stand up this program, identify shortages, and when possible, reduce the impact of shortages and supply chain disruptions in the U.S.

Funding will build a program to manage shortage assessments and mitigations. Expertise will be dedicated to rapidly responding to potential shortage threats and developing plans for mitigation. In addition to working closely with stakeholders, these plans will include flexible regulatory approaches and full transparency with the public. Expertise will also be dedicated to establishing

an Advanced Manufacturing Program to make manufacturing of critical need medical devices more efficient, productive, and resilient through the use of modern, intelligent technologies – such as digitization, computer modeling and simulation, and automation – and to incentivize manufacturing in the U.S. This effort will build on the one-time investments provided in the COVID-19 supplementals.

Funding will also increase the Devices Program's advanced manufacturing clearinghouse efforts to support adoption of digitalization, which will enable access to the data needed to evaluate and monitor the medical device supply chain, as well as the flexibility for rapid design and production changes. Equipping the MedTech industry with these technologies and approaches would provide the industry tools needed to manufacture more efficiently and rapidly, with higher quality, and less cost. This capability is needed to enhance the responsiveness and security of the U.S. medical device supply and enable increased U.S. manufacturing. This request will permit an initial foray into advanced manufacturing clearing house projects to support the adoption of the advanced methods that improve the medical device supply chain.

Through these efforts, FDA will develop a thorough understanding of the medical device supply chain and its inherent risks, including expanding our networks and ensuring data and information is used and shared appropriately to mitigate shortages. In addition, FDA will develop a method for evaluating and acting on the data regarding supply chain interruption and shortages provided to it through the CARES Act, and integrating it with other data sources to more completely understand the potential impact of supply chain disruptions that can inform directed mitigations to offset the disruptions.

The Devices Program would also leverage its existing relationships with stakeholders to deploy mitigations and communicate information about them. Mitigations include the use of alternative technologies and rapid ramp up of production of technologies in short supply by building on one-time efforts undertaken during the COVID-19 pandemic and establishing mechanisms to re-initiate those efforts seamlessly when needed. For example, working with ventilator manufacturers, FDA, NASA, and others, developed a rapidly manufactured ventilator using non-traditional parts thereby not putting any additional stress on the ventilator component supply chain. FDA would also work with the Strategic National Stockpile on purchasing and maintaining critical need devices.

Supplemental funding for the COVID-19 response was an important step in providing the Devices Program resources to support FDA's response to the pandemic. However, this funding is one-time and will not allow for the implementation of a permanent, mature and responsive program to address medical device shortages and U.S.-based manufacturing beyond COVID-19 or for FDA to support the U.S. Government's response to future emergencies. The Devices Program requests additional base funding to develop shortage management capabilities such as proactive assessment of the market and an improved understanding of how medical device availability may impact public health.

These resources will enable FDA to begin to address the critical first steps for establishing a comprehensive program - facilitating increased communication with industry, collaborative knowledge to help identify medical device shortages, and ability to respond to shortages more rapidly when they occur. In return, the Devices Program will be better able to provide more rapid

assessment of potential shortages, increase the efficiency and resiliency in the production of critical need devices, and facilitate the development of well-timed mitigation plans to reduce the risk of shortages from occurring. CDRH is uniquely qualified to perform these activities because the Center is not only responsible for reviewing and authorizing diagnostic and other medical devices, but we also have unique, collaborative relationships that allow us to engage directly with manufacturers, healthcare organizations and other stakeholders.

Advancing the Goal of Ending the Opioid Crisis: (+$2.0 million)
Center: +$2.0 million

The opioid epidemic has only worsened during the COVID-19 pandemic and the nation needs to use every tool at its disposal to address opioid use disorder (OUD). Medical devices play a critical role in FDA's all-hands on deck approach to confronting the opioid crisis. In particular, digital health technologies are being developed to identify those at risk for or to diagnose those with OUD as well as to treat or manage the disorder. CDRH is requesting $2 million to advance the development, evaluation, and market authorization of digital health medical devices that help address OUD. Funds will be used for actions that include establishing a streamlined framework for FDA market authorization based on evolving science and technology, enabling infrastructure to enhance capabilities to leverage real world data to support evaluation of OUD digital technology, and incentivizing the development of new safe, effective, high-quality digital risk assessments, diagnostics, and therapeutics, such as through a design-a-thon and other crowdsourcing measures.

Data Modernization and Enhanced Technologies – Medical Product Safety (+$2.8 million)

Center: +$2.8 million

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CDRH, $2.8 million is requested to support the Devices Program's Digital Transformation initiative.

FDA needs modern systems to support patients and the ecosystem. Timely patient and consumer access to new, safe, innovative devices and continued safeguards once available depend on FDA having modernized IT systems. Through the Devices Program's Digital Transformation initiative, FDA will be able to continue building an integrated knowledge management system and portal using modern, agile information technology systems with secure cloud-based data storage. This investment will enable safety issues to be better monitored throughout the total life cycle of the device from bench testing to premarket clinical trials to analysis of postmarket adverse events through leveraging real-world evidence. FDA will also expand its capability to quickly evaluate new questions, using laboratory research and other methods. This capability to better leverage data in near real time is essential for implementing FDA's new approaches for digital health technologies, as well as to support critical, ongoing programs for breakthrough devices, use of real-world evidence, and cybersecurity.

As part of this transformation, FDA will establish customer-friendly interfaces with industry, patients, and providers. These platforms will foster greater and more transparent interactions between FDA and its customers, including providing industry with the ability to track their premarket submissions. Funding for this initiative would also support building reliable,

connected environments that allow reviewers and users access to integrated data, tools, and knowledge. This transformation will reduce duplicative efforts and create one integrated environment for reviewers to analyze complete information to more efficiently process applications and respond to regulatory questions. Funding will also be used to recruit technical experts to ensure and maintain 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. To ease regulatory burdens and reduce uncertainty, FDA will continue to develop a regulatory paradigm for these products, build greater capacity to evaluate and recognize third party certifiers, and create a cybersecurity unit to complement the advances in software-based devices as well as to aid in review of cybersecurity vulnerabilities affecting the more traditional, hardware and software-based medical devices.

Implementing these technology and regulatory improvements are essential for improving the health and quality of life of patients while assuring critical safeguards. Overall, these investments will make the review of device applications and postmarket surveillance significantly more efficient and provide more timely patient access to innovative, safe, effective, high-quality devices.

Crosscutting (+$17.5 million / 19 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data: (+$6.0 million / 6 FTE)
Center: +$4.8 million / 5 FTE

Field: +$1.2 million / 1 FTE

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within CDRH, $4.8 million is requested to support the Enterprise Technology and Data crosscutting effort, and $1.2 million is for ORA.

Capacity Building: (+5.8 million / 3 FTE)
Center: +$4.6 million / 2 FTE

Field: +$1.3 million / 1 FTE

The FY 2022 Budget includes $40.3 million to support centrally-administered services to support critical, high-priority Capacity Building activities.

Inspections: (+$3.0 million / 10 FTE)
Field: +$3.0 million / 10 FTE

The FY 2022 Budget includes $18.8 million for inspections. ORA will increase site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID-19 related delays, and the Budget includes $3.0 million for the Field portion of Devices and Radiological Health.

Pay Costs: (+$2.7 million / 0 FTE)
Center: +$1.9 million / 0 FTE

Field: +$789,950 / 0 FTE

The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

USER FEES (+4.9 MILLION)

Center: +4.6 million

Field: + $311,292

The Devices Program request includes an increase of $4.9 million for user fees, 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
253203: Percentage of received Original Premarket Approval (PMA), Panel-track PMA Supplement, and Premarket Report Submissions reviewed and decided upon. (Outcome)	FY 2018: 97% in 180 days Target: 90% in 180 days (Target Exceeded)	90% in 180 days	90% in 180 days	Maintain
253204: Percentage of 180 day PMA supplements reviewed and decided upon within 180 days. (Outcome)	FY 2018: 100% 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 2018: 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 2018: 80% in 150 days Target: 50% in 150 days (Target Exceeded)	65% in 150 days	70% 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 2020: 100.0% Target: 65% (Target Exceeded)	65%	65%	Maintain
252203: Percent of total received Code Blue MDRs reviewed within 72 hours during the year. (Output)	FY 2020: 88% Target: 90% (Target Not Met)	NA	NA	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
252223: Percent of total received Code Blue MDRs reviewed within 10 days during the year. *(Output)*	FY 2020: xx% (New Measure Historical Baseline)	80%	90%	+10%
254203: Percentage of time CDRH meets the targeted deadlines for on-time recall classification (Output)	FY 2020: 85% Target: 85% (Target Met)	85%	85%	Maintain
252101: Number of technical analyses of postmarket device problems and performance. (Output)	FY 2020: 63 Target: 50 (Target Exceeded)	50	50	Maintain
253207: Number of technical reviews of new applications and data supporting requests for premarket approvals. (Output)	FY 2020: 2,183 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 2020: 99.6% 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 2020: 88.5% 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 2020: 84.1% 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 2018, 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. During FY 2020, the Agency strived to have all Code Blue MDRs read within 72 hours of receipt. CDRH did not meet the FY 2020 target of having 90% of the Code Blue reports read within 72 hours. Since the CDRH's reorganization, many staff acquired new reviewer responsibilities, requiring additional training with steep learning curves. Additionally, the COVID pandemic significantly impacted CDRH Staff workloads. An increase in the number of Emergency Use Authorization (EUA) were received by CDRH and the Center needed to shift resources and workloads to ensure that coverage of this unprecedented emergency was addressed. In support of this effort, MDR reviewers were asked to conduct other critical tasks associated with EUA devices, in addition to the review of adverse events. For effective workload management, CDRH changed their Code Blue performance expectations from 72 hours to 10 days, and has created a new performance measure to reflect this change.

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. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA's ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

CDRH Workload and Outputs	FY 2019 Actuals	FY 2020 Estimate	FY 2021 Estimate	FY 2022 Estimate
Original PMAs and Panel-Track Supplements (without Advisory Committee input)				
Workload [1]	56	71	65	65
Total Decisions [2]	63	59	61	62
Approved [3]	43	53	46	46
Original PMAs and Panel-Track Supplements (with Advisory Committee input)				
Workload	1	1	2	2
Total Decisions [2]	5	1	3	3
Approved	2	1	2	2
Modular PMAs				
Workload	90	75	77	77
Actions [4]	71	71	75	75
180-day PMA Supplements				
Workload	198	179	191	191
Total Decisions [5]	185	192	193	193
Approved	176	180	180	180
Real Time PMA Supplements				
Workload	375	367	361	361
Total Decisions [6]	354	352	346	346
Approved	314	341	323	323
510(k) Premarket Notifications				
Workload	3,776	3,754	3,754	3,754
Total Decisions [7] (SE & NSE)	3,046	3,293	3,293	3,293
Cleared [9] (SE)	2,929	3,143	3,143	3,143
Humanitarian Device Exemptions (HDE)				
Workload	6	1	3	3
Total Decisions [2]	5	2	3	3
Approved	3	1	2	2
Investigational Device Exemptions (IDE)				
Workload	309	352	352	352
Total Decisions [8]	311	344	344	344
Approved	161	202	202	202
Investigational Device Exemption Supplements				
Workload	1,799	1,798	1,798	1,798
Closures [10]	1,737	1,788	1,788	1,788
Pre-Submissions				
Workload	3,253	3,397	3,562	3,737
Closures [11]	3,228	3,409	3,574	3,749
De Novo				
Workload	62	61	61	61
Total Decisions [14]	51	50	50	50
Granted	21	25	25	25
Standards				
Total Standards Recognized for Application Review	1,385	1,395	1,425	1,455
Medical Device Reports (MDRs) [12]				
Reports Received	1,948,641	2,213,766	2,656,519	3,187,822
Analysis Consults [13]	627	590	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

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

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***1,084***	***100***	***2,546***
Bioresearch Monitoring Program Inspections	136	17	300
Pre-Market Inspections	26	4	60
Post-Market Audit Inspections	7	2	60
GMP Inspections	622	75	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	308	37	750
Domestic Radiological Health Inspections	27	4	50
Domestic Field Exams/Tests	18	2	100
Domestic Laboratory Samples Analyzed	82	72	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***175***	***5***	***613***
Foreign Bioresearch Monitoring Inspections	9	0	14
Foreign Pre-Market Inspections	12	0	30
Foreign Post-Market Audit Inspections	0	0	20
Foreign GMP Inspections	152	5	550
Foreign MQSA Inspections	0	0	14
Foreign Radiological Health Inspections	13	0	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***1,259***	***105***	***3,159***
IMPORTS			
Import Field Exams/Tests	16,641	16,650	19,800
Import Laboratory Samples Analyzed	303	310	670
Import Physical Exam Subtotal	**16,944**	**17,000**	**20,470**
Import Line Decisions	22,512,049	25,521,999	27,308,539
Percent of Import Lines Physically Examined	0.08%	0.08%	0.07%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***6,089***	***7,020***	***7,880***
Inspections (MQSA) by State Contract	6,071	7,000	6,800
GMP Inspections by State Contract	18	20	20
State Contract Devices Funding	$194,122	$200,000	$286,443
State Contract Mammography Funding	$10,593,830	$107,000	$11,240,003
Total State Funding	**$10,787,952**	**$11,297,711**	**$11,526,446**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***7,348***	***7,125***	***11,039***

[1] The FY 2020 actual unique count of foreign inspections includes 2 OGPS inspections (1 for China and 1 for India)

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

[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] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
National Center for Taxological Research (Budget Authority)....	66,712	66,702	66,712	76,994	10,282
FTE……....	276	296	276	277	*1*

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. 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 and regulatory data using bioinformatics and artificial intelligence (AI).
- Provide data surrounding understudied populations such as those belonging to the perinatal period (the period briefly before and after birth).

The following selected accomplishments demonstrate NCTR's delivery of its regulatory and public health responsibilities within the context of current priorities[106]. NCTR generates an extremely large amount of data to support the FDA regulatory centers and its scientists are committed to harnessing the power of this data to help FDA make better-informed regulatory decisions. The public health goal of NCTR is to conduct research to ensure the safety and efficacy of FDA-regulated products used in America and around the world.

COVID-19 RESPONSE

FDA continues to be at the forefront of the United States' response to the challenges associated with COVID-19. Many actions (such as Emergency Use Authorizations and Guidances[107]) have

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

[107] For more information, please visit: https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19#eua

been taken to address and combat the epidemic. NCTR was one of the first entities within FDA to initiate research on COVID-19 in March 2020. Since the epidemic began, NCTR has taken many actions to support FDA's regulatory role, some of which were supported by FDA's COVID Supplemental Funding[108] issued by Congress. Below are a few examples of NCTR's COVID-19 response:

- In March 2020, the NCTR Division of Microbiology initiated a project to develop an approach to rapidly indicate effectiveness of COVID-19 therapeutic treatments. Preliminary results are expected in FY 2021.

- NCTR leadership organized weekly/bi-weekly remote meetings to address the COVID-19 pandemic. Over 100 participants met routinely to maximize collaborative efforts between FDA/NCTR researchers and those from regional university/clinical facilities with critical biosafety level-3 (BSL-3) capability.

- NCTR initiated an AI project to support efforts to effectively treat COVID-19 patients. This project is in collaboration with the FDA Office of the Chief Scientist, Medical Countermeasures Initiative. Using computational drug-repositioning principles with AI, the project aims to systematically survey and prioritize approved or investigational drugs for their potential use to treat COVID-19. This research is projected to extend into FY 2022.

- The NCTR Division of Biochemical Toxicology developed methods to detect SARS-CoV-2 RNA in wastewater and is applying this methodology to selected metropolitan areas in Arkansas to monitor the presence and the extent of the COVID-19 epidemic. This method helps estimate viral spread at the community level without individual testing and may serve as an early warning tool for increased circulation of the virus.

- NCTR developed an AI-powered network pharmacology approach to comprehensively explore the opportunity of existing drugs for their potential to treat COVID-19 with over 3 million data points. Recently, the repurposing candidates were further prioritized for treating COVID-19 patients with different severity based on the COVID-19 patients' genomics profiles.

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. NCTR research focusing on oversight include projects in the areas of artificial intelligence (AI) and machine learning, cannabis and cannabis-derived products, and opioids.

[108] For more information, please visit: https://www.fda.gov/news-events/press-announcements/fda-signing-covid-19-emergency-relief-bill-including-landmark-over-counter-drug-reform-and-user-fee

Artificial Intelligence (AI) and Machine Learning

AI advances bioinformatics tools, computer software, and data science, which provide FDA tremendous opportunities to modernize tools and technologies that will assist in fulfilling the FDA mission. NCTR looks to capitalize on the variety of scientific opportunities available and realizes the major influence of AI on regulatory science research and regulations in the coming years.

Support for research and development of AI technologies at FDA can be found in FDA's Artificial Intelligence/Machine Learning Action Plan[109] and in Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS)[110] document. FDA data are unique with tremendous value for regulatory application and public health. Using advanced AI technologies, the value of these unique datasets to improve public health and fulfill the FDA review mission can be realized.

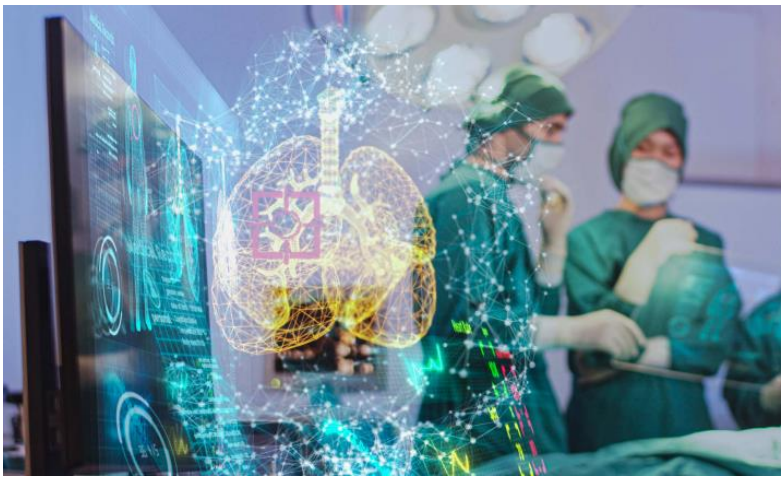


Figure 1: "Artificial intelligence (AI) and machine learning (ML) technologies have the potential to transform health care by deriving new and important insights from the vast amount of data generated during the delivery of health care every day."[4]

Applications or research areas of AI include:

- Personalized diagnostics or therapeutics
- Regulatory decision-making
- Early disease detection
- More accurate diagnosis
- Identification of new observations or patterns on human physiology
- Smarter food safety

NCTR continues to explore AI use-cases that serve FDA priorities. For example, in collaboration with FDA's Office of Regulatory Affairs (ORA) and Center for Veterinary Medicine (CVM), NCTR is designing and developing 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 risks from food and feed stuffs while

[109] For more information, please visit: https://www.fda.gov/news-events/press-announcements/fda-releases-artificial-intelligencemachine-learning-action-plan

[110] For more information, please visit: https://www.fda.gov/media/145001/download

decreasing costs associated with sample collections. A paper summarizing initial findings can be found in the *International Journal of Environmental Research and Public Health*[111].

Another ongoing AI-related study is in collaboration with the FDA Office of Women's Health (OWH). This project looks to develop an artificially intelligent virtual pregnant-woman modeling suite to support regulatory decisions. The modeling suite will save labor, resources, and time, and provide a consistent modeling and simulations framework across all FDA Centers to evaluate pregnant women's health outcomes. In addition to serving OWH's mission, the project also aligns with the FDA strategic priorities specifically with that of the 21st Century Cures Act. Furthermore, the proposed project better positions FDA and OWH among global federal partners who are similarly evaluating the utility of novel computational approaches as animal-free toxicity testing alternatives to address emerging public health concerns. An FY 2020 publication related to this research can be found in *Current Opinion in Toxicology*[112].

Cannabis and Cannabis-Derived Products such as Cannabidiol (CBD)

FDA recognizes the potential opportunities that cannabis or cannabis-derived compounds may offer and acknowledges the significant interest in these possibilities. However, FDA is aware that some companies are marketing products containing cannabis and cannabis-derived compounds in ways that violate the Federal Food, Drug, and Cosmetic Act (FD&C Act) and that may put the health and safety of consumers at risk[113]. Amid these safety concerns, FDA approved Epidiolex® —a CBD oral solution developed for the treatment of tuberous sclerosis complex and for seizures associated with two rare and severe forms of epilepsy in patients one year of age and older. Despite that approval, much is still unknown about the potential toxicities related to cannabis and cannabis-derived products. NCTR has several ongoing collaborative research projects that will generate data to evaluate the potential dangers associated with these substances.

FDA's Center for Drug Evaluation and Research (CDER) has received numerous applications for investigational new drugs (INDs) that contain cannabis. There is little information on the potential hazards associated with the consumption of smoke or vapors generated from cannabis; however, a review of current literature and reports has suggested that cannabis may be contaminated with heavy metals (e.g., lead) and microbiological organisms, such as bacteria, yeast, and mold. Those contaminants may harm individuals that inhale cannabis smoke or vapors, especially immune-compromised individuals. CDER's Office of Pharmaceutical Quality asked NCTR to identify and quantitate heavy metals and microbial species that may be present in cannabis raw material, and in cannabis vapors and cigarette smoke. This research will assist CDER's regulatory decision-making by providing the quality information needed for incoming

[111] For more information, please visit: https://pubmed.ncbi.nlm.nih.gov/31671576/

[112] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S2468202020300176

[113] For more information, please visit: https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd

cannabis-drug master files (DMFs) and will provide a framework for the quality considerations of INDs.

In collaboration with FDA's Office of the Chief Scientist, researchers in NCTR's Division of Neurotoxicology continue to examine the effects of CBD exposure during development. Effects from this early exposure will be evaluated throughout adulthood and include neurocognitive effects. This will create valuable information that currently does not exist or is unavailable publicly. NCTR expects the data from this study to aid FDA in regulatory decision-making and to help the public make healthier decisions regarding the use of CBD-containing products. This research is projected to be completed in FY 2023.

NCTR is also performing CBD research in collaboration with the Center for Food Safety and Applied Nutrition (CFSAN) and CVM through the CBD Policy Workgroup (led by the FDA's Office of the Commissioner). These recently initiated projects cover a variety of topics related to CBD, such as:

- Evaluation of male-reproductive toxicities induced by CBD
- Pharmacokinetics (movement of a substance within the body) of CBD by skin exposure
- Pharmacokinetics of CBD by oral exposure

Opioids

Drug overdose is the leading cause of death of Americans under the age of 45, with over half of these deaths attributable to opioids, according to data from the Center for Disease Control (CDC)[114]. The FDA Opioid Action Plan[115] provides comprehensive guidance for reestablishing safe-use standards for these products. In support, NCTR is conducting research related to opioid addiction and toxicity potential.

NCTR, in collaboration with CDER, continues to generate data on exposure of developing brain cells to opioids during perinatal development. The opioids hydrocodone, codeine, oxycodone, morphine, methadone, buprenorphine, fentanyl, and hydromorphone were evaluated on neural precursor cells. Preliminary results suggest that tested opioids have minimal effect on early growth and development. Continued experiments will focus on exposure of stem cells to investigate whether cells at different stages of development have differing sensitivities.

NCTR research continues to use imaging technologies to reveal the brain mechanisms of the abuse-related effects of opioids. 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

[114] National Vital Statistics System. Atlanta, GA: CDC, National Center for Health Statistics; 2017. Available at: https://www.cdc.gov/injury/wisqars/LeadingCauses.html

[115] For more information, please visit: https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm

explain an opioid's mechanism of action. Preliminary study results were presented at the Society for Birth Defects Research and Prevention's Annual Meeting in June 2020.

Additionally, NCTR is using computational models to assess the structure of addictive chemicals. 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, cannabinoids, and other structurally diverse chemicals. This technology could be used to prioritize the testing of chemicals with strong addiction potentials (such as synthetic opioids and cannabinoids), thus shortening the FDA regulatory-review process. A related FY 2020 publication can be found in *Archives of Toxicology*[116].

An innovative opioid-related project will utilize in silico (computer-based) methods to create the Opioid Agonists/Antagonists Knowledgebase (OAK). OAK will be used to assist the review and development of alternative pain-management products. FDA recently developed the Public Health Assessment via Structural Evaluation (PHASE) methodology. Combining PHASE with OAK will help FDA improve evaluation of opioid drug products. This project is in collaboration with the National Center for Advancing Translational Sciences (NCATS) and CDER. The project is expected to continue through FY 2023. A manuscript was recently submitted to the *Journal of Chemical Information and Modeling* for publication.

IMPROVING 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. To improve access, NCTR activities include: Perinatal Health Center of Excellence, pediatric medicine, maternal medicine, and antimicrobial resistance (AMR) and the microbiome.

Perinatal Health Center of Excellence (PHCE),[117] Pediatric Medicine, and Maternal Medicine

The focus of NCTR's Virtual Center of Excellence for Perinatal and Maternal Pharmacology and Toxicology—also known as the FDA Perinatal Health Center of Excellence (PHCE) —is on the perinatal period (the period-of-time including pregnancy, child birth, and infant/child development) which is a vastly understudied population. PHCE works to fill knowledge gaps about safety, efficacy, or potential toxicity that currently exist during the perinatal period, with the goal to strengthen the scientific basis of decision-making for FDA-regulated products used during pregnancy and in premature infants, newborns, and children.

Current PHCE projects have primary investigators representing CDER, CBER, CFSAN, CVM, and NCTR. A recently completed PHCE-funded study was a collaboration between CFSAN and NCTR scientists. This study examined polyfluorinated alkyl substance (PFAS)-based

[116] For more information visit: https://link.springer.com/content/pdf/10.1007/s00204-020-02684-8.pdf

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

compounds. PFAS is used in intravenous tubing on neonates in intensive care, and therefore it is important to better understand this substance and how it may affect the neonate population. The project studied specifically the persistence of PFAS-based compounds in various foods. These compounds are found in grease-proofing agents and can be used as stain- and waterproof-coatings for surfaces. A paper describing this work can be found in *Toxicology and Applied Pharmacology*[118].

Other PHCE research topics include, but are not limited to:

- Neonatal immune responses to vaccines
- Computer-based pregnancy models
- COVID-19 effects on pregnancy, prenatal, and postnatal development
- Drug labeling associated with pregnancy

Read more information about the PHCE and its progress.

Since many drugs and other medical products provided to pregnant women, neonates, and infants are used off-label, NCTR research is designed to stimulate robust efforts to provide faster, less expensive, and more predictive approaches and models, leading the way to improved safety and/or efficacy of FDA-regulated products in these susceptible populations. One such study looks at the long-term consequences of early-life exposure to anesthesia. While it is known that early-life exposure to anesthesia can cause neuronal degeneration, no study has directly studied the associated lack of oxygen and its role in the damage. This study will provide better quality data for FDA to use in its regulatory mission and possibly hasten the development of safer anesthesia regimens for use in a clinical setting.

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.

Figure 2: Photo of drug-resistant Salmonella/Centers for Disease Control and Prevention

Continuing AMR-related projects focus on bacterial plasmids (cellular structures which often provide bacteria with genetic advantages) and their role in antimicrobial resistance and increased pathogenesis. 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* and related pathogens. These studies build on previous NCTR efforts

[118] For more information, please visit: https://pubmed.ncbi.nlm.nih.gov/31923437/

examining the potential for increased virulence and refining our understanding of the plasmid-associated factors. Publications related to this project can be found in *BMC Microbiology*[119] and in *Genes*[120].

In FY 2020, NCTR scientists in the Division of Microbiology developed a database and analysis tool in collaboration with CVM scientists. These tools will aid FDA in understanding and controlling *Salmonella enterica* in foods and feeds. Genes with different functions, such as antimicrobial resistance, heavy metal/ biocide resistance, virulence and conjugation transfer, are currently being characterized. A review paper describing this work can be found in *Genes*[121].

Microorganisms associated with the human gut are known collectively as the "microbiome" or "microbiota" and play an important role in health and disease. NCTR uses the latest genomic and bioinformatic approaches to determine the interactions between the human microbiome and xenobiotics (antimicrobial agents, nanomaterials, food contaminants, and other FDA-regulated products). For example, the use of veterinary antimicrobial agents in food-producing animals may result in continuous human exposure to low levels of antimicrobial residues in food as part of their daily diet[122]. 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. Several NCTR scientists participated in a Health and Environmental Sciences Institute (HESI)-sponsored workshop on "The Gut Microbiome: Markers of Human Health, Drug Efficacy and Xenobiotic Toxicity." The recommendations from this workshop are published in *Toxicological Sciences*[123].

Some of NCTR's research accomplishments in the area of the microbiome include:

- Translating results from animal models to humans that come from studies on the interaction of any xenobiotics is very important in the xenobiotic safety assessment. This study evaluated the intestinal toxicity of corn oil (a commonly used vehicle for water insoluble drugs/xenobiotics) while using the two most common rodent models (rat and mice). The results illustrate how selection of the animal model and the vehicle/carrier can affect the results. This study is published in the journal *Toxicological Sciences*[124].

[119] For more information, please visit: https://bmcmicrobiol.biomedcentral.com/articles/10.1186/s12866-020-02008-x

[120] For more information, please visit: https://www.mdpi.com/2073-4425/11/11/1307

[121] For more information, please visit: https://pubmed.ncbi.nlm.nih.gov/33158112/

[122] For more information, please visit: https://onlinelibrary.wiley.com/doi/full/10.1111/jvp.12892

[123] For more information, please visit: https://academic.oup.com/toxsci/article/176/1/1/5862611?login=true

[124] For more information, please visit: https://academic.oup.com/toxsci/advance-article/doi/10.1093/toxsci/kfaa177/6017185

- NCTR scientists reported sex-dependent effects of silver nanoparticles on the gut-associated immune status and intestinal-barrier function using ex vivo human-intestinal tissues. A publication describing this work can be found in the *International Journal of Molecular Sciences*[125]. The same ex vivo model was also used to perform a safety assessment of carbon-based nanomaterials; a project initially funded by a Broad Agency Agreement (BAA) between the Arkansas Research Consortium in Nanotoxicity and FDA.

- In collaboration with the University of Arkansas for Medical Sciences, NCTR studied the sex-dependent effects on liver inflammation and gut microbiome that is associated with disease (dysbiosis) after continuous developmental exposure to the environmental contaminant trichloroethylene. More information can be found in *Frontiers in Pharmacology*[126].

- To protect consumers from foodborne pathogens, novel techniques are used for food storage. One technique is the use of silver or silver nanoparticles in food-contact materials (FCM). NCTR scientists initiated a study to assess the antimicrobial effects of FCM containing silver. The results showed that the amount of silver in each product was similar, although, migration varied considerably. Details of this study can be found in the journal *Food and Chemical Toxicology*[127].

- NCTR is also conducting a study which explores and provides research data on how fecal microbial transplantation (FMT) is an effective treatment for bacterial infections such as *Clostridioides difficile*. Recently, NCTR scientists observed that FMT bacteria affected the genetic mechanisms in human-intestinal cells infected with *Clostridioides difficile*. The understanding gained from these experiments provides new options for how to prepare a defined probiotic product to replace FMT and the risks of antimicrobial resistance it poses.

- NCTR is collaborating with CDER on a study that is assessing how nanoscale-size titanium oxide and zinc oxide in sunscreens interacts with the skin microbiome. Cosmetics are used by over 95 million U.S. women who are 18+ years old and the use of nanomaterials in cosmetic products is rapidly increasing. There are potential risks and 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 nanomaterials in cosmetics and provide data for safety assessments.

[125] For more information, please visit: https://pubmed.ncbi.nlm.nih.gov/33374948/

[126] For more information, please visit: https://www.frontiersin.org/articles/10.3389/fphar.2020.569008/full

[127] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S0278691520306189

SUPPORT SCIENCE-BASED DECISION-MAKING

NCTR research brings modern scientific tools into FDA to maintain FDA's gold standard for science-based product review, regulatory decision-making, 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 greater 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 regulations more efficient. The following section provides examples of NCTR's research in bioinformatics, nanotechnology, and NCTR's involvement with the Global Summit on Regulatory Science.

Bioinformatics

Bioinformatics uses computer software tools to develop and improve methods for storing, managing, and analyzing large quantities of biological data. NCTR develops, provides training for, and makes bioinformatics tools available to FDA and the global research community. FDA must have the software and database tools to manage the large amount of scientific data generated to improve product development, safety assessments, and risk analysis. Computer-based methods (in silico) are also important since, in some cases, they can be used as an alternative to animal methods (in vivo).

NCTR has developed a variety of bioinformatics datasets and tools for public use and continues to design and develop more and better tools. Among them, DILIrank is the largest publicly available annotated dataset of FDA-approved drugs for the study of drug-induced liver-injury (DILI) potential. Both the Endocrine Disruptor Knowledge Base (EDKB) (a database of about 3,000 chemicals that interfere with endocrine systems) and the Estrogenic Activity Database (part of EDKB) have been widely used by the research community and incorporated into larger government projects.

The FDALabel database is a web-based application used to perform full-text and customizable searches of over 130,000 human prescription, biological, over-the-counter (OTC), and animal-drug labeling documents. Recent publications related to FDALabel can be found in *Nature Biotechnology*[128] and *Drug Discovery Today*[129].

Differences in genes can make someone more or less likely to benefit from a drug, suffer side effects, or require a dose that is different from other people. Such pharmacogenomic (PGx) information can be used to improve the medical decision-making process and minimize severe adverse drug reactions. NCTR and CDER scientists, in collaboration with Virginia Commonwealth University, developed the Database of Pharmacogenomic Information in Ethnic Minority Populations (dbPGxEMP) to connect drugs and PGx biomarkers from drug labeling

[128] For more information, please visit: https://www.nature.com/articles/s41587-020-00751-0

[129] For more information, please visit: https://www.sciencedirect.com/science/article/pii/S1359644620300490?via%3Dihub

with allele frequencies of related genetic variations in different ethnic minority populations. A paper describing this work can be found in *Pharmaceutics*[130].

A new bioinformatics project uses AI-based Natural Language Processing for FDA documents, specifically FDA labeling documents. FDA has historically generated and continues to generate a variety of documents during the product-review process, leading to a large inventory of review documentation. Applying AI to the FDA documents allows FDA to harness scientific opportunities, helping to:

- Improve the agency's operation
- Develop science-based regulation of products containing AI components
- Communicate with the public for improved transparency.

In other bioinformatics-related research, NCTR scientists will also focus on developing techniques to predict drug-induced liver injury (DILI). NCTR, in collaboration with CDER, will benchmark and compare various computational methods to predict DILI-related factors in drug products. The goal of this project is to develop more accurate and reliable predictive models for DILI to support regulatory decisions during the review process, specifically the Investigational New Drug phase.

Nanotechnology

The NCTR/ORA Nanotechnology Core Facility (NanoCore) supports collaborative research within FDA and research between FDA and other government agencies and universities. This work provides information on nanomaterial characterization and the safety of products containing nanomaterials in FDA-regulated products. This research data is also used in staff and reviewer training and in establishing standards for use by stakeholders responsible for developing nanotechnology products. Nanomaterials can have different chemical, physical, or biological properties than their conventionally-scaled counterpart materials that are used in many products regulated by FDA. To date, over 700 drug products that contain nanomaterials have been submitted to FDA, with over 70 products approved for clinical use.

Studies being conducted in the NanoCore will help FDA to better understand the attributes of these emerging materials, their safety, and efficacy. Examples are listed below:

- In coordination with CDER, NCTR is studying how generic drug products containing nanomaterials disseminate to different parts of the body in animal models to determine their safety and efficacy.
- Partnering with OWH, NCTR is evaluating the potential migration of silver nanoparticles and their toxicity to the vaginal tissue when used in feminine-hygiene products.

[130] For more information, please visit: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693750/

Additionally, the FDA scientists are studying sex-based differences in immunotoxicity of nanomaterial.

- With the Office of the Chief Scientist (OCS) Coordinated Outbreak Response and Evaluation (CORES) grant support, NCTR is evaluating the immunotoxicity of nanomaterial generated from prosthetic implants after radiation exposure.

- A major project with significant impact to help industry is the collaborative-consensus standards development with support from the National Toxicology Program (NTP) and stakeholder involvement from academia and industry, NCTR is developing standards to include characterization methods to ascertain product quality, consistency, and in vitro safety. With the goal of providing common ground for product developers and FDA to help facilitate the development of FDA products containing nanomaterials. This is a major project with significant impact to help industry have collaborative consensus-standards development. These standards are identified by FDA and international regulatory agencies as a priority and are developed through the American Society for Testing and Materials (ASTM) E56 subcommittee on Nanotechnology and ISO Technical Committee 229. To date, two work items FDA developed, *Standard Practice for Performing Cryo-Transmission Electron Microscopy of Liposomes* and *Standard Test Method for Quantitative Measurement of the Chemoattractant Capacity of a Nanoparticulate Material in vitro* became standards in February 2019 and January 2020, respectively, and are available through ASTM International. Additional work items on nanotechnology are under development in the Nanocore and are going through the consensus-standard process at ASTM International E56 for quality assurance and testing for biocompatibility.

The FDA Nanotechnology Task Force (NTF), chaired by Dr. Anil Patri, Director of the NCTR Nanocore, published a comprehensive progress report, Nanotechnology—Over a Decade of Progress and Innovation, in July 2020. The report that highlights the current state of science in the area of nanotechnology and FDA's progress at FDA in research, infrastructure, guidances, standards, and inter-agency and international engagement.

FDA's Nano Day Virtual Research Symposium: "A Decade of Progress and Innovation in nanotechnology since 2007 and was featured in an FDA Grand Rounds public webinar which was recorded and publicly available.

Read more about nanotechnology at NCTR and nanotechnology at FDA.

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 eleventh year, the Global Summit's goal is to engage the global community and harmonize research strategies via collaborations that aim to build knowledge, promote regulatory science, define research needs, and strengthen product safety worldwide by training regulatory scientists. The Global Summit is led by the Global Coalition for Regulatory Science 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 Global Summit on Regulatory Science-2020 was held virtually on September 28-30, 2020 and was co-hosted by NCTR and National Center for Advancing Translational Sciences (NCATS). The theme of the 10th Global Summit was "Emerging Technologies and Their Application to Regulatory Science" with over 60 presentations and speakers from 14 different countries, including scientific leadership from FDA, National Institutes of Health (NIH), National Academy of Sciences (NAS), European Food Safety Authority (EFSA), Joint Research Centre (JRC), and Swissmedic to name just a few examples. Topics covered included:

- Emerging Technologies for the Safety Assessment of Food, Drugs, and Personal Care Products
- Approaches to Standardize and Validate Emerging Technologies for Regulatory Application
- Challenges and Opportunities of Emerging Technologies and Alternate Methods for Decision Making.

The 2021 GSRS is tentatively scheduled to be held virtually in October 2021. To stay abreast of upcoming meetings and for more information, please visit www.fda.gov/globalsummit.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2018 Actual	$64,512,000	$64,512,000	---
FY 2019 Actual	$66,712,000	$66,712,000	---
FY 2020 Actual	$66,702,000	$66,702,000	---
FY 2021 Enacted	$66,712,000	$66,712,000	---
FY 2022 President's Budget	$76,994,000	$76,994,000	---

BUDGET REQUEST

The FY 2022 President's Budget provides $76.9 million, an increase of $10.3 million compared to the FY 2021 Enacted, which is all Budget Authority.

The FY 2022 President's 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 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 biomarkers of toxicity.

These research areas include but are not limited to: COVID-19 Response, Artificial Intelligence and Machine Learning, Cannabis and Cannabis-Derived Products such as Cannabidiol (CBD), Opioids, Perinatal Health Center of Excellence (PHCE), Pediatric Medicine, and Maternal Medicine, Antimicrobial Resistance (AMR) and the Microbiome, Bioinformatics, and Nanotechnology. This research is collaborative 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

Food Safety: (+$900,000)

New Era of Smarter Food Safety: (+$750,000)
Center: +$750,000

NCTR will use funds to support FDA's New Era of Smarter Food Safety initiative to achieve the Administration's vision of a strong, reliable food safety system that also sustains the economic health of all segments of America's food industry. NCTR will focus research activities on the development of data-driven tools to increase access to data and information to better understand foodborne pathogens.

Emerging Chemical and Toxicological Issues: (+$150,000)
Center: +$150,000

NCTR will use these funds for Emerging Chemical and Toxicological Issues, in coordination with CFSAN. Specifically, NCTR will use these funds to develop research activities focused on the detection of novel sources, such as micro/nanoplastics found in foods.

Medical Product Safety: (+$7.5 million)

Predictive Toxicology Roadmap: (+$7.5 million)
Center: +$7.5 million

NCTR will utilize the funds to address important questions of validation and regulatory trust-building for the new alternative paradigms, which are key to enable the implementation of the strategies articulated in the FDA Predictive Toxicology Roadmap. Working in close collaboration with the product centers on study selection and design, NCTR will conduct studies aimed at appraising side-by-side the value of guideline and alternative testing paradigms.

Crosscutting: (+$1.8 million / 1 FTE)

Data Modernization and Enhanced Technologies – Enterprise Technology and Data (+$515,000 / 1 FTE)

The FY 2022 Budget includes $75.9 million to support data modernization by building core programs and infrastructure aligned to the specific needs in both Foods and Medical Product programs as well as FDA's enterprise technology capabilities. Within NCTR, $515,000 is requested for an Agency-wide centralized enterprise data modernization effort to strengthen the common data infrastructure established through the Technology Modernization Action Plan (TMAP) and Data Modernization Action Plan (DMAP).

Pay Costs: (+$402,000)
The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

Capacity Building: (+$916,000)
The FY 2022 Budget includes $40.3 million to support centrally-administered services to support critical, high-priority Capacity Building activities. Within NCTR, $916,000 is requested for these efforts.

