DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2023

Food and Drug Administration

Justification of
Estimates for
Appropriations Committees

Letter from the Commissioner

On behalf of the Food and Drug Administration (FDA), I am transmitting FDA's Congressional Justification for the fiscal year (FY) 2023 budget. This request for the $8.4 billion total program level is critical to support FDA's public health agenda including: public health and consumer protection; modernization to keep pace with evolving science and technology; and emergency preparedness and response. Since its inception in 1906, FDA's work has touched nearly every area of our lives. Each day FDA employees work to help ensure the safety, efficacy, quality of the products we regulate under our legal and regulatory frameworks. As a result, FDA is responsible for overseeing nearly three trillion dollars annually in medical products, food, and tobacco products. Combined, these products account for about 20 cents of every dollar spent on consumer goods in this country.

Every year the FDA reviews hundreds of product applications to determine which drugs, devices or biological products (e.g., vaccines) will be marketed in the U.S. The process is rigorous, thoughtful and always adheres to the most recent scientific standards for safety and effectiveness. We help to ensure that the human and animal food supply is safe, sanitary, and accurately labeled, and that cosmetic products are safe and properly labeled. The agency also protects Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products, and by educating the public about the dangers of tobacco products. We also ensure the public has the accurate, science-based information needed to make health decisions.

While much of the attention the agency received in 2021 focused on our response to the COVID-19 pandemic, I am pleased to note that, despite a great deal of uncertainty, the agency continued to accomplish a wide range of its non-COVID related priorities to protect the health and well-being of the people of the U.S. To carry out our mission during the pandemic, the agency made decisions guided by science, data and the best evidence. We continue to build on our accomplishments and lessons learned and request resources to modernize our agency to make our operations more efficient for the future.

The FY 2023 budget request for FDA requests a total of $6.8 billion in annual funding, an overall increase of $614 million compared to last year's level, including an increase of $458 million in direct discretionary budget authority. These critical discretionary investments will help us address our most urgent public health priorities, strengthen our public health capacity and business operations, advance agency-wide IT modernization and improve our agency-wide infrastructure. The budget proposes $100 million in additional 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. Finally, the budget requests $1.63 billion for FDA's responsibilities outlined in the HHS Pandemic Preparedness Plan. These resources will enable FDA to be better positioned to respond to future pandemics and support FDA's integral and unique federal regulatory pandemic preparedness responsibilities.

At a time when misinformation and disinformation are so prevalent, Americans can trust and depend on the FDA for essential information. We are driven to succeed in our public health mission and our focus is always on the well-being of patients and consumers.

On behalf of FDA, I extend my thanks for your support of FDA's mission and FY 2023 budget priorities.

Sincerely,

Robert M. Califf M.D., MACC
Commissioner of Food and Drugs, FDA

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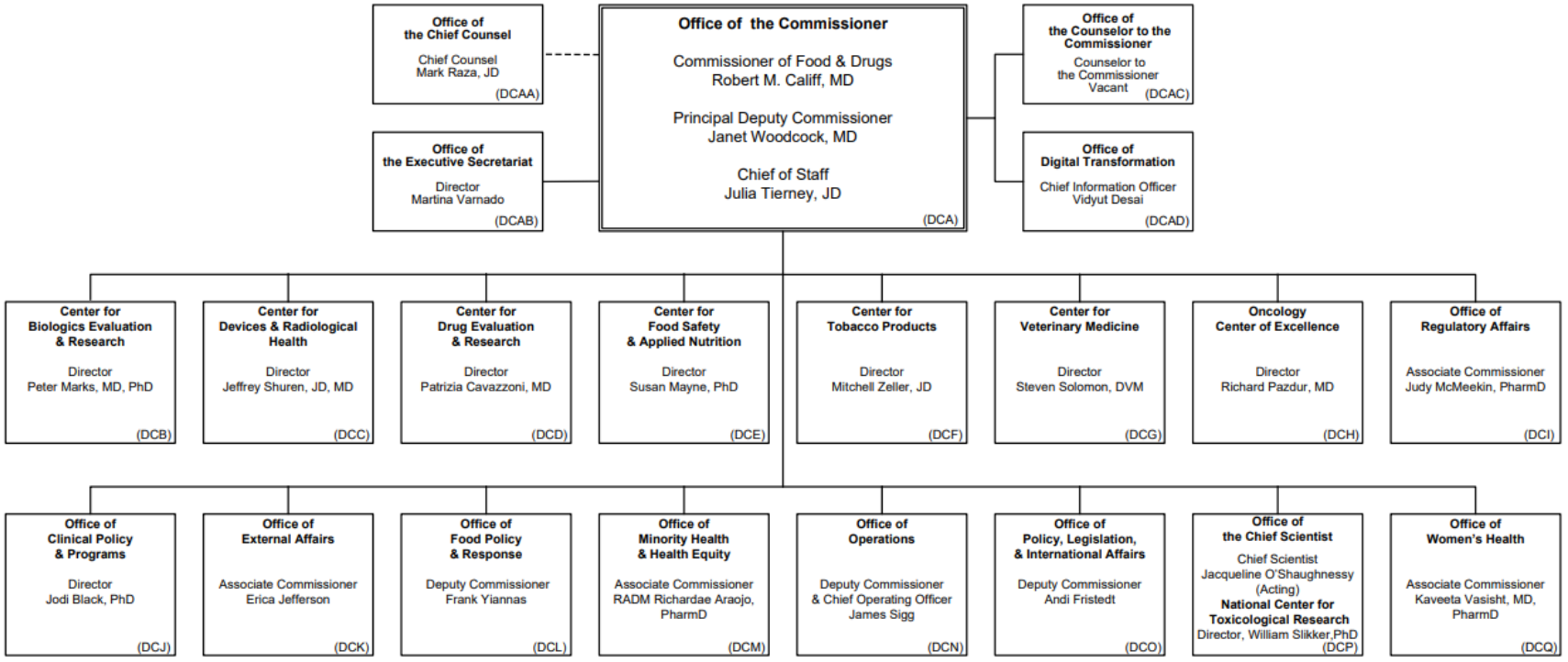
Table of Contents