PERFORMANCE

NCTR's performance measures focus on research to advance the safety of FDA-regulated products, to develop an FDA science base for alternative assays, and perinatal and maternal medicine solutions to protect and improve the health of the American public as represented by the following table:

Measure	Most Recent Result / Target for Recent Result	FY 2021 Target	FY 2022 Target
263103: Conduct translational and regulatory research to advance the safety of products that FDA regulates. (Output)	FY 2020: A method to detect *Burkholderia cepacia* in non-sterile pharmaceutical products and water was developed. A publication can be found in the *Journal of Industrial Microbiology and Biotechnology*. (Target Met) FY 2020: Data generation regarding the toxicity of small molecule kinase inhibitors was completed. A review manuscript was published in *Expert Opinion on Drug Metabolism & Toxicology*. (Target Met)	Finalize data regarding 3D molecular modeling of opioids and other chemicals. Provide preliminary results on the perinatal developmental toxicity and neurotoxicity of inorganic arsenic (present in foods) exposure using a zebrafish model.	In collaboration with the Office of the Chief Scientist, provide preliminary data on CBD exposure in the developing brain.
263201: Develop science base for supporting FDA regulatory review of new and emerging technologies. (Output)	FY 2020: In collaboration with CBER, NCTR scientists developed a safety assessment for gene editing therapies that are pending clinical trials. The findings were published in *Nature Communications*. (Target Met)	Report preliminary results on development of Alzheimer's disease-on-a-chip technology as a tool for toxicological screening of FDA-regulated products as reviewed and approved by the NCTR Director.	Initiate the development of an artificially intelligent virtual pregnant woman modeling suite to support regulatory decisions. Report preliminary findings related to COVID-

Measure	Most Recent Result / Target for Recent Result	FY 2021 Target	FY 2022 Target
			19 effects on pregnancy and prenatal/postnatal development.
262401: Develop biomarkers to assist in characterizing an individual's genetic profile in order to minimize adverse events and maximize therapeutic care. (Output)	FY 2020: NCTR scientists developed a database of information on how genetics effect drug efficacy and toxicity (pharmacogenomic data) in minority populations. A paper was published in *Pharmaceutics*. (Target Met) FY 2020: A manuscript regarding biomarkers for early detection of anticancer treatment-induced heart injury was published in *Clinical Pharmacology and Therapeutics*. (Target Met)	Develop biomarkers to better assess immunotoxicity associated with FDA products containing nanomaterials.	Perform research to identify potential biomarkers for the onset of prostate cancer.
264101: Develop risk assessment methods and build biological dose-response models in support of food protection. (Output)	FY 2020: A database and analysis tool was developed to better understand and control *Salmonella enterica* in foods and feeds in collaboration with CVM. A publication describing this work can be found in *Genes*. (Target Met)	Identify potential ways to minimize increased virulence and antimicrobial resistance in food animals.	Report preliminary findings regarding nanomaterial interaction with the gastrointestinal tract
263104: Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates. (Output)	FY 2020: NCTR scientists developed software to provide FDA reviewers with the ability to evaluate applications for genome assembly-based diagnosis of devices, products, and services. (Target Met)	Finalize data on the use of lipidomics to reveal factors influencing newborn susceptibility to vaccines.	Construct a database of opioid agonists/antagonists to assist the review and development of alternative pain management products.
263102: Develop computer-	FY 2020: NCTR scientists examined the utility of the In Vitro (lab-based) and In Vivo (animal-based)	In collaboration with CDER and Elsevier, NCTR scientists will report preliminary results	Provide initial data on a study to benchmark and compare computational and genomic predictive

Measure	Most Recent Result / Target for Recent Result	FY 2021 Target	FY 2022 Target
based models and infrastructure to predict the health risk of biologically active products. (Output)	Extrapolation (IVIVE) as a new tool for FDA safety assessments. A publication can be found in *Chemical Research in Toxicology*. (Target Met)	regarding the development of a predictive model for detecting drug-induced liver-injury (DILI) during the drug review process.	methods for toxicity for drug-induced-liver injury (DILI) using AI-based methods.

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

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 related to detecting contaminated pharmaceutical water and product as well as research related to small kinase inhibitors. In FY 2020, NCTR scientists developed a method to detect *Burkholderia cepacian* (BCC) in non-sterile pharmaceutical products and water. This research provides FDA with data and test methodology that can be recommended to assist industry in detecting the BCC from non-sterile pharmaceutical products and pharmaceutical water and more advanced rapid molecular detection methods. Additionally, in FY 2020, NCTR scientists gathered toxicity data on FDA-approved cancer fighting molecules, called kinase inhibitors (KI). This project continues and will provide a comprehensive picture of KI effects on the liver and heart that will help FDA better evaluate the use of KIs. In FY 2021, NCTR researchers will finalize data regarding 3D molecular modeling of opioids and other chemicals. The results of this project will allow better understanding of the structural requirements associated with a strong addiction potential.

SCIENCE BASE FOR ALTERNATIVE ASSAYS

NCTR continues to develop the science base to help FDA move towards alternative assays. These efforts look to replace research animal models with in vitro (lab-based) or in silico (computer-based) models. In FY 2020, in collaboration with CBER, NCTR scientists developed a safety assessment for gene-editing therapies that are pending clinical trials. This project continues and has the overall goal to enable more complete and accurate product safety assessment by creating new tools to assess the safety of CRISPR-mediated genome engineering therapies. In FY 2021, NCTR will report preliminary results on validating Alzheimer's disease-on-a-chip technology as a tool for toxicological screening of FDA-regulated products. And in FY 2022, NCTR scientists will initiate the development of an artificially intelligent virtual pregnant woman modeling suite to support regulatory decisions. The proposed pregnant woman modeling suite will be the first-of-its-kind in the field of biological modeling, pregnancy health, and regulatory science.

MATERNAL AND PERINATAL MEDICINE

Scientific expertise in the area of perinatal and maternal health has long been a strength of NCTR. In FY 2019, NCTR began the Perinatal Health Center of Excellence. The PHCE focuses on the perinatal period (the period-of-time including pregnancy, childbirth, and infant/child development) and the research covers a broad range of topics from chemical toxicology to new computer modeling methods. All PHCE projects have a common goal to fill knowledge gaps around perinatal safety and efficacy. In FY 2021, in collaboration with CFSAN, NCTR scientists will provide preliminary results on the perinatal developmental toxicity and neurotoxicity of inorganic arsenic (present in foods) exposure using a zebrafish model. In FY 2022, NCTR scientists in collaboration with the PHCE, will report preliminary findings related to COVID-19 effects on pregnancy and prenatal/postnatal development.

OFFICE OF REGULATORY AFFAIRS - FIELD ACTIVITIES

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Office of Regulatory Affairs	**1,230,480**	**1,224,332**	**1,244,765**	**1,330,373**	**85,608**
Budget Authority	***1,123,665***	***1,123,417***	***1,130,121***	***1,209,899***	***79,778***
User Fees	***106,815***	***100,915***	***114,644***	***120,474***	***5,830***
Prescription Drug (PDUFA)	*10,021*	*8,932*	*10,221*	*10,424*	*203*
Medical Device (MDUFA)	*2,586*	*2,463*	*2,597*	*2,682*	*85*
Generic Drug (GDUFA)	*53,124*	*55,022*	*54,096*	*55,019*	*923*
Biosimilars (BsUFA)	*1,472*	*1,303*	*1,322*	*1,344*	*22*
Animal Drug (ADUFA)	*383*	*391*	*390*	*426*	*36*
Animal Generic Drug (AGDUFA)	*228*	---	*224*	*277*	*53*
Family Smoking Prevention and Tobacco Control Act	*16,269*	*20,444*	*22,607*	*26,653*	*4,046*
Mammography Quality Standards Act (MQSA)	*11,281*	*11,963*	*11,507*	*11,737*	*230*
Food and Feed Recall	*1,020*	---	*1,040*	*1,061*	*21*
Food Reinspection	*5,490*	---	*5,600*	*5,711*	*111*
Voluntary Qualified Importer Program	*4,406*	---	*4,495*	*4,584*	*89*
Third Party Auditor Program	*147*	---	*150*	*153*	*3*
Outsourcing Facility	*388*	*396*	*395*	*403*	*8*
FTE	**4,878**	**4,894**	**4,901**	**5,017**	**116**

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 DESCRIPTIONS AND ACCOMPLISHMENTS

Overview

FDA is responsible for the regulatory oversight of food, medical, and tobacco products purchased and consumed by Americans. FDA-regulated products account for about 20 cents of every dollar spent in the United States. The Office of Regulatory Affairs (ORA) advances FDA's mission by conducting field operational activities for 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 FDA-regulated products offered for import into the United States,
- Oversight of recalls and execution of enforcement actions,
- Response to consumer complaints and emergencies,
- Development and promotion of state and local partnerships, and
- Review of inspectional information from international regulatory mutual reliance partners.

ORA has staff in 229 offices across 49 states, including the Commonwealth of Puerto Rico, with staff both temporarily and permanently assigned to foreign posts. ORA manages 16 scientific laboratories including three locations with co-located Human and Animal Food (HAF) labs and Medical Products and Specialty (MPS) labs, which perform specialized analyses of domestic and imported products. ORA works with each FDA center to implement a workplan that designates assignments for more than 500 activity areas, while maintaining flexibility to respond to unplanned activities (e.g., product recalls, emergencies, investigations of food-related illness outbreaks). This flexibility ensures quick containment and mitigation of the latter. ORA accomplishes FDA's mission through a highly skilled professional staff including:

- Consumer safety officers (CSOs), also known as investigators and compliance officers,
- Laboratory scientists, technicians and quality management staff,
- Scientific program coordinators,
- Occupational safety and health officers,
- Criminal investigators, and
- State cooperative program, public affairs, and communication specialists.

Recent Accomplishments

Three of ORA's 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, systems, and technology at the nine International Mail Facilities (IMFs) located throughout the country. Improvements at IMFs are in progress and ORA continues to implement 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.

FDA and Customs and Border Protection (CBP) developed a Memorandum of Understanding (MOU), signed October 28, 2020. The MOU addresses the areas of cooperation outlined in the Support Act, including information sharing, operational coordination for better targeting of higher risk parcels, collaborative strategies more specific to each agency's respective regulatory enforcement requirements, and facility improvements at IMFs.

The MOU also addresses FDA and CBP's commitment to partner in order to establish an expanded scientific presence at IMFs considered most at risk of receiving opioids and other illegal or dangerous drugs entering the United States. FDA and CBP are looking at ways to develop and deploy laboratory-based methods to identify unapproved, counterfeit and other unlawful controlled substances. Plans are underway that will provide permanent space for analytical equipment and laboratory analysts to conduct rapid screening testing. The first of these satellite laboratories was established at the Chicago O'Hare IMF. United States Postal Service (USPS), CBP, and FDA met in 2019 and mutually agreed on the arrangements, with FDA purchasing the laboratory unit from the U.S. Army with CBP responsible for site improvements. One additional IMF satellite laboratory is currently being established in or around the Miami IMF. Both satellite laboratories are expected to be operational during calendar year 2021.

Initiating a New Era of Smarter Food Safety

The New Era of Smarter Food Safety represents a new approach to food safety, leveraging technology and other tools to create a safer and more digital, traceable food system. Smarter food safety is about more than just technology. It's also about simpler, more effective, and modern approaches and processes. In FY20, ORA has made strides to advance the New Era through the use of remote regulatory activities.

ORA pilot tested the use of technology for virtual Subject Matter Experts (SMEs) participation during an onsite inspection, which allowed them to remain in a different location throughout various scenarios including travel restrictions under COVID-19. ORA was able to use this type of technology to engage SMEs from various physical locations during two field investigations within the United States. Use of the technology generated human and financial savings and created efficiencies in our processes. Agency SMEs were able to view in real time, what the investigation teams were viewing and provide expert guidance on locations for sampling and possible routes of contamination. This technology saved the agency funding for travel and lodging, lessened the size of the team at the firms and used Center SMEs for a small but necessary window during the investigations rather than monopolizing the SME for an entire week.

Expanding FDA Medical Product Safety

ORA has advanced two initiatives, both domestic and international, that are key in the area of medical product safety. First, ORA supports 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. The Center of Excellence on Compounding for Outsourcing Facilities will expand FDA's engagement with outsourcing facilities and state regulatory bodies in training and development to help this new industry sector achieve its intended function. ORA continues to support this center in areas such as the development of content for the delivery of planned outreach and training and inspections. In September 2020, the Compounding Quality Center of Excellence hosted its first-ever virtual conference to discuss the future of the compounding industry.

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 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 May 2020, FDA announced that human drug capability assessments had 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 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 the E.U. to include veterinary medicines and FDA is currently conducting capability assessments of E.U. veterinary agencies. To date, nine veterinary medicine authorities have been assessed by FDA, exceeding the goal of eight for the calendar year.

Expanding Public Health through Information Sharing

ORA actively engages with regulatory partners at all levels to share data in the interest of efficiency and public health and safety. This includes the development and maintenance of information technology systems used across FDA, industry, state and other regulatory partners to maximize the use and analysis of data collected in regulatory activities.

International information sharing with authorities with qualifying Confidentiality Commitments expanded in April 2020 with the implementation of sharing trade secrets pursuant to the Food Drug and Cosmetic Act (FD&C Act) section 708(c) after all relevant delegations of authority were obtained and procedures drafted. Since taking the necessary steps to share trade secret information with the applicable foreign authorities, ORA has responded to 38 requests related to this authority. Confidentiality Commitments enable this information sharing (limited in scope to drugs only) with the competent authorities for each European Union Member State.

FDA is currently limited in the information it can provide its domestic partners (local, state, tribal, and territorial), requiring extensive review, redaction, and valuable time.

Standardizing an Integrated Food Safety System and Program

ORA supports 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. FDA collaborates with other federal, SLTT, regulatory and public health association partners and the Department of Defense to advance an IFSS with the goal of protecting public health and reducing foodborne illness.

FDA works collaboratively with its SLTT and public health/regulatory association partners to develop, revise, and promote conformance with standardization programs such as Manufactured Food Regulatory Program Standards (MFRPS), Animal Feed Regulatory Program Standards (AFRPS), Voluntary National Retail Food Regulatory Program Standards (VNRFRPS), and Egg Regulatory Program Standards (ERPS). SLTT programs enrolled in these standardization programs are taking meaningful steps to ensure they have the regulatory foundation and framework necessary to protect public health. At the beginning of FY 2020, a total of 933 SLTT programs were enrolled in these standardization programs nationwide.

The bedrock of an effective IFSS is the assurance that FDA and its regulatory partners are building and maintaining consistent, quality, and capable programs to protect public health. To accomplish this objective, FDA has 259 cooperative agreement programs (CAPs) and/or grants with 49 states, American Samoa, and 11 associations. In FY 2020, to leverage the resources of its SLTT 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 will enable approximately 18,000 inspections, site visits, and sample collections, including an approximate 400 human food preventive controls (PC) inspections.

In FY 2020, FDA started a new Retail Food Safety Regulatory Association Collaboration CAP. This CAP leverages national retail food regulatory associations to promote development and implementation of intervention strategies to reduce foodborne-illness risk factors, SLTT adoption of FDA Food Code, implementation of risk-based inspections methods by SLTTs, and active participation and conformance with the VNRFRPS.

FDA continues 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. In an emergency, RRTs coordinate efforts to align the response activities of agencies that have overlapping jurisdiction. Since 2009, the RRT program has grown from nine to 20 states in 2020, and an additional four states participate in the program voluntarily (outside of the funded cooperative agreement).

ORA provides oversight of regulatory science standards in laboratories 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 focuses on collaboration up front. It allows stakeholders to take part in developing assignments and

strengthens the surveillance of FDA-regulated food products.

In FY 2020, FDA awarded 55 cooperative agreements to state labs under a new Laboratory Flexible Funding Model CAP. The Laboratory Flexible Funding Model (LFFM) allows local or state government labs to increase their testing capability and capacity, while offering the opportunity for state laboratories to participate in method development, method validation, and matrix extension studies. Participation in these studies help us ensure that the laboratory methods needed to support regulatory compliance, investigations and enforcement actions meet the highest analytical performance standards appropriate for their intended purposes.

In FY 2020, ORA enhanced the concept of an IFSS between FDA and the States by establishing a new mutual reliance program, the Non-Contract Inspection (NCI) program. The program allows the agency to obtain state inspection data for facilities and state performed non-contract inspections meeting identified criteria. The data is used by the agency to meet FSMA inspection mandates and expand the data in our official inventory. Additionally, the agency shares information in our systems with the states to help expand the state data. In FY 2020, the agency accepted data for more than 450 inspection reports, expanding our information, positively impacting FSMA cover-by-dates and saving the Agency thousands of dollars in human and financial resources.

Premarket and Bioresearch Monitoring Activities

To ensure products are produced as outlined in medical product applications, ORA inspects manufacturing facilities as part of the application review process. 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 device. The information and metrics contained in this report provide benchmark data to industry stakeholders regarding inspections related to product application approvals. ORA works in collaboration with the Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), and Center for Biologics Evaluation and Research (CBER) to publish these annual reports and guidance documents. These inspections provided additional regulatory coverage and assurance that these firms were in compliance with the regulations.

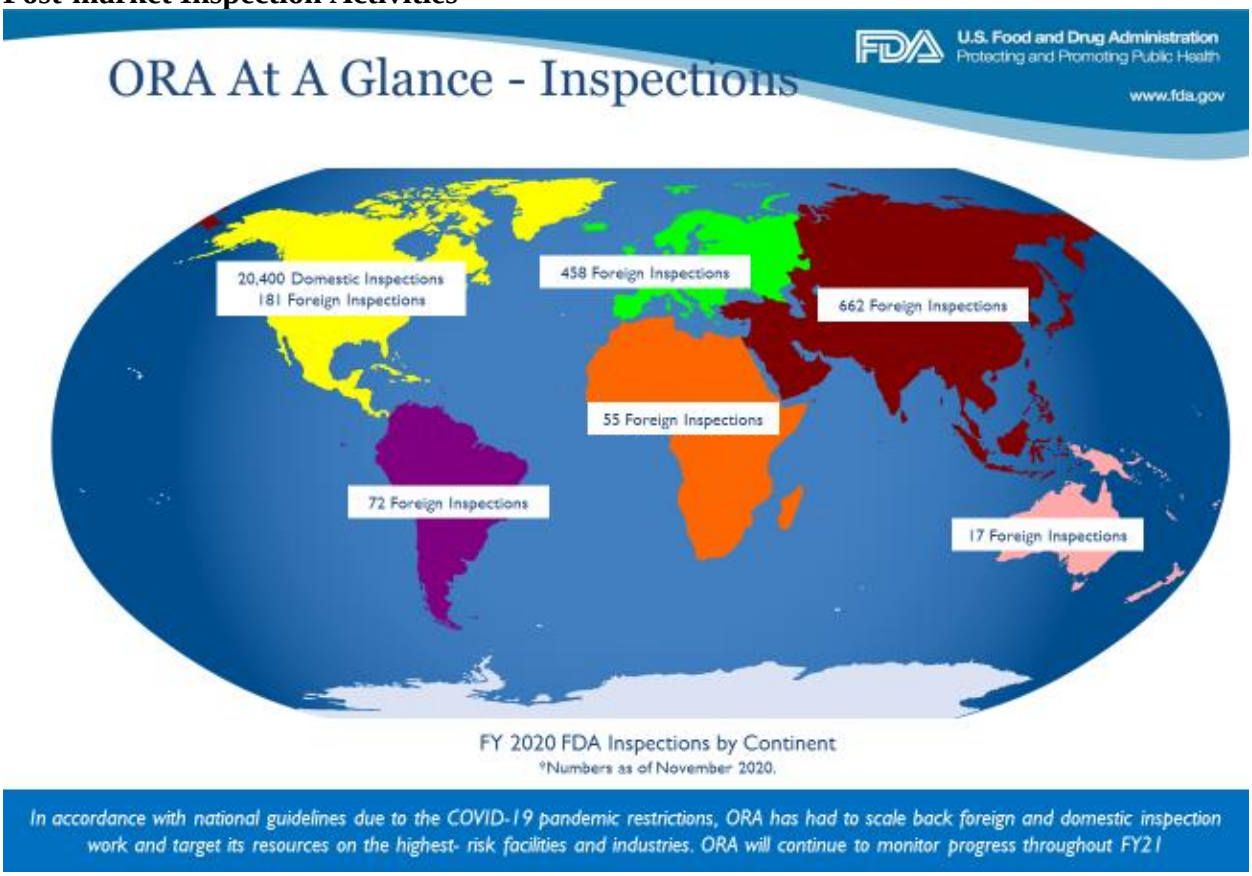
The premarket activities noted above help to protect patients and consumers by ensuring the medical products used are safe, effective, and manufactured in accordance with the parameters outlined in their applications. In addition to conducting these inspections and activities to support approval of medical product applications, ORA conducts Bioresearch Monitoring (BIMO) inspections and data audits to assure the quality and integrity of data submitted to the agency in support of new product approvals and marketing applications. BIMO activities provide for the protection of the rights and welfare of the thousands of human subjects and animals involved in FDA-regulated research. BIMO inspections and data audits are integral to ensuring the safety and effectiveness of new medicines, medical devices, food and color additives, and veterinary products, and the safety of new tobacco products, during the FDA preapproval process. For example, on October 1, 2020 the owner and operator of a site management organization was sentenced to over 28 years in prison on 47 counts including wire and mail fraud, fraudulently obtaining controlled substances, abuse of private and public trust, use of a person under 18 to commit a felony, and obstruction of justice all related to falsifying numerous clinical trials. The

owner and operator were also ordered to forfeit and pay over $7.5 million including restitution and penalties.

Under the BIMO 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 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.

In FY 2019, ORA added a dedicated foreign inspection cadre to augment the existing BIMO program for completing BIMO inspections abroad. Due to the initial success of the cadre, an additional member was added in January 2020. The cadre currently consists of nine investigators who completed 54 foreign BIMO inspections in FY 2020 prior to COVID-19 related international travel restrictions being imposed. The cadre allows ORA to quickly respond to application-driven inspection assignments with short review dates and for inspections staff to develop specialized skills. ORA enhances the overall coverage of the foreign establishment inventory by leveraging the work of its dedicated foreign inspection cadres, the inspection staff located at FDA's foreign offices, and domestic-based investigators.

Post-market Inspection Activities



FDA completes surveillance and enforcement activities throughout the distribution chain and allocates inspectional resources based on risk estimates associated with specific domestic and foreign firms. Using a preventive model to prioritize resources, ORA can efficiently focus inspection efforts, in conjunction with FDA centers as well as applicable SLTT regulatory partners.

As part of continued efforts to implement FDARA, ORA published the final guidance, *Process To Request a Review of FDA's Decision Not To Issue Certain Export Certificates for Devices*, in November 2019, and developed procedures to implement this guidance. The final guidance, *Review and Update of Device Establishment Inspection Processes and Standards*, was also published on June 26, 2020.

Over the years, sampling approaches have evolved to help expose risks, assess the value of strategies to control those risks, and prevent contaminated products from reaching consumers. The process is a mechanism to actively identify risks and areas where preventive controls should be placed to protect public health. As FDA increases its understanding of contamination sources in high-risk commodities and practices, resources can be effectively allocated to address public health risks through compliance sampling, targeted sampling, or other risk-mitigation strategies.

ORA is intensely involved in many critical aspects of FDA's human drug-compounding program including:

- Inspections and enforcement,
- Policy development and implementation,
- State collaboration and coordination, and
- Stakeholder outreach.

In FY 2020, ORA completed 54 inspections of compounding facilities. Compliance activity throughout FY 2020 resulted in 20 recalls, the issuance of 25 warning letters, 18 Untitled letters and 53 state referral letters. Additionally, in FY 2019, four permanent injunctions were issued against compound drug producers who did not comply with previous interventions from FDA.

ORA is responsible for surveillance inspections and investigations of human cells, tissues, cellular and tissue-based products (HCT/Ps) and cell and gene therapy drug products. The office is also charged with oversight of U.S. blood, blood components, and source plasma establishments. In FY 2020, ORA conducted 286 inspections of HCT/P establishments and 352 inspections of U.S. blood, blood components, and source plasma establishments. Although disruptions due to the COVID-19 pandemic caused a reduction in blood and HCT/P surveillance operations by over half in FY 2020, ORA continued to play an important role in maintaining the safety of the U.S. blood supply and the HCT/P industry.

In the 2019–2020 flu season, 174.5 million doses of influenza vaccine were distributed in the United States. In FY 2020, ORA completed surveillance inspections and records assessments of 26 domestic and foreign vaccine manufacturers to help ensure the safety and availability of vaccines for U.S. children and adults. ORA is also engaged in providing cGMP on-site feedback to COVID-19 vaccine manufacturers, to support the development of COVID-19 countermeasures.

Mammograms are critical to early detection of breast cancer and more than 39 million are performed on patients annually. Each year, FDA and inspectors in 44 states complete inspections at more than 8,500 mammography facilities. Radiological Health Representatives (RHR) within ORA work directly with the states to ensure that every mammography clinic is inspected annually.

Outreach

Aside from regulatory and enforcement activities, ORA participates, in collaboration with the Centers, in outreach activities such as meetings and publications. A few examples of FY 2020 ORA outreach activities include:

- ORA enhanced the Recall Enterprise System (RES), to include templates for recall determination, classification, and termination emails for voluntary firm-initiated recalls. These automated letters will save time, money, and resources, eliminating manual preparation. When these emails are sent, a permanent record will be created and stored in RES.
- To assist industry and provide clear recommendations, ORA collaborated with CDER to develop four guidance documents addressing compounding activities. Three of those

guidance documents are intended to provide recommendations to outsourcing facilities and pharmacy compounders currently not registered for certain compounding activities during the COVID-19 public health emergency.

- ORA led the development of four updated or new recall-related guidance documents to further help protect the public from violative or unsafe FDA-regulated products. These were issued to assist and provide recommendations and best practices to industry and FDA staff.
- ORA published "A Day in the Life" video series to provide education to the medical device industry and created a series of Frequently Asked Questions (FAQs) about combination products. Each of the five modules highlights "behind-the-scenes" perspectives that industry constituents will find valuable in learning about and understanding inspectional best practices.
- ORA virtually hosted its second annual conference with industry entitled "Cultivating Compliance." Over 168 industry members attended this collaborative day of sharing information and discussing opportunities for the most important public health issues impacting medical devices, including recalls, adverse events and compliance trends.
- On September 30 and October 1, 2020, ORA, in conjunction with CBER, hosted a virtual FDA Workshop for the Reproductive Tissue Industry in response to a trend of noncompliance within this industry. The workshop was held to educate the industry on FDA requirements. Approximately 695 industry members attended this workshop, which included discussions of donor screening and testing, donor eligibility determination, labeling, registration, and exemption requests.

Post-market Import Operations

Over the last decade, there has been a significant increase in FDA-regulated products introduced for import into the U.S. market (Table 1). While this growth has been difficult to match with available resources, FDA has made several advances in targeting and processing imported products for entry.

Table 1: Number of Import Lines by Program Area: FY 2014 through FY 2022 (Est.)

Program Area	2014	2015	2016	2017	2018	2019	2020	5 Yr Actual Percent Growth*	2020 Percent of Total Lines	Estimate 2021	Estimate 2022
Foods	12,180,223	13,080,429	13,952,537	15,251,687	16,859,790	17,722,742	16,983,686	4%	38.84%	17,000,000	17,850,000
Cosmetics	2,596,057	2,930,682	2,939,034	2,625,555	2,729,584	2,762,411	2,350,216	-4%	5.37%	2,375,673	2,494,457
Human Drugs	641,908	688,208	739,309	789,853	871,212	838,267	959,585	6%	2.19%	967,604	967,604
Animal Drugs & Feeds	391,388	416,860	434,384	426,484	456,684	410,237	493,192	3%	1.13%	479,518	503,494
Biologics	82,710	150,673	151,911	157,080	170,575	181,328	152,158	0%	0.35%	155,000	197,462
Medical Devices & Rad Health	16,668,422	17,252,283	18,757,725	20,584,138	22,291,902	22,967,758	22,512,049	4%	51.48%	25,521,999	27,308,539
Tobacco Products	20,161	16,680	32,972	199,066	281,097	280,901	275,261	109%	0.63%	289,024	303,475
Total	32,580,869	34,535,815	37,007,872	40,033,863	43,660,844	45,163,644	43,726,147	3%	100.00%	46,788,819	49,625,031

*Percent growth based on a five-year average of actuals from FY 2016 - FY 2020

ORA has continued oversight of food importers through establishment of the remote inspection protocol for FSVP Inspections. The FSVP rule specifically authorizes remote inspections of FSVP Importers. In FY 2020, ORA conducted 700 FSVP Inspections following the remote inspection protocol. Additionally, 97 of these inspections were inspections of FSVP Importers of product from Foreign Suppliers whose foreign inspection was postponed due to COVID-19.

Also, under the FSMA framework, ORA continued implementation of the Voluntary Qualified Importer Program (VQIP). On January 1, 2020, the VQIP application portal became available on www.fda.gov and remained open to accept completed VQIP applications through July 31, 2020. This year, FDA received three VQIP applications for FY 2021 benefits, including an extension from the sole approved applicant from FY 2020. The associated information for all importers approved for participation in this program may be found in the FDA Data Dashboard under 'Approved VQIP Importers'. In future years, the VQIP Application portal will be open between January 1 - May 31.

Leveraging Laboratory Capabilities

FDA laboratories support the agency's mission by performing scientific testing on regulated products, conducting applied research, and supporting inspectional and compliance operations, as well as criminal investigations. These laboratories support a broad spectrum of technical proficiencies and use cutting edge scientific instrumentation to provide analytical and microbiological testing on FDA-regulated products. ORA operates 16 field laboratories across the United States and Puerto Rico and is in the process of establishing satellite laboratories at selected (IMF) International Mail Facilities.

ORA laboratories continually strive to expand their analytical repertoire by developing new applied scientific methods to respond to emerging public health needs and promote compliance through routine surveillance. Analyses performed in the laboratories include: whole genome sequencing (WGS), which is used for epidemiological trace-back based on genetic fingerprinting; and the use of advanced mass spectrometry systems to detect and identify chemical contaminants in a vast variety of products including seafood, vaping liquids, and pharmaceutical drugs. ORA laboratories adhere to a strict quality system framework as they carry out their regulatory testing obligations and are all accredited to ISO 17025:2017 standard.

Analytical excellence has played a pivotal role in FDA's response to recent public health emergencies such as the opioid crisis, vaping related deaths, foodborne illnesses, and adverse events associated with quality and integrity of pharmaceutical and medical device products. New complex consumer products entering the marketplace present unique risks and analytical challenges requiring a responsive, flexible laboratory network. The active research portfolio and technical training programs of ORA laboratories provide analytical readiness to protect the public health from these future threats.

Compliance and Enforcement Activities

The ORA-led Operation Quack Hack was launched in March 2020 to proactively identify and neutralize public health threats related to the COVID-19 pandemic. The Operation Quack Hack task force leverages agency expertise and advanced analytics to protect consumers from fraudulent medical products, including unproven cures, illegitimate test kits and substandard or

counterfeit respirators during the COVID-19 pandemic.

To date, Operation Quack Hack has identified more than 1360 fraudulent and unproven medical products related to COVID-19, reviewed thousands of websites, social media posts, and online marketplace listings resulting in over 170 warning letters to sellers most of which were issued jointly with the Federal Trade Commission., The task force has issued more than 300 reports sent to online marketplaces, and more than 290 abuse complaints to domain registrars. The agency has taken civil enforcement action including the first temporary restraining orders in several decades, as well as criminal prosecutions. An Order for Permanent Injunction was granted in August 2020 against an online retailer with claims on the firm's website indicating the product is intended to cure, mitigate, treat, or prevent COVID-19 in addition to other diseases such as HIV, Alzheimer's, multiple sclerosis, autism, and brain cancer. The permanent injunction enjoins the Defendants from directly or indirectly labeling, holding, and/or distributing any drugs.

ORA continues active surveillance of online marketplaces for unapproved products, including those that contain hidden drug ingredients. In December 2020, FDA announced the laboratory findings of 50 products collected from Amazon and eBay – 46 of which were found to contain dangerous, undeclared drug ingredients. To date, nine companies have conducted voluntary recalls of these tainted products purchased from Amazon and eBay. Since 2007, FDA has uncovered more than 1000 tainted products and pursued hundreds of recalls, warning letters or other compliance actions for sellers of these unlawful products.

ORA also maintains its investigative work with unlawfully marketed cannabidiol (CBD) products, working with agency programs and the Federal Trade Commission (FTC) to act against companies marketing CBD products with false health claims for numerous medical conditions, including Alzheimer's disease, cancer, opioid addiction and withdrawal, and autism.

In FY20, ORA issued 24 public notifications for products with harmful, hidden ingredients (i.e. "tainted products") and achieved 12 voluntary recalls of tainted products. At just the midpoint of 2021, ORA has already issued 76 public notifications and achieved 11 voluntary recalls for tainted products.

FDA also obtained signatures for three Consent Decrees of permanent injunction. The first was for a contract manufacturer of dietary supplements for a firm with a long regulatory history that includes a warning letter, a regulatory meeting, and three separate recalls involving their products. The consent decree permanently restrains and enjoins the defendants from receiving, manufacturing and distributing dietary supplements pending certification of compliance by FDA. Further the decree requires the defendants to recall and destroy all dietary supplements and drugs received, manufactured and distributed since 2013.

The second signed Consent Decree of permanent injunction was against a manufacturer of hot and cold smoked seafood products. Despite a prior warning letter and regulatory meeting, an August 2018 inspection found 16 of 138 swabs positive for *Listeria*, violations to the seafood Hazard Analysis and Critical Control Point (HACCP) regulations, and failure to monitor sanitation procedures.

The third signed Consent Decree of permanent injunction was the first consent decree against a firm or grower for violating public safety standards under the Produce Safety Rule enacted under FSMA. The Produce Safety Rule requires, among other things, that covered sprout operations take measures to prevent the introduction of dangerous microbes into seeds or beans used for sprouting; test spent sprout irrigation water (or, in some cases, in-process sprouts) for the presence of certain pathogens; test the growing, harvesting, packing and holding environment for the presence of the Listeria species or Listeria monocytogenes; and take corrective actions when needed.

Criminal Investigations

ORA has the primary responsibility for criminal investigations conducted by FDA and for all law enforcement and intelligence issues pertaining to threats against FDA-regulated products and industries.

In FY 2020, the criminal investigative efforts resulted in:

- 202 domestic arrests;
- 5 foreign arrests;
- 171 convictions; and
- More than $481 million in forfeiture, fines, and restitutions.

The arrests and criminal convictions occur in all areas of FDA's jurisdictions and include: product tampering, illicit vaping products, falsely labeled food, counterfeit pharmaceuticals, opioids, adulteration and misbranding of drugs, illegal importation of drugs, fraud involving medical products, tainted cosmetics, misbranded and adulterated animal drugs, and misbranded medical devices.

A series of events impacting public health in FY 2020 have underscored the importance of FDA's criminal investigations. The opioid crisis, which has taken countless lives, continues to be a major concern to FDA. ORA has responded by conducting several criminal investigations impacting how prescription opioids are marketed and highlight the availability of counterfeit opioids for sale on the internet. ORA investigations have involved medical professionals, transnational drug counterfeiting groups and multi-national pharmaceutical companies that recklessly contribute to the opioid crisis.

To highlight the serious crime of tampering with opioids intended for patient use by health care professionals, a recent case involved a registered nurse who tampered with morphine sulfate prescribed to an 89-year old hospice patient. Analyses by FDA's Forensic Chemistry Center (FCC) indicated that the nurse replaced the extracted medication with another liquid to avoid detection, diluting the morphine to just 26% of the prescribed concentration. The hospice patient received the diluted morphine and suffered unnecessary pain. In September 2020, the registered nurse was sentenced in federal court.

In yet another example of the contribution to the opioid crisis, Insys Therapeutics was involved in the illegal promotion of Subsys, a powerful opioid painkiller. In January 2020, the founder and one executive were sentenced related to their involvement in prescribing the fentanyl-based pain

medication, often when medically unnecessary. In 2019, the company agreed to enter a $225 million global resolution of criminal and civil investigations. Additionally, the U.S. Department of Justice had reached a $1.4 billion settlement with Reckitt Benckiser Group and Indivior Solutions to resolve criminal and civil investigations related to OCI's investigation of the marketing of the opioid addiction treatment drug Suboxone.

Online, ORA's Cybercrime Investigation Unit (CcIU) is targeting online marketplaces and vendors manufacturing and selling counterfeit opioids through arrest and the seizure of assets. Operation CyberPharma targets suspected darknet vendors selling counterfeit drugs. Thus far, Operation CyberPharma has led to the arrest of 14 darknet vendors and aided in the takedown of a major darknet marketplace as well as the seizure of drug counterfeiting tools and tens of thousands of dollars in virtual currencies and other assets. Additional arrests and seizures are anticipated with this on-going operation.

Protecting U.S. Consumers in the Global Market

To combat the increasingly global nature of crime related to FDA-regulated commodities, ORA 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. Two examples of the intersection of these three pivotal areas is the 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. ORA criminal investigators prosecuted a U.K. importation nexus and many involved bad actors misusing the internet to distribute non-FDA-approved drugs and medical devices as well as assisted U.K. law enforcement counterparts in the prosecution of an individual attempting the sale of fraudulent cures for COVID-19 in the United States.

Recently, ORA merged the Import Operations Program and ORA's international network to encompass one program, the International Operations Program (IOP), to engage with global law enforcement partners to identify illicit products in the United States and identify global threats to public health. IOP detects violative shipments of FDA-regulated products entering the domestic ports and facilities. IOP's priorities include responding to IMFs, 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 FDA's support of the overall United States government-wide effort to combat cross-border crime. In response to the COVID-19 pandemic, IOP targeted illicit imports of FDA-regulated products, including drugs and medical devices, from overseas that were fraudulent, misbranded, and adulterated.

ORA conducted its first bilateral enforcement operation, Operation Broadsword, at the IMFin Chicago, Illinois. Operation Broadsword targeted packages of violative FDA-regulated products transshipped through third-party countries to conceal their point of origin to avoid detection. The operation was a collaboration with India's Directorate of Revenue Intelligence and U.S. Customs and Border Protection.

ORA'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 in Charleston, South Carolina, and with FDA placement of an OCI special agent within the European Union Agency for Law Enforcement Cooperation (EUROPOL) in The Hague, Netherlands. ORA 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. 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.

ORA's Internet-related criminal investigations are led by its 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 ORA's cybercrime specialists and experts from the online ecosystem.

Enhancing Opioids Enforcement

Leadership from FDA, CBP, and the U.S. Immigration and Customs Enforcement, Homeland Security Investigations (ICE-HSI) signed a MOU to stop harmful products that pose a threat to public health and attempt to enter the United States through IMFs. The SUPPORT Act was enacted to address the opioid epidemic and directs the agencies to work collaboratively in preventing the importation of unapproved prescription medications and illicit drugs from entering the U.S. through the IMFs. The MOU will maximize inspection and detection capabilities in order to prevent this illegal activity.

The MOU identifies specific roles and responsibilities for DHS, CBP, ICE-HSI, and FDA to coordinate activities to respond to illegal controlled substances and drug imports, medical devices, and combination products at IMFs. Such activities include facility improvements and increased technological and inspection capacity at the IMFs through collaborative information sharing, shared facilities, and coordinated operations at the IMFs.

Section 3022 of the SUPPORT Act added section 801(u) [21 U.S.C. § 381(u)] to the FD&C Act, giving FDA 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." In FY 2019, an initial list was developed of nine APIs that meet both the "significant public health concern" and the approval/investigational use authorization conditions described above and ORA implemented this new authority using the initial list of indicated APIs at the IMFs. In FY 2020, ORA worked with CDER to identify an additional nine APIs that meet the statutory criteria in section 801(u). FDA will continue to update the API list, as additions are approved throughout FY 2021.

A section of FDA's authority, section 801(u), authorizes FDA to treat an imported article as a "drug" if the product contains an active ingredient in a drug that is currently approved by FDA. The implementation of 801(u) is an unquestioned success. In FY 2020, ORA raised its overall

destruction rate to more than 77% of violative refused drug products, up from a destruction rate of 48% of refused drug products in FY 2019.

The partnership between CBP and FDA included an increase in scientific resources at selected IMFs and sharing of space, technologies and information. Based on benchmarking with Federal partners, FDA identified specially trained field-based scientists using an established set of analytical tools to be the most scientifically reliable and efficient approach to rapid identification of illicit FDA-regulated products, such as counterfeit pharmaceuticals, including opioids, and adulterated supplements. Ten ORA chemists were trained at FDA's FCC on the use of these instruments, a satellite laboratory unit procured from the U.S. Army and pilot operations were initiated at the Chicago O'Hare IMF. These chemists working with ORA import investigators, processed over 900 samples in 68 working days. Of those samples, 20% were found to contain either DEA-scheduled substances or represented FDA violations. The pilot was halted in March 2020 due to COVID-19 related complications and a pilot summary report was issued in July 2020. Plans are in progress to establish a network of IMF located satellite laboratories, and hire and train additional scientists, establishing full operations at two IMF locations by the second quarter of FY 2021. The increased analytical capabilities at the IMFs will facilitate immediate science-based entry decisions.

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, as tobacco products. ORA's tobacco operations staff completed 78 inspections of domestic tobacco product manufacturers, three inspections of foreign tobacco manufacturers, 74 investigations, and investigated five free-sample events in FY 2020. In response to evidence of increasing youth use of Electronic Nicotine Delivery Systems (ENDS) products, FDA prioritized enforcement of certain flavored ENDS Products. 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. Additionally, ORA performed multiple foreign and domestic Premarket Tobacco Application (PMTA) inspections. 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.

In January 2020, FDA published the guidance for industry, Enforcement Priorities for Electronic Nicotine Delivery System, (ENDS) and Other Deemed Products on the Market Without Premarket Authorization to describe how FDA intends to prioritize enforcement resources regarding the marketing of certain deemed tobacco products that do not have premarket authorization. As part of the implementation strategy for this enforcement policy, ORA worked with CTP to increase surveillance of those products described in the guidance, specifically flavored, cartridge-based ENDS, that are offered for import into the U.S. This heightened surveillance of indicated ENDS products since January 2020 led to ORA almost doubling examinations of ENDS products from FY 2019 to FY 2020, with approximately 42% of the lines examined in FY 2020 found to be in violation.

In August 2019, FDA worked with the Centers for Disease Control and Prevention (CDC) and state/local public health partners to investigate a multistate outbreak of severe pulmonary illness/injury, which CDC has labeled EVALI (e-cigarette, or vaping, product use associated lung injury). As of February 2020, a total of 2,711 hospitalized cases of EVALI were reported to CDC and 60 deaths were confirmed.

In response to this outbreak, FDA activated its Agency Executive Group (AEG) and Incident Management Group (IMG) to coordinate FDA's activities for this investigation. The IMG focused on whether there was a relationship between any specific products or substances and the reported cases. FDA's work included collecting critical details about the products or substances involved, where they were purchased and how they were being used by specific patients and analyzing product samples. ORA and the CDC laboratories collaborated in this effort with FDA conducting the majority of product testing. In February 2020, FDA received over 1,300 samples to evaluate for a broad range of chemicals, nicotine, tetrahydrocannabinol (THC) and other cannabinoids, cutting agents/diluents and additives, pesticides, opioids, poisons, heavy metals and toxins. Based on FDA and CDC testing, results of e-liquids with linked epidemiological data provided evidence supporting an association of EVALI with THC and vitamin E acetate containing products. FDA also responded to inquiries from media, Congress, and international public health partners. FDA's investigational findings, preliminary lab results, guidance and recommendations to consumers, healthcare providers, and state health departments were shared on FDA's public webpage.

Data Modernization and Enhanced Technologies

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 described in the accomplishments above. The modernization approach focuses on the top-level strategic goals of the agency and office, including:

- Increase information and data-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.

In FY 2020, ORA made significant technological advancements utilizing novel technology to engage subject matter expertise located remotely during an investigation in real-time. Use of the technology allowed experts in the Centers to engage with the investigation team, helping to

address unexpected circumstances as they occurred, providing guidance on next steps, activities to accomplish and highlighting new areas of focus in the field based on real-time observations. Use of this technology was an instrumental step in advancing our field operations, created great efficiencies in the investigation and saved the agency human and financial resources.

ORA enhanced external information sharing and management capability with internal and external partners. Some examples of ORA's collaborative enhancements are:

- The National Food Safety Data Exchange (NFSDX), a system that enables data sharing to support food safety programs across produce safety, sample collection, inspections, and other FSMA programs. Currently 27 states are accessing this data, and nine more are engaged.
- ORA implemented Document Retrieval and Management Service (DRMS), a system that allows FDA to share and submit documents, FDA inspection reports, and other artifacts related to inspections with internal and external partners.
- ORA improved data management, reporting, and business intelligence capabilities to support CDER's Opiate Data Warehouse Initiative as well as other center wide initiatives such as CFSAN Enterprise Information Repository for Research and Analytics (CEIRRA) and OFPR's big data initiatives to support high priority analytical work.
- ORA rolled out the System for Entry Review and Import Operations (SERIO) to meet the needs of ORA's Import Investigational and Compliance staff which will enhance productivity across the board, particularly in the IMFs.

Managing a World-Class Workforce and Promoting a Culture of Excellence

Recruitment and Retention

ORA's ability to advance its mission of protecting and promoting public health relies on ORA's ability to recruit a highly skilled, professional workforce. From successfully filling vacancies to providing a pathway for career advancement, ORA will ensure that best management practices are consistently employed across the organization and throughout the lifecycle of the employee.

Through consolidated and coordinated cohort hiring, ORA re-engineered the hiring process by establishing a talent acquisition plan, standardizing the interview and selection process, and utilizing every additional direct hire method made available including Schedule A, veteran hiring, Returned Peace Corps hiring, Commissioned Corps and COVID-19 Direct Hire Authority. As a result, in FY20, ORA experienced an overall increase in hiring of 106% for all job series. This included 264 net gains overall, and of these 175 were Consumer Safety Officers (CSOs) in 95 locations nationwide, which increased the hiring of CSOs by 144% over last year. At the halfway point in FY21, ORA selected 84 total candidates via CSO Direct Hire Authority and 213 candidates overall, continuing the significantly increased hiring trend.

Additionally, in FY 2020, ORA for the first time offered and implemented the use of the Student Loan Repayment Program (SLRP) for use in retaining current employees. Over 150 applicants were approved with $1.3 million awarded.

Training and development of ORA staff is critical. In FY 2020, ORA held 86,267 face-to-face courses and 28 virtual Instructor Led Training (vILT) courses with 2,769 students in attendance. Meeting the training needs of state, local, and territorial regulators is also a high priority. ORA developed a process map for the implementation of third-party delivery of ORA regulatory training courses, including pilot program testing Qualified Instructor and Train-the-Trainer Programs. ORA also partnered, using cooperative-agreements with several organizations and two State partners, to deliver training on its behalf.

Coronavirus (COVID-19) Pandemic

ORA has supported efforts related to the COVID-19 pandemic through a wide range of activities. ORA has conducted domestic/foreign inspections of viable manufacturers, pre-market/post-market inspections, import activities (such as screenings, entry review), and PPE for personnel performing their duties. ORA will continue to support the issuance of import screening associated with products and manufacturers affected by impacts of COVID-19 on FDA operations and inspections. ORA also supports health fraud investigational related activities such as purchase of undercover/anonymous browser software and health fraud laptops, sample purchasing, and laboratory analysis.

ORA has been on the forefront of the COVID-19 response and has adapted regulatory work to meet the challenges created by the pandemic including:

- Development and implementation of remote regulatory activities to maintain oversight and engagement with regulated industry.
- Adjusting the entry screening to provide greater oversight of products imported from foreign firms where travel restrictions have postponed inspections.
- Tackling substandard and dangerous hand sanitizers through increased screening coordinated with CBP and testing in ORA's Medical Products Laboratories. As a result, 47 foreign suppliers have been added to the import alert to deny future shipments.
- Implementing rigorous safety procedures to allow ORA laboratories to perform mission critical work including the analysis of food samples associated with outbreaks and analysis of large numbers of fraudulent hand sanitizers and other fraudulent COVID remedies and tests.
- Facilitating the entry of effective and necessary personal protective equipment, by working with FDA centers to streamline the entry process for products meeting emergency use authorizations (EUA) and immediately-in-effect (IIE) enforcement guidance documents.
- Investment in projects to assist with acquiring data, conducting research, and developing analytic methodologies to identify products at risk of a drug shortage and conduct other supply chain vulnerability assessments.
- Ensuring continued investigator training through collaboration with grant partners and contractors to complete conversions of 15 courses from instructor-led training to virtual instructor-led training (vILT), adapting course content, exercises, and facility tours to virtual formats while engaging the same level of interactivity in virtual vs in-person courses.
- Migrating more than 3,000 foreign firms into a new database that will allow for efficient

targeting of resources by enhancing our data and maintaining a level of regulatory oversight.

- Expanding its long-standing information sharing with the Securities Exchange Commission (SEC) during the Covid-19 pandemic to mitigate risk of fraudulent products. This information sharing led to the suspension of trading in 35 companies and fraud charges against at least three companies related to marketing illegal medical supplies during the COVID-19 pandemic.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$1,224,332,000	$1,123,417,000	$100,915,000
FY 2021 Enacted	$1,244,765,000	$1,130,121,000	$114,644,000
FY 2022 President's Budget	$1,330,373,000	$1,209,899,000	$120,474,000

BUDGET REQUEST

The FY 2022 President's Budget request for the Office of Regulatory Affairs Program is $1,330,373,000, of which $1,209,899,000 is budget authority and $120,474,000 is user fees. Within the FY 2022 President's Budget request, the budget authority increases by $79,778,000 compared to the FY 2021 Enacted level and user fees increase by $5,830,000. The FY 2022 President's Budget request allows FDA to continue to ensure that the food, feed, and medical products available to the American public are safe and effective.

BUDGET AUTHORITY

Medical Product Safety (+$10.0 million / 25 FTE)

Advancing the Goal of Ending the Opioid Crisis: (+$10.0 million / 25 FTE)
Field Human Drugs (+$10.0 million / 25 FTE)

ORA requests funding to expand the current International Mail Facilities (IMF) initiative to interdict shipments of opioids, unapproved foreign drugs, counterfeit pharmaceuticals and health fraud related shipments. FDA reviews in the IMF have increased from just under 14,000 to more than 50,000 in FY 2020, with a commensurate increase in destructions of non-compliant drugs. Under the current IMF initiative, ORA has multiple laboratory subcomponents that support drug testing efforts including illegal, unapproved, counterfeit and opioid testing. Laboratory resources will be used to establish IMF satellite laboratories, develop field deployable toolkits, train and deploy laboratory personnel, and analyze additional samples associated with regulatory and criminal investigations. As the program matures, additional resources are required to meet the increased volume and complexity of the samples as well as for management and support of new or existing analytical tools deployed for field use; development of new analytical methods or strategies; development and support of laboratory reach back capabilities, accreditation/proficiency requirements; and expansion of the safety program for the geographically diverse locations.

Compounding and outsourcer inspections have added an investigational assessment for compounding of opioids and opioid products. This expanded investigation involves tracking and tracing supply chains along with production activities at the compounding facilities. Additional will support the outsourcer inventory as it has grown and the products produced, and supply chains have become more complex.

Food Safety (+$21.3 million / 8 FTE)

New Era of Smarter Food Safety/Data Modernization & Enhanced Technology (DMET)
Field Human Foods (+6.6 million)
Field Animal Drugs and Foods (+0.6 million)

FDA requires additional resources in FY 2022 to strengthen its data infrastructure and technical platforms to support advanced analytical tools and improved processes supporting the New Era Initiatives. These investments will enable acquisition of new tools, systems and capabilities to support dictive analytics targeting imported food; enhancement and modernization of inspection, training, and compliance tools; data exchange to improve outbreak response; and support to modernize recall data delivery. FDA will evaluate existing ways non-traditional data sources are being utilized and expand into predictive models. As more data streams and tools for rapidly analyzing data become available, FDA will evaluate how we can best use predictive analytics tools to identify when and where contamination might be likely to occur, to prevent contaminated products from entering the food supply, and target efforts to remove potentially contaminated product from the market.

This request will enable improvements to the program and systems supporting the data and information exchange elements of Mutual Reliance; adding capabilities to the systems that support data exchange and state system interoperability for work planning, firm inventories, inspection data, laboratory results and enforcement actions. This funding will also support IT development and contracts for development of enhancements to various consumer notification processes related to recall modernization and investment towards systems enhancements to support a two-tier inspection program.

New Era/Mutual Reliance: Animal Food Safety Oversight
Field Animal Drugs & Foods (+14.1 million / 8 FTE)

With this increase, FDA will provide funding to states to expand efforts to modernize, harmonize, and transform the U.S. animal food inspection system into one that is comprehensive, and prevention oriented utilizing the Food Safety Modernization Act (FSMA) authorities including Preventive Control for Animal Food framework. FDA will also update inspection and enforcement programs, develop outreach and training initiatives, and devote resources to the analysis of controls for expected and understanding unknown animal food hazards. The One Health initiative has sown a clear linkage between animal health and human health, namely animals have died, and humans have been sickened because animal food has been contaminated by preventable hazards. FDA has historically relied on states to conduct 80% of animal food safety inspections. In FY 2020, FDA received $3.2M as an initial investment in cooperative

agreements with just 13 states. With existing resources, FDA and its state partners need these resources to help address the risk-based oversight needed of the existing inventory of approximately 34,000 animal food facilities subject to FDA's food safety regulations, including FSMA.

Crosscutting (+$48.4 million / 83 FTE)

Data Modernization and Enhanced Technologies: (+ $10.6 million / 12 FTE)
Field Human Foods (+$6.4 million/ 7 FTE)
Field Human Drugs (+$1.8 million/ 2 FTE)
Field Biologics (+$0.5 million/ 1 FTE)
Field Animal Drugs and Foods (+$0.7 million/ 1 FTE)
Field Devices (+$1.2 million/ 1 FTE)

The FY 2022 Budget includes $11.0 million to support data modernization by building core programs and infrastructure aligned to FDA's enterprise technology capabilities.

Inspections: (+$18.8 million / 65 FTE)
Field Human Foods (+$3.5 million/ 12 FTE)
Field Human Drugs (+$7.5 million/ 26 FTE)
Field Biologics (+$4.5 million/ 16 FTE)
Field Animal Drugs and Foods (+$0.3 million / 1 FTE)
Field Devices (+$3.0 million/ 10 FTE)

ORA is the lead on increasing site inspections and the number of unannounced inspections of regulated facilities manufacturing essential medicines, medical countermeasures, and critical inputs. The additional resources will help address the postponed FDA facility inspections caused by COVID related delays. The additional resources will go directly to defining methods for flagging these facilities manufacturing essential medicines in the inventory as a manufacturer of essential medicines. In addition, the funding will also allow ORA to invest in technological advances to streamline the inspectional process.

Capacity Building: (+$11.6 million / 6 FTE)
Field Human Foods (+$7.0 million/ 4 FTE)
Field Human Drugs (+$2.0 million/ 1 FTE)
Field Biologics (+$0.6 million)
Field Animal Drugs and Foods (+$0.8 million)
Field Devices (+$1.3 million/ 1 FTE)

The FY 2022 Budget includes $11.6 million to support centrally administered services to support critical, high-priority Capacity Building activities.

Pay Costs: (+$7.0 million)
Field Human Foods (+$4.3 million)
Field Human Drugs (+$1.1 million)
Field Biologics (+$0.4 million)
Field Animal Drugs and Foods (+$0.4 million)

Field Devices (+$0.8 million/ 1 FTE)
The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

User Fees

Current Law User Fees: +$5.4 million
Field Human Drugs: $1.1 million
Field Biologics: $0.1 million
Field Animal Drugs and Foods: $0.1 million
Field Devices: $0.1 million
Field Center for Tobacco: $4.0 million

The ORA Program request includes an increase of $5,368,000 for user fees authorized, 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

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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2020: 93.4% 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 2020: 77.7% Target: 80% (Target Not Met)	80%	80%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2020: 70.0% Target: 70% (Target Met)	70%	70%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
254221: Percentage of Medical Device and Radiological Health significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2020: 88.5% 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 2020: 76.2% 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 2020: 69.3% 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 2020: 77.8% 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 2020: 84.1% 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 2020: 100.0% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2020: 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 2020: 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.

COVID Impact on ORA Field Performance Measures

Due to COVID-19, ORA faced many challenges in meeting the FY 2020 performance targets. FDA paused on-site surveillance inspections due to COVID-19, needing to balance our public health mission with investigator safety concerns, geographic and establishment restrictions, and increased work related to public health need during the pandemic. Despite these challenges, ORA continued conducting its mission critical work, and met all of the performance goals, except one. Given the 3-year rolling basis methodology of this performance goal and the continued prioritization of follow-up after regulatory actions, the inspections not conducted toward this goal in FY 2020 will be a responsibility in FY 2021. Depending on COVID-19 restrictions and continued safety concerns, COVID-19 may have an impact on ORA’s ability to meet the FY 2021 performance targets.

PROGRAM ACTIVITY DATA

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate[5]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	3941	***2,500***	***8,000***
Domestic Food Safety Program Inspections	2,312	**Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high**	**Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high**
Imported and Domestic Cheese Program Inspections	64		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	124		
Domestic Fish & Fishery Products (HACCP) Inspections	338		
Import (Seafood Program Including HACCP) Inspections	90		
Juice HACCP Inspection Program (HACCP)	93		
Interstate Travel Sanitation (ITS) Inspections	245		
Domestic Field Exams/Tests	805	*850*	2,500
Domestic Laboratory Samples Analyzed	11,238	*11,500*	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***641***	***50***	***1,400***
All Foreign Inspections	912	*50*	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***4,582***	***2,550***	***9,400***
IMPORTS			
Import Field Exams/Tests[2]	82,382	*82,500*	168,200
Import Laboratory Samples Analyzed	11,750	*12,000*	35,300
Import Physical Exam Subtotal	**94,132**	**94,500**	**203,500**
Import Line Decisions	16,983,686	17,000,000	17,850,000
Percent of Import Lines Physically Examined	0.55%	0.56%	1.14%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***5,476***	***2,500***	***2,078***
State Contract Food Safety (Non HACCP) Inspections	4,960	4,090	5,000
State Contract Domestic Seafood HACCP Inspections	365	327	400
State Contract Juice HACCP	34	29	35
State Contract LACF/Acidified Food Inspections	64	61	75
State Contract Foods Funding	$13,727,413	$13,756,200	$13,893,762
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***10,058***	***5,050***	***11,478***

[1] The FY 2020 actual unique count of foreign inspections includes 38 OGPS inspections (22 for China, 9 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.

[4] FERN State Laboratory funding has ended in FY20. It been removed from PAD.

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2020Actuals	FY 2021 Estimate[2]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***25***	***5***	***100***
		5	
Domestic Inspections	25	5	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***3***	***0***	***0***
Foreign Inspections	3	0	0
IMPORTS			
Import Field Exams/Tests[1]	3,210	3300	1,600
Import Laboratory Samples Analyzed	208	215	400
Import Physical Exam Subtotal	**3,418**	**3,500**	**2,000**
Import Line Decisions	2,350,216	2,375,673	2,494,457
Import Line Decisions	0.15%	0.15%	0.08%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***28***	***5***	***100***

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

[2] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate[4]	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***882***	***150***	***1,695***
Pre-Approval Inspections (NDA)	55	10	100
Pre-Approval Inspections (ANDA)	41	6	90
Bioresearch Monitoring Program Inspections	411	66	600
Drug Processing (GMP) Program Inspections	315	52	650
Compressed Medical Gas Manufacturers Inspections	13	2	50
Adverse Drug Events Project Inspections	25	4	88
OTC Monograph Project and Health Fraud Project Inspections	6	1	70
Compounding Inspections[1]	54	9	127
Domestic Laboratory Samples Analyzed	818	701	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS[2]	***516***	***40***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	58	11	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	89	16	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	139	24	255
Foreign Drug Processing (GMP) Program Inspections	251	44	900
Foreign Adverse Drug Events Project Inspections	4	1	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,398***	***190***	***3,055***
IMPORTS			
Import Field Exams/Tests	7,096	7,100	10,000
Import Laboratory Samples Analyzed	841	850	620
Import Physical Exam Subtotal	**7,937**	**7,950**	**10,620**
Import Line Decisions	959,585	967,604	967,604
Percent of Import Lines Physically Examined	0.83%	0.82%	1.10%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,398***	***190***	***3,055***

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

[2] The FY 2019 actual unique count of foreign inspections includes 36 OGPS inspections (16 for China, 16 for India, and 0 for Latin America).

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

[4] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***744***	***100***	***1,892***
Bioresearch Monitoring Program Inspections	69	8	100
Blood Bank Inspections	233	90	900
Source Plasma Inspections	106	12	190
Pre-License, Pre-Market Inspections	44	5	55
GMP Inspections	17	2	28
GMP (Device) Inspections	3	1	7
Human Tissue Inspections	283	30	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***29***	***5***	***47***
Bioresearch Monitoring Program Inspections	8	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	0	1	7
Pre-License, Pre-market Inspections	7	1	7
GMP Inspections (Biologics & Device)	0	1	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***773***	***105***	***1,939***
IMPORTS			
Import Field Exams/Tests	85	45	45
Import Line Decisions	152,158	155,000	197,462
Percent of Import Lines Physically Examined	0.06%	0.02%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***773***	***105***	***1,939***

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

[2] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Animal Drugs & Feeds Program Activity Data (PAD)

Field Animal Drugs and Feeds Program Workload and Outputs	FY 2020 Actuals			FY 2021 Estimate[5]			FY 2022 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	***598***	***78***	***520***	***105***	***5***	***100***	***1,696***	***298***	***1,398***
Pre-Approval /BIMO Inspections	3	3	0	1	1	0	79	79	0
Drug Process and New ADF Program Inspections	51	51	0	9	9	0	175	175	0
BSE Inspections	87	0	87	16	0	16	1,205	0	1,205
Feed Contaminant Inspections	0	0	0	0	0	0	25	0	25
Illegal Residue Program Inspections	120	0	120	20	0	20	450	0	450
Feed Manufacturing Program Inspections	54	0	54	10	0	10	200	0	200
Domestic Laboratory Samples Analyzed	463	1	462	421	17	404	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS[1]	***52***	***19***	***33***	***5***	0	5	***5***	***0***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	6	6	0	0	0	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	14	14	0	0	0	0	33	33	0
Foreign Feed Inspections	2	2	0	2	0	2	5	0	5
BSE Inspections	2	0	2	2	0	2	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***650***	***97***	***553***	***110***	***5***	***105***	***1,701***	***298***	***1,403***
IMPORTS									
Import Field Exams/Tests	1,467	491	976	1,500	500	1000	3,795	495	3,300
Import Laboratory Samples Analyzed	363	0	363	400	0	400	867	2	865
Import Physical Exam Subtotal	**1,830**	**491**	**1,339**	**1,900**	**500**	**1,400**	**4,662**	**497**	**4,165**
Import Line Decisions	493,192	68,371	424,821	479,518	68,500	425,000	503,494	71,925	446,250
Percent of Import Lines Physically Examined	0.37%	0.72%	0.32%	0.40%	0.73%	0.33%	0.93%	0.69%	0.93%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***1,543***	***0***	***1,543***	***1,000***	***0***	1,000	***1,600***	***0***	1,600
State Contract Inspections: BSE	637	0	637	403	0	403	650	0	650
State Contract Inspections: Feed Manufacturers	382	0	382	248	0	248	400	0	400
State Contract Inspections: Illegal Tissue Residue	0	0	0	0	0	0	0	0	0
State Contract Animal Feeds Funding	$3,123,039		$3,123,039	$3,200,000	0	$3,200,000	$3,296,000	0	$3,296,000
State Contract Tissue Residue Funding			$0	$0	0	$0	$0	0	$0
Total State Funding	**$3,123,039**	**$0**	**$3,123,039**	**$3,200,000**	**$0**	**$3,200,000**	**$3,296,000**	**$0**	**$3,296,000**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***2,193***	***97***	***2,096***	***1,110***	***5***	***1,105***	***3,301***	***298***	***3,003***

[1] The FY 2019 actual unique count of foreign inspections includes 1 OGPS inspections (1 for China).

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

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

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

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries. ORA will continue to monitor progress throughout FY21.

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***1,084***	***100***	***2,546***
Bioresearch Monitoring Program Inspections	136	17	300
Pre-Market Inspections	26	4	60
Post-Market Audit Inspections	7	2	60
GMP Inspections	622	75	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	308	37	750
Domestic Radiological Health Inspections	27	4	50
Domestic Field Exams/Tests	18	2	100
Domestic Laboratory Samples Analyzed	82	72	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***175***	***5***	***613***
Foreign Bioresearch Monitoring Inspections	9	0	14
Foreign Pre-Market Inspections	12	0	30
Foreign Post-Market Audit Inspections	0	0	20
Foreign GMP Inspections	152	5	550
Foreign MQSA Inspections	0	0	14
Foreign Radiological Health Inspections	13	0	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***1,259***	***105***	***3,159***
IMPORTS			
Import Field Exams/Tests	16,641	16,650	19,800
Import Laboratory Samples Analyzed	303	310	670
Import Physical Exam Subtotal	**16,944**	**17,000**	**20,470**
Import Line Decisions	22,512,049	25,521,999	27,308,539
Percent of Import Lines Physically Examined	0.08%	0.08%	0.07%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***6,089***	***7,020***	***7,880***
Inspections (MQSA) by State Contract	6,071	7,000	6,800
GMP Inspections by State Contract	18	20	20
State Contract Devices Funding	$194,122	$200,000	$286,443
State Contract Mammography Funding	$10,593,830	$107,000	$11,240,003
Total State Funding	**$10,787,952**	**$11,297,711**	**$11,526,446**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***7,348***	***7,125***	***11,039***

[1] The FY 2020 actual unique count of foreign inspections includes 2 OGPS inspections (1 for China and 1 for India)

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

[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] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA has had to scale back foreign and

TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Tobacco	**680,437**	**752,921**	**681,513**	**780,812**	**99,299**
Center	664,168	732,476	658,906	754,159	95,253
User Fees	664,168	732,476	658,906	754,159	95,253
Family Smoking Prevention and Tobacco Control Act	*664,168*	*732,476*	*658,906*	*654,159*	*-4,747*
Expand tobacco products (Proposed)	---	---	---	*100,000*	*100,000*
Field	16,269	20,444	22,607	26,653	4,046
Family Smoking Prevention and Tobacco Control Act	*16,269*	*20,444*	*22,607*	*26,653*	*4,046*
FTE	**1,012**	**1,040**	**1,279**	**1,368**	***89***

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 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

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
- Establishing and 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,[131] and nearly 1,500 youth aged 12 to 17 smoke their first cigarette every day in the United States.[132] 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 Addiction 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 products, including electronic nicotine delivery systems (ENDS) - such as e-cigarettes, cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels.

[131] 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.

132 Substance Abuse and Mental Health Services Administration. (2020). *Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health* (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/

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 4

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.[133] 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 were current e-cigarette users (having used within the last 30 days) – with a majority reporting cartridge-based products as their usual brand. Additionally, for the first time ever, the total number of middle and high school students reporting past month use of e-cigarettes surpassed 5 million (an estimated 4.11 million high school students and 1.24 million middle school students).[134]

[133] Cullen KA, Ambrose BK, Gentzke AS, Apelberg BJ, Jamal A, King BA. *Notes from the Field:* Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students — United States, 2011–2018. MMWR Morb Mortal Wkly Rep 2018;67:1276–1277. DOI: http://dx.doi.org/10.15585/mmwr.mm6745a5

[134] Cullen KA, Gentzke AS, Sawdey MD, et al. e-Cigarette Use Among Youth in the United States, 2019. JAMA. 2019;322(21):2095–2103. doi:10.1001/jama.2019.18387

Published 2019 NYTS data in the *Journal of the American Medical Association (JAMA)* [135] shows that e-cigarettes remain the most commonly used tobacco product among youth: 27.5 percent of high school students and 10.5 percent of middle school students were current e-cigarette users. Published data from the 2020 NYTS, collected prior to the COVID-19 pandemic, shows a decline in current e-cigarette use: 19.6 percent high school students and 4.7 percent of middle school students were current e-cigarette users. Despite the decline in current use, approximately 3.6 million U.S. youths reported current e-cigarette use in 2020, more than 8 out of 10 youth users reported current use of flavored e-cigarettes, and disposable e-cigarette use increased significantly from 2019.[136]

FDA's ongoing oversight of e-cigarettes and other ENDS products remains a high priority and 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 who are over 21 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 youth. Years of progress to combat youth use of tobacco – to prevent lifetimes of addiction to nicotine – is now threatened by an epidemic of e-cigarette use by young people.

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 required 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). Due to the impact of the COVID-19 pandemic, the Agency requested, and the Court granted a 120-day extension of the deadline. The new deadline for submission of premarket applications for new deemed tobacco products on the market as of August 8, 2016 was September 9, 2020. FDA has received these submissions and is working to accelerate the review of premarket applications for e-cigarettes and other new tobacco products. FDA strives to be as transparent as possible with regards to the status of these submissions and plans to provide regular updates to the public over the course of the next year.

On August 19, 2020, the U.S. District Court for the District of Columbia issued a ruling, in part, to prohibit FDA enforcement of the Tobacco Control Act's premarket authorization requirement for premium cigars, as defined by the court, until after the agency considers developing a streamlined substantial equivalence process specifically for premium cigars. Accordingly, FDA will not enforce the premarket review requirement against manufacturers of premium cigars, as defined by the court, that did not submit premarket applications for these products by the Sept. 9, 2020 deadline. FDA also has updated its Guidance titled "FDA Deems Certain Tobacco Products Subject to FDA Authority, Sales and Distribution Restrictions, and Health Warning Requirements for Packages and Advertisements" to reflect this U.S. District Court ruling.

[135] Cullen KA, Gentzke AS, Sawdey MD, et al. e-Cigarette Use Among Youth in the United States, 2019. JAMA. 2019;322(21):2095–2103. doi:10.1001/jama.2019.18387

[136] Wang TW, Neff LJ, Park-Lee E, Ren C, Cullen KA. King BA. E-cigarette Use Among Middle and High School Students—United States, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1310-1312. DOI: http://dx.doi.org/10.15585/mmwr.mm6937e1

FDA remains committed to tackling the epidemic of youth vaping using all available regulatory tools at our disposal. On January 2, 2020, FDA issued a final guidance, revised in April 2020, for industry entitled "Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization."[137] 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) risk FDA enforcement actions.

FDA is prioritizing 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.

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.
In light of the alarming uptick in youth use of disposable e-cigarettes revealed in the 2020 NYTS data, flavored disposable ENDS products have also become an enforcement priority for FDA.

For ENDS products other than those in the groups described above, if premarket applications were submitted by September 9, 2020, FDA generally intends to continue to exercise enforcement discretion for up to one year pending FDA review of the application, unless there is a negative action by FDA on such application.

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. Toward that end, FDA has issued draft guidance entitled "Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies." This draft guidance is intended to help applicants design and conduct tobacco product perception and intention studies that may be submitted as part of a modified risk tobacco product application, premarket tobacco product application, or substantial equivalence report.

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

In addition, on December 20, 2019, legislation was signed into law 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 tobacco products – including cigarettes, cigars and e-cigarettes – to anyone under 21. FDA announced in the Spring 2020 Unified Agenda its intent to issue a regulation to fully implement this legislation.

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 and is currently working to publish final rules on these topics.[138] In addition, as described in the Unified Agenda, FDA is working towards a proposed rule regarding requiring manufacturers to establish tobacco product manufacturing practices.

On April 29, 2021, FDA announced[139] that it is committing to advancing two tobacco product standards to significantly reduce disease and death from using combusted tobacco products, the leading cause of preventable death in the U.S. FDA is working toward issuing proposed product standards within the next year to ban menthol as a characterizing flavor in cigarettes and ban all characterizing flavors (including menthol) in cigars. This decision is based on clear science and evidence establishing the addictiveness and harm of these products and builds on important, previous actions that banned other flavored cigarettes in 2009.

Menthol Product Standard

The 2009 TCA did not include menthol in its ban on characterizing flavors in cigarettes, leaving menthol cigarettes as the only flavored combusted cigarettes still marketed in the U.S. The law instructed FDA to further consider the issue of menthol in cigarettes.
Since then, FDA sought input from an independent advisory committee as required by the TCA, and further demonstrated its interest by issuing an Advance Notice of Proposed Rulemaking, undertaking an independent evaluation and supporting broader research efforts—all to better understand the differences between menthol and non-menthol cigarettes and the impact of menthol on population health. In the U.S., it is estimated that there are nearly 18.6 million current smokers of menthol cigarettes. But use of menthol cigarettes among smokers is not uniform: out of all Black smokers, nearly 85% smoke menthol cigarettes, compared to 30% of White smokers who smoke menthols. In addition, among youth, from 2011 to 2018, declines in menthol cigarette use were observed among non-Hispanic White youth but not among non-Hispanic Black or Hispanic youth.

Cigar Flavor Product Standard

[138] FDA has drafted final rules regarding PMTA and SE Reports. Both rules displayed in the Federal Register on January 19, 2021. However, pursuant to the White House Memorandum titled "Regulatory Freeze Pending Review," these rules have been withdrawn and returned to the Agency. FDA is working with the new Administration to allow these rules to proceed to publication in the Federal Register.

[139] https://www.fda.gov/news-events/press-announcements/fda-commits-evidence-based-actions-aimed-saving-lives-and-preventing-future-generations-smokers

After the 2009 statutory ban on flavors in cigarettes other than menthol, use of flavored cigars increased dramatically, suggesting that the public health goals of the flavored cigarette ban may have been undermined by continued availability of these flavored cigars.

Flavored mass-produced cigars and cigarillos are combusted tobacco products that can closely resemble cigarettes, pose many of the same public health problems, and are disproportionately popular among youth and other populations. In 2020, non-Hispanic Black high school students reported past 30-day cigar smoking at levels twice as high as their White counterparts. Nearly 74% of youth aged 12-17 who use cigars say they smoke cigars because they come in flavors they enjoy. Among youth who have ever tried a cigar, 68% of cigarillo users and 56% of filtered cigar users report that their first cigar was a flavored product. Moreover, in 2020, more young people tried a cigar every day than tried a cigarette.

The Tobacco Control Act also requires FDA to include new warning labels on cigarette packages and in cigarette advertisements. On March 17, 2020, FDA issued a final rule[140] to require new health warnings on cigarette packages and in cigarette advertisements. The warnings feature textual statements with photo-realistic color images depicting some of the lesser-known, but serious health risks of cigarette smoking, including impact to fetal growth, cardiac disease, diabetes, and more.

The 11 finalized cigarette health warnings represent the most significant change to cigarette labels in more than 35 years and will considerably increase public awareness. In addition, FDA has issued a guidance to accompany the final rule. The "Required Warnings for Cigarette Packages and Advertisements: Small Entity Compliance Guide"[141] guidance for industry will assist small businesses in understanding and complying with the final rule. FDA also has issued a guidance titled "Submission of Plans for Cigarette Packages and Cigarette Advertisements" to provide recommendations for industry regarding the submission of cigarette plans for cigarette packages and advertisements.

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, if they are substantially equivalent to an eligible predicate tobacco product, or if they are exempt from the requirements of substantial equivalence. 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 resulting from product changes are submitted for FDA review under one of these three marketing pathways:

- Premarket tobacco product application (PMTA)

[140] https://www.federalregister.gov/documents/2020/03/18/2020-05223/tobacco-products-required-warnings-for-cigarette-packages-and-advertisements

[141] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/required-warnings-cigarette-packages-and-advertisements-small-entity-compliance-guide-revised

- 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 and educate the public on 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

FDA is actively working to complete and publish this final rule.[142]

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. This rule 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. FDA is actively working to complete and publish this final rule.[143]

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

[142] FDA's final rule regarding SE Reports displayed in the Federal Register on January 19, 2021. However, pursuant to the White House Memorandum titled "Regulatory Freeze Pending Review," this rule was withdrawn from the Federal Register. The final rule is now under review at OMB.

[143] FDA's final rule regarding PMTAs displayed in the Federal Register on January 19, 2021. However, pursuant to the White House Memorandum titled "Regulatory Freeze Pending Review," this rule was withdrawn from the Federal Register. The final rule is now under review at OMB.

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 had authorized the marketing of four new tobacco products through the PMTA pathway. Through 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 placed stringent marketing restrictions on the products.

On December 17, 2019, FDA announced it 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 combusted 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.

As an alternative to the PMTA pathway, eligible 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[144] 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. FY 2020 performance measures are not yet available because FDA has been focused on the intake and processing of premarket submissions covering millions of deemed products received in September 2020.

FDA continues scientific review of provisional SE Reports.[145] 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. Approximately 1,400 reports were 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.

In April 2019, FDA posted six appendices containing common issues found in SE Reports, broken down by product type, on the Agency's website. 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

[144] http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm

[145] 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 had 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". 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.

On July 7, 2020, FDA announced the second set of tobacco products to be authorized as MRTPs and these are the first products to receive exposure modification orders, which permits the marketing of a product as containing a reduced level of or presenting a reduced exposure to a substance or as being free of a substance when the issuance of the order is expected to benefit the health of the population. Importantly, the authorization for these products requires the company to conduct postmarket surveillance and studies to determine whether the MRTP orders continue to be appropriate, including assessing the potential for increased use among youth. FDA previously authorized the marketing of these non-combusted cigarette products without modified risk information on April 30, 2019, as noted above via the PMTA pathway.

Status of Submitted Applications

The following table summarizes the status of tobacco product applications received, including Exemption Requests, Regular SE Reports, PMTA and MRTPA through December 31, 2020. Due to the large volume of PMTAs received and not yet fully processed, the numbers for PMTAs are expected to change as we continue to process applications submitted by September 9, 2020 and receive new applications. Therefore, in the PMTA column of the following table, the number of received and open applications is not available at this time. As of February 16, 2021, FDA has processed submissions that cover over 5 million products under the PMTA pathway. FDA is posting expanded data on our new Tobacco Product Application Metrics & Reporting webpage which can be found here: *https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/tobacco-product-applications-metrics-reporting*. For the first time, we will be posting all metrics both by pathway (SE, EX REQ, and PMTA) and by product category type (e.g., cigarette, ENDS, cigars, smokeless). This webpage will be updated regularly and will provide more detailed updates of the Agency's progress on premarket application review than previously available. The new website includes:

- List of deemed new tobacco products with applications pending with FDA https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/deemed-new-tobacco-product-applications-list
- List of negative actions and other actions that impact marketing (includes refuse-to-accept, refuse-to-file, marketing denial order, not substantially equivalent, not exempt, withdrawals by applicant, and administrative closures)
- List of positive marketing orders (includes marketing granted order, SE orders, and exempt orders)

Tobacco Product Applications Received, Open, Pending, and Closed by Product Class

Application Status	Product Class[146]	Cumulative through 12/31/2020				
		Exemption Requests	Regular SE Reports	Provisional SE Reports	Premarket Tobacco Applications	Modified Risk Tobacco Applications
Received[147]	Cigarettes	801	1,442	2,392		14
	Roll Your Own	25	1,158	646		0
	Smokeless	57	480	589		19
	ENDs	0	2	18		14
	Cigars	182	3,135	0		0
	Pipe Tobacco Products	0	1,759	0		0
	Waterpipe Tobacco Products	200	2,569	0		0
	Other	0	1	0		0
	Total	**1,265**	**10,546**	**3,645**		**47**
Open	Cigarettes	98	80	395		2
	Roll Your Own	0	124	13		0

[146] Other includes tobacco products that are not defined (e.g., nicotine gel, dissolvable products from extracts) and products not under CTP jurisdiction.

	Smokeless	0	65	78		7
	ENDs	0	0	0		5
	Cigar	62	2,937	0		0
	Pipe Tobacco Products	0	1,528	0		0
	Waterpipe Tobacco Products	114	1,142	0		0
	Other	0	1	0		0
	Total	**272**	**5,877**	**486**		**14**
Closed[148]	Cigarettes	703	1,362	1,997	12	12
	Roll Your Own	25	1,034	633	4	0
	Smokeless	59	415	511	14	12
	ENDs	0	2	18	4,384	9
	Cigar	120	198	0	0	0
	Pipe Tobacco Products	0	231	0	0	0
	Waterpipe Tobacco Products	86	1,427	0	64	0
	Other	0	0	0	1	0
	Total	993	4,669	3,159	4,479	33

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

[148] Closed includes refuse-to-accept, refuse-to-file, remove from review, issuance of an order, environmental information request, withdrawn, or closure due to administrative issues.

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 2020, FDA invested more than $220 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 across populations
- Health Effects: understanding the short- and long-term health effects of tobacco products across populations of special relevance, as appropriate
- Behavior: understanding the knowledge, attitudes, and behaviors related to tobacco product use and changes in tobacco product characteristics across populations, as appropriate
- 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 among different populations
- Impact Analysis: understanding the impact of potential FDA regulatory actions

In addition to conducting independent research to support regulatory science, CTP partners with several other FDA Centers including the National Center for Toxicological Research (NCTR) and Center for Food Safety and Nutrition (CFSAN), and FDA's Southeast Tobacco Laboratory, as well as other governmental agencies, including the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC). By leveraging the expertise of other Federal agencies, FDA brings science-based regulation to the manufacturing, marketing, and distribution of tobacco products.

FDA has also undertaken efforts to further the discussion and understanding around e-cigarette or vaping product use-associated lung injury (EVALI). This includes a request for information (RFI) that could help identify and evaluate additional steps the Agency could take to "address the recent pulmonary illnesses reported to be associated with the use of e-cigarettes and vaping products."[149]

NIH Tobacco Regulatory Science Program (TRSP)

[149] https://www.federalregister.gov/documents/2020/02/18/2020-03160/request-for-information-on-vaping-products-associated-with-lung-injuries

Through a collaboration with NIH, FDA is able to tap into NIH's well-established infrastructure for the solicitation, review, and management of scientific research. In FY 2020, FDA funded more than 100 research projects via NIH TRSP. These research projects include grants 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 FDA research priority areas, such as:

- 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
- Studying the impact of flavor and sweetness of different tobacco products on use behaviors such as experimentation and initiation among youth and young adults

FDA also recommends research studies include, where appropriate to the research question, populations of special relevance, including (but not limited to): youth, socioeconomically disadvantaged populations, racial/ethnic minorities, underserved rural populations, people with comorbid mental health conditions and/or substance use disorders, military/veteran populations, pregnant women or women of reproductive age, and sexual and gender minorities.

A key component of the CTP – NIH TRSP collaboration includes funding 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). CASEL's objective is to facilitate synthesis, coordination, and communications of research and career enhancement within the scientific program by FDA.

Population Assessment of Tobacco and Health (PATH) Study

FDA funds the PATH Study[150] via NIH's National 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.

[150] https://www.fda.gov/tobacco-products/research/fda-and-nih-study-population-assessment-tobacco-and-health

Research topics in the PATH Study include examining 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 tobacco products. The study also assesses exposures from tobacco use, related biomarkers, and potential health outcomes.

Figure 5 Population Assessment of Tobacco and Health logo

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. This data collection is referred to as "Special Collection Wave 4.5". A second special data collection of approximately 16,000 PATH Study youth and young adult respondents began December 2019 and concluded December 2020. This data collection is referred to as "Special Collection Wave 5.5". A special collection of approximately 13,000 adult respondents began September 2020 and concluded December 2020. This data collection, referred to as "PATH Adult Telephone Survey" or "PATH ATS" examines adult tobacco use during the COVID-19 pandemic.

Wave 4 questionnaire data were released to researchers in May 2019 and to the public in November 2019. Wave 5 questionnaire data is scheduled for release Spring 2021. Wave 3 biomarker data were released in March and June 2020. Initial Wave 4 biomarker data were released to researchers in August 2020. A Special Collection of data collected from youth ages 12-17 (Wave 4.5) was released to researchers in March 2020 and to the public in September 2020.

Laboratory Analyses

FDA has extensive tobacco regulatory science laboratory capabilities. CTP, in partnership with the Office of Regulatory Affairs (ORA), has established a dedicated tobacco product laboratory, the Southeast Tobacco Laboratory (STL), to conduct various tests to verify information in premarket applications, develop product standards, and to support enforcement. The STL houses a wide range of capabilities include chemical and physical testing of tobacco filler, e-liquid, smoke, and aerosol. Additional specialized tobacco testing support activities have also been established at the FDA Winchester Engineering Analytical Center, which supports engineering and battery safety testing for electronic nicotine delivery device and endotoxin testing in e-liquids, and at the FDA Forensic Chemistry Center, which supports tobacco products testing for counterfeit markers, both chemical and physical as well as testing associated with adverse events and emergency responses (i.e. EVALI). 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 FDA's Center for Drug Evaluation and Research (CDER) to understand the toxicity of e-cigarette aerosol through in vivo inhalation studies.

FDA partners with CDC to address priority research needs with the Division of Laboratory Sciences at CDC on the analyses of tobacco exposure biomarkers from research data collected in the PATH Study.

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 expands the scope and increases 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[151]. On November 5, 2019, data from this survey were published in the *Journal of the American Medical Association (JAMA)*[152] 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. On September 18, 2020, published data from the 2020 NYTS, collected prior to the COVID-19 pandemic, shows a decline in current e-cigarette use—19.6 percent high school students and 4.7 percent of middle school students were current e-cigarette users. Despite the decline in current use, approximately 3.6 million U.S. youths reported current e-cigarette use in 2020, more than 8 out of 10 youth users reported current use of flavored e-cigarettes, and disposable e-cigarette use increased significantly from 2019.[153] 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-cigarette among recently pregnant women in the Pregnancy Risk Assessment Monitoring System (PRAMS). 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. The National Longitudinal Mortality Study (NLMS) links TUS-CPS data with health data under a separate interagency agreement. The interagency agreement was recently expanded as part of the Tobacco Longitudinal Mortality Study (TLMS) to include more records in the linkage, as well as linking

[151] Cullen KA, Ambrose BK, Gentzke AS, Apelberg BJ, Jamal A, King BA. *Notes from the Field:* Use of Electronic Cigarettes and Any Tobacco Product Among Middle and High School Students — United States, 2011–2018. MMWR Morb Mortal Wkly Rep 2018;67:1276–1277. DOI: http://dx.doi.org/10.15585/mmwr.mm6745a5

[152] Cullen KA, Gentzke AS, Sawdey MD, et al. e-Cigarette Use Among Youth in the United States, 2019. JAMA. 2019;322(21):2095–2103. doi:10.1001/jama.2019.18387

[153] Wang TW, Neff LJ, Park-Lee E, Ren C, Cullen KA. King BA. E-cigarette Use Among Middle and High School Students—United States, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1310-1312. DOI: http://dx.doi.org/10.15585/mmwr.mm6937e1

with health expenditure data from the Centers for Medicare and Medicaid Services (CMS) and cancer incidence data from NCI's SEER program.

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.