Department of Health and Human Services
Food and Drug Administration

February 17, 2022



Legend:
- - - Direct report to DHHS General Counsel

FY 2023 EXECUTIVE SUMMARY

PERFORMANCE BUDGET OVERVIEW

EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2023 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; regulated industry; academia; and, state, local, federal and international governmental agencies.

ALIGNMENT TO ADMINISTRATION PRIORITIES AND HHS STRATEGIC PLAN

FDA is committed to supporting the national priorities set by the Administration. FDA collaborates closely with other HHS Agencies and Federal departments on crosscutting topics, especially where there are initiatives and activities where coordination and collaboration to protect patients and consumers is critical. FDA contributes to all five strategic goals of the HHS Strategic Plan. FDA actively implements strategies in support of these efforts, such as:

- Advancing health equity through outreach, collaborative research, and regulatory efforts;
- Building diverse, agile supply chains for human and animal food and medical products to reduce and prevent shortages and to ensure continued access and continuous supply;
- Strengthening regulatory and compliance capacity and leveraging technology to anticipate and respond to rapid increase in research technology and data capabilities;
- Taking actions to reduce the use of tobacco products, to protect American families and improve public health;
- Modernizing legacy information technology infrastructure, processes and systems to deploy emerging technologies, such as artificial intelligence and machine learning; and
- Advancing strong strategic management to foster prudent use of resources, strengthen human capital management, and enhance public trust.

Additional detail outlining FDA's recent accomplishments may be found in the Program chapters and in FDA 2021 Year in Review - Working for You.

HEALTH EQUITY

FDA's mission to facilitate the development and availability of therapeutics, vaccines, diagnostics, and other medical products, as well as advance efforts to ensure food safety and promote healthy eating, has a clear impact on underserved and vulnerable communities. FDA is dedicated to advancing the health of our nation's most vulnerable and underrepresented populations to achieve health equity for all and is working to support the Administration's

Executive Orders, including Executive Order 13950, "On Advancing Racial Equity and Support for Underserved Communities Through the Federal Government."

FDA continues to work to address gaps, including efforts to advance clinical trial diversity. Moreover, health disparities that existed long before COVID-19 have been amplified during the pandemic, especially for racial and ethnic minority and other underserved populations. FDA's responsibilities to protect those most at risk and advance health equity, including across racial, ethnic, and rural/urban lines, have exponentially grown and become increasingly complex. FDA expects health equity focused efforts to significantly increase, including the amount and urgency of work, not only to address current priorities and COVID-19, but also efforts to address the gaps and needs of racial and ethnic minority, and other diverse populations disproportionately impacted by certain diseases and conditions (e.g., lupus, cardiovascular disease, Sickle Cell Disease, HIV/AIDS etc.).