On March 18, 2020, FDA announced the temporary postponement of all routine domestic surveillance facility inspections due to health and safety concerns related to the COVID-19 pandemic. FDA also issued related partial stop work orders to the contractors engaged in tobacco retail compliance check inspections and vape retail inspections. The Agency subsequently extended the partial stop work orders through the end of FY 2020. Guided by health and safety considerations, FDA took appropriate actions, as outlined by its priorities. For example, certain enforcement efforts, such as monitoring the online marketing and sale of regulated tobacco products and issuing import alerts for unauthorized tobacco products, remained uninterrupted by COVID-19.

In July 2020, FDA announced the development of a risk assessment level to help FDA, as well as the states, make informed risk-based decisions on when and where to resume prioritized domestic inspections. This "Advisory Level" qualitatively assesses the status of COVID-19 cases in a local area based on county, state, and national criteria, using three metrics: the phase that the state is in as defined by the White House guidelines, and two information sources measured at the county level that are intended to indicate the current trend and intensity of infection. These metrics assist FDA in identifying and prioritizing the types of field operations that can safely occur within a region. States that conduct work for FDA under contract may use the Advisory Level to inform their decisions regarding inspectional assignments and other field operations.

In FY 2021, some tobacco manufacturer and retailer inspections resumed in certain areas where the spread of COVID-19 was less prevalent. FDA will continue taking appropriate actions that are guided by health and safety considerations and as outlined by the Agency's priorities.

Since October 1, 2019, as part of the Youth Tobacco Prevention Plan and consistent with FDA's policy to prioritize the enforcement of certain e-cigarettes and other deemed products on the market, the Agency has taken the following actions to stop youth use of, and access to, ENDS products:

- Prior to the partial stop work order issued in March 2020 due to the COVID-19 pandemic, conducted over 65,000 retail inspections to crack down on the sale of tobacco products, including ENDS products, to minors at both brick-and-mortar and online retailers
- Issued more than 7,000 warning letters and civil money penalties to retailers for illegally selling tobacco products, including ENDS products, to minors
- Issued over 200 warning letters to online and brick-and-mortar establishments, including 7-Eleven and Shell, for selling unauthorized flavored, cartridge-based e-cigarette products

- Prior to temporarily halting inspection activities due to the COVID-19, conducted inspections of over 140 tobacco manufacturing establishments and over 400 vape shops and conducted investigations involving thousands of websites, issued warning letters to manufacturers, importers, and vape shops for illegally marketing over 100 unauthorized ENDS products
- Issued 96 warning letters to companies that have not submitted premarket applications to FDA and are continuing to sell or distribute unauthorized ENDS after September 9, 2020. Collectively, the 96 companies that received those warning letters have over 826,000 products listed with FDA
- Issued a warning letter to XL Vape LLC (doing business as Stig Inc.), a popular disposable e-cigarette brand among youth, for the unauthorized sale of their ENDS products
- Issued warning letters to two companies for illegally marketing unauthorized menthol-flavored e-liquids that feature cartoon images, such as vampires and kings
- Issued warning letters to ten companies, including the maker of Puff Bar, for the unauthorized sale of flavored disposable e-cigarettes and e-liquids that imitate packaging for products such as Cinnamon Toast Crunch cereal, Twinkies, and Cherry Coke
- Issued warning letters to companies for marketing unauthorized products, such as a backpack and sweatshirt with hidden pockets to conceal an e-cigarette
- Issued warning letters to companies for marketing unauthorized products that resemble smartwatches and children's toys, such as a video game system and a fidget spinner
- Issued warning letters to companies marketing e-liquids that imitate packaging for food products that appeal to youth, such as candy, or feature cartoon characters like SpongeBob SquarePants
- Issued a warning letter to e-liquid manufacturer StemStix Inc. for marketing new tobacco products without authorization, marketing tobacco products with false and misleading advertising, and marketing unauthorized modified risk tobacco products
- Refused admission into the U.S. of at least 300 lines of ENDS products, including disposables, for violations of the FD&C Act
- In collaboration with U.S. Customs and Border Protection, seized more than 33,000 units of counterfeit, unauthorized e-cigarettes coming from China

Figure 6 Examples of unauthorized ENDS products targeted to minors.

In March, FDA also sent official requests to four e-cigarette brands – each active and with large followings on social media and not using age restriction tools on those platforms – to submit information about their marketing practices to FDA. This information will allow FDA to further understand the relationship between rising youth exposure to online e-cigarette marketing and youth use. Based on what FDA learns from the information these companies provide, the Agency will explore its regulatory options, including using the full scope of its authority to target youth exposure and access to, and appeal of, these products.

Tobacco Retailer Inspection Program

As of February 28, 2021, FDA had contracts for tobacco retailer compliance check inspections in approximately 50 states and territories, and one tribal jurisdiction, though as mentioned above, a stop work order starting March 19 was issued as a safety measure due to the COVID-19 pandemic. In FY 2021, retailer inspections resumed on a limited basis in certain areas where the spread of COVID-19 was less prevalent. 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 FDA commissioned inspectors in the jurisdiction 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 2020 Actuals	FY 2021 (as of 2/28/2021)	Total Since the Program's Inception (as of 2/28/2021)
Retailer Inspections	65,716	3,642	1,205,423
Total Warning Letters	4,906	11	98,054
Warning Letters Resulting from the Sale of ENDS Products to Minors	1,166	3	11,565
Total Civil Money Penalties	2,327	8	25,828
Civil Money Penalties Resulting from the Sale of ENDS Products to Minors	480	2	2,057
No-Tobacco-Sale-Orders	37	1	220

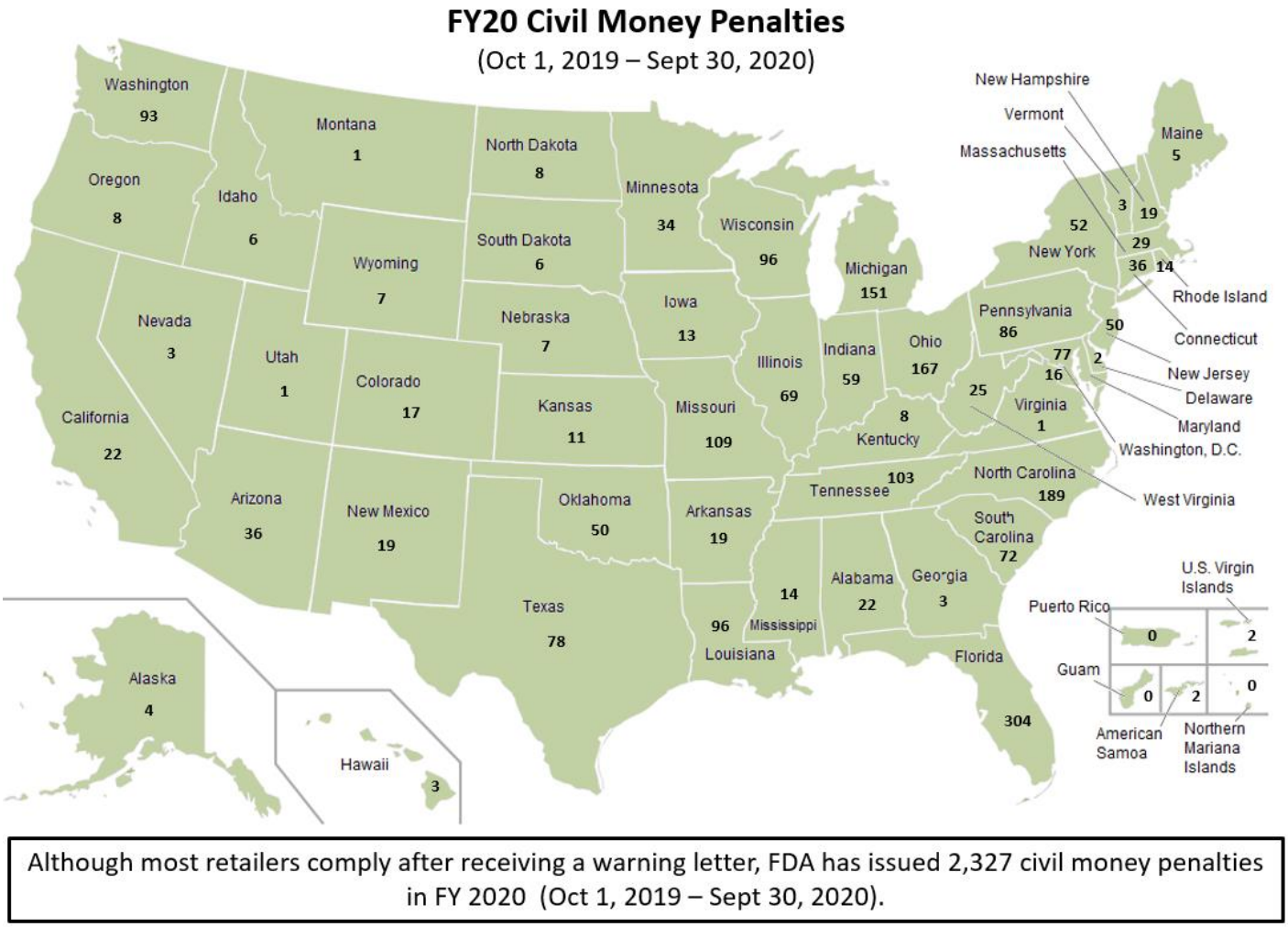


Figure 3 The number of Civil Money Penalty Complaints filed by the Center for Tobacco Products in FY 2020.

Tobacco 21

As stated above, it is now illegal for a retailer to sell tobacco products – including cigarettes, cigars and e-cigarettes – to anyone under 21. The legislation also required FDA to publish a final rule making conforming amendments to our regulations to reflect this statutory change. The law also provides that such final rule must increase the federal minimum for verification of tobacco product purchaser age by retailers, from under 27 years of age to under 30 years of age. FDA is currently working to issue this final rule. Until the regulation is changed, the current requirement of verifying identification by means of photo identification for those under 27 years of age remains in effect.

FDA's enforcement of the new federal minimum age law is generally carried out using the same process that was used to enforce the previous minimum age of sale. The Agency continues to conduct compliance check inspections of tobacco product retailers to determine a retailer's compliance with federal laws and regulations. During Undercover Buy inspections, underage tobacco product purchasers (who are under the supervision of FDA-commissioned inspectors)

attempt to purchase tobacco products. If, during these inspections, a tobacco product is sold to an underage purchaser, FDA sends the retailer a Compliance Check Inspection Notice which informs the retailer that a potentially violative inspection occurred at the establishment.

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 those for 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.[154] 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; however, Federal law enacted in December 2019 prohibits retailers from selling tobacco products to anyone under 21.

In addition, the agency created the "FDA's Age Calculator" mobile application (app) to help retailers, through the use of their personal smartphone, determine if the purchaser is of legal sales age. This app has allowed users to update it to reflect the change of the federal minimum age of sale of tobacco products from 18 to 21 years that became effective on December 20, 2019.

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 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. Since the inception of the Tobacco Program's manufacturer inspection activities through February 28, 2021, CTP has overseen the completion of more than 2,300 inspections of vape shops to verify whether they were engaged in manufacturing activities, and ORA has completed over 900 routine biennial inspections of tobacco manufacturers. As mentioned above, in March 2020, FDA temporarily postponed manufacturing inspections, including tobacco, due to the COVID-19 pandemic and the related stop work order for inspection contracts impacts work related to FDA's vape shop inspections. In FY 2021, to determine manufacturers' compliance with applicable FDA laws and regulations, the agency is utilizing remote regulatory assessments and domestic manufacturer inspections, which resumed on a limited basis where the spread of COVID-19 is less prevalent.

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. Since the inception of the Tobacco Program's internet and publication surveillance activities through February 28,

[154] https://digitalmedia.hhs.gov/tobacco/print_materials/search.protocol=https?page=1&tag=This+Is+Our+Watch

2021, FDA has issued over 900 warning letters as a result of these surveillance activities. This includes issuance of well over 140 warning letters in FY 2020. 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 79 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

Beginning in 2014, FDA began implementing multiple public education campaigns designed to reduce cigarette initiation among populations who continued to have high prevalence of use and remained susceptible to cigarette use. With the changing tobacco landscape and the increased youth initiation and use of e-cigarettes, FDA began prioritizing prevention efforts to address youth use of vaping products in 2017 and has steadily increased budget allocation to reverse escalating youth use. FDA also continuously monitors national usage rates of all tobacco products to determine the most pressing needs and then align the best approaches for campaign messaging and development. In 2020, several public education campaigns and their related outcome evaluation research were completed. Going forward, FDA will continue comprehensive youth prevention efforts based on prevalence of use. A concerted focus will remain on driving down e-cigarette use, the most used tobacco product among all youth. While cigarette use has declined to the lowest recorded rates, cigarettes remain the most harmful combustible tobacco product and therefore an area of concern. Research is in progress to explore the need for additional new programs to educate youth about the harms of cigarette and other tobacco product use.

FDA's tobacco 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 cigarette use among high at-risk African American, Hispanic, and Asian American/ Pacific Islander youth ages 12-17.
"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 – ENDS Prevention

FDA's award-winning youth tobacco prevention campaign, "The Real Cost," continues 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. "The Real Cost" launched in 2014 with cigarette prevention messaging using a robust media strategy to effectively reach teens and change their tobacco-related knowledge, attitudes, beliefs, and behaviors. The campaign expanded to include smokeless tobacco messaging in 2016, and then FDA began prioritizing e-cigarette messaging in 2017 due to the high youth usage rates.

Figure 18 "The Real Cost" campaign logo

In September 2018, FDA launched "The Real Cost" E-Cigarette Campaign 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, and highlights information about the potential risks of e-cigarette use. The campaign launched with national digital advertising and posters placed in all public and private school bathrooms. In 2019, campaign advertising expanded to television and remains FDA's highest public education priority. FDA will be expanding e-cigarette prevention messaging to American Indian/Alaska Native (AI/AN) youth audiences, a population that has historically had higher tobacco usage rates. FDA has conducted research with AI/AN youth to understand tobacco beliefs and perceptions and is determining best messaging approaches to reach this at-risk audience.

Since the launch, the campaign has shown positive results for effective reach and engagement. This campaign has reached up to 85 percent of all teenagers nationwide and has generated over 4.7 billion views from teen exposure and high online engagement. Across social media platforms, FDA has engaged teen audiences with more than 3.1 million likes, over 337,000 shares, and over 80,000 comments. Additionally, on the campaign's social media channels approximately 10% of the total comments from teens are asking for help and resources to quit vaping. In an ongoing collaboration with the National Cancer Institute (NCI), FDA and NCI developed vaping cessation content for teens to be added on the Teen.SmokeFree.gov website. Since the web content launched in July 2019, there have been over 1.6 million page views with visitors spending an average of 4 minutes per page to learn how to quit vaping, manage nicotine withdrawal and acquire tips for managing stress and anxiety.

The Real Cost – Cigarette Prevention

In February 2014, FDA launched its first ever national youth tobacco prevention campaign, "The Real Cost," which was designed to prevent youth who were open to using tobacco from doing so and to reduce the number of youths who moved from experimenting with tobacco to regular use. Overall, nationally representative data suggests that the percentage of youth who currently use cigarettes has declined from 3.8 percent in 2018 to 3.2 percent in 2020. Although the decline at the national level is evident, state-level prevalence of current cigarette smoking has remained higher than the national average in certain states. In 2021, to address the remaining high usage rates of cigarettes in key locations across America, "The Real Cost" Cigarette Campaign will continue to provide national paid media messages, while focusing on states that have the highest

youth cigarette usage rates, which include Alabama, Arkansas, Kentucky, Louisiana, North Carolina, North Dakota, Oklahoma, South Dakota, Tennessee, West Virginia, Iowa, Mississippi, Montana, New Mexico, Alaska, Pennsylvania, South Carolina, Virginia, and Wyoming. Additionally, the campaign is exploring opportunities to deliver critical cigarette prevention messaging to specific audiences that are at higher risk of smoking. FDA launched new advertising for the campaign in December 2020.

The Real Cost – Smokeless Tobacco

To educate youth about the dangers of smokeless tobacco use, the FDA expanded "The Real Cost" campaign in April 2016 to include new advertising targeting the hard-to-reach rural male youth ages 12-17 at-risk of smokeless tobacco use. The campaign advertisements, built on extensive qualitative research and theories of health behavior change, aimed to deliver facts about the dangers of smokeless tobacco use in relevant and attention-grabbing ways. The overall strategic platform for this messaging area was "smokeless doesn't mean harmless." The campaign advertisements were in market at high reach and frequency levels using a variety of tactics, including local television and radio, outdoor signs, as well as precise targeting on digital and social media platforms based on teen's passion points. The advertisements initially educated nearly 600,000 rural male youth in 35 rural media markets where smokeless tobacco use was relatively high. In January 2019, the campaign expanded to 20 states after the end of the evaluation period, reaching nearly 3 million male youth, using a digital-only media strategy.

During the three years the campaign was in market, "The Real Cost" Smokeless Campaign was able to achieve significant reach to the rural male youth audience. The messaging resonated with the audience and the campaign achieved high levels of receptivity among the audience. Overall, the campaign was able to reach more than 90 percent of the audience and there were over 14 million social media engagements with the campaign's social media channels.

As a result of prioritizing e-cigarettes and combustible tobacco products, the smokeless public education campaign ended in December 2020. FDA will continue to provide youth messaging and resources for stakeholders on smokeless tobacco prevention.

Overall, "The Real Cost" campaign has received a number of accolades from the advertising and marketing industry for its creativity and effectiveness. The North American Effie Effectiveness Awards awarded the campaign with a 2015 Gold Effie, a 2017 Bronze Effie, a 2019 Silver Effie and a 2020 Bronze Effie. The campaign also earned 2017 and 2019 Clio Awards; and 2016 Shorty Awards. The campaign has also been recognized in various advertising industry publications, including *Advertising Age*, *AdWeek, Campaign Magazine*, and *The Drum.*

Fresh Empire

The "Fresh Empire" Campaign was implemented from October 2015 through June 2020 and educated the nearly five million at-risk African American, Hispanic, and Asian American/Pacific Islander youth who were open to smoking, or experimenting with cigarettes, about the harms of tobacco use. The campaign used broadcast TV, radio, digital advertising, and social media to reach the audience with messaging on addition caused by cigarette smoking.

During the four years the campaign was in market, "Fresh Empire" was able to achieve significant reach to the at-risk youth audience through engaging, cutting-edge marketing approaches. Innovative tactics, such as the use of influencers and brand ambassadors, casting authentic and aspirational talent related to teens' interests of music, dance and fashion, and aligning digital and social advertising with key cultural moments all worked in tandem to increase the saliency of the tobacco messaging and build a significant brand following. Campaign messaging focused on being a positive influence for younger siblings and the cosmetic and health consequences of smoking cigarettes. These messages resonated with the audience and the campaign achieved high levels of receptivity. Overall, the campaign was able to reach 95 percent of the audience and there were over 424 million social media engagements with the campaign's social media channels. "Fresh Empire" also received several Hermes and Telly awards, which recognize excellence in advertising and marketing. While paid media efforts for "Fresh Empire" have ended, insights from the campaign implementation are being used to inform current youth prevention campaigns and have provided FDA valuable learnings in how best to use media to reach sub-populations for future prevention efforts.

Figure 19 "Fresh Empire" campaign logo

This Free Life

FDA ran the "This Free Life" Campaign from May 2016 through February 2020. 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 was 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

During the campaign's three-year implementation, "This Free Life" was able to reach 95 percent of the audience through primarily digital only tactics. "This Free Life" was also able to reach LGBT subpopulations by using innovative approaches with influencers and tailored messaging. The campaign's messaging resonated with the audience and received over 172 million likes, comments and shares on the campaign's social channels. The campaign also received several prestigious marketing and advertising awards, including an Association of National Advertisers (ANA) Multicultural Excellence Award, multiple Hermes awards, and multiple Telly Awards. Insights from the "This Free Life" campaign implementation are being used to inform future youth prevention and adult cessation messaging and have provided FDA valuable learnings in how best to use media to reach LGBT audiences who remain at higher risk for tobacco usage.

Every Try Counts

FDA's first adult cessation campaign, "Every Try Counts," encouraged cigarette smokers to quit through messages of support that underscore the health benefits of quitting. The campaign leveraged a novel strategic approach that utilized positive, non-graphic messaging and reframed past quit attempts not as failures, but as important steps towards future success. The paid media portion of the campaign was in market from January 2018 through April 2020. The campaign was initially implemented in point-of-sale (POS) retail locations where cigarettes are sold. As the first multi-city POS tobacco cessation campaign, "Every Try Counts" delivered messages where smokers often encounter tobacco advertising and triggers for smoking relapse. Additionally, each ad included a call to action to drive smokers to the campaign website, which features quitting tips, "practice the quit" text message programs, and online cessation counseling. In February 2020, "Every Try Counts" expanded to a national digital campaign to reach a broader audience and messaging reached over 45 million adult smokers. Overall, "Every Try Counts" served over 769 million digital impressions and drove more than 1.6 million unique visitors to EveryTryCounts.gov, prompting over 15,000 sign-ups for text message programs designed to help smokers quit.

Figure 21 "Every Try Counts" campaign logo

While there will be no continued paid media efforts for "Every Try Counts" in 2021, FDA plans to continue to develop a range of education materials for adults that message on the benefits of cessation and address nicotine misperceptions. Assets will be disseminated to public health partners and stakeholders. Knowledge from "Every Try Counts" and ongoing research among adult smokers have provided FDA with valuable learnings about how to best reach smoking adults and will inform future educational efforts.

Select print ads are available for use via both CTP's content sharing platform, the Exchange Lab, and the CDC's Media Campaign Resource Center (MCRC). The Exchange Lab and MCRC provide access to cessation materials for use by states and/or other public health organizations and agencies.

American Indian/Alaska Native Campaign

FDA will be expanding e-cigarette prevention messaging to American Indian/Alaska Native (AI/AN) youth audiences, a population that has historically had higher tobacco usage rates. FDA has conducted research with AI/AN youth to understand tobacco beliefs and perceptions and is determining the best messaging approaches to reach this at-risk audience.

Scholastic

Since the fall of 2018, FDA has collaborated with Scholastic, the global children's publishing, education, and media company, to develop youth e-cigarette prevention resources for middle and high school educators. Resources are available in English and Spanish and include lesson plans, activity sheets, and videos to help teachers start educational conversations about the harms of youth e-cigarette use. These free educational materials, as well as a teacher resource guide and youth addiction and cessation materials, have been distributed to more than 1.3 million educators

and have reached an estimated 2.7 million students. In January 2021, FDA and Scholastic developed new content for the 2020-2021 school year including a student magazine, an e-cigarette prevention poster contest, and a content refresh of previous materials.

Outcome Evaluations

A critical factor in reducing youth tobacco use is to produce and maintain effective levels of campaign awareness within the target population. Studies have specifically confirmed the effectiveness of media campaigns in reducing youth tobacco use. The NIH NCI's 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 for the Agency's public education campaigns. For example, the study design for the original Cohort and now Cohort 2 of "The Real Cost" E-Cigarette Campaign is longitudinal, meaning the study will attempt to follow the same individuals over time to track changes in targeted tobacco-related knowledge, attitudes, and beliefs.

An evaluation found that in the first two years of the "The Real Cost" smoking prevention effort 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.

Due to collective public health efforts, beliefs and risk perceptions about vaping are rapidly evolving among teens. Twenty-nine of 34 items assessing youth beliefs about vaping in the "The Real Cost" E-Cigarette Campaign evaluation changed in the direction of increased perceptions of risk and improved knowledge of harm. In addition, recent outcome evaluation data showed that approximately 79% of youth were aware of at least one campaign ad from "The Real Cost" E-Cigarette Campaign and 75% of teens were aware of "The Real Cost" brand.

These results not only reinforce the importance of these 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 which can garner huge returns: during the first two years of "The Real Cost" smoking prevention campaign, FDA realized a cost savings of $180 for every dollar of the nearly $250 million invested.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2018 Actual	$625,406,000	---	$625,406,000
FY 2019 Actual	$686,991,000	---	$686,991,000
FY 2020 Actual	$752,921,000	---	$752,921,000
FY 2021 Enacted	$681,513,000	---	$681,513,000
FY 2022 President's Budget	$780,812,000	---	$780,812,000

BUDGET REQUEST

The FY 2022 Budget is $780.8 million all from user fees. This amount is $100 million above the FY 2022 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 $99.3 million above the FY 2021 Enacted. The Center for Tobacco Products amount in this request is $754.2 million.

Currently, the Tobacco Control Act does not provide a means for FDA calculation of user fees for e-cigarettes and other 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. 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 e-cigarettes, through the support of FDA's Youth Tobacco Prevention Plan, which includes compliance and enforcement efforts for all tobacco products, 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 all regulated tobacco products, including e-cigarettes, which currently have high rates of youth use, as well as new public health threats of tomorrow.

In FY 2022, 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, 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 marketed and sold. Manufacturers are required to obtain FDA authorization before marketing new[155] tobacco products:

- By demonstrating they are appropriate for protection of the public health, or
- By demonstrating substantial equivalence[156] to predicate tobacco products, or
- By demonstrating they are exempt from the requirements of substantial equivalence

The deadline for submission of marketing applications for new deemed tobacco products that were on the market on August 8, 2016 was September 9, 2020.

CTP is currently addressing comments to proposed rules and draft guidances as well as developing additional rules and guidances in support of the 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. For example, FDA has issued draft guidance entitled "Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies." This draft guidance is intended to help

[155] 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.

[156] 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.

applicants design and conduct tobacco product perception and intention studies that may be submitted as part of a modified risk tobacco product application, premarket tobacco product application, or substantial equivalence report. In addition to developing rules and guidances, CTP will continue to monitor performance measures for product review, including the more recent performance measures that became 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.

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 exploring potential product standards for addictiveness, toxicity, and appeal in a strategic effort to yield strong standards and improve public health.

Public Education

FDA maximizes impact on public health by focusing public education efforts on at-risk audiences such as youth who are already experimenting with tobacco or are open to it. FDA began prioritizing prevention efforts to address youth use of vaping products in 2017 through "The Real Cost" campaign and will continue prioritize reducing youth e-cigarette initiation and usage. FDA also continuously monitors national usage rates of all tobacco products to determine the most pressing needs and then align the best approaches for campaign messaging and development.

Campaign messaging and outreach tactics for different product types, include e-cigarettes, cigarettes and little cigars and cigarillos, 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 2022, 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
- Expand education efforts, such as "The Real Cost" campaign, to educate youth about the dangers of using tobacco products, including e-cigarettes
- Conduct and share findings from its campaign outcome evaluation studies
- Develop interactive digital communication technologies and products such as CTP's content sharing platform, the Exchange Lab
- 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:

- Investigating whether manufacturers may be marketing new ENDS products that have not gone through premarket review or submitted a premarket application as of the September 9, 2020 deadline
- Prioritizing the enforcement of unauthorized ENDS on the market to prevent youth use of these products
- Continuing inspections and investigations at brick and mortar locations, to the extent possible using FDA's COVID Advisory Levels, and online websites to monitor, enforce, and prevent ENDS sales
- Closely evaluating manufacturers' internet storefronts and distribution practices and taking enforcement actions if violations of the restrictions on sales to minors are found
- Conducting inspections to the extent possible using FDA's COVID Advisory Levels and remote regulatory assessments of tobacco manufacturing facilities
- Inspecting vape shops, to the extent possible using FDA's COVID Advisory Levels, 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

FDA is focused on growing our workforce to support our strategic initiatives and continues to invest in the Agency's 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 has significantly increased 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, and improve management and analysis of research and regulatory data
- Conduct surveillance and evaluation of tobacco products and the use of such products by monitoring data sources such as national surveys and retail sales data, and reviewing adverse events reporting, such as 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
280005: Total number of compliance check inspections of retail establishments in States under contract. *(Outcome)*	FY 2020: 65,716 Target: 130,000 (Target Not Met)	10,000	75,000	+65,000
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: 97% 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 2020: 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.

In March 2020, FDA issued stop work orders to the contractors engaged in tobacco retail compliance check inspections and vape retail inspections due to COVID-19. The Agency subsequently extended the stop work orders through the end of FY 2020. As a result, FDA conducted 65,716 retailer inspections, far fewer than the projected target of 130,000. Prior to FY 2020, FDA consistently exceeded its annual retailer inspections target. FDA has also reevaluated its FY 2021 and FY 2022 targets with respect to the impacts of COVID-19.

Though we expect some jurisdictions may be able to contract with FDA in FY 2021 and FY 2022 to conduct inspections, we anticipate that many jurisdictions may have significant challenges related to the pandemic and resource constraints that will prevent them from contracting with the agency or operating at previous levels.

REGULAR SE REPORTS

"Review and act on" includes issuing a Deficiency letter (deficiency notification), Cancellation, Closure, Environmental Information Request letter, SE Order, or NSE Order.

FY 2020 performance results are not yet available because FDA has been focused on the intake and processing of premarket submissions which, as of February 16, 2021, cover over five million deemed products. This influx of applications is the result of the July 2019 U.S. District Court ruling that required makers and importers of e-cigarettes and other ENDS and certain other tobacco products to submit applications for their currently marketed products to FDA by May 12, 2020. Due to the COVID-19 pandemic, FDA requested, and the Court granted, a new deadline of September 9, 2020. FDA has received these submissions and is working to accelerate the review of premarket applications for e-cigarettes and other new tobacco products and the Agency will report FY 20 results for Regular SE Reports as soon as they are available.

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's "The Real Cost" Cigarettes campaign and "The Real Cost" E-Cigarette campaign are active in market.

PROGRAM ACTIVITY DATA

CTP Workload and Outputs	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
Tobacco Retailer Inspections			
Number of Inspections[1]	65,716	10,000	75,000
Tobacco Manufacturer Inspections			
Number of Inspections[28,29]	541	100	250

[28] FY 2021 and FY2022 estimates have been decreased due to stop work orders and interruptions related to COVID-19. FY 2021 and FY 2022 estimates also assume that at least 30% of firms are in the "green" or "yellow" status and inspections can be conducted safely. FY 2022 estimates assume that COVID-19 is largely under control.
[29] Outyear estimates are based on the number of firms registered with FDA. FDA works to inspect each registered firm biennially. The tobacco manufacturer inspections for FY 2020 actuals and outyear estimates include vape manufacturer inspections conducted by contractors.

FDA HEADQUARTERS

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
FDA Headquarters	**302,289**	**308,089**	**319,572**	**345,079**	**25,507**
Budget Authority 1/	***186,920***	***186,919***	***194,951***	***221,834***	***26,883***
User Fees	***115,369***	***121,170***	***124,621***	***123,245***	***-1,376***
Prescription Drug (PDUFA)	*56,756*	*60,918*	*60,354*	*58,773*	*-1,581*
Medical Device (MDUFA)	*9,219*	*8,306*	*10,459*	*11,185*	*726*
Generic Drug (GDUFA)	*32,834*	*37,214*	*34,575*	*34,517*	*-58*
Biosimilars (BsUFA)	*1,331*	*1,657*	*1,417*	*1,372*	*-45*
Animal Drug (ADUFA)	*914*	*724*	*1,172*	*1,279*	*107*
Animal Generic Drug (AGDUFA)	*756*	*594*	*740*	*895*	*155*
Family Smoking Prevention and Tobacco Control Act	*12,169*	*11,757*	*14,485*	*13,777*	*-708*
Mammography Quality Standards Act (MQSA)	*74*	---	*76*	*77*	*1*
Food and Feed Recall	*77*	---	*78*	*80*	*2*
Food Reinspection	*489*	---	*499*	*509*	*10*
Voluntary Qualified Importer Program	*283*	---	*288*	*294*	*6*
Third Party Auditor Program	*40*	---	*41*	*41*	---
Outsourcing Facility	*427*	---	*437*	*446*	*9*
Innovative Food Products (Proposed)	---	---	---	---	---
FTE	**931**	**954**	**927**	**980**	***53***

1/ FDA Headquarters Budget Authority shown inclusive of the $1.5M OIG transfer amount

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), Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019 (P. L. 115-92).

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[157].

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

New Era of Smarter Food Safety

In July 2020, FDA released the New Era of Smarter Food Safety Blueprint.[158] The blueprint outlines goals to enhance traceability, improve predictive analytics, expand collaboration with our regulatory and public health partners, respond more rapidly to outbreaks, address new business models (such as online ordering and direct delivery of foods), advance the safety of foods sold in retail establishments, and foster strong food safety cultures. This approach builds on the progress that continues to be made in FDA's implementation of the Food Safety Modernization Act, 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. The ultimate goal of the New Era of Smarter Food Safety is to bend the curve of foodborne illness in this country by reducing the number of illnesses and injuries attributed to FDA-regulated foods.

The New Era of Smarter Food Safety Blueprint is centered around four core elements:

- Tech-enabled Traceability
- Smarter Tools and Approaches for Prevention and Outbreak Response
- New Business Models and Retail Modernization
- Food Safety Culture.

These are the foundational pillars of the New Era of Smarter Food Safety, covering the range of technologies, analytics, business models, behaviors, and values that are its building blocks. The blueprint also outlines partnerships between government, industry and public health advocates based on a commitment to create a more modern approach to food safety. The on-going COVID-19 pandemic has highlighted the need for many of the goals in the blueprint, such as enhancing traceability to better understand the supply chain, exploring the use of remote and virtual food inspections, addressing safety vulnerabilities for foods ordered online, and strengthening food safety culture to change behaviors to decrease illness.

While we published the blueprint in July 2020, the development of the New Era of Smarter Food Safety began over a year ago. In April 2019, FDA announced a new approach to food safety to leverage technology and other modern tools and practices, to create a more digital, traceable, and safer food system. After engaging our internal experts, FDA held a public meeting in October 2019 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.

There continues to be high levels of stakeholder interest in the New Era of Smarter Food Safety. Following the launch of the blueprint, FDA conducted a First 100 Days of the New Era of Smarter Food Safety webinar in October 2020 to inform industry, government, academia, and consumer groups about FDA's efforts, which drew more than 2,600 registrants. Additional accomplishments towards the goals of the Blueprint are detailed below.

[158] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint

Imported Seafood Artificial Intelligence/Machine Learning Pilot
As part of efforts to better leverage predictive analytics, FDA implemented a pilot program to understand the abilities of artificial intelligence (AI), specifically machine learning (ML), to rapidly analyze data for screening foods imported into the United Sates. Machine learning is a type of AI that makes it possible to rapidly analyze data, automatically identifying connections and patterns in data that people or even our current rules-based screening system cannot see. In August 2020, the FDA announced the results of the proof-of-concept for imported seafood, which demonstrated that machine learning could almost triple the likelihood of identifying a shipment containing potentially contaminated products. This is especially important since the United States imports upwards of 94 percent of its seafood supply. In February 2021, FDA launched the second phase of the AI imported seafood pilot, an in-field pilot, which is designed to enhance and improve the agency's ability to quickly and efficiently identify imported seafood products that may pose a threat to public health.

Tracking and Tracing of Food
In September 2020, FDA issued the Proposed Rule for Food Traceability as the first step toward enhanced traceability through harmonization of proposed key data elements and critical tracking events. Food traceability is the ability to follow the movement of a food product and its ingredients through all steps in the supply chain, both backward and forward. Traceability involves documenting and linking the production, processing, and distribution chain of food products and ingredients. In the case of a foodborne illness outbreak or contamination event, efficient product tracing helps government agencies and those who produce and sell food to rapidly find the source of the product and where contamination may have occurred. This enables faster removal of the affected product from the marketplace, reducing incidences of foodborne illnesses. Following the release of the proposed rule, FDA conducted three public meetings to discuss the rule and accepted public comments through the Federal Register. The proposed rule, when finalized, would establish a standardized approach to traceability recordkeeping, paving the way for industry to adopt, harmonize, and leverage more digital traceability systems in the future, as part of the goals of FDA's New Era of Smarter Food Safety.

In March 2020, FDA released the Leafy Greens STEC Action Plan to foster a more urgent and collaborative approach to preventing leafy greens outbreaks caused by STEC. While millions of servings are consumed safely every day, fresh leafy greens have been implicated in outbreaks of foodborne illness caused by Shiga toxin-producing *E. coli*. While most strains of *E. coli* are harmless, Shiga toxin-producing *E. coli*, or STEC, can be life-threatening. Between 2009 and 2018, the FDA and the Centers for Disease Control and Prevention (CDC) identified 40 foodborne outbreaks of STEC infections with a confirmed or suspected link to leafy greens in the United States.

Produce Safety
In March 2020, FDA released the Leafy Greens STEC Action Plan to foster a more urgent and collaborative approach to preventing leafy greens outbreaks caused by STEC. While millions of servings are consumed safely every day, fresh leafy greens have been implicated in outbreaks of foodborne illness caused by Shiga toxin-producing *E. coli*. While most strains of *E. coli* are harmless, Shiga toxin-producing *E. coli*, or STEC, can be life-threatening. Between 2009 and 2018, the FDA and the Centers for Disease Control and Prevention (CDC) identified 40

foodborne outbreaks of STEC infections with a confirmed or suspected link to leafy greens in the United States.

In 2020, FDA made significant progress on the Leafy Greens STEC Action Plan by enhancing prevention strategies, improving response activities by the agency and other entities, and identifying and addressing the knowledge gaps that exist around STEC contamination of leafy greens. FDA launched the California Longitudinal Study, developed an efficacy protocol for the development and registration of antimicrobial treatments for pre-harvest agricultural water and took critical steps to advance traceability of leafy greens. FDA has also conducted several focused inspections, follow-up investigations and sampling assignments.

In April 2021, FDA took additional steps to advance the safety of leafy greens. FDA released a report on the investigation into the Fall 2020 outbreak of *E. coli* O157:H7 illnesses linked to the consumption of leafy greens. The report describes findings from the investigation, as well as trends key to understanding leafy greens outbreaks linked to the California Central Coast growing region (encompassing the Salinas Valley and Santa Maria growing areas) that have occurred every fall since 2017. Based on this investigation, FDA recommends that growers of leafy greens in the California Central Coast Growing Region consider this reoccurring *E. coli* strain a reasonably foreseeable hazard, and specifically of concern in the South Monterey County area of the Salinas Valley.

FDA also released an updated version of the Leafy Green STEC Action Plan, reaffirming the need for collaborative action to improve the safety of leafy greens, and building on the work accomplished in 2020. The updates for 2021 include a renewed emphasis on actions to help prevent contamination from adjacent land, to include new actions that build on the accomplishments and learnings from the 2020 plan, and to renew our commitment to actions that were difficult to accomplish in 2020 due to challenges presented by the COVID-19 pandemic.

In addition to work on the Leafy Greens STEC Action Plan, FDA also conducted a root cause investigation into a multi-state outbreak of *Cyclospora* infections in the summer of 2020 that found the parasite in the surface water of a canal near the farm suspected of being the source of contaminated produce. FDA scientists pioneered ways to detect the parasite in produce and water that were employed in this outbreak investigation.

Throughout 2020, FDA also worked to strengthen the safety of papayas imported from Mexico and minimize the risk of contamination with *Cyclospora*. FDA collaborated with Mexican authorities and industry to develop improved production practices and deliver training to papaya producers. FDA also worked with Mexican authorities and key industry and academic partners to hold both an in-person seminar and a virtual webinar on *Cyclospora cayetanenesis* for fresh herb growers and packers from the state of Puebla, Mexico. FDA data shows that about one-third of all agency-regulated human food imported into the U.S. is from Mexico, including 60 percent of fresh produce imports.

FDA-Mexico Food Safety Partnership

In October 2020, the United States and Mexico officially launched the FDA-Mexico Food Safety Partnership[159] (FSP), broadening and strengthening the scope of our existing partnership to include the safety of all human food regulated by the FDA. The earlier Produce Safety Partnership, signed in 2014, had created a framework for Mexico and the U.S. to work together to contain potentially serious outbreaks related to produce and to lessen consumer exposure to foodborne disease. In addition to produce, the new FSP includes all human food regulated by the FDA, as Mexico exports seafood, processed fruits and vegetables, and snack foods to the U.S. — totaling about $25 billion in 2019, according to the Office of the U.S. Trade Representative and the National Oceanic and Atmospheric Administration. The FSP also embraces the use of new and emerging technologies, including elements of the FDA's New Era of Smarter Food Safety initiative, to solve complex public health challenges. Further, it strengthens collaboration with academia, consumer groups, and other governmental offices in the U.S. and Mexico.

Third-Party Food Safety Standards

In October 2020, FDA announced a new third-party food safety standards alignment pilot program that is designed to help both FDA and industry better understand how to determine whether these standards align with FDA regulations to help ensure safer food for consumers. This goal is consistent with and an important element of our New Era of Smarter Food Safety Blueprint. Many throughout the food industry voluntarily rely on private audit standards to evaluate their suppliers' performance. Determinations that third-party audit standards align with FSMA regulations could provide importers and receiving facilities with confidence that these audits could also be used to fulfill certain FSMA supplier verification requirements. In addition, alignment determinations could help the FDA's investigators more efficiently determine whether importers and receiving facilities are in compliance with certain FSMA supplier verification requirements.

COVID-19 Response Efforts

Temporary Guidance on Reporting Closures/Reduced Production Capacity

In May 2020, FDA issued guidance to provide certain FDA-regulated food establishments (i.e., human food facilities and farms, but not restaurants and retail food establishments), with a convenient mechanism to voluntarily report to FDA if they have temporarily ceased or significantly reduced production or if they are considering doing so. This reporting mechanism may also be used to request dialogue with FDA on issues related to continuing or restarting safe food production during the pandemic.

Food Supply Chain Continuity and COVID-19 Vaccine Distribution to Food and Agriculture Workers

[159] https://www.fda.gov/food/cfsan-constituent-updates/fda-and-mexico-sign-statement-intent-forging-food-safety-partnership

To help ensure the continuity and resiliency of the food and agriculture sector, FDA developed a new data analysis tool called 21 *Forward* to identify where risks for interruptions in the continuity of the food supply may be the greatest because of the pandemic. The unprecedented scale and pace at which the COVID-19 pandemic has spread presents unique challenges to the food supply chain. Specifically, there is a risk of shortages and an imbalance of supply and demand. Some large food facilities temporarily closed or reduced operations due to COVID-19-related impacts. Manufacturers whose products are sold in grocery stores have seen spikes in demand for particular commodities, while producers reliant on the restaurant industry have experienced excess supply, and challenges in redistributing foods that are packaged for foodservice.

Utilizing a combination of FDA and USDA data and CDC forecasting for COVID-19, the 21 *Forward* platform is used to help FDA identify where there may be risks for interruptions in the food supply chain and conduct targeted outreach to the food industry to offer additional resources and technical assistance in addressing challenges. In collaboration with HHS, CDC, and USDA, data from 21 *Forward* are also being made available to assist states with their planning efforts for vaccine distribution to workers in the food and agriculture sectors.

Emergency Preparedness and Response

Accomplishments during COVID-19 include playing key critical rolls in the COVID-19 FDA Incident Management Group. These HQ staff members were crucial to the effective evaluation, determination, and execution of the numerous requests for assistance by the impacted states, jurisdictions, and impacted industry sectors, as they ensured that all relevant information was communicated to the various stakeholders. In FY 2020 over six hundred requests for information have been responded to from public and private sector individuals and entities.

The team played a major technical and managerial role developing the COVID-19 Advisory Level Rating system (COVID-19 Advisory Matrix) to qualitatively assess the number of COVID-19 situation in a local area based on state and county metrics. This COVID-19 Advisory Level, informs the FDA's risk-based decisions on activities, including when and where to resume prioritized surveillance inspections. The states that conduct work for the FDA under contract also use this tool to inform their decisions regarding domestic regulatory inspection assignments. HQ also quickly tailored the "Pandemic Influenza Incident Annex" to the FDA Emergency Operations Plan (EOP) into the "Coronavirus Disease 2019 Outbreak (COVID-19) Concept of Operations Plan (CONPLAN)".

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.

Through 2020, FDA HQ coordinated emergency response to 86 significant incidents including:

- two serious adverse or injury event incidents
- 64 natural disasters
- 19 man-made disasters
- one National Special Security Event

Additionally, FDA HQ received and coordinated 846 emergency Investigational New Drug (eIND) calls and 102 non-eIND calls. FDA HQ also activated Incident Management Groups (IMGs) to provide headquarters coordination for COVID-19.
FDA HQ evaluated 5,425 consumer complaints (including 12 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 2020, FDA HQ:

- coordinated 20 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 100 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.
- conducted, evaluated and reported on TableTop and Full-Scale Exercises for two Center Select Agent Laboratory facilities, including a medically downed patient in a High Containment Laboratory.
- conducted a mandated Radiation Laboratory Security table top exercise
- 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.

Critical Public Health and Economics Analyses

ECON and PHSA staff responded to the critical data analysis needs of FDA at the outset of the COVID-19 pandemic. Economists and social science analysts mobilized quickly to work with Senior FDA leadership on the analysis of supply chain information for both prescription drugs and medical devices. These initial analyses helped inform FDA leadership of key trends in the supply and demand of products during the pandemic.

The PHSA staff, along with its partners in CDER and at the World Health Organization (WHO), created and implemented a ground-breaking pilot program to share FDA reviews of HIV drugs that have been approved or tentatively approved by the FDA under the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). The aim is to assess whether such sharing will expedite WHO reviews of these drugs, and thereby get these drugs into high-burden countries faster.

In support of the Agency's initiative to examine prescription drug pricing and drug importation, the PHSA and ECON staff jointly conducted several innovative analyses characterizing the international market dynamics of drugs and biosimilars as well as drug importation and drug prices. They also provided technical support for modeling the state of prescription pricing and drug trade and completed a regulatory impact analysis in a month's time for a rule-making to create a drug importation pipeline. These efforts were in support of FDA's goal to enhance drug availability and increase competition.

Economic Analysis and Support for Regulations Published

In 2020, along with the publication of the proposed and final rules themselves, FDA published the economic analyses for a number of high priority Agency rules, while working under very tight deadlines and within unique legal constraints, including:

- Importation of Prescription Drugs
- Requirements for Additional Traceability Records for Certain Foods
- Submission of Food and Drug Administration Import Data in the Automated Commercial Environment for Veterinary Devices
- Postmarketing Safety Reports for Approved New Animal Drugs; Electronic Submission Requirements
- Tobacco Products; Required Warnings for Cigarette Packages and Advertisements

The support provided by these economic analyses 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 August 1, 2019 through January 31, 2021 FDA HQ issued/held:

- 282 MedWatch Safety Alerts (FDA's second largest e-list) to more than 350,000 subscribers and over 51,000 MedWatch Twitter followers;
- Nearly 800 News Releases and other press announcements in English and/or Spanish to more than 100,000 subscribers, including for numerous COVID-related actions;
- 57 FDA Voice Blogs with more than 66,000 subscribers;

- About 125 individual Consumer Updates (both new and updated content) offered in English and Spanish, in additions to four Asian languages for all the COVID-19 articles, to more than 125,000 subscribers in English and 38,000 in Spanish;
- 48 Consumer Videos in English and Spanish uploaded to YouTube with 900 views and nearly 58,000 subscribers; and
- More than 100 newsletters, which reach approximately 71,000 health care professionals, consumers and patients and targeted emails to specific organizations.
- Approximately 40 Stakeholder Calls with the Commissioner and issued over 70 stakeholder targeted outreach emails.
- 100 tweets per month, 125 Facebook posts per month with an estimated 5 million views per month. Of note, FDA has 1 million followers on Office of Media Affairs accounts, and 2.6 million followers on all social media accounts across FDA.

MedWatch Update Reporting: FDA's ongoing work to promote MedWatch presents numerous opportunities to increase awareness about the importance of health professional, patient and consumer reporting adverse events and problems with medical products to FDA.
FDA HQ has worked to make updates to the MedWatch forms to simplify reporting of MedWatch reports for health professionals, patients and consumers. FDA has also worked to expand access of MedWatch reporting with the release of a newly translated Form FDA 3500B in Spanish which can be uploaded electronically, mailed or faxed to FDA.

FDA Office of Women's Health (OWH) conducts educational initiatives and outreach to connect women with FDA health and safety information. The Outreach and Communications Program utilizes a multi-pronged approach that includes:

- Monthly OWH newsletter
- social media and digital outreach
- outreach collaborations and partnerships with stakeholders
- stakeholder conference presentations and exhibitions
- dissemination of women's health publications

Notable accomplishments throughout calendar year 2020:

- In February 2020, launched new KNOWH (Knowledge and News on Women's Health) campaign designed to educate and share the latest women's health information and insights that may not be well known to women, consumers, industry, healthcare providers, partners, and stakeholders.
- In conjunction with American Heart Month, released first video under the KNOWH campaign umbrella, Getting a Beat on Women's Heart Health, a "woman on the street" style video to raise awareness of heart disease among women and dispel some common myths about heart disease. The full video lives on the OWH heart health landing page and has garnered over 9,000 pageviews (or impressions) since its launch, and 107,000 cumulative video views inclusive of the longer form video and associated takedowns (shorter versions of the video).

Scheduled to release in FY 2021 are the following:

- A new video is under development featuring women sharing their experiences living with diabetes and addressing the importance of diabetes management.
- Under development, video content with the goal of educating the public and raising awareness of uterine fibroids as a chronic women's health condition.

In May 2020, during National Women's Health Week, launched new OWH blog, Knowledge and News on Women to share important information about women's health topics with consumers and healthcare professionals. This blog reminded women of the importance of wellness checks during the COVID-19 pandemic. Subsequent blog post topics included the following:

- During Fibroid Awareness Month, July's blog focused on uterine fibroids and highlighted the agency's efforts to combat this issue including the approval of a new option to treat heavy menstrual bleeding associated with fibroids in women, research developments on fibroids, and insights from stakeholders who shared their personal experiences. women and their experiences.

So far in FY 2021 OWH has created three additional blogs post on the following topics.

- In November 2020 during National Diabetes Month, OWH collaborated with the FDA Center for Food Safety and Applied Nutrition to share insights on how recent updates to the Nutrition Facts label can help individuals living with diabetes.
- In January 2021, the OWH blog post was dedicated to encouraging women to prioritize their health throughout 2021 with tips and resources to encourage self-care physically and mentally.
- In February 2021, a guest blogger and selected speaker for the OWH Scientific Speaker series shares insights on how women can focus on and protect their heart health.

To date, the five blog posts have garnered nearly 9,000 page views.

- Developed and disseminated FDA safety alerts and women's health information via the OWH Twitter account to over 76 thousand followers. Received over 1.4 million twitter impressions and nearly 5,000 engagements. An ad campaign highlighting National Rural Health Day was promoted, which garnered over 19k impressions and 169 retweets. The FDA For Women webpage had approximately 1.5 million website visits across various topic pages.
- Featured COVID-19 specific updates from FDA and agency partners (e.g. CDC) in monthly electronic newsletters beginning in April of 2020 and regularly each month, which included vaccine approvals and updates regarding safety and advisory meetings. COVID-19 related information and links are highlighted on the *For Women* homepage, with specific information and resources for pregnant and breastfeeding women. Information regarding COVID-19 and pregnancy and breastfeeding is also highlighted on the FDA dedicated pregnancy page[160].

[160] http://www.fda.gov/pregnancy

In FY 2021, OWH plans to develop a dedicated webpage to provide a plain language comparison of the approved COVID-19 vaccinations to date.

- Developed and disseminated 18 FDA Office Women's Health e-Updates to over 100,000 subscribers, including virtual presentations and exhibits (a new outreach medium for OWH to promote and disseminate women's health resources and materials), targeted agency health alerts for women, monthly and bi-monthly newsletters, and college women's campaign targeted outreach communications.
- Developed the content and recorded an Inside FDA podcast to bring awareness to OWH research and outreach activities including the OWH Diverse Women in Clinical Trials Campaign.
- Updated existing publications in other languages and created additional publications in new languages, to include: mammograms, heart health, medicine and pregnancy. The focus for 2021 is ensuring the publications are available in the top 12 languages spoken in the US: Spanish, Chinese, Vietnamese, Korean, Russian, Arabic, Tagalog, Polish, French, Haitian Creole, Portuguese, and Japanese.
- Medicine booklets currently being revised include cholesterol and high blood pressure. Additional publications under revision include birth control, and mammography awareness guide. Approximately 2 million OWH women's health publications were ordered and distributed from the Government Publishing Office (GPO). Specific visits to the "*Free Publications for Women*" webpage was over 700,000.

The FDA Office of Minority Health and Health Equity (OMHHE) develops culturally and linguistically tailored health education materials for racial and ethnic minority, underserved, and underrepresented consumer groups, written at low literacy levels and translated into multiple languages. These communications are designed to strengthen consumer's decision-making regarding FDA-regulated products and include items like brochures, fact sheets, post cards, and digital content such as videos and social media messages.

In FY 2020 and FY 2021, over 2,400 health education materials were disseminated to stakeholder organizations, with over 19 health educational materials translated into ten languages. OMHHE reached over 168 million consumers through digital outreach such as social media messages, six Twitter chats, three blogs, weekly communications with FDA COVID-19 updates, and over 50 e-alerts focused on health topics disproportionately impacting minority groups. OMHHE continued promotion of two public service announcements and a podcast as part of the Diversity in Clinical Trials Initiative featuring Veterans sharing their stories to promote clinical trial participation that reached over 126,000 consumers. OMHHE also added multi-media health education resources in multiple languages to our ongoing Diversity in Clinical Trials Initiative to help address barriers preventing diverse people from participating in clinical trials. In FY 2020, added a new video, "Medical Device Clinical Trials," developed in collaboration with FDA's Center for Devices and Radiological Health that addresses the need for diverse participants in clinical research for medical devices. To date, the video has received over 1,800 views on YouTube. In addition to the Diversity in Clinical Trials Initiative, the Office also created a PSA video, "Creating a World Where Health Equity is a Reality for All," as part of OMHHE's 10-year anniversary celebration that launched in April 2020.

In addition, in FY 2020 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". Findings from this training were presented at the American Public Health Association's annual meeting (October 2019) and a manuscript[161] was published in the Journal of Primary Care and Community Health and downloaded over 150 times to date. In FY 2020 OMHHE adapted the training to a virtual format and offered four additional training opportunities in September 2020 with over 100 staff trained. Additionally, OMHHE partnered with the Office of Regulatory Affairs to adapt the training for their field staff and will offer four sessions in FY2021 as well as offering the training FDA-wide four times in FY2021 (April-July).

OMHHE continued to expand training opportunities and developed a new curriculum for a web-based training on "Communicating with Confidence: The Impact of Bias on Health Education and Communications" in FY2020. Four virtual trainings were delivered in September 2020 with more than 85 staff trained. The training aimed to provide the knowledge and skills to recognize bias, identify the impact of biased thinking and actions, and gain the ability to apply self-reflective and cultural knowledge-building practices to address biases that can hinder effective and culturally competent communication and education for diverse audiences. Findings from this training were presented at the American Public Health Association Annual meeting in October 2020. Four additional trainings are being held in FY2021 (April through July).

OMHHE sponsored a health equity "Special Collections Issue: FDA's Strategies to Close the Health Equity Gap Among Diverse Populations[162]" in the Journal of Primary Care and Community Health. This issue featured a collection of seven manuscripts highlighting FDA's work across the agency to address health disparities related to nutrition, devices, immunizations, training, and social science research. The issue was launched in March 2021.

FDA OMHHE also sponsored a journal supplement on "Tobacco and Health Equity" in Health Promotion Practice. The journal supplement launched in January 2020 and featured a collection of 18 articles on tobacco cessation and prevention through innovative programs, strategies, and policies to address the needs of racial and ethnic minorities, underserved, and underrepresented groups. The supplement included a commentary published in collaboration with the Center for Tobacco Products highlighting FDA's efforts to address tobacco use. To date, the articles have a combined download of over 21,000.

During FY 2020 and FY 2021, FDA OMHHE continued to lead the Language Access Program (LAP) (FDASIA Section 1138); continued to manage the Translation Excellence language access services contract to provide a flexible means for OMHHE and other FDA centers and offices to acquire language services; continued to lead the LAP Cross-Agency steering committee aimed at strengthening culturally appropriate communications for LEP consumers/patients; continued providing support to FDA centers and offices on the implementation of language access services across the agency; and continued leading the LAP

[161] https://journals.sagepub.com/doi/full/10.1177/21501327211003688

[162] https://journals.sagepub.com/topic/collections-jpc/jpc-1-fda_strategies_to_close_health_equity_gap/jpc

Volunteers' Group with native speakers from across the agency that help review/proofread translated materials for accuracy and cultural sensitivity.

During the COVID-19 Pandemic, OMHHE increased amplification of clinical trial diversity messages and provided tailored FDA COVID-19 communications to racial and ethnic minority stakeholders. FDA OMHHE also increased outreach by disseminating COVID-19 health education materials for consumers in multiple languages and distributed a weekly e-alert updating consumers on pertinent FDA COVID-19 information. OMHHE supported COVID-19 translations, with over 20 health education materials translated to more than 10 languages.

FDA OMHHE assisted the Office of External Affairs and FDA Centers in translation of materials for the agency's official COVID-19 webpage in Spanish (among other languages) and supported the development of the FDA COVID-19 Multilingual Resources webpage that features a growing collection of educational materials in Spanish, Simplified Chinese, Korean, Vietnamese, Tagalog, among other languages. To further enhance outreach and dissemination, FDA OMHHE launched a COVID-19 Bilingual (English/Spanish) Social Media Toolkit that features consumer friendly messages and culturally appropriate graphics and assisted in the development of the FDA "Patient Outreach" Toolkit. The office also joined the U.S. Department of Health and Human Services' "Vaccine Ready" campaign and released a set of public service announcement videos (PSAs) to address vaccine confidence among diverse populations. The videos were translated into multiple languages and an accompanying social media toolkit with Twitter and Facebook messages was developed as well.

In February 2021, OMHHE collaborated with the Center for Biologics Research (CBER) and conducted a virtual Q and A session with Dr. Peter Marks for the "Health Equity and COVID-19: What Minority Communities Need to Know" webinar. Following the webinar, OMHHE and CBER co-authored a blog for National Minority Health Month (April 2021) addressing vaccine hesitancy concerns among racial and ethnic minority and Tribal groups. Additionally, FDA OMHHE assisted in the planning and implementation of listening sessions with minority health organizations to update them on FDA's COVID-19 activities and to learn more about the gaps and needs of minority communities to help inform future programming.

Support for FDA's Priority Rulemakings and Guidance Documents

In 2020, FDA's Office of Policy (OP) continued to advance the agency's public health mission. In addition, OP played a pivotal role in supporting FDA's response to the COVID-19 public health emergency.

As part of FDA's COVID-19 response, under OP's leadership, approximately 64 guidance documents have been developed and issued based on sound scientific data that address the various medical products needed to diagnose, treat, and protect the public from COVID-19. OP created a framework to streamline the availability of these guidance documents, which assist industry and others in understanding FDA's current thinking and regulatory decision-making. These guidance documents also support the rapid development and review of important products desperately needed in the fight against the pandemic. OP has facilitated the issuance of guidance documents to describe, among other things, enforcement discretion and guidelines for Emergency Use Authorizations to facilitate the appropriate availability of various medical products.

OP has also worked hard to continue advancing mission priorities other than those related to COVID-19. OP supports all the agency's components in the development and issuance of regulations, guidance documents, and other Federal Register documents, which, in total, routinely exceed 700 or more actions per year. From October 2019 through September 2020, OP facilitated issuance of 717 documents in the Federal Register. OP also coordinated the clearance and issuance of a final rule that clarifies the use of the term "gluten-free" in food labeling. This will enable consumers that are sensitive to gluten to make better informed decisions when grocery shopping. OP also coordinated the clearance and issuance of the cigarette warnings rule for cigarette packages and advertisements. The final rule provides consumers with more easily understood information detailing the public health concerns associated with cigarette use through the use of graphic figures.

In addition, OP facilitated clearance and publication of policy initiatives described in the Drug Competition Action Plan and Biosimilars Action Plan. These efforts include publication of guidance related to Competitive Generic Therapies, opening a public docket soliciting input to improve the Orange Book, and leading a panel in the joint FDA-FTC Public Workshop on a competitive marketplace for biosimilars. OP also worked closely with colleagues across the agency to ensure a smooth transition in the regulation of certain biological products that were originally approved as drugs, which will help facilitate greater choice and competition for critical medicines such as insulin.

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 2020, FDA HQ:

- received 706 first-time requests for orphan drug designation and designated 438 promising drugs and biological products for rare diseases
- received 14 first-time requests for Humanitarian Use Device designations and designated 12 promising devices for rare diseases and conditions
- received 272 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 235 drugs and biologics for rare pediatric diseases[163]
- funding approximately 70 clinical studies of promising therapies for rare diseases and new clinical trial grant awards
- funding 7 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

Jurisdictional Determinations and Support for Combination Products Regulation

In FY 2020, with respect to combination products, FDA HQ provides clarifications and support for approximately 1146 inter-center consults and 113 post-market activities. FDA HQ issued 9 formal requests for classification and assignment decisions (7 combination products and 2 non-combination products), with 100% of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also provided timely classification and jurisdictional feedback for 79 separate Pre-Request for Designation (Pre-RFD) submissions (informal inquiries) and 79 center-requested classification and assignment consultations. In FY 2020, FDA HQ also responded to 188 requests for product-specific assistance, the responses to which contributed to ensuring the timely and effective review of combination products. FDA HQ began work to develop a new electronic system for Pre-RFD and RFDs using Salesforce software to harmonize workflow and data collection.

In FY 2020, FDA HQ published a draft guidance in December 2019 entitled Requesting FDA Feedback on Combination Products which discusses ways in which combination product sponsors can obtain feedback from FDA on scientific and regulatory questions, and best practices for FDA and sponsors when interacting on these topics. The guidance also discusses the new combination product agreement meeting (CPAM) mandated under section 3038 of the Cures Act. FDA HQ also led a cross-agency group that developed the compliance program for inspections of CDER-led or CDRH-led combination products, published in June 2020. FDA HQ also participated in the implementation of PDUFA VI activities as it relates to combination products (e.g., independent assessment of combination product processes, bridging and human factor guidance documents).

FDA HQ enhanced the technology platform to facilitate cross-Center collaboration for the review of combination products. FDA HQ implemented a project to integrate into a single point

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

of reference, to the extent feasible, data on combination products from different data sources such as premarket systems, registration & listing, and adverse event reporting systems from all three medical product centers, to enhance the efficiency and consistency of postmarket safety activities.

Regarding staff development and support, FDA HQ continued to provide Agency staff training on combination product regulation, including how to identify such products, inter-center coordination for premarket review and postmarket regulation, inspectional processes, postmarketing safety reporting requirements for combination products

Pediatric Coordination

FDA HQ continued collaborations with all the Agency Centers and external stakeholders to enhance pediatric specific efforts, including providing support for COVID-19 related activities.

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 the European Medicines Agency (EMA), Health Canada (HC), PMDA, and TGA. In FY 2020, these efforts included discussion of 227 issues, where several issues could be discussed with respect to an individual product. Out of the 227 issues discussed, harmonization was achieved for 72 percent. Examples of the most frequent issues discussed included scope of pediatric development, safety, study design, dosing and extrapolation. Also, in FY2020, this Cluster was utilized as a forum for the timely discussion of 3 potential therapeutics for the treatment of COVID-19 in pediatric patients.

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 56 consult reviews in FY 2020 as well as ongoing work in developing guidance documents. These ethical issues included pediatric rare disease populations study design considerations and informed consent requirements.

FDA HQ continued its pediatric safety review process which involves collaboration with the Agency Centers to examine and provide post-market pediatric adverse events and safety reporting issues to the Pediatric Advisory Committee (PAC). In FY 2020, these efforts included completing 31 web-posted pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews). In addition, a virtual PAC Meeting was held on September 15, 2020. Six products (CDER-4, CDER-1, CDRH-1) were discussed before the PAC, including two drug product class safety signals.

FDA HQ promoted the support of therapeutic product development for neonates through internal and external collaborative efforts. These collaborative efforts included initiating and participating in guidance development with colleagues across the FDA Centers as well as contributing to consortium efforts developing tools to streamline therapeutic development programs. The consultation service provided neonatal-perinatal medicine consultations across the FDA Centers with 54 consults completed in FY 2020. Neonatology consultation was included in the discussion of iPSPs for COVID-19 products.

FDA HQ promoted the study of pediatric regulatory science through support of:

- Global Pediatric Clinical Trials Network grant
- Advancing standards and methodologies to generate real world evidence from real world data through a neonatal pilot project grant
- BAAs to study:
- Actigraphy in Pediatric Pulmonary Artery Hypertension
    - Comparative Safety of Complex Feeding Device Types among NICU Graduates

FDA HQ promoted pediatric outreach activities through collaboration with the American Academy of Pediatrics (AAP) (monthly newsletter), and consortium activities through the International Neonatal Consortium, the Multi-Regional Clinical Trials Center Pediatrics Project, the International Society for Pharmacoepidemiology, the Children's Hospitals Neonatal Consortium, and the Newborn Brain Society.

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

Since the establishment of the Office of Women's Health (OWH), FDA HQ has funded 436 projects. Scientific data from these research projects have contributed to FDA guidance development, labeling changes, and evidence-based support for consumer decision making. OWH provides subject matter expertise on FDA policy, including the 2020, FDA guidance entitled Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry which recommended the inclusion of women in clinical trials in adequate numbers to allow for analysis by sex by avoiding unjustified exclusion based on sex and suggested other actions to promote inclusion.

In FY 2020, OWH continues to advance the science of pregnancy and lactation by funding research involving pregnant and lactating women, including one study to identify unique antibody characteristics for prediction of effective influenza vaccination in pregnant and lactating women, one on the Pregnancy and Lactation Labeling Rule (PLLR): Health Care Provider Testing to Improve Health Communications Related to Lactation, the CURE Pregnancy Treatment Repository, and one assessing real-world use of pharmaceuticals among pregnant women.

Over the past year, Office of Women's Health has continued to support women's health research, and in FY 2020, funded a total of 13 research projects. Eight were funded through the OWH intramural program on a wide variety of topics relevant to women, including research assessing hormone release from contraceptive devices, research identifying characteristics for predicting effective antibody response to influenza vaccine in pregnant and lactating women, and a study

evaluating the genotoxic potential of black cohosh – a dietary supplement widely marketed for relief of gynecologic disorders and menopausal symptoms.

In FY 2020, through OWH's special funding mechanism, the Office funded 3 projects: a project to develop an integrated database for gender-based toxicological assessments, a project on the determination of sex differences in immune responses to nanoparticles, and a project on the qualitative development of a patient preference survey tool for contraception products.

Office of Women's Health is also an active participant in the Centers of Excellence in Regulatory Science and Innovation (CERSI) and the Broad Agency Announcement (BAA) programs, collaborating on one study with the University of California San Francisco-Stanford University CERSI on identifying genetic mechanisms of doxorubicin-induced cardiotoxicity.

In 2020, OWH staff and funded investigators published over fifteen manuscripts in peer-reviewed scientific and medical journals detailing findings from their research which help to not only advance the scientific basis for important sex and gender considerations, but also impact FDA's regulatory work.

In FY 2020 and continuing into FY 2021-2022, OWH plans to support women's health research by providing funding for research initiated by FDA investigators and their collaborators. In response to the COVID-19 pandemic, OWH is soliciting research proposals on the effect of SARS-CoV-2 on the health of women of every age and ethnicity. Potential research topics include sex and gender influences on the susceptibility and response to SARS-CoV-2/COVID-19, and implications for treatment. OWH is also interested in topics relevant to SARS-CoV-2/COVID-19 and pregnancy and lactation.

FDA HQ has also used the Research Impact and Outcomes (RIO) Framework to evaluate the performance of programmatic initiatives, including funded research portfolios and to select proposals for funding with the greatest potential impact. In FY21-22, the RIO Framework will be updated to facilitate prospective evaluation of the potential impact of research submitted for OWH funding and to simplify retrospective evaluation of the Office's research portfolio. This update will also allow OWH to identify areas of improvement and existing knowledge/research gaps to advance the health of all women. Once these knowledge and research gaps are identified, OWH plans to update its Research Roadmap to help guide future research.

Additionally, Office of Women's Health partners with FDA Centers, academic institutions, and other external organizations to investigate sex differences and its impact on regulatory science. The OWH Women's Health Center Staff Fellowship program, officially launched as a pilot in 2020, funded a full-time research fellow in CDER to conduct research to evaluate the participation of women in clinical trials supporting FDA approval of HIV drugs and to asses sex differences in efficacy and selected safety events from 2011-2020. The study will also compare weight gain in people who take certain antiretroviral therapies for HIV.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ promotes women's health through medical and scientific education and collaborations with health professional organizations. FY 2020 program accomplishments include:

Maternal Health: FDA HQ works to advance the health of pregnant and lactating individuals. OWH serves as the FDA Commissioner's representative to the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)[164], established in 2016 by the 21st Century Cures Act[165] (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[166] to the HHS Secretary and Congress and OWH has also participated in briefing Congressional staff regarding PRGLAC. OWH maintains a public list of pregnancy exposure registries for FDA-regulated medical products, thus raising awareness of an important data source and encouraging women to help improve safety information for medications and vaccines used during pregnancy by enrolling in registries.

- Hosting a quarterly Scientific Speaker Series to provide scientific evidence and consideration regarding sex and gender differences to support regulatory decision-making across FDA. Topics covered include **safety of asthma medications during pregnancy,** sex differences in vaccine efficacy, COVID-19 and pregnancy, and sex differences in COVID-19. These popular lectures have increased reviewer understanding of the importance of sex and gender differences and their application to regulatory science.
- Launching the "Bench to Bedside: Integrating Sex and Gender to Improve Human Health" online course, which aims to educate scientists and health professionals about the importance of understanding sex and gender influences on health and disease and incorporating sex as a biological variable into research. FDA developed this innovative six-hour continuing education series in partnership with the NIH Office of Research on Women's Health. In FY20-21, educational modules on immunology, cardiovascular disease, pulmonary disease, neurology, endocrinology, and mental health were launched.
- Opening a public docket to solicit comments from stakeholders interested in informing OWH's scientific, educational, and outreach priorities. FDA HQ published this Federal Register notice to better understand the health concerns, research topics, and outreach areas that are important to OWH stakeholders and will consider this feedback while developing OWH's strategic plan.

In FY 2021, OWH will continue to promote women's health through medical and scientific education. To date, OWH has:

- Hosted a full-day Scientific Conference on **CBD & Other Cannabinoids: Sex and Gender Differences in Use and Responses.** Presentations addressed patient and healthcare provider perspectives on CBD and other cannabinoid use, sex differences in the effects of CBD and other cannabinoids, use of CBD and other cannabinoids in pregnancy, and government agency perspectives on CBD research and evaluation.

[164] For more information please visit https://www.nichd.nih.gov/about/advisory/PRGLAC

[165] 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

[166] Report is available at https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf

- Scheduled a Scientific Speaker Series on **Sex Differences in Ischemic Heart Disease: Pathophysiology, Presentation, and Diagnosis** to discuss the unique presentation of ischemic heart disease (IHD) in women, including differences in presentation, diagnosis, and pathophysiology.
- Presented at numerous conferences nationally and with international engagement, developed webinars and presented at schools of Pharmacy with a focus to educate on various FDA related women's health topics such as the need for participation of women in clinical trials, consideration for pregnant and lactating people and the importance of sex and gender consideration from an FDA perspective.
- Provided subject matter expertise on cross Agency Committees and working groups to coordinate women's health efforts across the federal landscape.

Minority Health Research Engagement

FDA's Office of Minority Health and Health Equity (OMHHE) provides leadership and policy direction on minority health, health disparity, and health equity matters for FDA. OMHHE works with FDA centers, offices, and public- and private-sector stake holders, including, academia, government agencies, and non-profit organizations to advance health equity-focused research, education, and scientific exchange. OMHHE's efforts enable innovative intramural and extramural research to answer pressing health disparity and regulatory science research questions to deliver valuable public health information to diverse communities and to aid in shaping regulatory decisions.

OMHHE Intramural Challenge Grants enables OMHHE to support innovative, minority health focused research that contributes to the reduction of health disparities. During FY 2020 and FY 2021, OMHHE continued to collaborate across FDA product Centers and funded and/or participated in intramural projects on the safety and health of patients living with sickle cell disease undergoing blood group genotyping for transfusion; scientific knowledge and innovation in phantom-based test methods for evaluating photoacoustic breast imaging systems; validation of epigenetic biomarkers in Systemic Lupus Erythematosus; and racial and ethnic differences in severe and critical hospitalizations among COVID-19 patients under age 65.

FDA OMHHE Extramural Research Program leverages various funding mechanisms, collaborations, and partnerships to achieve its mission to include supporting extramural research through the FDA Broad Agency Announcement (BAA), Centers of Excellence in Regulatory Science and Innovation (CERSI), Interagency Agreements (IAA), and Research Collaborative Agreements (RCA). During FY 2020- FY 2021 OMHHE collaborated with FDA Center and Offices on project areas including diabetes, opioid prescribing, cardiovascular disease, and COVID-19. Additionally, during FY2020-2021, FDA OMHHE supported the following scientific projects to advance health equity.

- Funded a BAA on "Leveraging community engagement and electronic health record strategies to promote diverse participation in COVID-19 clinical trials" with Yale University and the Cultural Ambassadors Program. The study seeks to (1) understand factors or combination of factors that contribute to COVID- 19 morbidity and mortality in minority populations (2) utilize real time data and EHR data to provide population health management and access to COVID-19 clinical trials information, including

integration of community level social determinants of health information (3) understand ways to amplify linguistically and culturally appropriate information related to COVID-19 research awareness, participation, and retentions as well as prevention strategies.

- Developed a Research Collaborative Agreement (RCA) with the Hepatitis B Foundation to increase understanding of how people living with hepatitis B in the U.S. vs. globally perceive clinical trials and barriers to clinical trial participation.
- Developed an Interagency agreement (IAA), in collaboration with CDER, on utilization of VA electronic health care records and artificial intelligence options to increase understanding of direct oral anticoagulant treatment outcomes in racial and ethnic minority populations.
- Funded a UCSF CERSI study on understanding of biological clinical asthma profiles in racial and ethnic minorities. The study found that peripheral blood parameters and asthma subtypes are differentially associated with asthma outcomes across pediatric African American, Mexican American, and Puerto Rican patients.
- Funded a UCSF CERSI study on usability testing of virtual reality for pain management among diverse patients
- Funded a UCSF CERSI study on understanding of health literacy in children with chronic illness.
- Funded a BAA on "Using Big data, machine learning, and infoveillance approaches to detect and characterize adoptions and adherence to PReP therapy among minority populations". The study used big data, machine learning, and social media surveillance to elucidate knowledge, attitudes and behaviors associated with Pre-Exposure Prophylaxis (PrEP) therapy among minority populations for the treatment of HIV/AIDS. Specifically, the project advanced computational methods to detect, characterize, and assess self-reported experiences with PrEP among minority populations as expressed on popular social media platforms.
- Co-funded with CBER a UMD CERSI project on "Patient and Caregiver Diversity in FDA Patient Engagement Activities and CBER-regulated therapeutic." The goal of the project is to increase understanding of diverse patient and caregiver engagement in food allergy.
- Collaborated with the VA on a project aimed at understanding minority Veterans' use of opioids and adverse events and established an IAA between OMHHE and the Veterans Administration to advance collaborative engagement.

During FY 2020 - FY2021, OMHHE supported advancement of social and behavioral sciences, by chairing the OCS FDA Social and Behavioral Sciences Work Group. The FDA OMHHE Extramural Research Program led the creation of the PRA Generic Clearance for Data to Support Cross-Center Collaboration for Social and Behavioral Sciences Associated with Disease Prevention, Treatment, and the Safety, Efficacy, and Usage of FDA Regulated Products. The PRA Generic Clearance will support cross-center collaboration for social and behavioral science research utilizing both qualitative and quantitative data. Additionally, OMHHE cohosted the Social Science Forum, which convened social scientists from different offices and centers, to discuss important social and behavioral topics, highlight research, and encourage collaborations (with more than 80 multidisciplinary FDA staff in attendance).

In FY 2020, FDA published the article "Assessment of Public and Patient Online Comments in Social Media and Food and Drug Administration Archival Data" in Research in Social and Administrative Pharmacy. The study explored leveraging technological advances and multiple patient experience data sources to capture the patient perspective beyond clinical delivery to aid in understanding the picture of medical product functioning beyond controlled randomized clinical trials. "Lee C, St. Clair Chris, Merenda C et al. Assessment of Public and Patient Online Comments in Social Media and Food and Drug Administration Archival Data. Social Adm Pharm. 2020 Jul;16(7):967-973. https://doi.org/10.1016/j.sapharm.2019.10.009".

In FY 2021 OMHHE led the Social and Behavioral Sciences Workgroup in publishing a cross-center manuscript highlighting social and behavioral sciences research advancing health equity in the Journal of Primary Care and Community health. "FDA's Diverse and Dynamic Activities in the Social and Behavioral Sciences: Advancing and Supporting Health Equity "

The FDA Office of Minority Health and Health Equity (OMHHE) also supports efforts to diversify the workforce by precepting pharmacy students who applied to the FDA Pharmacy Student Experiential Program and expressed an interest in minority health as part of their elective rotation. Students gained enhanced regulatory science skills and knowledge to address health disparities. During FY 2020-2021, FDA OMHHE precepted five students, several of whom went on to present abstracts/posters at national conferences, enroll in additional degree-granting programs, and/or enter residencies. Other efforts in FY 2020 to advance regulatory science and minority health include continuing to support of the CFSAN Professional Development Program in Food Science by funding three teachers serving students in underserved areas to virtually learn the accredited "Science and Our Food Supply" curricula.

In FY 2021 OMHHE developed an Intra-Agency Agreement (IAA) with the National Human Genome Research Institute (NHGRI) to support the Postdoctoral Fellowship in Genomic Science and Health Equity. The post-doctoral fellowship co-sponsored by the NHGRI and OMHHE will prepare fellows to use genetic, genomic and pharmacogenomic approaches to advance minority health and health equity.

To provide awareness about research, programs, and scientific initiatives that address issues which impact racial and ethnic minority populations, OMHHE hosted six scientific lectures on topics including clinical trials, tobacco use among Latinx communities, precision medicine, asthma drug response, Hepatitis B and Asian Americans, and the HIV epidemic in Indian Country under the "Health Equity Lecture Series", with over 200 attendees. These lectures provided continuing education credits for physicians, pharmacists, nurses, and health educators.

During FY 2021, OMHHE funded a small conference grant with The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) to host a virtual two-day conference on "Heterogeneity of Treatment Effects in Clinical Trials: Methods and Innovations." The conference was held on November 30 through December 1, 2020, with an expert meeting held on December 2, 2020, to further discuss information shared during the conference. Presenters included experts in biostatistics from across academia, industry, and FDA, including CDER's Office of Biostatistics and Office of New Drugs, Office of the Commissioner, CDRH, and CBER, among a range of other stakeholders, with over 240 attendees.

On February 10, 2021, OMHHE held a workshop with the UMD CERSI on "Collaborating to Advance Health Equity for Diabetes and chronic Kidney Disease", with 281 attendees. The workshop brought together stakeholders from the FDA, academia, patients, community members, advocacy organizations, policy makers, and clinicians to advance the understanding of the following: (1) Leveraging patient experience data and community/system approaches to inform care, drug development and overall research agenda to improve patient outcomes and reduce health inequities for diverse communities living with diabetes and chronic kidney disease (CKD). (2) Explore barriers to diversity in clinical trials for CKD and diabetes and strategies to improve diversity in clinical trials. (3) Utilization of real-world data to inform strategies and decision making on the management of diabetes and CKD.

OMHHE also partnered with the Yale Cultural Ambassadors Program to host a "Diversity Day: Patient Centered Approach to Care and Research" in February 2020 with speakers from across government, academia, public and private sector organizations, among other stakeholders to advance clinical trial diversity (more than 300 attendees).

To inform and advance OMHHE strategic priorities, OMHHE published a notice in the Federal Register in January 2020, to ensure important health concerns are carefully considered when developing OMHHE priorities that can have the most impact for diverse communities. (OMHHE reopened the comment period in April 2020).

To advance scientific partnerships and collaborations, OMHHE continued its efforts through Memorandums of Understanding (MOUs) established 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; and with Yale University to advance the Yale Cultural Ambassadors Program, an engagement of community partners to increase diverse participation in clinical research.

OMHHE met with multiple stakeholders, participated in workshops, and meetings 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.

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

Communication with Stakeholders - Improvements to FDA.gov

FDA continued to make iterative improvements to its public-facing website, FDA.gov. The new user-friendly look of the website was launched in April 2019, and 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. For example, during the ongoing COVID-19 pandemic FDA was able to quickly set-up a mobile-friendly, easy to navigate COVID-19 landing page with all the important content our stakeholders need to make informed decisions. Through the first year of the pandemic this page has grown considerably and serves as the agency's hub to provide visitors with vital information on vaccines, testing, personal protective equipment, Emergency Use Authorizations (EUAs). In addition, FDA is continuing to work towards iterative improvements to 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 – GovDelivery Email Service

FDA HQ implemented a new, state-of-the-art email marketing system called GovDelivery to make it easier for stakeholders to sign up to receive critical public health information from FDA. In addition, this new, mobile-friendly and easy-to-use product simplifies the process of sending emails for the FDA administrators who manage the email lists. Currently, FDA has over 180 content topics available and over 1 million stakeholders who have subscribed to receive information. GovDelivery has been an important communication channel throughout the

pandemic as it is a fast way to share critical COVID-19 related information with our stakeholders.

Stakeholder Outreach Activities

FY 2020 engagement activities were impacted due to adherence to implementation of public health authorities' pandemic migration strategies impacting all non-essential travel and limiting attendance at large meetings that are not mission-critical.

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.

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.

Listening Session on COVID-19: FDA HQ coordinated over 75 listening sessions since February 2020 to gather stakeholder concerns, feedback and useful information regarding interest about testing, clinical trials, and therapeutic development in response to the pandemic.

Speaker Requests: FDA HQ manages 1,065 speaker requests received from over 186 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.

Since October 2019, OMHHE participated and/or exhibited at over 110 meetings and conferences and participated in media interviews that reached diverse consumers.

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 provided remarks; plus 23 speakers representing patients, patient advocacy groups, Department of Health and Human Services, Department of Justice, and the Veterans Health Administration gave presentations on their unique efforts to address the opioid crisis.

During the COVID-19 Pandemic, FDA OMHHE collaborated with the Office of External Affairs/Stakeholder Engagement Office and held listening sessions with diverse stakeholders to learn more about the gaps and needs of minority communities and to share information on FDA's COVID-19 activities.

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 January 2019 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 across all Centers. 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 further 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; and the History of FDA and PHS collaborations, Part I: 1906-1962. Efforts are underway to work with the Smithsonian to fabricate an extensive fixture suitable to present a recently acquired collection of 3000 pharmaceuticals documenting the 100-plus years of FDA's oversight of drugs.

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 Associate Commissioner for Regulatory Affairs, 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. FDA and the Office of Equal Employment Opportunity launched a collaborative program to jointly develop staff recognition programs, beginning with Black History Month. 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 about 250 interviews, as well as 3400 A/V recordings, and many of the latter have been incorporated into a year-long program of historically-informed social media.

FDA provided bi-weekly in-person and online-based training on agency history to all 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; historical background to print and broadcast media interested in agency policy; and perspective for Congressional testimony by agency officials. FDA also participated in the Interagency Working Group on Scientific Collections to study the economics of the government's scientific collections. FDA contracted for a comprehensive external expert assessment of the agency's historical collections and recommendations for short- and long-term maintenance and preservation needs. Finally, FDA is working across the agency and networking with HHS OPDIVS and other institutions to document FDA's response to the COVID-19 crisis by planning strategic oral histories with key

personnel, identifying key objects of regulatory and other interest, and tracking the records of the IMG and others.

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[167]

Congressional Engagement

The Office of Legislation (OL) has provided information requested by Congress in order to inform policymaking on new issues. 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, responding to over 300 requests pertaining to members' policy interests, including issues surrounding the use of public health data and real-world evidence. OL has also managed over 700 congressional outreaches and engagements, such as the Agency's "New Era of Smarter Food Safety" initiative and through our Real-World Evidence program established under The 21st Century Cures Act. OL has responded to more than 1,000 inquiries regarding the COVID-19 pandemic and FDA's response efforts.

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. This includes proposals on drug

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

importation, exclusivity, price disclosure, publication of biologic patents, the use of citizen petitions, access to reference listed drugs, and biosimilars. OL has assisted Congress to legislation that could impact medical product approval standards and regulatory pathways in an effort to expedite getting innovative products onto the market. Examples include passage of legislation to reform the regulation of over-the-counter drugs, and the passage 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 has also extensively engaged with Congress on efforts to ensure the safety of imported products and protect consumers from fraudulent or counterfeit goods, as well as legislative issues surrounding new innovative technologies across the medical products and foods regulatory space. OL has worked closely with Congress to advance congressional and legislative efforts to provide Americans with competitive and innovative food and medical products. For example, OL has worked on advancing unique approval pathways for innovative products, such as the expanded conditional approval pathway for animal drugs, the Orphan Drug Designation Program, the Humanitarian Use Device Program, and the Rare Pediatric Disease Priority Review Voucher Program. OL has also worked on legislative issues surrounding new, innovative technologies across the medical products and foods regulatory space. All of these efforts have strengthened American patients and consumers decision making.

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, and territorial officials and regulatory partners. In addition, per the Agency's Tribal Consultation Policy, the IGA staff has been designated as the Agency's primary liaison with tribal governments.

In addition to proactively providing timely information on the important activities of the Agency, the IGA staff serves as a primary entry point for these important stakeholders on issues of significant concern to states, localities, territories and tribes, and works to ensure that questions from these stakeholders related the Agency's policies and programs are addressed in as timely a manner as possible.

In FY 2021, significant engagement by the IGA team with state, local, territorial and tribal 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. In addition, IGA has been an active participant in the agency's response to the COVID-19 pandemic by supplying information proactively to state, local, territorial and tribal officials, as well as responding to COVID-19 inquiries from these stakeholders.

The IGA team is also 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 9th such meeting was held in FY 2021 (October 27-28, 2020) and brought together regulatory officials from 44 jurisdictions, as well as leadership and staff from the National Association of State Boards of Pharmacy (NABP). The meeting featured sessions on: FDA's and states' oversight of compounding issues raised during the COVID-19 public health emergency; sharing information on inspectional processes, and providing insights from FDA's inspections conducted over the previous year; discussing the recently finalized FDA-State Memorandum of

Understanding (MOU), and the information-sharing system under development by NABP that is intended to support state reporting under the MOU; and a variety of other topics.

Regarding food safety, the IGA team interfaces with Governors' offices, state legislators, state/local/territorial elected leadership, and tribal governments to ensure that important information regarding food recalls, outbreaks of foodborne illnesses, and other important food safety issues are shared in a timely manner. IGA works in close coordination with FDA's Office of Food Policy and Response, Center for Food Safety and Applied Nutrition, and/or Office of Regulatory Affairs on all food safety matters.

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.[168]

FDA HQ continues to coordinate with the Centers, ORA and the National Institutes of Health 21stof clinical trial registration and results information reporting to the ClinicalTrials.gov databank (42 CFR part 11). FDA HQ continues to provide consultation to NIH to support the reports required under the Cures Act related to ClinicalTrials.gov. In accordance with Section 2052 of the Cures Act, a Report to Congress was submitted on April 17, 2019. NIH and FDA are working on the next Report to Congress which is due on April 18, 2021. FDA HQ also coordinates with NIH on messaging and frequently asked questions around compliance and enforcement of ClinicalTrials.gov requirements.

Regulatory Policy and Guidance

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. This proposed rule, if finalized, would implement Section 3024 of the Cures Act and harmonize with the revised Common Rule. FDA issued the NPRM in November 2018 and is in the process of reviewing and responding to public comments received on this proposed rule.

Guidance Documents – Human Subject Protection and Good Clinical Practice

In August 2020, FDA issued a final guidance entitled, "Civil Money Penalties Relating to ClinicalTrials.gov Databank." This final guidance describes FDA's thinking regarding the assessment of civil money penalties under section 303(f)(3) of the FD&C Act for failing to submit clinical trial registration and/or results information to the ClinicalTrials.gov data bank and/or certain certifications to FDA.

Each year, FDA HQ responds to approximately 1,600 inquiries on human subject protection, informed consent, and best practices for the conduct of clinical trials. Archives of these

[168] https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf The compliance date of the revised Common Rule was delayed until January 21, 2019; see https://www.gpo.gov/fdsys/pkg/FR-2018-06-19/pdf/2018-13187.pdf

questions and answers are available on FDA's website. Additionally, FDA HQ coordinated with the Centers to respond to approximately 250 inquiries related to the COVID-19 public health emergency from the healthcare community and patients.

FDA HQ promotes high standards of scientific integrity and human subject protection by providing expert ethical advice to agency Centers and Offices on a variety of ethical and clinical trial design concerns identified during the review of research and marketing applications. FDA HQ annually provides over 120 (formal and informal) inter-Center ethics consultations for studies involving adult research participants. The consults opine on complex ethical issues, such as research involving life-threatening conditions in which there is no time to obtain consent and the review of research involving rapidly evolving gene editing technologies. In FY 2020, FDA HQ advised on challenging ethics issues arising during the conduct of research related to or impacted by the COVID-19 pandemic, including obtaining informed consent from patients in strict isolation and mitigating risk to those not participating as subjects in the clinical trial, but who could be exposed to research-related risks.

Additionally, FDA HQ participated in a wide variety of activities, such as serving as ex-officio on the Secretary's Advisory Committee on Human Research Protections (SACHRP), participating at FDA Advisory Committees, and conducting training for internal staff and external stakeholders on the principles of human subject protection and good clinical practice.

Geographic Information System Mapping

Accomplishments during COVID-19 include creation of the COVID-19 FDA Advisory level, a qualitative way to indicate the status of COVID-19 outbreak in an area based on county and state metrics and is intended to inform FDA decision makers. It allowed FDA to make effective, safe decisions for their investigators as they resumed surveillance inspections.

In FY 2020 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 2020 COVID-19 Response. FDA HQ completed maps for 90 GIS project requests involving FDA-regulated industry.

Global Health Security

FDA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security. FDA HQ:

- serves as point of entry on policy and planning matters related to global health security
- serves as a focal point for the FDA's involvement in the HHS-led Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and the Department of Defense (DoD) medical countermeasure (MCM) programs
- coordinates the Medical Countermeasures Initiative (MCMi) to facilitate the development and availability of safe and effective MCMs against chemical, biological, radiological, and nuclear (CBRN) agents and emerging threats, such as pandemic influenza, Ebola virus, and Zika virus, and SARS-CoV-2 virus (the causative agent of COVID-19)
- provides leadership and coordination for FDA responses to health security threats

FDA HQ provided leadership and support for FDA's response to the COVID-19 pandemic including supporting the development of MCMs, the issuance of over 250 EUAs to enable the emergency use of hundreds of medical products (including diagnostic tests, personal protective equipment and treatments), working closely with interagency partners and regulated industry to identify and mitigate supply shortages of FDA-regulated products, and proactively communicating FDA's Agency-wide response efforts (including the issuance of 200+ press releases, 150+ new web pages, 30+ weekly MCMi COVID-19 email updates, 10+ videos, and thousands of tweets).[169] Additionally, FDA HQ continued to facilitate coordination of FDA response activities to the Ebola outbreak in the Democratic Republic of Congo. FDA HQ also supported the issuance of numerous amendments to current EUAs upon request from the product manufacturers to add additional instruments or specimen types or make clarifications, and several EUA revocations, (e.g., when Ebola and Zika diagnostics previously available under EUA were authorized for marketing, or when revocation criteria were met for COVID EUAs).

FDA HQ also supported monitoring for products with unsubstantiated or fraudulent claims for the diagnosis, treatment, or prevention of COVID-19, Ebola and Zika; led domestic and supported international policy development activities related to COVID-19, Ebola and Zika virus response; provided technical support to the World Health Organization and international regulatory counterparts.

FDA HQ continued to work to resolve MCM shortages as quickly as possible when they occurred. For example, FDA HQ provided critical leadership through the USG supply chain task force and provided FDA collaboration and technical assistance to USG-wide efforts to mitigate the impact of COVID on shortages of FDA-regulated products.

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 include:

- developing reagents and new methods to sequence the SARS-CoV-2 virus to create profiles of coronavirus for the rapid characterization of these viruses in humans and animal models
- using innovative imaging approaches to better understand viral infection and immune responses to SARS-CoV-2 in non-clinical and clinical studies
- development of reagents for expansion of specific and sensitive diagnostic devices for emergent viruses, including Zika and SARS-CoV-2
- development of assays to support evaluation of vaccine immune responses for SARS-CoV-2
- developing gastrointestinal, bone marrow, and lung 'organs-on-a chip' models of acute radiation syndrome for evaluation of candidate therapeutics, 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

[169] More information about FDA's COVID response efforts is available on the FDA website at: www.fda.gov/coronavirus

- 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 in collaboration with NIAID, 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 vaccine recipients 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 that support MCM availability and access include:

- addressing issues related to use of expanded access mechanisms and EUAs to make available unapproved MCMs for CBRN and other emerging infectious disease threats, including COVID response efforts
- implementing novel EUA approaches, including use of templates to facilitate reviews, development of "umbrella" EUAs to authorize use of multiple MCMs through issuance of a single authorization, issuance of EUAs that cover multiple products regulated by different Centers, and assuring consistency between Centers on approaches to issuance, revision, termination and transparency of EUAs and use of other emergency authorities (e.g., waivers of cGMPs)
- providing technical assistance to legislative proposals that amend MCM-related authorities, including proposals to provide authorities related to, among others: waivers for imports during certain declared emergencies, enforcement discretion for imports,

stockpiling MCMs, liability protections, expanded EUA transparency, mitigation of shortages, and advanced manufacturing.
- implementing, developing guidance, 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
- clarifying regulatory issues around the conduct of clinical studies during public health emergencies, including continued efforts to advanea national capability to track, collect, analyze, and evaluate information related to MCMs used during public health emergencies
- supporting FDA MCM-related collaborations, including enhanced DoD collaborations under Public Law 115-92 as implemented under the DoD-FDAMOU
- 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, including the COVID response
- 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 establishment of a generic framework for sharing medical countermeasures

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.[170]

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 15 USC 3710 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 Development Agreements (CRADAs) and out-licensing of FDA technologies, the Agency

[170] More information about these efforts is available on the FDA website at: https://www.fda.gov/medicalcountermeasures

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.

International Inspections, Information Sharing and Strategic Engagement, and Continued Implementation of China Safety Initiative

FDA engages strategically with global regulatory counterparts and stakeholders to assure that products coming to the U.S. market are safe and effective. FDA's Office of Global Policy and Strategy (OGPS) is comprised of three headquarters offices (Office of Global 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 through the Office of Global Operations. Bilateral engagements for countries where there is not an FDA Office are managed by OGDP. OGPS collaborates with FDA Centers and Offices to ensure global issues are reflected in policy and regulatory actions, and that priority regulatory initiatives are advanced 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 in India and Mexico; advocacy in bilateral and multilateral settings for the importance of strong regulatory systems to enhance public health or facilitate international trade; representation of FDA's regulatory equities in trade negotiations and at the WTO; negotiation and development of international arrangements or agreements which facilitate the exchange of regulatory information with our global counterparts; and continued implementation of the China Safety Initiative by the FDA China Office.

COVID-19 Response

OGPS supported the Agency's COVID-19 response by working collaboratively with regulatory partners around the globe, and the U.S. interagency to expand knowledge and compliance with FDA's emergency use authorizations. FDA China Office worked to mitigate Chinese export barriers for critical medical countermeasures. OGPS' China Office and headquarters offices played a vital coordinating role in the Mission China PPE Task Force, which was a round-the-clock effort to safely and quickly import critical PPE and test kits from China. This effort included OGPS-led high-level dialogues with Chinese regulatory counterparts. OGPS headquarters offices contributed to international understanding of the FDA essential medicines list and to ensuring that diplomatic considerations were reflected in all of FDA's public messaging related to COVID-19.

The OGPS Europe Office developed and hosted a global vaccine regulators forum to exchange best practices and regulatory strategies to facilitate development of a SARS-CoV-2 vaccine, which established common understanding related to preclinical data requirements in support of first-in-human clinical trials and promoted FDA-EU regulatory cooperation related to the pandemic. The India Office mitigated any possible disruptions to the U.S. pharmaceutical supply chain from India's COVID-19 lockdown by engaging with municipal and federal regulators in India. The OGPS Latin America Office coordinated across the region to assure that both

regulatory partners and regulated industry understood the requirements of FDA's emergency use authorizations.

Inspections

FDA foreign office staff as well as ORA investigators on short-term assignment to the China, India, and Latin America offices conduct inspections in their respective country or region. These inspections provide valuable insights and information regarding manufacturing, quality controls, and processing occurring in those facilities which support FDA's risk-based inspection models workplan, providing oversight to the highest risk facilities and strengthening FDA's regulatory knowledge. In fiscal year (FY) 2020, a total of 42, 37, and 7 inspections were conducted by FDA investigators based in-country or on temporary duty assignments in China, India and Latin America respectively, before normal in-country operations were suspended through authorized departures or local government-initiated shelter-in-place requirements due to the Covid-19 pandemic. In addition, during FY 2020, OGPS completed 25 remote assessments of critical drug facilities and sites conducting clinical trials of drugs and biologics while in-person inspections were suspended.

The China Office also conducted high-profile inspections that led to enforcement actions, completing 42 inspections in Fiscal Year 2020 OGPS China Office plays a critical role in vetting facilities for FDA inspection, assuring that their registration information is correct and that they do export products to the United States, this improves the efficiency of FDA inspectional resources in China.

In FY 2020, the India Office conducted an analysis of inspection trends, export data, and seasonal harvesting, which resulted in a better understanding of how inspections of FDA-regulated commodities should be targeted. They also developed a Foreign Export Inspection Guidance to support FDA investigators conducting inspections in India.

The India Office 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, leading to the discovery of the industry practice of the use of third-party solvent recovery facilities and contamination of APIs with nitrosamine impurities, resulting in multiple-observation FDA 483's.

Information Sharing and Strategic Engagement

FDA engages strategically to ensure 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 regulators around the globe. International arrangements with foreign authorities, including confidentiality commitments and cooperative arrangements, facilitate regulatory cooperation, including the sharing of certain types of non-public information.

During FY 2020, FDA established one new trade secret information confidentiality commitment with Germany pursuant to Section 708c of the Food, Drug, and Cosmetic Act, to help advance implementation of the Revised Pharmaceuticals Annex to the United States – European Union Mutual Recognition Agreement (MRA). In addition, FDA completed a Memorandum of

Understanding with India's Central Drugs Standard Control Organization to strengthen cooperative engagement in scientific and technical matters for the oversight of medical products; confidentiality commitments with Canada (tobacco and vaping products) and Argentina (foods, drugs, medical devices, cosmetics and biologics); and a statement of intent with Mexico that revised and expanded the Produce Safety Partnership (PSP) to include all human food and rebranded the effort as the Food Safety Partnership when signed by the Deputy Commissioner.

In FY 2020, OGPS led the finalization and issuance of FDA's first-ever equivalence determination. The equivalence determination will enable Spain and the Netherlands to export raw bivalve molluscan shellfish to the United States. Specifically, FDA's equivalence determination finds that the adoption and implementation by Spain and the Netherlands of the European Union's (EU's) system of food safety control measures for raw bivalve molluscan shellfish, along with their application of additional measures specifically adopted for export to the United States, provides at least the same level of sanitary protection as comparable food safety measures in the United States and is therefore equivalent..

The China Safety Initiative enables FDA to strengthen its efforts to regulate the 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, and conducts regulatory trend analysis to support risk-based decision making. These contribute to FDA regulatory policies and actions, provides critical regulatory intelligence to Centers and ORA to mitigate public health risks, and promotes greater oversight of products manufactured in China.

To better inform the public about OGPS' many activities, the OGPS Communications Team established both a new monthly newsletter and an international blog (11 blogs issued to date) and launched a new Twitter handle (@FDA_Global that now has more than 2,100 followers. In addition, we continued to distribute Dear International Colleague emails highlighting notable FDA actions to a list-serve of nearly 20,000 subscribers.

Facilitating competition and innovation through International Partnerships
FDA collects, analyzes and shares high-quality information to strengthen science, enhance risk-management of FDA regulatory resources and 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 protecting and promoting public health and facilitating international trade. In FY 2020, FDA's partnerships included multilateral institutions such as the World Health Organization (WHO), the Pan American Health Organization (PAHO), the Organization of Economic Cooperation and Development (OECD), the Joint Institute for Food Safety and Applied Nutrition (JIFSAN), and the Inter-American Institute for Cooperation on Agriculture

(IICA). FDA also engages with other institutions, including the Bill & Melinda Gates Foundation, and the National Academies of Science, Engineering and Medicines (NASEM).

OGPS commissioned studies to initiate a global dialogue and increase understanding of the value of strengthening regulatory systems. This included a PAHO landscaping paper on medical product regulations in the Americas and two separate NASEM reports; the first on stronger food and drug regulatory systems and the second on mutual recognition and reliance for medicines.

Building on the momentum of the first international global food safety conferences co-convened by WHO, WTO and FAO in FY2019, FDA worked with HHS and the U.S. interagency and other governments to request that the WHO Member States discuss key food safety issues in FY 2020. This multi-country, cross-regional effort resulted in the World Health Assembly adopting the first resolution in a decade focused specifically on strengthening food safety efforts.

During FY 2020, OGPS, in collaboration with FDA Centers, catalyzed global efforts related to whole-genome sequencing of foodborne pathogens; the regulation of artificial intelligence within a global context; the exploration of mobile-accessible information platforms to strengthen regulatory competency and capacity; and the case for risk-based surveillance for substandard and falsified medical products through economic modeling.

OGPS serves as FDA's policy lead for the negotiation of new free trade agreements and FDA's engagement in relevant WTO Committees. The objective of FDA's participation in trade agreements is to align trading partners' regulatory practices with FDA's established regulatory programs in a manner which better protects U.S. consumers and patients, and which enhances competition by leveling the playing field for American manufacturers. In FY 2020 OGPS led FDA's participation in the negotiation and implementation of trade agreements with China, Mexico and Canada (USMCA), the United Kingdom, Kenya, and Brazil.

Leveraging the Authority of Foreign Regulators

FDA leverages partnerships to protect and promote public heath through diplomacy and global leadership. OGPS efforts increase foreign stakeholders' understanding of FDA regulations and guidance documents, drawing the links between strong regulatory systems and public health, development and trade.

OGPS is FDA's lead for the negotiation of MRAs and other arrangements. Title VII, Section 712 of the Food and Drug Administration Safety and Innovation Act (FDASIA) allows FDA to enter into written arrangements and agreements with foreign governments to recognize the inspection of foreign drug establishments for the purpose of facilitating FDA's risk-based inspection schedule. 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. In FY 2020, OGPS furthered implementation of the Revised Pharmaceuticals Annex to the United States – European MRA by completing eight capability assessments of Member States for their ability to perform GMP inspections of veterinary drug facilities.

In FY 2020 The Europe Office effectively used diplomacy and partnership so the European Food Safety Agency would align more closely with FDA‘s approach to agricultural genome editing, and helped develop a global biotechnology communications toolkit to assure factual messages on topics such as genetic modification techniques; and, in response to the COVID-19 pandemic the Europe Office and relevant USG agencies, brought together (digitally) other regulators from Europe, and around the world for an emergency vaccine regulators forum to discuss the different vaccine approval frameworks.

Through the leadership and efforts of the Latin America Office in FY 2020, regional implementation of FSMA's rules for produce safety and third-party verification continues. These included a revised and updated Food Safety Partnership agreement with Mexican regulatory authorities, on-farm-readiness review training workshops in Chile, and development and delivery of on-line, train-the-trainer capacity building workshops in collaboration with IICA to enhance competencies of food producers and manufacturers exporting to the United States.

GAO/OIG Engagement and Responses

The GAO/OIG Liaison team continued to lead the agency in responding timely, accurately, and completely to GAO and OIG engagements, providing responses to GAO and OIG recommendations, and addressing GAO's High-Risk Issues. As part of this work, the GAO/OIG Liaison Team continues to cultivate relationships with GAO, HHS, and FDA programs to ensure that GAO and OIG studies at FDA are handled effectively.

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

Beginning in March 2020, the staff began handling the heavy volume of GAO and OIG oversight related to the COVID-19 pandemic. 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 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 Actual	$308,089,000	$186,919,000	$121,170,000
FY 2021 Enacted	$319,572,000	$194,951,000	$124,621,000
FY 2022 President's Budget	$345,079,000	$221,834,000	$123,245,000

BUDGET REQUEST

The FY 2022 Budget Request for FDA Headquarters is $345,079,000, of which $221,834,000 is budget authority and $123,245,000 is user fees. The budget authority increases by $26,883,000 compared to the FY 2021 President's Budget. User Fees decrease by $1,376,000. The request builds upon the initiatives enacted in the FY 2021 appropriation and includes new initiatives supporting the FDA mission. The FDA Headquarters Budget Authority shown is inclusive of the $1,500,000 to transfer to OIG.

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 (+$2.5 million / 5 FTE)

Data Modernization and Enhanced Technologies – New Era of Smarter Food Safety Headquarters (+$2.5 million / 5 FTE)

The FY 2022 Budget includes $2.5 million in targeted investments to ensure effective strategic and project management across the four core elements of the New Era of Smarter Food Safety Blueprint[171], as part of the $45 million total request for Smarter Food Safety. These resources are also a portion of FDA's cross-cutting Data Modernization and Enhanced Technologies initiative, which aligns to FDA's Technology and Data Modernization Action Plans as well as the Blueprint. The public health objective of the New Era of Smarter Food Safety is to reduce the number of illnesses and injuries attributed to FDA-regulated human and animal foods.

The New Era of Smarter Food Safety Blueprint outlines achievable goals to enhance traceability, improve predictive analytics, expand collaboration with our regulatory and public health partners, respond more rapidly to outbreaks and other food safety problems, address new business models (such as online ordering and direct delivery of foods that has accelerated due to the COVID-19 pandemic), advance the safety of foods sold in traditional retail establishments, and foster strong food safety cultures. This approach builds on the modernized food safety regulatory framework created by the FDA Food Safety Modernization Act (FSMA) and is also closely connected with FDA's response to the unprecedented challenges of the on-going COVID-19 pandemic by fortifying our public health infrastructure to help ensure that consumers have access to safe food when public health emergencies arise in the future.

With new resources in FY 2022, FDA will ensure effective strategic and project management across the four core elements of the New Era of Smarter Food Safety Blueprint. This investment includes hiring experts in emerging technologies and cutting-edge food safety science, as well as support for comprehensive project management, strategic engagement, and IT system requirements analysis. As a critical component of the $45 million total request for the New Era of Smarter Food Safety in FY 2022, these resources will allow FDA to successfully manage the implementation the Blueprint, including effective use of new and emerging technologies and data-driven approaches that strengthen our predictive capabilities, accelerate prevention, and speed traceback when contaminated foods are identified.

FDA continues to have significantly increased responsibilities in responding to the on-going COVID-19 pandemic that require coordinated support, analysis, and stakeholder engagement. Continuous improvements have allowed FDA to maximize and exhaust the efficient use of all current resources, but additional resources are necessary in order to fulfill the full scope of the New Era of Smarter Food Safety Blueprint. Without new resources, FDA's ability to maintain appropriate safeguards will significantly lag behind changes occurring in the marketplace, potentially putting consumers at risk and adversely impacting industry. In addition, lack of learning from the COVID-19 pandemic will prevent us from being better prepared for future public health challenges.

[171] https://www.fda.gov/media/139868/download

Crosscutting (+$20.1 million / 46 FTE)

Data Modernization and Enhanced Technologies – Enterprise Wide Headquarters (+$6.1 million / 7 FTE)
FDA will strengthen the common data infrastructure established through the Technology Modernization Action Plan (TMAP) and COVID-19 investments as well as leverage Agency-wide data and technology governance model, accelerate the development and deployment of new data-rich capabilities like AI.

Office of Minority Health and Health Equity Headquarters (+$4.7 million / 3 FTE)
The FY 2022 Budget includes an increase of +$4.7 million, to enhance FDA's ability to support and expand health equity and health disparity efforts. This funding will allow FDA to expand culturally and linguistically tailored communication and outreach efforts, establish new scientific initiatives, support novel health disparity and health equity focused intramural and extramural research, advance activities that enhance meaningful inclusion of minority populations in clinical trials, understand and address health disparities (including, but not limited to, ethnicity, race, age, geography, and disability), increase engagement with Historically Black Colleges and Universities, Minority Serving Institutions, and other collaborators to address gaps and needs of diverse communities, and develop FDA-wide training programs that focus on the reduction of health disparities and advancement of health equity. OMHHE will utilize 3 new FTEs, contracts, and grants to support these activities.

Capacity Building: Essential Services Headquarters (+$0.009 million)
The FY 2022 Budget includes $40.3 million to support the Essential Services component of the Capacity Building initiative. The FY 2022 Budget Request supports the Headquarters components of vital cross-agency services. The funds support FDA's operations and FDA's ability to keep pace with new requirements, legislation, and regulatory responsibilities.

The Budget will allow FDA to more efficiently recruit and hire staff, as well as properly award, manage, and monitor grants and contracts. The funding will help to ensure proper budget planning and control, and help FDA effectively manage and address Enterprise Risks. These funds will support FDA's security and project management of over 360 FDA-owned, GSA-owned, and GSA-leased buildings, and allow FDA to conduct an agency-wide comprehensive security vulnerability assessment. The funds will also address workload challenges to ensure compliance with ethics and equal opportunity requirements.

The Budget includes investments in eDiscovery which are critical to building and expanding the infrastructure needed to respond to growing demand and for future pandemic or public health crises. eDiscovery – the process of identifying, collecting, processing, reviewing, and producing electronic information relevant to civil, criminal, or regulatory matters – is critically needed to support litigation, third party subpoenas, FOIA requests, and criminal investigations.

The Budget will support critically needed equipment replacement, including replacing end-of-life servers, updating network devices, and upgrading storage solutions. The Budget also

includes funding for Cybersecurity to address real, critical threats to FDA's underlying cybersecurity infrastructure with outdated solutions.

These capacity building investments are critical to supporting FDA's ability to operate sufficiently and effectively and support the expansive range of responsibilities.

Capacity Building: Laboratory Safety
Headquarters (+$6.6 million / 11 FTE)
FDA Office of Laboratory Safety (OLS) supports the FDA mission by providing policy, resources, and oversight for occupational safety and health, environmental management programs, and laboratory quality management. OLS' goals are to reduce risk from laboratory work, increase laboratory security and data quality, increase efficiencies across the Centers/ORA, and enhance the culture of responsibility and safety. To achieve these objectives, the office directs the short-, mid-, and long-term strategy for developing new Agency-wide standards and policies in collaboration and coordination with the Centers and Offices, as appropriate; provides training, tools, and resources associated with implementing standards and policies; provides quality and safety assessment and improvement strategies; and leads activities that emphasize the benefits of a safety-oriented culture. In addition, OLS is responsible for ensuring integrated, timely, and quality customer service delivery and appropriate communication between stakeholders.

The FY 2022 Budget request includes an increase of $6.6 million to support these efforts. The investment will ensure that the FDA workforce is able to carry out FDA's critical public health mission safely. The increase will enable OLS to effectively serve as the Agency's coordinator and lead for implementation of policies and procedures, centralized training, and oversight for occupational safety and health, and laboratory security related activities. These funds will be used to support the:

- Inspection of FDA laboratories including the development and implementation of a standardized laboratory safety inspection program (29 CFR 1960.25c);
- Enhancement of communication efforts; collaboration, coordination and partnership inter- and intra-agency to further enhance laboratory security, environmental, occupational safety and health programs, and laboratory quality management; and the culture of responsibility and safety;
- Development of Agency Safety Manuals, Plans, and Guides and perform annual updates (29 CFR 1960.10 and 12; 42 CFR 73, 9 CFR 121, 10 CFR 31 and 35);
- Coordination and implementation of Agency wide laboratory quality management program (FDA SMG 2130.11);
- Develop and implement IT solutions (Inventory Control and Information Management System) for efficient Occupational Safety and Health program management including workplace incident reporting and management (29 CFR 1904, 29 CFR 1960.25-26, 29 CFR 1960.70 & 72, and Executive Orders 13410, 13335, and 12196);
- Development of FDA-wide training programs and perform annual updates (29 CFR 1910, 29 CFR 1904, 49 CFR 171, 10 CFR31, and 29 CFR 1926);
- Establishment of a safety and engineering contract to provide on demand resources and industrial hygiene support to the Center and ORA programs; and

- Administration of the FDA Institutional Biosafety Committee and other safety committees, councils, and working groups, Environmental Compliance and Audit Program, Employee Compensation Program, Hazardous Waste Management Program FDA White Oak Radiation Safety Program.

Capacity Building: Office of Chief Counsel
Headquarters (+$6.6 million / 25 FTE)
The Office of Chief Counsel (OCC) has a critical need for increased funds for legal services to support crucial pandemic-related matters, as well as the range of "normal" FDA regulatory activities such as medical product reviews, food safety assessments, enforcement cases, defense of agency decisions, and other high-profile matters involving multiple motivated stakeholders. OCC attorneys have been crucial to the agency's immediate and short-term response to the COVID-19 crisis and will remain critical well into the future. The FY 2022 Budget Request will support hiring 25 additional staff attorneys. Additional staffing would support FDA's ability to provide legal counsel on Emergency Use Authorizations, including ongoing and future Emergency Use Authorizations, product reviews, technical and enforcement guidance for industry, importation and product quality, and other regulatory activities associated with devices related to the diagnosis, treatment, or mitigation of COVID-19. OCC's responsibilities have grown alongside FDA's complex regulatory responsibilities. New OCC staff are needed to support legal work such as those that impact food producing and handling facilities and those that mitigate disruption in the food supply for both human and animal food. New OCC staff also are needed to handle matters to determine whether and how to exercise enforcement discretion on regulatory requirements without undermining the underlying regulatory programs. Additional OCC staff are needed to support and advise on cross-cutting matters including disclosure matters and privacy issues, ethics and conflict of interest matters, and implementation of regulatory reform activities.

Pay Costs
Headquarters (+$1.0 million)
The FY 2022 Budget provides half of the estimated cost to FDA to address the 2.7% pay cost requested in the President's Budget. The funding will support FDA public health employee costs and is critical to avoid program erosion. The remaining costs are assumed within FDA's base funding level.

USER FEES

Current Law User Fees (-$1.4 million / 2 FTE)

FDA HQ will utilize the 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 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products.*(Output)*	FY 2020: Developed 90 mapping products to support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinated 86 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 2020: FDA completed annual milestones for 6 additional projects, for a total of 58 intramural research projects under the Nanotechnology CORES program to promote cross-center and external collaborative regulatory science research opportunities, focusing on studies evaluating nano-materials. (Target Met)	64 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards	70 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards	+ 6 Maintain
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship programs. (Outcome)	FY 2020: 80% Target: 50% (Target Exceeded)	20%	20%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 +/- FY 2021
293205: Percentage of requests for combination product designations processed within the 60-day statutory requirement. *(Output)*	FY 2020: 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, Canada, and Australia. *(Output)*	FY 2020: 227 Target: 90 (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 2020: 37 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 FDA's global mission. *(Outcome)*	FY 2020: 73 Target: 35 (Target Exceeded)	40	45	Maintain
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2020: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain

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

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. 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. FDA reset the retention target to 20% in FY 2021 to reflect the new expanded program's expected baseline. For now, the retention target will remain at 20% in FY 2021 and 2022. Although it's unclear what the ultimate impact on the program will be, COVID-19 and the recent shutdown has affected FDA's ability to sponsor fellows, and has limited the experience of those fellows to train onsite in FDA labs, and with the appropriate mentors. FDA will continue to monitor and adjust this goal moving forward as necessary.

INFRASTRUCTURE - GSA RENT, OTHER RENT, AND WHITE OAK

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
FDA White Oak Complex	**53,913**	**59,744**	**52,944**	**55,892**	**2,948**
Budget Authority	***45,914***	***45,913***	***45,914***	***48,414***	***2,500***
User Fees	***7,999***	***13,831***	***7,030***	***7,478***	***448***
Prescription Drug (PDUFA)	*3,848*	*11,082*	*3,886*	*3,925*	*39*
Medical Device (MDUFA)	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	*4,151*	*2,749*	*3,144*	*3,553*	*409*
Other Rent and Rent Related	**132,970**	**119,877**	**136,257**	**155,096**	**18,839**
Budget Authority	***80,173***	***80,172***	***84,262***	***102,095***	***17,833***
User Fees	***52,797***	***39,705***	***51,995***	***53,001***	***1,006***
Prescription Drug (PDUFA)	*26,389*	*17,796*	*26,652*	*26,919*	*267*
Medical Device (MDUFA)	*5,291*	*5,291*	*5,344*	*5,398*	*54*
Generic Drug (GDUFA)	*13,206*	*11,467*	*13,338*	*13,472*	*134*
Biosimilars (BsUFA)	*1,081*	*543*	*1,092*	*1,102*	*10*
Animal Drug (ADUFA)	*797*	*797*	*805*	*813*	*8*
Animal Generic Drug (AGDUFA)	*266*	*266*	*269*	*272*	*3*
Family Smoking Prevention and Tobacco Control Act	*5,283*	*3,506*	*4,001*	*4,522*	*521*
Food and Feed Recall	*44*	---	*45*	*46*	*1*
Food Reinspection	*208*	---	*212*	*216*	*4*
Voluntary Qualified Importer Program	*173*	---	*177*	*180*	*3*
Third Party Auditor Program	*24*	*5*	*25*	*25*	---
Outsourcing Facility	*35*	*34*	*35*	*36*	*1*
GSA Rental Payments	**240,549**	**219,334**	**235,961**	**236,214**	**253**
Budget Authority	***171,208***	***171,208***	***167,119***	***166,286***	***-833***
User Fees	***69,341***	***48,126***	***68,842***	***69,928***	***1,086***
Prescription Drug (PDUFA)	*35,695*	*24,354*	*36,052*	*36,412*	*360*
Medical Device (MDUFA)	*8,395*	*6,097*	*8,479*	*8,563*	*84*
Generic Drug (GDUFA)	*12,847*	*8,335*	*12,975*	*13,105*	*130*
Biosimilars (BsUFA)	*455*	*190*	*460*	*465*	*5*
Animal Drug (ADUFA)	*847*	*635*	*856*	*864*	*8*
Animal Generic Drug (AGDUFA)	*310*	*233*	*314*	*317*	*3*
Family Smoking Prevention and Tobacco Control Act	*9,960*	*8,277*	*8,857*	*9,336*	*479*
Food and Feed Recall	*74*	---	*76*	*77*	*1*
Food Reinspection	*355*	---	*362*	*369*	*7*
Voluntary Qualified Importer Program	*296*	---	*302*	*308*	*6*
Third Party Auditor Program	*48*	*5*	*49*	*50*	*1*
Outsourcing Facility	*59*	---	*60*	*62*	*2*

Authorizing Legislation: The Federal Food Drug and Cosmetic Act (21 U.S.C. 321 399); Radiation Control for Health and Safety Act (21 U.S.C. 360hh 360ss); The Federal Import Milk Act (21 U.S.C. 142 149); Public Health Service Act (42 U.S.C. 201, et seq.); Foods Additives Amendments of 1958; Color Additives Amendments of 1960; Animal Drug Amendments (21 U.S.C. 360b); Controlled Substances Act (21 U.S.C. 801 830); The Fair Packaging and Labeling Act (15 U.S.C. 1451 1461); Safe Drinking Water Act (21 U.S.C. 349); Saccharin Study and Labeling Act; Federal Anti-Tampering Act (18 U.S.C. 1365); Medical Device Amendments of

1976; Infant Formula Act of 1980; Drug Enforcement, Education, and Control Act of 1986; Generic Animal Drug and Patent Term Restoration Act; Prescription Drug Marketing Act of 1987; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Nutrition Labeling and Education Act of 1990; Prescription Drug Amendments of 1992; Safe Medical Device Amendments of 1992; Dietary Supplement Health and Education Act of 1994; Animal Medicinal Drug Use Clarification Act of 1994; Animal Drug Availability Act of 1996; Food Quality Protection Act of 1996; Federal Tea Tasters Repeal Act (42 U.S.C. 41); Safe Drinking Water Act Amendments of 1996 (21 U.S.C. 349); Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Medical Device User Fee and Modernization Act of 2002; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Animal Drug User Fee Act of 2003 (21 U.S.C. 379j 11 - 379j 12); Project Bioshield Act of 2004 (21 U.S.C.360bbb 3); Minor Use and Minor Species Animal Health Act of 2004; Food Allergy Labeling and Consumer Protection Act of 2004 Medical Device User Fee Stabilization Act of 2005; Sanitary Food Transportation Act of 2005 Dietary Supplement and Nonprescription Drug and Consumer Protection Act (21 U.S.C. 379aa 1); Food and Drug Administration Amendments Act of 2007; The Family Smoking Prevention and Tobacco Control Act of 2009 (P.L. 111 31); Protecting Patients and Affordable Care Act of 2010; The Federal Cigarette Labeling and Advertising Act (15 U.S.C. 1333); FDA Food Safety Modernization Act, Public Law 111 353 (January 4, 2011); The Food and Drug Administration Safety and Innovation Act (P.L. 112 144); the Drug Quality and Security Act (2013.

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Infrastructure Program directly supports FDA's priorities by providing secure, modern, and cost-effective office and laboratory space that empowers FDA's workforce to protect and promote the safety and health of families; to foster the competition and innovation that will improve healthcare, expand access to medical products, and advance public health goals; to empower consumers and patients to make better choices; and to strengthen science and efficient risk-based decision making. The Infrastructure Program consists of:

- General Services Administration (GSA) Rental Payments
- Other Rent and Rent Related Activities
- White Oak

The Infrastructure Program supports FDA's offices and labs across the country and its headquarters White Oak Campus in Silver Spring, Maryland. Investing in FDA's facility objectives will provide the high-quality infrastructure and facilities needed for FDA employees to work to ensure FDA can achieve its strategic priorities: unleashing the power of data, empowering American patients and consumers, and innovation, choice and competition. Without adequate investment, FDA would be unable to respond to food safety, medical product, and public health emergencies, such as the COVID-19 pandemic, 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.

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; however, 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 operations including:

- Conducting inspections of more than 35,000 regulated products and manufacturers annually
- Collecting and analyzing more than 40,000 samples of regulated products annually
- Recalling unsafe products, like the 7,893 recalls in FY 2019 alone
- Reviewing more than 45.2 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 E. coli in clover sprouts, listeria monocytogenes in enoki mushrooms, Cyclospora in bagged salad, and salmonella Newport in red onions
- Interdicting opioids at International Mail Facilities (IMFs) to combat the addiction crisis, which is a dominant public health problem in the U.S., killing 841,000 people in our nation from 1999 to 2019, and 71,000 in 2019 alone.
- Conducting criminal investigations, which resulted in 259 arrests, 242 convictions, $1.4 billion of assets forfeited and seized, and $1.6 billion in fines and restitution in FY 2019 alone.

FDA occupies almost 6.9 million rentable square feet of GSA-owned and GSA-leased office, laboratory, warehouse, and border/inspection-station space.

Approximately 69 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 268 buildings, including district offices, laboratories, resident posts, border stations, and field offices across the nation and in Puerto Rico.

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 2020, FDA:

- 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
- continued coordinating 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)
- began coordinating the design and construction activities required to renovate and expand operations at ORA's Forensic Chemistry Center located in Cincinnati, Ohio
- continued coordinating leasing/relocation activities for ORA resident posts, border stations, district offices, and field offices to enhance inspection and criminal-investigation operations that protect public health
- continued coordinating leasing, design, and construction activities required to expand ORA's presence near nine IMFs, enhance opioid interdiction efforts, and combat the addiction crisis threatening American families
- continued coordinating the expansion CDER's laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis
- coordinated design activities for a new CDER laboratory near the White Oak Campus to house a pilot plant for simulating the processing of drug substances and products manufacturing
- completed the renovation of an existing building to provide a security center on the White Oak Campus to protect FDA's expanding operations and growing workforce
- continued coordinating the renovation of an existing building to provide additional storage on the White Oak Campus to support FDA's expanding operations and growing workforce

In FY 2021, FDA plans to:

- complete the construction of and relocate operations to the ORA laboratory near Kansas City, Kansas
- complete the 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 Laboratory and the Southeast Tobacco Laboratory
- begin coordinating the design activities required to replace an aging facility and improve operations of ORA's human and animal foods laboratory near Denver, Colorado
- continue coordinating the design activities required to renovate and expand operations at ORA's Forensic Chemistry Center located in Cincinnati, Ohio
- coordinate activities for a GSA 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
- continue coordinating leasing/relocation activities for ORA resident posts, border stations, district offices, and field offices to enhance inspection and criminal-investigation operations to 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
- continue to coordinate 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 an existing building to provide additional storage on the White Oak Campus to support 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 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 $0.3million annually, and a simple payback of approximately eight years. This project included an upgrade of HVAC controls, replacement of air valves, retro-commissioning, replacement of electric motors with more efficient units with variable frequency drives, and improvements to building envelopes such as adding solar film and weather stripping.

FDA awarded a UESC with Southern California Edison Company at the Irvine, CA location with a capital investment of $5.3M and utility cost savings of $0.35million annually with a simple payback of 15 years. This project includes installation of solar systems, an LED lighting

upgrade, and replacement of electric motors with more efficient units with variable frequency drives.

FDA initiated a feasibility study in FY 2020 to address additional facility improvements at four sites, including the Muirkirk Road Complex, Jefferson Labs Complex, and Irvine and San Juan locations. The evaluation identified items such as: cooling tower improvements; air handling unit replacement; boiler stack economizer metering and boiler venting improvements; pump enhancements 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 and efficiency of failing infrastructure systems and allow the Centers for Food Safety and Applied Nutrition (CFSAN), Center for Veterinary Medicine (CVM), National Center for Toxicological Research (NCTR), and the Office of Regulatory Affairs (ORA) to continue their research, testing and oversight programs without disruption. CFSAN and CVM 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. NCTR conducts FDA mission-critical, peer-reviewed, critical path (translational) research targeted to develop a scientifically sound basis for regulatory decisions and reduce risks associated with FDA-regulated products. ORA is the lead office for all agency field activities. ORA inspects regulated products and manufacturers, conducts sample analyses of regulated products and reviews imported products offered for entry into the United States.

Awarding additional UESCs, procuring renewable energy and incorporating energy efficiency measures in FDA's newly constructed facilities 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, renewable energy and energy conservation measures 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, such as the COVID-19 pandemic, 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 7 State-of-the-Art Laboratories at White Oak

Figure 8 State-of-the-Art Laboratories at White Oak

Figure 9 Anechoic Chambers Laboratory

Figure 10 Nuclear Magnetic Resonance Laboratory Supporting CBER and CDER

Figure 11 State-of-the-Art White Oak Infrastructure: Advanced Air Terminal Units Supporting Laboratories

Figure 12 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 the Campus infrastructure, building fit-out, and specialized equipment required to make the base buildings operational (often called *above-standard* or *above-GSA-standard* items), as well as 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, 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 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 Actual	$219,334,000	$171,208,000	$48,126,000
FY 2021 Enacted	$235,961,000	$167,119,000	$68,842,000
FY 2022 President's Budget	$236,214,000	$166,286,000	$69,928,000

FUNDING HISTORY - OTHER RENT AND RENT-RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$119,877,000	$80,172,000	$39,705,000
FY 2021 Enacted	$136,257,000	$84,262,000	$51,995,000
FY 2022 President's Budget	$155,096,000	$102,095,000	$53,001,000

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actual	$59,744,000	$45,913,000	$13,831,000
FY 2021 Enacted	$52,944,000	$45,914,000	$7,030,000
FY 2022 President's Budget	$55,892,000	$48,414,000	$7,478,000

BUDGET REQUEST

The FY 2022 President's Budget Request for the Infrastructure Program is $447,202,000, of which $316,795,000 is budget authority and $130,407,000 is user fees. In the request, the budget authority increases by $19,500,000 compared to the FY 2021 Enacted, and user fees increase by $2,540,000.

The President's Budget net increase for GSA Rent – based on a decrease in budget authority and an increase in user-fees – will cover rent costs that the agency anticipates in FY 2022 related to market changes, including new Occupancy Agreements replacing those expiring in FY 2021 and FY 2022 for approximately 76 GSA Occupancy Agreements that will cause rental rates to reset to market rates. The request includes a reasonable contingency for new field locations required by FDA to execute its regulatory responsibilities.

The increase in budget authority and user fees reflected in the President's Budget request for OR&RR is needed to meet cost escalations associated with security, operations and maintenance contracts, utilities, and Energy Savings Performance Contract payments for FDA's owned and GSA-managed buildings nationwide. Additionally, 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 2022 Budget request includes funding to address ongoing, above GSA-standard repairs and improvements and to meet program needs, including campus utility infrastructure capacity and reliability improvements; 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, supporting FDA's facilities will provide the high-quality infrastructure and facilities needed for FDA to achieve its strategic priorities: unleashing the power of data, empowering American patients and consumers, and innovation, choice and competition.

GSA RENTAL PAYMENTS

The FY 2022 President's Budget Request for GSA Rental Payments is $236,214,000, of which $166,286,000 is budget authority and $69,928,000 is user fees. The budget authority decreases by $833,000 compared to the FY 2021 Enacted Budget and user fees increase by $1,086,000. The request continues the initiatives included in the FY 2021 President's Budget.

The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2022 Budget Request for GSA Rental Payments covers the cost of rental payments to GSA for FDA's approximately 6.9 million square feet of existing GSA-managed space and the rental payments to GSA for the expansion of FDA's footprint to approximately 7.0 million square feet. The expanded footprint is required for FDA to fully execute its expanding mission and public health responsibilities by increasing its presence in the field.

The requested budget for GSA Rent, including the decrease, considers new leases coming on line for which rent will begin, free-rent periods associated with some new leases, expected market rates for GSA-owned and leased locations, and that FDA will incur a double-rent period when it relocates a field lab as part of FDA's Lab Modernization effort, which is required to provide time to decommission the vacated lab.

OTHER RENT AND RENT-RELATED

The FY 2022 President's Budget Request for Other Rent and Rent-Related is $155,096,000, of which $102,095,000 is budget authority and $53,001,000 is user fees. The budget authority increases by $17,833,000 compared to the FY 2021 Enacted Budget, and user fees increase by $1,006,000. The request continues the initiatives included in the FY 2021 President's Budget.

The FY 2022 Budget Request 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 2022 President's Budget Request for White Oak is $55,892,000, of which $48,414,000 is budget authority and $7,478,000 is user fees. The budget authority increases by $2,500,000 compared to the FY 2021 Enacted Budget and user fees increase by $448,000.

The FY 2022 Budget provides the necessary resources for increased above GSA-standard repairs and improvements as well as the most critical 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, including, transportation services, labor and loading dock services, and a centralized safety program. Additionally, this request ensures that FDA has the necessary resources to move forward with additional infrastructure and reliability improvements, prevent facilities from degrading, and assure that facilities remain state-of-the-art to support ever evolving science.

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 efforts to control COVID-19 and U.S. readiness for seasonal and pandemic influenza. CBER's laboratories play several critical roles in the development and manufacture of vaccines, from participating in global surveillance for circulating virus strains and developing candidate vaccine strains to deriving and distributing critical reagents for manufacturers to use in their assessment of 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 deaths.

BUILDINGS AND FACILITIES

(Dollars in Thousands)	FY 2020 Final	FY 2020 Actuals	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Buildings and Facilities (Budget Authority).....	31,788	43,289	12,788	30,788	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 high-quality infrastructure and facilities needed for FDA employees to work to ensure FDA can achieve its strategic priorities: unleashing the power of data, empowering American patients and consumers, and innovation, choice and competition.

Supporting the FDA Mission

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. Accordingly, 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 13 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, Jefferson, Arkansas
- Muirkirk Road Complex, Laurel, Maryland
- Pacific Southwest Laboratory, Irvine, California
- San Juan District Office and Laboratory, San Juan, Puerto Rico
- Winchester Engineering & Analytical Center, Winchester, Massachusetts

Activities in FY 2020 and Planned for FY2021

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 2020, FDA developed a Program of Requirements for a new laboratory and office building that will replace or consolidate several existing buildings and executed an Interagency Agreement with the U.S. Army Corps of Engineers to design and construct the new building.

In FY 2021, FDA will not initiate any new projects at this location and will continue the design and construction of the new laboratory and office building noted above.

Jefferson Laboratories Complex (JLC) – Jefferson, Arkansas

The JLC houses the National Center for Toxicological Research (NCTR) and the Office of Regulatory Affairs (ORA) Arkansas Laboratory (ARKL). Additional details of the vital NCTR 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 2020, FDA initiated projects to:

- design a new main sewer line on the south side of the site
- complete modifications to the site master plan

- repair and improve the site water treatment plant
- design a renovation for a critical Pathology lab
- design a new Central Chiller Plant

In FY 2021, FDA plans to initiate projects to:

- design and replace the campus motor control center
- replace an air-handling unit (AHU) in a lab building
- replace the capacitor bank in the main electrical substation
- upgrade exterior lighting to address a safety deficiency
- replace roofs for several buildings
- make additional repairs to site infrastructure (roadways, drainage, sidewalks)
- design the replacement of the main sewer line from JLC to the Pine Bluff Arsenal's wastewater treatment plant

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 2020, FDA initiated a project to renovate the aquaculture research facility and also provided supplemental funding for the Non-Recurring Expenses Fund (NEF) project to replace AHUs.

In FY 2021, FDA will initiate projects to:

- replace the substation housing, switchgear and electrical feeders on campus
- provide supplemental funding, if necessary, for the NEF projects for facility improvement measures to replace generators and correct the main laboratory's AHUs
- provide eyewash stations in select MOD2 research buildings to correct a safety deficiency

Pacific Southwest Laboratory – Irvine, California
The Pacific Southwest Laboratory provides analytical laboratory support to FDA's regulatory mission in the Pacific Region.

In FY 2020, FDA initiated a project to replace security gates at building exits.

In FY 2021, FDA will initiate projects to:

- design and upgrade for the HVAC in the LAN closets to support additional IT equipment
- test exterior building shear walls for withstanding seismic activity and modify interior wall supports to remediate cracked walls

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 2020, FDA initiated projects to:

- repair or replace HVAC systems in three buildings
- repair and paint exterior of multiple buildings
- replace windows and repair ceilings, lights and walls in an administrative building
- repair and maintain the site emergency generator
- perform underwater inspection of the seawall and boat ramp
- replace doors in two buildings
- repair perimeter fencing and boat ramp gates to improve site security
- replace the water chiller and variable frequency drive pumps for the main administrative building
- replace the roof membrane on the laboratory building
- purchase a new emergency generator and main power transformer
- install new pumps for the site domestic water system

In FY 2021, FDA will provide supplemental funding for the NEF project to design and construct a new office building for the District Office.

Winchester Engineering and Analytical Center (WEAC) – Winchester, Massachusetts

WEAC 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.

In FY 2020, FDA provided supplemental funding for the NEF project for the construction of the new WEAC facility.

In FY 2021, no new projects will be initiated at this facility.

FDA Owned Facilities Condition and Sustainability Assessment
In FY 2020, FDA initiated a project to assess the condition of owned facilities at JLC, MRC, Irvine, and San Juan. A report will be produced for each site that will include the updated FCI and BMAR for site infrastructure and buildings by site. The GCSL and WEAC sites were not assessed since the projects in progress to construct new buildings will eliminate the BMAR at these two locations.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2018 Actual	$14,618,000	$14,618,000	---
FY 2019 Actual	$11,477,000	$11,477,000	---
FY 2020 Actual	$43,289,000	$43,289,000	---
FY 2021 Enacted	$12,788,000	$12,788,000	---
FY 2022 President's Budget	$30,788,000	$30,788,000	---

BUDGET REQUEST

The FY 2022 President's Budget Request is $30,788,000, an increase of $18,000,000 compared to the FY 2021 Enacted Budget, consisting solely of budget authority.

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 buildings and facilities.

At the Gulf Coast Seafood Laboratory facility, FDA will continue the project to construct a new laboratory/office building and will not initiate any new projects.

At the Jefferson Labs Complex, FDA will initiate critical infrastructure projects to:

- upgrade the campus fire alarm system to have one campus-wide system
- replace the fuel system in the boiler plant
- upgrade domestic water system towers, including code compliance

Additional projects will be initiated to:
- replace roofs for four mission-critical lab and animal research buildings
- renovate two lab and animal research buildings
- perform upgrades and repairs of air handling units (AHUs) in a lab building

- renovate a maintenance building
- upgrade ventilation in the site data center to protect equipment
- repair or replace a freight elevator
- design a renovation to the food service and conference building
- repaint and seal the exterior of an administrative building

At the Muirkirk Road Complex, FDA will:

- replace the campus backflow preventors and install a bypass backflow system
- renovate the aquaculture research facility
- install an air conditioning unit in an animal research building
- install an exhaust fan in an animal research building

At the Pacific Southwest Laboratory, FDA will:

- replace the cooling towers
- upgrade the fire alarm system
- upgrade the house nitrogen system for the lab
- replace the vacuum pump servicing the lab
- remediate exterior building wall cracks
- upgrade HVAC in LAN closets

At the San Juan District Office and Laboratory, FDA will:

- replace front sections of the perimeter security fencing
- install additional exterior lighting
- replace five roof top AHUs, ductwork and compressed air lines in the lab building

At the Winchester Engineering and Analytical Center, FDA will continue the project to construct a new laboratory building and will not initiate any new projects.
The following table provides an allocation plan by site for use of the FY 2022 funds.

FY 2022 BUILDINGS AND FACILITIES ALLOCATION PLAN

BUILDINGS AND FACILITIES ALLOCATION PLAN FY 2022 Congressional Justification	
Site	**President's Budget**
CFSAN Gulf Coast Seafood Laboratory – Dauphin Island, AL	$0
Jefferson Laboratories Complex (NCTR & ORA Arkansas Lab) – Jefferson, AR	$21,550,000
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	$1,538,000
ORA Pacific Laboratory SW – Irvine, CA	$6,400,000
San Juan District Office and Laboratory – San Juan, PR	$1,300,000
Winchester Engineering and Analytical Center – Winchester, MA	$0
B&F Project Total	**$31,788,000**

In FY 2022, 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 2022 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 2020 Actual	**FY 2021 Enacted**	**FY 2022 Request**
CFSAN Gulf Coast Seafood Laboratory	**83**	**81**	**81**
Jefferson Laboratory Complex	**66**	**65**	**65**
Muirkirk Road Complex	**54**	**49**	**49**
ORA Pacific Regional Laboratory Southwest	**94**	**94**	**94**
San Juan District Office and Laboratory	**73**	**62**	**62**
Winchester Engineering and Analytic Center	**62**	**62**	**100[2]**

[1]The Backlog of Maintenance and Repair (BMAR) at each site is significant. Funding is allocated to projects at sites to reduce the BMAR and sustain or improve the average Facility Condition Index (FCI) for the site. Based on funding levels enacted in FY 2020 and FY 2021 and requested in FY 2022, coupled with NEF resources, FDA's total remaining BMAR after FY 2022 is estimated to be $216 million, with escalation.

[2]The project to construct the new laboratory building will be complete in FY 2022, which will eliminate the BMAR at the WEAC location.

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 group is in the Office of Finance, Budget, Acquisitions and Planning (OFBAP) 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)
- Business Managers (Operations service 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, 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 OFBAP. 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, service rates, efficiency and performance targets, and 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 centrally administered 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

Budget Summary

(Dollars in Thousands)

	FY 2020[2]	FY 2021[3] [4]	FY 2022[5]
FDA NEF Requests[1]	$59,300	$8,000	TBD

Authorizing Legislation: Section 223 of Division G of the Consolidated Appropriations Act, 2008

Allocation Method: Direct Federal, Competitive Contract

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Non-recurring Expenses Fund (NEF) permits HHS to transfer unobligated balances of expired discretionary funds from FY 2008 and subsequent years into the NEF account. Congress authorized use of the funds for capital acquisitions necessary for the operation of the Department, specifically information technology (IT) and facilities infrastructure acquisitions.

FDA's Buildings & Facilities (B&F) and Infrastructure budgets have been unable to sustain the level of its backlog of maintenance and repairs at owned assets. Additionally, they have not provided adequate funding for owned-laboratory repairs, improvements, and replacements. FDA's Infrastructure budget has been inadequate to fund leased-laboratory relocations, repairs, and improvements, forcing FDA to use program funds for these purposes.

From FY 2015 through FY 2021, FDA has requested $360.4 million from the HHS NEF and has received $311.5 million.

PROGRAM ACCOMPLISHMENTS

From FY 2015 through FY 2019, FDA received a total of $244.2 million from the NEF to replace one owned laboratory, significantly renovate two owned laboratories, address other urgent owned-facilities and infrastructure needs, and relocate three aged and deteriorated leased laboratories. 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

[1] Pursuant to Section 223 of Division G of the Consolidated Appropriation Act, 2008, notification is required of planned use.

[2] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on July 20, 2020.

[3] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on October 22, 2020.

[4]The projects described below are the current list of approved projects through FY 2021. Additional projects may be funded from the FY 2021 notification letter upon approval from OMB.

[5] HHS has not yet notified for FY 2022.

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. Funds were also used for building and site infrastructure improvements, such as renovations, building system upgrades, roadway/drainage repairs, and building equipment replacement, at FDA owned locations. NEF resources have also allowed FDA to initiate the process to relocate ORA's aged, leased laboratories in Kansas City, Kansas, Atlanta, Georgia, and Denver, Colorado, into new, modern, and efficient leased laboratories designed to meet ORA's mission. Without NEF resources received for leased-laboratory relocations, ORA would have had to cut critical items in its foods programs, such as delaying hiring, which would reduce ORA's ability to train staff and conduct inspections, and/or delaying laboratory equipment purchases required to keep up with changing technology.

FY	Project Title	Amount Allocated/Approved
2015	Jefferson Labs Complex, Jefferson, AR, Buildings 14 & 53A Renovations	$30,000,000
2016	Winchester Engineering & Analytical Center, Winchester, MA, Replacement	$45,029,905
2016	Kansas City Laboratory, Lenexa, KS, Relocation	$8,093,971
2016	Southeast Laboratory, Atlanta, GA, Relocation	$45,876,124
2017	Winchester Engineering & Analytical Center Replacement, Supplemental Funding	$15,000,000
2017	Kansas City Laboratory, Relocation – Supplemental Funding	$7,185,966
2017	Jefferson Labs Complex, Building 53B Renovation	$4,200,000
2019	Denver Laboratory, Lakewood, CO, Relocation	$36,000,000
2019	San Juan Laboratory, San Juan, PR, Toro Building Addition	$8,000,000
2019	Southeast Laboratory, Relocation – Supplemental Funding	$17,300,000
2019	Pacific Southwest Laboratory, Irvine, CA, Retaining Wall	$3,300,000
2019	Jefferson Labs Complex, New Chiller Plant – Design Phase	$1,185,000
2019	Muirkirk Road Complex, Laurel, MD, Replace Eight Air-Handling Units	$5,000,000
2019	Gulf-Coast Seafood Laboratory, Dauphin Island, AL, Replace Two Office Trailers with an Office Building	$2,400,000
2019	Jefferson Labs Complex, Renovation of Infrastructure	$4,600,000
2019	Pacific Southwest Laboratory, Repair Surface Parking Lot	$5,000,000
2019	Pacific Southwest Laboratory, Repair Heating, Ventilation, and Air-Conditioning (HVAC) System and Building Automation System Controls	$6,000,000
	Total	**$244,170,966**

In FY 2020 and FY 2021, FDA was allocated a total of $67.3 million in resources in order to advance the ongoing laboratory relocation project at ORA's Southeast Laboratory in Atlanta and to support infrastructure and laboratory renovation projects at FDA's Muirkirk Road Complex and Pacific Southwest Laboratory.

FY	Project Title	Amount Allocated/Approved
2020	Southeast Laboratory, Relocation – Supplemental Funding	$47,900,000
2020	Muirkirk Road Complex, Replace Four Emergency Generators	$9,000,000
2020	Pacific Southwest Laboratory, Renovate Several Labs	$2,400,000
2021	Muirkirk Road Complex, Correct MOD1 Infrastructure Deficiencies	$8,000,000
	Total	**$67,300,000**

FY 2015 ($30.0M)

Jefferson Labs Complex, $30.0M – for renovating existing, functionally obsolete laboratories in Buildings 14 and 53A Jefferson Laboratories Complex, in Jefferson, Arkansas.

FY 2016 ($99M)

Winchester Engineering & Analytical Center, $45M – for replacing the existing aged and functionally obsolete building, with a new, flexible, modern laboratory building.

Kansas City Laboratory, $8.1M – for relocating the laboratory from an aged and functionally obsolete GSA-leased building to a new, flexible, modern GSA-leased laboratory in the same geographic area.

Southeast Laboratory, $45.9M – for relocating the laboratory from an aged and functionally obsolete GSA-leased building to a new, flexible, modern GSA-leased laboratory in the same geographic area.

FY 2018 ($26.4M)

Winchester Engineering & Analytical Center, $15M – for supplemental funding required to replace the existing aged and functionally obsolete building, with a new, flexible, modern laboratory building.

Kansas City Laboratory, $7.2M – for supplemental funding required to address changing market conditions and implement laboratory quality-assurance requirements associated with relocating the laboratory from an aged and functionally obsolete GSA-leased building to a new, flexible, modern GSA-leased laboratory in the same geographic area.

Jefferson Labs Complex, $4.2M – for renovating a processing area in Building 53B.

FY 2019 ($88.8M)

Denver Laboratory, $36.0M – for replacing the existing laboratory in an aged and functionally obsolete GSA-owned building with a new, flexible, modern GSA-owned laboratory building.

San Juan, $8.0M – for the construction of an addition to the Toro Building to consolidate all District Office staff and functions currently housed in multiple buildings across the site.

Southeast Laboratory, $17.3M – for supplemental funding required to address changing market conditions and implement laboratory quality-assurance requirements associated with relocating the laboratory from an aged and functionally obsolete GSA-leased building to a new, flexible, modern GSA-leased laboratory in the same geographic area.

Pacific Southwest Laboratory, $3.3M – to design and construct a retaining wall to stabilize soil and correct a safety hazard on the site.

Jefferson Labs Complex, $1.2M – for the design of a new central chiller plant to replace two separate, functionally obsolete chiller plants in accordance with the campus master plan.

Muirkirk Road Complex, $5.0M – for replacing eight air-handling units to ensure operational reliability and continuity of mission critical work.

Gulf Coast Seafood Lab, $2.4M – for demolishing two office trailers and replacing them with a one-story office building on an elevated concrete slab.

Jefferson Lab Complex, $4.6M – for renovating failing infrastructure components including roads, sidewalks, storm drainage piping, and pavement in accordance with the campus master plan.

Pacific Southwest Laboratory, $5.0M – for repairing the south surface-parking lot damaged by the settlement.

Pacific Southwest Laboratory, $6.0M – for repairing HVAC system and Building Automation System Controls to correct deficiencies impairing the proper operation of the laboratory and office areas.

FY 2020 ($59.3M)

Southeast Laboratory, $47.9M – for supplemental funding required to address changing market conditions associated with relocating the laboratory from an aged and functionally obsolete GSA-leased building to a new, flexible, modern GSA-leased laboratory in the same geographic area.

Muirkirk Road Complex, $9M – for replacing four aged emergency generators in the MOD1 laboratory building that support lab and animal research and offices for lab staff.

Pacific Southwest Laboratory, $2.4M – for renovating several functionally obsolete labs.

FY 2021 ($8.0M)

Muirkirk Road Complex, $8M – for correcting MOD1 laboratory building infrastructure deficiencies by replacing two cooling towers; three air-handling units; miscellaneous boiler components, pumps, piping, and valves; and control systems.

SUPPLEMENTARY TABLES

OBJECT CLASSIFICATION TABLES

(Dollars in Thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	944,464	964,509	1,030,186	65,676
Other than full-time permanent (11.3)	88,193	90,065	96,197	6,133
Other personnel compensation (11.5)	50,964	52,046	55,589	3,544
Military personnel (11.7)	88,573	91,230	93,694	2,463
Special personnel services payments (11.8)	1,015	1,037	1,107	71
Subtotal, Personnel Compensation	**1,173,209**	**1,198,886**	**1,276,773**	**77,887**
Benefits:				
Civilian benefits (12.1)	378,601	386,636	412,963	26,327
Military benefits (12.2)	8,998	9,268	9,518	250
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**387,599**	**395,904**	**422,481**	**26,577**
Total Personnel Compensation and Benefits	**1,560,808**	**1,594,790**	**1,699,255**	**104,464**
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0)	22,739	22,581	25,820	3,239
Transportation of things (22.0)	3,653	3,627	4,148	520
Rental payments to GSA (23.1)	171,208	167,119	166,286	-833
Rent payments to others (23.2)	300	298	341	43
Communication, utilities, and misc. charges (23.3)	16,314	16,200	18,524	2,324
Printing and reproduction (24.0)	1,966	1,953	2,233	280
Subtotal, Contractual Services	**216,180**	**211,779**	**217,352**	**5,573**
Other Contractual Services:				
Consulting services (25.1)	51,203	50,847	58,141	7,294
Other services (25.2)	466,222	462,985	529,398	66,413
Purchase of goods and svcs from Govt Acts. (25.3)	397,178	394,420	450,998	56,578
Operation and maintenance of facilities (25.4)	72,213	71,712	81,999	10,287
Research and Development Contracts (25.5)	36,961	36,704	41,969	5,265
Operation and maintenance of equipment (25.7)	42,485	42,190	48,242	6,052
Subsistence and support of persons (25.8)	---	---	---	---
Subtotal, Other Contractual Services	**1,066,261**	**1,058,858**	**1,210,747**	**151,889**
Supplies and Materials:				
Supplies and materials (26.0)	40,680	40,397	46,192	5,795
Equipment (31.0)	105,435	104,703	119,722	15,019
Land and Structures (32.0)	66,562	66,100	75,582	9,482
Grants, subsidies, and contributions (41.0)	208,592	207,143	236,857	29,714
Insurance claims and indemnities (42.0)	448	445	509	64
Interest and dividends , Refunds (43.0, 44.0)	---	---	---	---
Receivables-collected (61.7)	---	---	---	---
Subtotal, Supplies and Materials	**421,717**	**418,789**	**478,862**	**60,073**
Total Contractual Services and Supplies	**1,704,158**	**1,689,426**	**1,906,961**	**217,536**
Total Budget Authority by Object Class	**3,264,966**	**3,284,216**	**3,606,216**	**322,000**

(Dollars in Thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	739,068	788,398	820,267	31,869
Other than full-time permanent (11.3)	98,181	104,734	108,968	4,234
Other personnel compensation (11.5)	82,733	88,256	91,823	3,568
Military personnel (11.7)	71,071	73,203	75,180	1,976
Special personnel services payments (11.8)	166	177	184	7
Subtotal, Personnel Compensation	**991,219**	**1,054,768**	**1,096,422**	**41,654**
Benefits:				
Civilian benefits (12.1)	312,745	333,619	347,105	13,486
Military benefits (12.2)	10,820	11,145	11,445	301
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**323,565**	**344,764**	**358,551**	**13,787**
Total Personnel Compensation and Benefits	**1,314,784**	**1,399,532**	**1,454,973**	**55,441**
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0)	7,908	7,949	8,555	605
Transportation of things (22.0)	608	612	658	47
Rental payments to GSA (23.1)	69,341	68,842	69,928	1,086
Rent payments to others (23.2)	52	52	56	4
Communication, utilities, and misc. charges (23.3)	2,219	2,230	2,400	170
Printing and reproduction (24.0)	2,490	2,503	2,693	191
Subtotal, Contractual Services	**82,618**	**82,188**	**84,291**	**2,102**
Other Contractual Services:				
Consulting services (25.1)	54,719	55,004	59,193	4,189
Other services (25.2)	513,657	516,333	555,658	39,324
Purchase of goods and svcs from Govt Acts. (25.3)	393,113	395,161	425,257	30,096
Operation and maintenance of facilities (25.4)	26,877	27,017	29,074	2,058
Research and Development Contracts (25.5)	52,240	52,513	56,512	3,999
Operation and maintenance of equipment (25.7)	39,645	39,852	42,887	3,035
Subsistence and support of persons (25.8)	---	---	---	---
Subtotal, Other Contractual Services	**1,080,250**	**1,085,879**	**1,168,581**	**82,702**
Supplies and Materials:				
Supplies and materials (26.0)	11,802	11,863	12,767	904
Equipment (31.0)	37,926	38,124	41,028	2,904
Land and Structures (32.0)	18,692	18,789	20,220	1,431
Grants, subsidies, and contributions (41.0)	103,630	104,170	112,103	7,934
Insurance claims and indemnities (42.0)	239	241	259	18
Interest and dividends , Refunds (43.0, 44.0)	24,667	24,796	26,684	1,888
Receivables-collected (61.7)	---	---	---	---
Subtotal, Supplies and Materials	**196,957**	**197,983**	**213,062**	**15,079**
Total Contractual Services and Supplies	**1,359,825**	**1,366,050**	**1,465,933**	**99,883**
Total Reimbursable by Object Class	**2,674,609**	**2,765,582**	**2,920,906**	**155,324**

*FY2020 Actuals includes $26.6M for refunds FDA returned for work not accomplished in FY 2020

(Dollars in Thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	1,683,532	1,752,907	1,850,453	97,546
Other than full-time permanent (11.3)	186,374	194,799	205,165	10,366
Other personnel compensation (11.5)	133,697	140,301	147,413	7,112
Military personnel (11.7)	159,644	164,434	168,873	4,440
Special personnel services payments (11.8)	1,181	1,214	1,292	78
Subtotal, Personnel Compensation	**2,164,428**	**2,253,654**	**2,373,195**	**119,541**
Benefits:				
Civilian benefits (12.1)	691,345	720,255	760,068	39,813
Military benefits (12.2)	19,818	20,413	20,964	551
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**711,164**	**740,668**	**781,032**	**40,364**
Total Personnel Compensation and Benefits	**2,875,592**	**2,994,322**	**3,154,228**	**159,906**
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0)	30,647	30,530	34,375	3,845
Transportation of things (22.0)	4,261	4,239	4,806	567
Rental payments to GSA (23.1)	240,549	235,961	236,214	253
Rent payments to others (23.2)	352	350	397	47
Communication, utilities, and misc. charges (23.3)	18,532	18,431	20,925	2,494
Printing and reproduction (24.0)	4,456	4,455	4,926	471
Subtotal, Contractual Services	**298,798**	**293,967**	**301,643**	**7,676**
Other Contractual Services:				
Consulting services (25.1)	105,922	105,851	117,334	11,483
Other services (25.2)	979,878	979,318	1,085,056	105,738
Purchase of goods and svcs from Govt Acts. (25.3)	790,291	789,581	876,255	86,674
Operation and maintenance of facilities (25.4)	99,090	98,728	111,073	12,344
Research and Development Contracts (25.5)	89,201	89,217	98,481	9,264
Operation and maintenance of equipment (25.7)	82,130	82,041	91,128	9,087
Subsistence and support of persons (25.8)	---	---	---	---
Subtotal, Other Contractual Services	**2,146,512**	**2,144,737**	**2,379,328**	**234,591**
Supplies and Materials:				
Supplies and materials (26.0)	52,481	52,260	58,959	6,698
Equipment (31.0)	143,361	142,827	160,750	17,923
Land and Structures (32.0)	85,254	84,889	95,802	10,913
Grants, subsidies, and contributions (41.0)	312,221	311,313	348,961	37,648
Insurance claims and indemnities (42.0)	688	686	768	82
Interest and dividends , Refunds (43.0, 44.0)	24,667	24,796	26,684	1,888
Receivables-collected (61.7)	---	---	---	---
Subtotal, Supplies and Materials	**618,673**	**616,772**	**691,924**	**75,152**
Total Contractual Services and Supplies	**3,063,983**	**3,055,476**	**3,372,894**	**317,418**
Total Program Level by Object Class	**5,939,575**	**6,049,798**	**6,527,122**	**477,324**

SALARY AND EXPENSES

(Dollars in Thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 President's Budget +/- FY 2021 Enacted
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	944,464	964,509	1,030,186	65,676
Other than full-time permanent (11.3)	88,193	90,065	96,197	6,133
Other personnel compensation (11.5)	50,964	52,046	55,589	3,544
Military personnel (11.7)	88,573	91,230	93,694	2,463
Special personnel services payments (11.8)	1,015	1,037	1,107	71
Subtotal, Personnel Compensation	**1,173,209**	**1,198,886**	**1,276,773**	**77,887**
Benefits:				
Civilian benefits (12.1)	378,601	386,636	412,963	26,327
Military benefits (12.2)	8,998	9,268	9,518	250
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**387,599**	**395,904**	**422,481**	**26,577**
Total Pay Costs	**1,560,808**	**1,594,790**	**1,699,255**	**104,464**
Travel and transportation of persons (21.0)	22,739	22,581	25,820	3,239
Transportation of things (22.0)	3,653	3,627	4,148	520
Rental payments to GSA (23.1)	171,208	167,119	166,286	-833
Rent payments to others (23.2)	300	298	341	43
Communication, utilities, and misc. charges (23.3)	16,314	16,200	18,524	2,324
Printing and reproduction (24.0)	1,966	1,953	2,233	280
Subtotal, Contractual Services	**216,180**	**211,779**	**217,352**	**5,573**
Other Contractual Services:				
Advisory and assistance services (25.1)	51,203	50,847	58,141	7,294
Other services (25.2)	466,222	462,985	529,398	66,413
Purchase of goods and svcs from Govt Acts. (25.3)	397,178	394,420	450,998	56,578
Operation and maintenance of facilities (25.4)	72,213	71,712	81,999	10,287
Research and Development Contracts (25.5)	36,961	36,704	41,969	5,265
Operation and maintenance of equipment (25.7)	42,485	42,190	48,242	6,052
Subtotal, Other Contractual Services	**1,066,261**	**1,058,858**	**1,210,747**	**151,889**
Supplies and materials (26.0)	40,680	40,397	46,192	5,795
Total Non-Pay Costs	**1,323,121**	**1,311,034**	**1,474,291**	**163,257**
Total Salary and Expense	**2,883,929**	**2,905,824**	**3,173,546**	**267,721**
Direct FTE	**9,939**	**10,042**	**10,417**	**375**

DETAIL OF FULL-TIME EQUIVALENTS

	FY 2020 Actuals			FY 2021 Enacted			FY 2022 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Food Safety and Applied Nutrition	1,079	46	1,125	1,111	46	1,157	1,196	46	1,242
Center for Drug Evaluation and Research	4,902	497	5,399	5,203	497	5,700	5,268	497	5,765
Center for Biologics Evaluation and Research	1,161	52	1,213	1,158	52	1,210	1,165	52	1,217
Center for Veterinary Medicine	685	12	697	714	12	726	748	12	760
Center for Devices and Radiological Health	1,585	80	1,665	1,759	80	1,839	1,784	80	1,864
National Center for Toxicological Research	296	---	296	276	---	276	277	---	277
Office of Regulatory Affairs	4,547	347	4,894	4,554	347	4,901	4,670	347	5,017
Headquarters and Office of the Commissioner	892	62	954	865	62	927	918	62	980
Export Certification	24	---	24	26	---	26	26	---	26
Color Certification	34	---	34	37	---	37	37	---	37
##	924	41	965	1,149	41	1,190	1,238	41	1,279
##	49	---	49	11	---	11	11	---	11
Opiods - No Year	33	---	33	---	---	---	---	---	---
21st Century Cures (BA Only)	187	---	187	187	---	187	187	---	187
Total	**16,398**	**1,137**	**17,535**	**17,050**	**1,137**	**18,187**	**17,525**	**1,137**	**18,662**

Five Year History of GS/GM Average Grade

Year	Grade
FY 2017	13
FY 2018	13
FY 2019	13
FY 2020	13
FY 2021	13

* FTE figures do not include an estimated 80 reimbursable, 1 FOIA, 27 PEPFAR and 7 COVID Supplemental.

DETAIL OF POSITIONS

	FY 2020 Final	FY 2021 Enacted	FY 2022 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	**$194,495**	**$195,954**	**$199,922**
Executive Service (ES)			
Executive Service	68	70	72
Total Executive Service	**68**	**70**	**72**
Total - ES Salary	**$13,225,660**	**$13,735,715**	**$14,404,279**
General Schedule (GS)			
GS-15	1,412	1,455	1,496
GS-14	3,877	3,997	4,108
GS-13	4,850	5,000	5,139
GS-12	1,956	2,016	2,072
GS-11	699	720	740
GS-10	8	8	9
GS-9	542	559	574
GS-8	47	49	50
GS-7	268	277	284
GS-6	60	62	64
GS-5	42	43	45
GS-4	33	34	35
GS-3	33	34	35
GS-2	9	9	9
GS-1	8	8	9
Total General Schedule	**13,845**	**14,272**	**14,670**
Total - GS Salary	**$1,650,476,295**	**$1,714,127,901**	**$1,797,560,312**
Administrative Law Judges (AL)	---	---	---
Scientific/Senior Level (ST/SL)	5	5	5
Senior Biomedical Research Service (RS)	45	46	48
Scientific Staff Fellows (RG) (Title 42)	1,168	1,204	1,238
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	152	157	161
Former Performance Mgmt Recognition System Employees (GM)	1	1	1
Physicians and Dentists - (GP) (Title 38)	836	862	886
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06	284	284	284
Commissioned Corps - Other	853	853	853
Total Commissioned Corps	**1,137**	**1,137**	**1,137**
Administratively Determined (AD) (includes Title 42)[2]	384	396	407
Wage Grade	13	13	14
Consultants[2]	22	23	23
Total FTE (End of Year)[1]	**17,677**	**18,187**	**18,662**
Average ES Level	3	3	3
Average ES Salary	$194,495	$195,954	$199,922
Average GS grade	13	13	13
Average GS Salary	$119,211	$120,105	$122,537
Average GM Salary	$157,684	$158,867	$162,084
Average GP Salary	$225,894	$227,588	$232,197

[1] Does not include FTE estimates for 80 reimbursable, 1 FOIA, 27 PEPFAR and 7 COVID Supplemental.

[2] Includes consultants appointed under 5 U.S.C. 3109, those appointed under similar authorities, and those appointed to serve as advisory committee members. However, scientists hired under Title 42 are now included in the Distinguished Consultants/Senior Science Managers (RF) category.

SIGNIFICANT ITEMS

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (116-446)

1. Donor Human Milk

The Committee urges the FDA to develop a plan for classifying all donor human milk. It further urges FDA to continue to regulate human milk-derived products that meet the statutory definition of infant formula and that are intended for consumption by low birth weight infants or those infants who otherwise have unusual medical or dietary problems as exempt infant formulas, and to regulate them as specified by the Infant Formula Act.

FDA Response:
Products that are composed solely of human milk are foods and subject to applicable requirements for foods, including applicable requirements established under the FDA Food Safety Modernization Act (FSMA). FSMA requires food facilities, including donor human milk facilities covered by FSMA requirements, to establish and implement hazard analysis and risk-based preventive controls for human food.

Additionally, facilities covered by FSMA requirements that produce human milk products are subject to FSMA's risk-based mandated inspection frequencies. High-risk domestic facilities will be inspected every three years and non-high-risk facilities every five years. Between 2012 and January 2020, FDA conducted inspections at 14 registered donor human milk banks and found no serious problems raising public health concerns as a result of the inspections.

FDA shares the Committee's commitment to regulating human milk-derived products that meet the statutory definition of infant formula and are intended for consumption by low birth weight infants, infants who have inborn errors of metabolism, or infants who otherwise have unusual medical or dietary problems as exempt infant formulas under 21 CFR 107.50, and to regulating these products as specified by the Infant Formula Act. FDA is committed to protecting these vulnerable populations through rigorous regulatory oversight of infant formula, which is often used as the sole source of nutrition for infants during a critical period of their growth and development.

While products composed solely of human milk do not qualify as infant formulas, some products that contain donor human milk do qualify as infant formula, and FDA regulates them under the exempt infant formula provisions in §107.50. Exempt infant formula products containing human milk typically consist of human milk to which nutrients have been added to meet increased nutrient requirements of preterm infants. FDA critically examines any change, even a small one, to donor human milk on a case-by-case basis to determine whether that change would cause the donor human milk to be an infant formula under the Infant Formula Act and then regulates the product accordingly.

2. Food Traceability

The Committee provides an increase of $1,240,000 to investigate and prevent foodborne outbreaks. The Committee is encouraged by the work the FDA has put forth in developing a comprehensive food traceability system. The Committee directs FDA to continue 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 recall through their New Era of Food Safety Initiative. The Committee looks forward to the FDA's Blueprint that is expected 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. This Blueprint is to be made available on the FDA website within 60 days of the date of enactment of this Act. Further, the Committee recommends the research, investment, and implementation of artificial intelligence and other emerging technologies to assist with these aims.

FDA Response:
In July 2020, FDA announced the New Era of Smarter Food Safety Blueprint and published it on the Agency's website (https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-blueprint). The Blueprint outlines goals to enhance traceability, improve predictive analytics, respond more rapidly to outbreaks, address new business models, reduce contamination of food, and foster the development of stronger food safety cultures.

In September 2020, FDA published the Food Traceability proposed rule, which is mandated by the FDA Food Safety Modernization Act (FSMA). The proposed rule, when finalized, will lay a foundation for the tech-enabled traceability core element of the Blueprint. The requirements in the proposed rule would help FDA rapidly and effectively identify recipients of certain foods to prevent or mitigate foodborne illness outbreaks and address credible threats of serious adverse health consequences or death. FDA has also engaged stakeholders in a series of three public meetings to discuss the proposed rule.

As part of the New Era initiative, FDA is enhancing its processes for investigation and prevention of foodborne outbreaks, including consideration of technology solutions. FDA also is encouraging industry adoption of tech-enabled tracing systems for all foods, while leveraging artificial intelligence and other emerging technologies to assess risk and help prioritize the Agency's work and resources.

3. High-Risk List

The Committee expects FDA to release a list designating high risk foods in September 2020 as required by FSMA. FSMA also requires that foods designated as high-risk will be subject to more stringent recordkeeping requirements in order to improve traceability efforts during foodborne outbreaks. The Committee encourages FDA to ensure that any additional recordkeeping and traceability requirements are required throughout the supply and distribution chain as FDA continues to develop rules and regulations for compliance with FSMA.

FDA Response:
In September 2020, FDA published the Food Traceability proposed rule and released the Food Traceability List that tentatively identifies foods for which additional traceability records will be required. The Food Traceability proposed rule would require those who manufacture, process, pack, or hold foods on the Food Traceability List to establish and maintain records containing Key Data Elements (KDEs) associated with different Critical Tracking Events (CTEs). Establishing the KDEs and CTEs will provide a foundation for traceability that will allow stakeholders in the supply chain to facilitate rapid and accurate tracing needed to prevent or mitigate foodborne illness outbreaks.

4. In-Home Drug Disposal

The Committee directs the FDA to evaluate and consider updating current drug disposal guidance to reflect the availability of in-home disposal technology intended to deactivate and dispose of prescription drugs in a manner that renders the controlled substance unavailable and unusable for all practical purposes. The Committee also encourages the FDA to closely consider whether opioid labeling, REMS materials, and other prescriber information should include language on co-dispensing of in-home drug disposal technology, particularly for prescriptions connected to acute pain such as post-surgical pain.

FDA Response:
The Agency supports and encourages the continued development of innovative solutions for appropriate drug disposal.

FDA is aware of some consumer-focused opioid disposal programs in the U.S., including opioid disposal programs offered voluntarily by large retail chain pharmacies (e.g. CVS, Walmart) and state-required drug disposal programs required by some states and operated by drug manufacturers. We are planning a public meeting, aimed for June 2021, with the assistance of the Duke Margolis Center for Health Policy, to facilitate an exchange of information and opinions about in-home disposal options. The Agency is also seeking proposals to evaluate technologies, including disposal options, designed to reduce nonmedical use and overdose involving opioids and other medications with abuse potential.

FDA is considering whether messaging regarding proper drug disposal should be created or revised, including drug labeling and FDA's "Remove the Risk" toolkit (see https://www.fda.gov/drugs/ensuring-safe-use-medicine/safe-opioid-disposal-remove-risk-outreach-toolkit).

In addition, section 3032 of the SUPPORT Act provided FDA with new REMS authority to mandate safety-enhancing packaging or disposal in certain circumstances. We are considering how, and under what circumstances, we might use this authority.

5. Inspections at Land Ports of Entry

A record volume of FDA-regulated commodities are being introduced for import inspections, which include examination and sample collections of FDA goods at the U.S.-Mexico border. The

Committee is concerned that this is outpacing the Administration's processing operations resources at Land Ports of Entry, and has resulted in increased cargo backlogs or, otherwise, compromised the Administration's ability to detect and seize violative products. In order to improve and streamline the inspection process and expedite the release of compliant products, the Committee directs FDA to support increased import operations at Land Ports of Entry, near the U.S.-Mexico border.

FDA Response:
FDA acknowledges that there has been an increase in certain commodities being imported across land ports of entry along the southern border. The Agency works to support the timely flow of trade while protecting the public from products that adversely impact health and safety. To help reduce the potential for backlogs, the Agency guides the use of resources to areas of higher risk. To accomplish this, FDA continues to rely on a proven system-based screening tool, the Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting (PREDICT). To further augment FDA's risk-based screening efforts, the Agency is exploring the use of other modern tools such as artificial intelligence (AI) and machine learning (ML) to improve FDA's ability to target and screen higher-risk products to most effectively leverage current resources. Leveraging these new technologies will further enhance existing resources to improve import operations.

Additionally, FDA relies on a number of existing tools to support import operations at the southern border. This includes the Foreign Supplier Verification Program (FSVP) regulation and the Voluntary Qualified Importer Program (VQIP), which reduces the need for the Agency to inspect lower-risk products and allows FDA to expend its resources screening higher-risk product areas for import inspections, including through examinations/sample collections by FDA staff.

Other existing tools to accommodate the volume of imported products submitted to FDA for review on the southern border include the implementation of weekend entry review coverage at most major southern border ports of entry. Saturday and Sunday coverage at critical ports of entry has been in place for several years within specific land border ports along the southern border to support expedited entry review and admissibility dispositions of highly perishable regulated products and high-priority products with a high-risk association during peak produce seasons. During peak seasons, FDA also has utilized extended entry review conducted by remote offices in different time zones to provide additional entry review coverage. For example, FDA staff located in California review perishable products that are offered for entry late in the afternoon and early in the evening in Texas.

6. Menstrual Product Labeling

The Committee is concerned with the lack of labeling requirements for menstrual hygiene products and directs FDA to revise existing guidance for industry to include recommendations concerning menstrual hygiene product labeling and material lists, including recommendations that ingredient lists be included on packaging.

FDA Response:

FDA appreciates the Committee's concerns about the safety of menstrual products and ensuring that consumers and health care providers have transparency regarding the ingredients that compose these products. The Agency will work to update its existing guidance to recommend that ingredient lists be included in packaging, and looks forward to engaging with patients, health care providers, and others during a public comment period when those guidance updates are proposed.

7. Non-Human Primates

The Committee looks forward to receiving the report requested in last year's House Report regarding a strategy and timeline for reducing intramural primate research. The Committee continues to encourage the FDA to reduce primate testing, prioritize alternative research methods, and seek opportunities to relocate primates to sanctuaries. The Committee requests an update be included as part of the FDA's fiscal year 2022 budget request.

FDA Response:
FDA takes seriously the responsibility to ensure the welfare of research animals in our care and strictly adheres to the highest standards of humane animal care, including the ethical mandates to replace, reduce, and refine the use of animals. FDA is reducing the need for nonhuman primates in FDA intramural research and, whenever possible, has taken steps to reduce nonhuman primate use in both intramural and extramural research and testing.

The Agency notes that FDA provided the Committee with the requested report on intramural research involving nonhuman primates March 9, 2021. We look forward to continuing to work with the Committee on this important issue.

8. Olive Oil Standards of Identity

The Committee directs the FDA to continue working 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. The Committee remains particularly concerned with the number of different oil state standards for olive oils in the U.S. and believes it is important to determine if establishing a uniform set of the standards would better inform and protect consumers. The FDA is directed to consult and meet with domestic producers and importers of olive oil to develop a science-based Standard of Identity for extra virgin olive oil and olive oil to ensure the integrity of these products for U.S. consumers. The Committee directs the Commissioner of the FDA to brief the Committee by December 31, 2020 on the status of the agency's progress in developing a U.S. Standard of Identity for different grades of olive oil.

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, on February 21, 2020, FDA re-opened the

comment period on a proposed rule[172] seeking to establish general principles to update the framework for standards of identity. The comment period closed on July 20, 2020, and the Agency has completed its review of the comments received and is considering next steps. While FDA is working hard on this comprehensive effort to modernize food standards, the Agency is also proceeding with ongoing work on standards and labeling consistent with our priorities and resources, including looking at individual standards of identity.

FDA has met with the olive oil industry several times over the last few years. Specifically, 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 Association, American Olive Oil Producers Association, and Deoleo SA to discuss their interest in a standard of identity for olive oil. During these meetings, the Agency discussed what needs to be in a citizen petition for a standard of identity and emphasized the benefit of submitting requests for a standard of identity that align.

At this time, FDA is reviewing two citizen petitions requesting a standard of identity for olive oil. FDA received one citizen petition from the American Olive Oil Producers Association (FDA-2019-P-5191) in November 2019 and another citizen petition from the North American Olive Oil Association (FDA-2020-P-1423) in May 2020. There are differences in the citizen petition requests which complicates the Agency's review and increases the time needed to reach a decision. FDA is reviewing the petitions and will continue to discuss this matter with industry representatives.

9. Plant Product Labeling

The Committee notes the increase of plant-based products labeled and marketed with meat, dairy, eggs, seafood and other animal food product terminology that may be advertised as a more healthful alternative to conventional animal-based food products. Such representations may cause consumer confusion. As FDA works to modernize standards of identity and evaluate related product labeling, the Committee directs the Commissioner to consult with FSIS to prevent misleading labeling of these food products that do not contain any animal-based ingredients and to continue to engage with stakeholders and the public on this issue.

FDA Response:
FDA appreciates the Committee's support of its work on standards of identity and related product labeling. FDA shares the concern that food should be properly labeled and that the representations in food labeling should not deceive consumers. FDA is working diligently to provide clarity around the labeling of plant-based alternatives to dairy products, which is an Agency priority. FDA continues to assess products currently on the market to ensure that consumers are not being deceived or misled by product labeling.

[172] https://www.fda.gov/food/cfsan-constituent-updates/fda-extends-reopened-comment-period-general-principles-food-standards-modernization

FDA considers product labeling, and the statements and representations made on product labels, on a case-by-case basis. Generally, FDA considers the terms used within the context of the entire label, including qualification of any statements or names with additional terms or information. FDA expects the labeling of plant-based alternative products to distinguish these products from traditional animal-based products. FDA may also consider data and information that indicate whether the words or representations in the labeling cause consumers to confuse these alternative products with traditional animal-based products or mislead consumers about the nature or source of the food. While there are First Amendment considerations about restricting the use of certain words on food labels regardless of context that FDA must take into account, FDA continues to welcome and consider all additional data and information about this matter, including consumer understanding of product labeling.

Additionally, FDA has been and remains committed to maintaining regular, open communication with USDA's FSIS regarding the labeling of plant-based products. FDA will continue to use its authorities and work collaboratively with USDA to ensure that Americans have access to a safe and properly labeled food supply.

10. Radiation Exposure in Medical Imaging

The Committee urges FDA to collaborate with the medical imaging industry and radiological professional societies to address the safety of all x-ray imaging modalities and promote the use of international consensus standards and alternative technologies when appropriate.

FDA Response:
FDA's Radiological Health Program works to protect 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 has and will continue working with manufacturers, the Image Gently Alliance[173], and many other professional organizations to:

- Promote reducing the radiation dose used in imaging children, and using the minimum radiation dose necessary to obtain an acceptable image.
- Educate imaging professionals on the optimal use of imaging equipment.
- Alert users when imaging may involve use of an excessive amount of radiation.
- Improve the international standards concerning the safety of imaging equipment.
- Promote quality assurance programs in imaging facilities to utilize the most up-to-date protocols.
- Promote development of new image quality evaluation methodologies.

Additional FDA collaborations that support protection of patients and reduction of the incidence and severity of radiation injury include:

[173] https://www.imagegently.org/. For example, CDRH and the Critical Path Program funded contracts awarded to the Image Gently Alliance that supported the development of educational tools for imaging practitioners to encourage reduction of radiation dose to pediatric patients.

- Work with the American College of Radiology to develop a dose index registry for interventional fluoroscopy procedures.
- Work with the National Council on Radiation Protection and Measurements to develop reports on Evaluating and Communicating Radiation Risks for Studies Involving Human Subjects and Routine Gonadal Shielding of Patients During Abdominal and Pelvic Radiography.
- Participation in American Association of Physicists in Medicine Work Groups on Fluoroscopy Dose Management, Pediatric Fluoroscopic Exposure Rates, User Instructions for International Electrotechnical Commission (IEC) X-ray Performance Tests, and other areas.
- Participation in the International Atomic Energy Agency Technical Meeting on the Justification and Optimization of Protection of Patients Requiring Multiple Imaging Procedures in October, 2020.
- Participation in the drafting or revision of multiple IEC standards related to x-ray imaging devices.
- Work with the American Association of Physicists in Medicine and industry to include Size Specific Dose Estimates on CT scanners.

11. Skin Lightening

The Committee is concerned about the availability of illegal skin lightening products containing dangerous levels of mercury and hydroquinone that are available to consumers, particularly through online retailers. With the passage of the CARES Act, FDA has new authorities to address the safety and effectiveness of OTC drug products, including those containing hydroquinone. The Committee encourages the Office of Cosmetics and Colors, within CFSAN and the Office of Non-Prescription Drugs within CDER to collaborate to combat online sales of illegal skin lightening products, including testing to determine compliance with FDA content limits. The Committee provides an increase of $1,000,000 to FDA's Office of Minority Health and Health Equity to educate the public on the dangers of cosmetics containing these ingredients, including partnering with community-based organizations with records of reaching out to communities. The FDA should coordinate with the National Institute of Health's National Institute on Minority Health and Health Disparities to ensure any potential interventions or educational efforts are complementary and not duplicative.

FDA Response:
Ensuring that cosmetics are safe for their intended use and properly labeled is one of FDA's important public health priorities. Below please find a short summary of the regulatory status of mercury and hydroquinone under applicable FDA authorities.

Mercury. Mercury is currently listed as one of the prohibited or restricted ingredients found in the regulations under 21 CFR Part 700, specifically, 21 CFR 700.13. This regulation generally prohibits the marketing of cosmetics, including skin lightening/bleaching creams, containing mercury. However, 21 CFR 700.13 recognizes that a trace amount of mercury may be unavoidable despite use of good manufacturing practice but limits such trace amount to less than 1 part per million (ppm). It also provides an exception for use as a preservative in eye-area

cosmetics, permitting no more than 65 ppm of mercury as a preservative in cosmetics for use around the eye when no other safe or effective alternative preservative exists for use in such cosmetic. Mercury-containing cosmetics not in compliance with one of these conditions would be deemed to be adulterated under sec. 601(a) of the FD&C Act. In addition, in 1990, FDA made a final determination under 21 CFR Part 330 that drug products containing ammoniated mercury for skin bleaching and mercury oleate for the treatment of dandruff, seborrheic dermatitis, and psoriasis are not generally recognized as safe and effective for these uses and are subject to the requirement for a new drug application.[174] Accordingly, under section 505G(a)(5) of the FD&C Act, as added by the Coronavirus Aid, Relief, and Economic Security (CARES) Act, these drug products are deemed to be a new drug under section 201(p), misbranded under section 502(ee), and subject to the requirement for an approved new drug application under section 505.[175]

FDA is committed to compliance with the terms of the Minamata Convention on Mercury (2013) (MCM) and has already taken steps to reduce to a de minimis level the manufacture, import, and export of most of the products listed in Part I of Annex A to the MCM. FDA has also implemented measures to reduce the use of mercury in additional products not listed in Part I of Annex A.

FDA Import Alert # 53-18 ("Detention Without Physical Examination of Skin Whitening Creams Containing Mercury"; https://www.accessdata.fda.gov/cms_ia/importalert_137.html), which has been in effect since July 5, 1973, provides guidance to FDA field personnel at U.S. ports of entry about imported cosmetics that may contain mercury in violation of FDA regulations at 21 CFR 700.13. Products that appear to contain mercury, as identified in the import alert, are subject to detention without physical examination.

This import alert was published to reduce the occurrence of unlawful skin lighteners being imported into the U.S. The import alert lists those companies in the past that were found to be non-compliant. Since 2009, FDA has identified at least 27 products that are subject to the import alert.

For FY 2018-2020, 53 lines of skin-lightening products were flagged under IA 53-18. Of those 53 none of them were refused based on findings of mercury in the product.

Hydroquinone. Unlike mercury, there are no regulations specifically prohibiting the use of hydroquinone (HQ) in cosmetics. When HQ is used as a cosmetic ingredient, it is usually in lower concentrations than when used in drugs. HQ typically is used in a cosmetic as an antioxidant, reducing agent, processing aid, or as hair color components in coal tar hair dyes.

HQ has also been marketed as an over-the-counter (OTC) drug for skin bleaching under the OTC monograph system. It is classified as a drug for any skin bleaching indication including "gradual

[174] Status of Certain Over-the-Counter Drug Category II and III Active Ingredients, 55 FR 46914, 46918, 46919, 46920, 46921 (November 7, 1990).

[175] FD&C Act §505G(a)(5).

fading of 'age spots', 'liver spots', freckles, and melasma (the mask of pregnancy . . .); or "lightens dark pigment of the skin.[176]" These are considered drug claims because agents intended to lighten areas of hyperpigmented skin affect the structure or function of the body by acting through the suppression of melanin pigment formation within skin cells.[177]

Pursuant to section 505G(a)(4) of the FD&C Act, as added by the CARES Act, OTC skin bleaching drug products containing hydroquinone as an active ingredient are now deemed to be new drugs under section 201(p), misbranded under 502(ee), and subject to the requirement for an approved new drug application under section 505 of the FD&C Act as of September 23, 2020.

Education
The FDA appreciates the Committee's interest in this area. The appropriated $1 million in funding will be used to develop culturally and linguistically tailored multi-media health education for the public on the dangers of unsafe skin lightening products that contain hydroquinone and mercury and have been disproportionately targeted towards and used by racial and ethnic minority groups. Formative research, through focus groups and/or key informant interviews, in collaboration with community organizations, will be used to inform content development and dissemination. Additionally, through engagement with community organizations that have relationships with diverse communities, the FDA Office of Minority Health and Health Equity (OMHHE) will expand the reach and dissemination to the public. Activities will be conducted by the FDA OMHHE in coordination with the Center for Drug Evaluation and Research and the Center for Food Safety and Applied Nutrition. The FDA OMHHE will also engage with the National Institutes of Health's National Institute on Minority Health and Health Disparities to ensure efforts are synergistic and not duplicative.

12. Thalassemia

Recent studies have shown that the length of time between when blood is donated and transfused does not impact outcomes for patients in need of an emergency blood transfusion. However, the Committee is aware that these studies do not determine the impact on chronically transfused patients, such as those with thalassemia, in which administration of older red cells may exacerbate iron loading and contribute to worse outcomes. The Committee urges FDA to review scientific literature on this issue and provide a brief to the Committees on potential steps to address safety.

FDA Response:
Individuals with beta-thalassemia major require chronic blood transfusions, and adults usually receive approximately two units of blood every three to four weeks. An essential component of the treatment of every adult on simple chronic transfusion therapy is iron chelation therapy. Iron

[176] Skin Bleaching Drug Products for Over-the-Counter Human Use; Establishment of a Monograph; Notice of Proposed Rulemaking, 43 FR 51546, 51547, 51553 (November 3, 1978).

[177] *Id*. at 43 FR 51547. *See also* Skin Bleaching Drug Products For Over-the-Counter Human Use; Proposed Rule, 71 FR 51146, 51152 (August 29, 2006).

chelation therapy is now possible with both oral agents, as well as parenteral ones.[178] When properly administered, chelation therapy can adequately remove the excess iron administered through transfusion. Whether a reduction in the time between when blood is donated and transfused would lead to an improvement in clinical outcomes due to reduction in iron loading could be quite challenging to evaluate in this setting, requiring large clinical trials. Differences in other outcomes that might be benefited by the transfusion of younger red blood cells could require large clinical trials as well.

While it is not within FDA's purview to sponsor such clinical trials, FDA would certainly support such studies on the age of red cells and thalassemia outcomes should they be conducted by academic or other researchers.

[178] For reference see https://www.ncbi.nlm.nih.gov/books/NBK269373/

JOINT EXPLANATORY STATEMENT

1. Opioid Epidemic

The agreement remains deeply concerned about the opioid epidemic that has taken the lives of thousands of Americans and continues to support FDA's investments into International Mail Facilities to stop drugs from entering the United States. The agreement directs FDA to comply with Section 3001 of the SUPPORT Act (Public Law 115-271). The agreement continues to direct FDA to refer any drug application for an opioid to an advisory committee for their recommendations prior to approval, unless FDA finds that holding such committee is not in the interest of protecting and promoting public health. The agreement also directs FDA to comply with Section 3032 of the SUPPORT Act and encourages the agency to continue to monitor the effectiveness of existing Opioid Analgesic Risk Evaluation and Mitigations Strategy to determine whether further modifications are necessary.

FDA Response:
One of the highest priorities of FDA is advancing efforts to address the crisis of misuse and abuse of opioid drugs harming families. The Agency appreciates the Committee's continued support of the FDA's efforts, including our investments into International Mail Facilities (IMF) to stop drugs from entering the United States. Our IMF efforts include ongoing work to expand space, increase staffing, increase scientific detection tools and improve IT infrastructure at the different IMF locations.

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. The Agency has taken a number of actions pursuant to section 3001 of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act. For example, 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.
- Issued draft guidance on June 20, 2019, "Opioid Analgesic Drugs: Considerations for Benefit-Risk Assessment Framework," which describes the benefit-risk assessment framework the agency uses in evaluating applications for opioid analgesic drugs. This draft guidance also summarizes the information that can be supplied by applicants to assist the Agency's benefit-risk assessment, including public health considerations.
- Held a public hearing on September 17, 2019 titled, "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 existing therapies, among other factors, in reviewing applications.

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 continues 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 and overdose of opioids. Pursuant to section 3032 of the SUPPORT Act, the Agency 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. FDA is analyzing comments from the docket and will take action as appropriate. FDA is also continuing to consider whether and how to use authority under SUPPORT Act section 3032 to mandate the dispensing of disposal technologies to patients receiving opioids for at-home use.

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).

2. Pesticides Residues in Imported Human Food

The agreement notes that imported human food continues to have higher pesticide violation rates than domestically produced food and directs FDA to continue to partner with State inspection services and develop emerging technologies to enhance the imported food sampling efforts. Additionally, the agreement encourages FDA to work with partners such as the U.S. International Trade Commission to conduct a multi-year data review to better identify imported food samples that are more likely to have pesticide violations to assess whether giving special attention to certain imported products with significantly higher rates of violations compared to domestic products would change the planning of the pesticide sampling plan for future years.

FDA Response:

As part of FDA's New Era of Smarter Food Safety Initiative, FDA is committed to advancing emerging technologies in support of the Agency's predictive analytics capabilities, including expanded use of artificial intelligence (AI) and machine learning tools, beginning with expanding on the proof of concept completed by the Agency on using AI for screening of imported foods at ports of entry. FDA appreciates the Committee's support for these efforts.

Under FDA's pesticide residue monitoring program, FDA collects samples from individual lots of domestically produced and imported foods and analyzes them to determine whether they contain pesticide chemical residues that are "unsafe" within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA enforces tolerances established by EPA (see tolerances for pesticide residues in food at 40 CFR part 180). A food that bears or contains the

pesticide chemical residue is deemed to be adulterated under section 402(a)(2)(B) of the FD&C Act if the pesticide chemical residue is in excess of the established tolerance or if the pesticide chemical residue does not have an established tolerance or exemption from the requirement for a tolerance.

When planning sampling for the pesticide residue monitoring program, FDA experts primarily consider violation history and food consumption patterns. Additional factors such as data from other federal agencies (e.g., EPA, USDA) and state partners, foreign pesticide usage data, and analytical programs such as PREDICT (Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting), a risk-based analytics program that electronically screens all regulated shipments imported or offered for import, help identify foods that may warrant increased inspections. Pesticide violations in imported products may result in the addition of the product/firm to an FDA Import Alert, which alleviates the need for increased examination and testing of future shipments by FDA. When products are subject to detention without physical examination because they are listed on an import alert, importers are responsible for demonstrating the admissibility of their products. As a result, the importers (not FDA) assume the burden for any product sampling and must demonstrate their food products were produced in accordance with FDA requirements. A high violation rate for an imported targeted commodity affirms the success of FDA's sampling design to select commodities and production sources that are likely to be higher risk and to remove these products from commerce.

The annual FDA Pesticide Residue Monitoring Reports currently include a list of imported foods that may warrant special attention based on a violation rate above 10 percent, and considering the number of samples analyzed. FDA is planning to review data in the forthcoming 2019 report to determine if it is appropriate to modify the special attention list to also include imported products that have a violation rate below 10 percent, but for which imported products have significantly higher violation rates than identical domestic products. FDA experts also are currently conducting a multi-year data review that may aid in identifying imported food samples that are more likely to have pesticide violations. The Agency will review relevant U.S. International Trade Commission reports (e.g., Volumes 1 and 2 of *Global Economic Impact of Missing and Low Pesticide Maximum Residue Levels*) to determine if the reports would be helpful for sampling design.

3. Polypharmacy

The routine usage of five or more prescription medications within the same period is becoming increasingly prevalent among older adults, elevating risk factors for drug-drug interactions and adverse events. Therefore the agreement encourages FDA to assess potential impacts of polypharmacy.

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 and biological product 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.

As part of the clinical trial process, FDA 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 prescription and over-the-counter medications, dietary supplements, and other substances. FDA provides guidance and recommendations for sponsors on how to evaluate drug-drug interactions (DDIs) during drug development. In January 2020, FDA published a final guidance entitled: "Clinical Drug Interaction Studies – Cytochrome P450 Enzyme-and-Transporter-Mediated Drug Interactions Guidance for Industry." This guidance describes clinical studies to evaluate the DDI potential of an investigational drug including: (1) the timing and design of the clinical studies; (2) the interpretation of the study results; and (3) options for managing DDIs in patients. More recently in November 2020, the Agency published final guidance entitled: "Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs". This document, provides 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 geriatric patients) so that we better understand the safety and efficacy of new drugs, including biologics, for these patients.

Modernization of the Public-Facing Digital Services – 21st Century Integrated Digital Experience Act

The 21st Century Integrated Digital Experience Act (IDEA) was signed into law on Dec. 20, 2018. It requires data-driven, user-centric website and digital services modernization, website consolidation, and website design consistency in all Executive Agencies. Departments across the federal landscape are working to implement innovative digital communications approaches to increase efficiency and create more effective relationships with their intended audiences. The American public expects instant and impactful communications – desired, trusted content available when they want it, where they want it, and in the format they want it. If the consumer is not satisfied, they move on and our opportunity for impact is lost.

Modernization Efforts

In FY 2019 HHS engaged Department leadership and developed a Digital Communications Strategy that aligns with the requirements of IDEA. In FY 20, HHS Digital Communications Leaders began implementation of the Strategy in alignment with IDEA, beginning to align budgets to modernization requirements.

As the result of a comprehensive review of costs associated with website development, maintenance, and their measures of effectiveness, HHS will prioritize:

- modernization needs of websites, including providing unique digital communications services, and
- continue developing estimated costs and impact measures for achieving IDEA

Over the next four years HHS will continue to implement IDEA by focusing extensively on a user-centric, Digital First approach to both external and internal communications and developing performance standards. HHS will focus on training, hiring, and tools that drive the communication culture change necessary to successfully implement IDEA.

Over the next year, HHS Agencies and Offices will work together to continue to implement IDEA and the HHS Digital Communications Strategy across all communications products and platforms.

FDA DRUG CONTROL PROGRAM AGENCY

Budget Authority (in millions)	FY 2020 Final	FY 2021 Enacted	FY 2022 Request
Drug Resources by Function			
Research and Development: Treatment & Prevention (CDER)	$20.00	$20.00	$46.00
Interdiction (ORA)	$44.50	$44.50	$54.50
Total Drug Resources by Function	**$64.50**	**$64.50**	**$100.50**
Drug Resources by Decision Unit			
Center for Drug Evaluation and Research	$20.00	$20.00	$46.00
Office of Regulatory Affairs	$44.50	$44.50	$54.50
Total Drug Resources by Decision Unit	**$64.50**	**$64.50**	**$100.50**
Drug Resources Personnel Summary			
Total FTEs (direct only)	159	159	199
Drug Resources as a percent of Budget			
Total Agency Budget (in Billions)	$3.265	$3.286	$3.609
Drug Resources percentage	1.98%	1.96%	2.78%

PROGRAM SUMMARY

MISSION

The Food and Drug Administration (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 human and animal food, cosmetics, and radiation-emitting products; and regulating tobacco products. FDA's customers and key stakeholders include American patients and consumers; healthcare professionals; veterinarians; regulated industry; academia; and, state, local, federal and international governmental agencies.

Addressing the opioid crisis is one of the FDA's highest priorities. Opioid analgesics are effective medications that can help manage pain when properly prescribed for the right condition and used properly. 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, and we are engaged in many ongoing activities aimed at furthering the overarching strategy.

FDA recognizes both the benefits of these opioid medications for patients who need them, including those with debilitating chronic pain conditions as well as the risks associated with the treatment. We are taking immediate steps to reduce the scope of the opioid addiction epidemic and continuously examine our role and policies in the regulation of opioids, drugs used in pain treatment, and in opioid addiction and overdose. To apply its public health expertise, 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:

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
4. Improving Enforcement and Assessing Benefit-Risk

METHODOLOGY

FDA identified the drug control budget by using the dedicated budget authority for opioids activities. This includes opioids dedicated base activities conducted by the Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA).

BUDGET SUMMARY

FDA's FY 2022 request of $100.5 million for drug control activities is +$36.0 million above FY 2021 Enacted.

Center for Drug Evaluation and Research

FY 2022 Request: $46.0 million, +$26.0 million above FY 2021 Enacted

The FY 2022 Budget for drug-related activities includes $46.0 million for CDER. FDA requests an additional $26.0 million to further develop and advance strategies to confront the opioid crisis.

CDER is committed to supporting research that addresses questions that are critical to our work on the opioid crisis. In particular, the FY 2019 appropriation provided CDER with base funding for regulatory science, enforcement, and innovation activities, to combat the opioid epidemic. In FY 2020, CDER utilized the $20.0 million in opioids base funding to further develop and implement evidence-based actions to address FDA's opioid priority areas.

Some of CDER's recent research initiatives include:

- Advancing the development of evidence-based clinical practice guidelines on the appropriate management of acute dental pain (as part of SUPPORT Act Sec. 3002 implementation)
- Research on chronic pain therapies to inform the ongoing discussion about the appropriate use of opioid analgesics in chronic pain care
- Study on how comparative feedback to providers would impact the number of left-over opioid pills to help inform and improve safety of opioid prescribing practices for acute pain
- Studies to enhance FDA's opioids systems model, a U.S. population-level systems dynamics model, used to improve understanding of/reaction to the opioid crisis and inform FDA's decision-making regarding the treatment of Opioid Use Disorder (OUD)
- Research using predictive modeling to evaluate drug interactions, risk assessment, and drug development to further inform FDA's regulatory actions on opioids and other drug products with abuse potential
- Enhancing the Opioid Data Warehouse, a cloud-based large data warehouse and analytical capability which allows FDA to better assess opioid vulnerability points in the

population, anticipate changes in the opioid crisis, and target regulatory changes required for opioids
- Continuing implementation of the "Remove-the-Risk" campaign to advance FDA's consumer-focused outreach efforts, which has been an asset for the agency in efforts to address the opioid crisis on an individual level
- Studies examining characteristics of abuse deterrent formulations (ADF) to help FDA evaluate the best approach to assessing generic ADF formulations, support the FDA's regulatory science capabilities, and improve access to opioid alternatives

FDA supported research initiatives that have enhanced our understanding of appropriate opioids use as pain treatments, as well as risks and mitigating factors to address opioid misuse, abuse, overdose, and death. However, as opioid related deaths continue to increase in the U.S., further research is needed to address the opioid crisis including the impact of COVID-19 on patients with opioid use disorder.

Office of Regulatory Affairs – Field Activities

FY 2022 Request: $54.5 million, +$10.0 million above FY 2021 Enacted

The FY 2022 Budget for drug-related activities includes $54.5 million for the ORA. FDA requests an additional $10.0 million for ORA:

- to establish satellite laboratories at the International Mail Facilities (IMFs) to include staffing by scientists along with expanding ORA's use of analytical tools for expedited screening of packages, and
- expand the current IMF initiative to interdict shipments of opioids, unapproved foreign drugs, counterfeit pharmaceuticals, and health fraud related shipments.

In response to the current opioid crisis, ORA prioritized protecting the public health by monitoring FDA-regulated products shipped into the nation's nine IMFs in order to prevent unsafe, counterfeit, and unapproved drugs from entering the U.S. FDA's IMF staff works diligently to examine and document suspicious contents, however FDA investigators are only able to inspect a fraction of the incoming international mail packages. It is estimated that FDA is able to physically inspect less than 0.06 percent of the packages that are presumed to contain drug products that are shipped through the IMFs. Recognizing these hurdles, FDA is increasing existing resources, working more efficiently, and identifying innovative ways to expand the impact of its efforts. During FY 2018, FDA increased the number of investigators it has in the IMFs from 8 to 22 full-time employees (FTEs). The 2018 Omnibus Spending Bill provided FDA with additional resources for the IMFs, that will bring FDA to a total of 70 FTE in the IMFs when fully staffed. Thus far over 90 percent of these FTE have been hired and it is anticipated the IMFs will be fully staffed by the end of the 2021 calendar year. In FY 2020, FDA reviewed over 50,000 products at the IMFs. When fully staffed and once the additional space and IT improvements are completed at the IMFs, FDA is planning to increase the number of products reviewed.

Section 3022 of the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (SUPPORT Act), signed into law on October 24,

2018, added section 801(u) [21 U.S.C. § 381(u)] to the Food Drug and Cosmetic Act (FD&C Act), giving the FDA 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 substantial clinical trial has been instituted and made public, if the article is an "ingredient that presents significant public health concern."

FDA first implemented this new authority in FY 2019, developing an initial list of nine APIs meeting the 801(u) criteria. FDA IMF staff began using the initial list of indicated APIs in March 2019. In January 2020, FDA added nine more APIs to the 801(u) list, bringing the total number of APIs on the list to 18. FDA will continue to update the API list, as additions are approved through the established review process.

In FY 2018, ORA destroyed approximately 6% of refused drug products; in FY 2019, prior to implementing 801(u), that number was about 16%. Since 801(u) implementation, FDA has raised the overall destruction rate to more than 77% of violative drug products offered for import via international mail, and that destruction rate continues to increase.

Improvements at IMFs will continue, as ORA implements new authorities included in the SUPPORT Act. 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 (LOI) 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 LOI notes the history of collaboration between FDA and CBP to protect the public from illegal or harmful products entering the United States and outlines the intent of each agency to establish and implement strategies through separate written agreements by the end of FY 2019 to enhance knowledge-transfer to increase efficiency, reduce duplication of efforts and facilitate mission responsibilities.

FDA, CBP, and Homeland Security Investigations have since signed a Memorandum of Understanding (MOU) on October 28, 2020. The MOU addresses the areas of cooperation outlined in Section 3014, including information sharing, operational coordination for better targeting of higher risk parcels, and collaborative strategies specific to each agency's respective regulatory enforcement requirements, expansion of the presence of scientific personnel at selected IMF locations, and facility improvements at the IMFs.

FDA's Office of Regulatory Affairs' (ORA) Office of Criminal Investigations (OCI) continues to selectively target rogue healthcare providers misusing their positions of public trust, breaches in the FDA-regulated pharmaceutical supply chain, and bad actors operating on the surface and dark nets who distribute counterfeit and other illicit opioid products to unsuspecting consumers.

In an attempt to better understand and disrupt the threat posed by illicit pharmaceuticals, including opioid products, in FY 2020 ORA, with the support of CBP, executed the first joint international enforcement operation conducted by the Indian Directorate of Revenue Intelligence. In recognition of the shared threat posed by illicit opioid products, Operation Broadsword, which was supported by the Indian diplomatic mission to the U.S. as well as senior customs officers flown in from India, targeted inbound parcels from India at the U.S. Chicago O'Hare IMF, some of which included opioid products. Preliminary discussions have taken place with the

Government of India, regarding the potential for conducting a second Operation Broadsword at an IMF in India, COVID-19 dependent, during FY 2021.

Section 3022 of the SUPPORT Act also amended section 306 of the FD&C Act to give FDA new authority to debar persons from importing drugs into the U.S. if they have been convicted of a felony for conduct related to the importation of any drug or controlled substance. On June 24, 2019, FDA issued its first notice of debarment for a felony conviction involving two counts of illegal importation of a drug under this new authority. Since that time, FDA has issued eight (8) more notices of debarment based on felony convictions. Additionally, the first debarment case for a U.S. addressee, not based on a conviction but who exhibited a pattern of attempted importation posted in the Federal Register November 30, 2020. This individual attempted to import several shipments consisting of large amounts of sildenafil in various forms into the U.S. via international mail. The amounts, frequency, and dosage this individual attempted to import were inconsistent with personal or household use.

ORA continues to increase analytic capability and capacity at the IMFs. Based on benchmarking with Federal partners and discussions with OCC, ORA identified specially trained field-based scientists using an established set of analytical tools to be the most scientifically reliable and efficient approach to rapid identification of illicit FDA-regulated products, such as counterfeit pharmaceuticals, including opioids, and adulterated supplements. Ten ORA chemists were trained at the Forensic Chemistry Center (FCC) on the use of these instruments, a satellite laboratory unit was procured, and pilot operations were initiated at the U.S. Chicago O'Hare IMF. These chemists participated in 30-day details and working with ORA Consumer Safety Officers, processed over 900 samples in 68 working days. Twenty percent of the samples were found to contain either U.S. Drug Enforcement Administration scheduled substances or violative FDA products. The pilot was halted in March 2020 due to the COVID-19 pandemic. A pilot summary report was issued in July 2020. Additional scientists are being hired and trained with plans to establish full operations at two IMF locations by the end of CY 2021.

PERFORMANCE

At this time, FDA does not have specific performance measures tracking completion of drug control activities such as efforts related to opioids. FDA is reviewing the potential and practicality of developing specific performance measures for tracking these activities for inclusion in future Drug Control Budget submissions.

FDA SPECIFIC ITEMS

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES

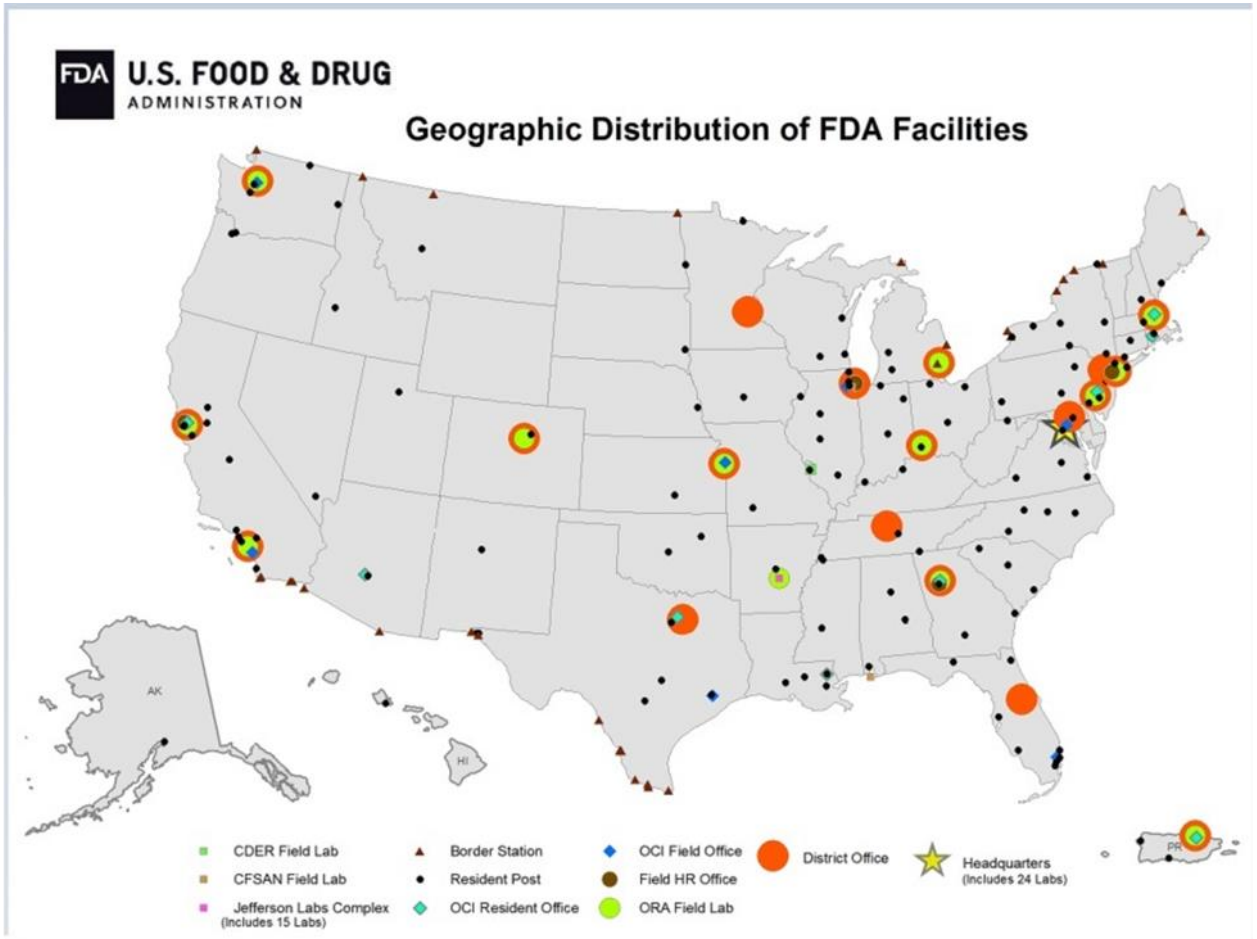


Figure 1 Geographical Distribution of FDA Facilities

HIV/AIDS FUNCTIONAL TABLE

Food and Drug Administration
HIV/AIDS Resource Funding
(Dollars in Thousands)

Program	FY 2020 Estimate	FY 2021 Estimate	FY 2022 Estimate
Human Drugs	$29,869	$29,869	$29,869
Biologics	$21,934	$21,998	$22,885
Medical Devices	$422	$431	$440
Field Activity	$36,960	$37,620	$38,280
Other Activities	$3,395	$3,395	$3,395
Total HIV/AIDS	**$92,580**	**$93,313**	**$94,869**

CROSSCUTS

Food and Drug Administration
FY 2020-FY 2022 Crosscutting Information
(Program Level in Thousands)

(dollars in thousands)	FY 2020 Estimate	FY 2021 Estimate	FY 2022 Estimate
Alzheimer's Disease	9,560	8,291	8,745
HIV/AIDS	92,580	93,313	94,869
Antimicrobial Resistance	47,571	50,118	49,369
Bioterrorism-Medical Countermeasures	145,237	149,501	153,113
Cosmetics	14,331	14,668	15,405
Diabetes	24,274	24,644	24,984
Drug Abuse	13,976	14,079	14,079
Global Health	61,347	60,684	62,640
Immunization	137,818	143,324	147,554
Mental Health	21,044	21,528	21,273
Minority Health	4,118	4,880	5,122
Opioids 1/	75,011	75,011	113,011
Pandemic Influenza	35,610	38,628	39,591
Patient Safety	603,043	604,063	638,605
Pediatric Drugs	6,451	6,717	6,349
Tobacco	712,000	712,000	812,000
Women's Health	81,050	84,004	86,716

*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 2021 Operating Plan

CENTRAL ACCOUNTS

Program (dollars in thousands)	FY 2020 Actuals		FY 2021 Estimates		FY 2022 Estimates	
	BA	UF	BA	UF	BA	UF
Foods	**16,599**	-	**13,961**	-	**13,528**	-
Center	5,164	-	4,334	-	4,199	-
Field	11,435	-	9,628	-	9,329	-
Human Drugs	**20,720**	**51,786**	**17,589**	**43,067**	**17,042**	**41,729**
Center	16,280	50,584	13,876	42,127	13,445	40,818
Field	4,440	1,202	3,713	940	3,597	911
Biologics	**6,335**	**5,245**	**5,140**	**4,566**	**4,980**	**4,424**
Center	5,364	5,201	4,322	4,528	4,188	4,388
Field	971	44	818	38	792	37
Animal Drugs and Feeds	**3,926**	**1,028**	**3,252**	**878**	**3,151**	**851**
Center	2,594	1,028	2,129	878	2,063	851
Field	1,332	-	1,123	-	1,088	-
Devices and Radiological Health	**10,637**	**4,844**	**8,853**	**4,083**	**8,578**	**3,956**
Center	8,526	4,713	7,071	3,968	6,851	3,845
Field	2,112	131	1,783	115	1,727	112
National Center for Toxicological Research	**760**	**-**	**645**	**-**	**625**	**-**
Family Smoking Prevention and Tobacco Control Act	-	**5,840**	-	**4,861**	**-**	**4,710**
Center	-	5,716	-	4,764	-	4,616
Field	-	124	-	97	-	94
FDA Headquarters	**11,662**	**5,929**	**8,369**	**6,347**	**8,109**	**6,150**
Total	**70,640**	**74,671**	**57,810**	**63,802**	**56,013**	**61,820**

HHS CHARGES AND ASSESSMENTS

Assessments:	**276,451**
NIH eRA Grants Management System Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	271,459
Federal Audit Clearinghouse	4,992
Fee For Service:	**68,800,193**
Program Support Center/ Office of the Secretary Provides various services to the FDA, including some Information and Systems Management Services	**18,141,678**
Financial Management Portfolio (FMP)	596,888
Real Estate and Logistics Portfolio Includes building operations, shredding, storage, property disposal	9,120,726
Equal Employment Opportunity Compliance and Operations Includes Complaint Investigations, FAD/Counseling, Mediation	741,875
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	7,682,189
Occupational Health Portfolio FDA agency health units and services	**2,967,047**
Information & System Management Services	**38,635,155**
Freedom of Information (FOIA)	57,000
Unified Financial Management Systems (UFMS) Includes services for Consolidated Financial Reporting System (CFRS), Financial Business Intelligence System (FBIS), Governance and UFMS O&M support	13,674,569
HCAS Operations and Maintenance HCAS O&M services provide support for daily operations of the HCAS application.	2,670,354
Office of Operations Telecommunications team offers expertise on Application Support / Capacity Management / Intranet	2,777,844
Office of Enterprise Services	2,287,255
Office of Chief Project Officer Services include activities for HHS' civilian employees and Commissioned Corps Officers, and maintenance and operation of the systems housing current and historical pay and leave records	5,018,957
Office of Information Security (OIS) Includes computer security incident reponse center. Trusted Internet Connections and IT Security.	4,726,176
Digital Communications	7,423,000
Office of Human Resource Services Includes HR Center services teir I, payroll liaison, systems planning and implemenation	**9,056,313**
Jointly Funded Projects:	**$3,596,853**
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	1,500,000
Other Jointly Funded Projects	**2,096,853**

CFO Audit of Financial Statements 518,379

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.

Office of Public Health/Blood Safety 300,000

Agreement to provide funding for the advisory committee on Blood Safety

Regional Health Administrators 308,010

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.

Intra-department Council on Native American Affairs 17,000

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

National Science Advisory Board for Biosecurity 225,000

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

NIH Negotiation of Indirect Cost Rates 34,125

Agreement with NIH/OD to support costs associated with the negotiation of indirect cost rates with commercial organizations

OPM USAJOBS 129,579

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.

President's Advisory Committee on Combating Antibiotic-Resistant Bacteria 175,000

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"

Biosafety and Biosecurity Coordinating Council 82,778

This will support the administrative management of the Council in efforts to coordinate and collaborate on biosafety and biosecurity issues within HHS.

Implementation of the DATA Act (PMO) 58,982

Tick-Borne Disease Working Group 150,000

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.

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.

National Clinical Care Commission 90,000

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.

Secretary's Tribal Advisory Committee 8,000

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.

Activity	FY 2020 Actuals	FY 2021 Estimate	FY 2022 Estimate
Assessments	**$ 276,451**	**$ 285,544**	**$ 294,845**
Fee for Service	**$68,800,193**	**$70,184,494**	**$71,461,387**
Program Support Center/OS	$18,141,678	$21,134,946	$21,587,052
Occupational Health Portfolio	$ 2,967,047	$ 1,739,548	$ 1,774,339
Information System Management Service	$38,635,155	$37,775,000	$38,374,297
Office of Human Resource Services	$ 9,056,313	$ 9,535,000	$ 9,725,700
Jointly Funded Services	**$ 3,596,853**	**$ 3,877,525**	**$ 3,877,197**
International Health - Bilateral Agreement	$ 1,500,000	$ 1,550,000	$ 1,565,500
Other Jointly Funded Projects	$ 2,096,853	$ 2,327,525	$ 2,311,697
Total	**$72,673,497**	**$74,347,563**	**$75,633,430**

GLOSSARY

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 s
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
CY	Calendar Year
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

FY	Fiscal Year
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
IGAs	Intentional Genomic Alterations
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
MCL	Mantle Cell Lymphoma
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
PHE	Public Health Emergencies
PHEIC	Public Health Emergency of International Concern
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PKU	Phenylketonuria
PMA	Premarket Approval
PMTA	Premarket tobacco product applications
PPE	Personal Protective Equipment
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
SaMD	Software as a Medical Device
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
VRBPAC	Vaccines and Related Biological Products Advisory Committee
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