As described in the Budget request section, FDA's FY 2023 Budget provides funding to advance Health Equity. The agency also is working to advance equity through our present work utilizing multiple strategies and approaches. For example:

- FDA's active and passive vaccine surveillance systems can be leveraged to assess safety in specific subpopulations, including underserved communities.
- FDA's advancements can support communities with a high prevalence of medical comorbidities, as well as those individuals with rare diseases by allowing for monitoring of the safety and effectiveness of therapies in specific populations, and by addressing supply chain challenges and mitigating drug shortages to improve overall availability of critical drugs and devices.
- Finally, FDA utilizes acquisition strategies to ensure that our funding announcements provide opportunities for minority-owned, women-owned, veteran-owned and HUBZone small businesses, as well as minority institutions of higher learning. FDA coordinates with the Small Business Administration (SBA) for contract actions prior to their announcement. Any contract not designated for a small business will include a requirement for subcontracting with small businesses, if applicable.

COVID-19 SUPPLEMENTAL FUNDING AND RESPONSE

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, issued an unprecedented number of 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 drugs 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 COVID-19 strains on authorized and approved 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 due to 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 $940.5 million in appropriations or allocations 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) for COVID-19 response work. 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, tests, vaccines, therapies, and PPE to diagnose, treat, and prevent COVID-19; surveille supply chains for potential shortages or disruptions and fraudulent products; and help to mitigate risks related to such impacts, as necessary to protect human and animal health. The funds support critical research to provide essential data and new tools using Artificial Intelligence (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 the configuration and ongoing use of FDA's foundational surveillance systems to monitor postmarket safety and effectiveness for authorized and approved vaccines to allow near real-time surveillance through coordination with several partners, including government, academic and large non-government healthcare data systems.

Over the last two years, FDA worked tirelessly to respond to the COVID-19 public health emergency, while continuing our other mission critical public health work reinforcing FDA's essential role within the HHS. Despite the agency's remarkable progress, the FY 2023 Budget includes areas of opportunity to improve overall operations and performance and provides critical targeted resources to minimize risks that threaten our ability to meet our responsibilities. This request will directly support targeted efforts to modernize the agency's workforce, operations, and regulatory framework across a variety of programmatic activities to be responsive to evolving human and animal health needs.

ENTERPRISE RISK MANAGEMENT

To support the FDA core mission, operations, and functions, FDA employs Enterprise Risk Management (ERM) practices to assess, prioritize, manage, and oversee the agency's top risks. FDA's approach ensures that these risks are understood and examined to mitigate challenges as well as identify potential opportunities to accomplish the agency's public health mission and goals. FDA's employment of ERM practice 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 FY 2023 Budget identifies investments that address enterprise risks as part of the alignment of budget and enterprise risk management activities. This includes, yet is not limited to, the following risks: IT stabilization and modernization of our public health data enterprise, food safety oversight, minority health and health equity, emerging chemical and toxicological issues, controlled substances (opioids), medical device cybersecurity, youth e-cigarette use, and shortages and supply chain disruptions.

OVERVIEW OF BUDGET REQUEST

The FY 2023 Budget request for FDA includes a total program funding level of $8.4 billion, an overall increase of 36 percent or $2.2 billion above the FY 2022 Annualized Continuing Resolution (CR) level. The request includes $3.7 billion for budget authority – an increase of $458.4 million compared to the FY 2022 Annualized CR – and $3.0 billion for user fees – an increase of $156.7 million compared to the FY 2022 Annualized Continuing Resolution (CR). The request also includes $1.6 billion of mandatory funding for Pandemic Preparedness.

The Budget invests in FDA's discretionary budget priorities that further HHS's mission including Enhancing Food Safety and Nutrition, Advancing Medical Product Safety, Investing in Core Operations, and Modernizing Buildings and Facilities. FDA's Budget overview provides additional details on each initiative including Food Safety and Medical Product Safety funding levels. The Budget requests the following budget authority initiatives in comparison to the FY 2022 Annualized CR level:

Budget Authority requests in comparison to FY 2022 Annualized CR

Enhancing Food Safety and Nutrition	**New Era of Smarter Food Safety**	**+$51.8 million**
	Smarter Food Safety Data Modernization	*+$22.8 million (non-add)*
	New Era of Smarter Food Safety	*+$12.7 million (non-add)*
	Animal Food Safety Oversight	*+$16.4 million (non-add)*
	Healthy and Safe Food for All	**+$13.5 million**
	Maternal and Infant Health and Nutrition	**+$18.0 million**
	Emerging Chemical and Toxicological Issues	**+$19.7 million**
Advancing Medical Product Safety	**Cancer Moonshot**	**+$20.0 million** (one-time funding)
	Premarket Animal Drug Review Workload	**+$5.0 million**
	Medical Device Cybersecurity	**+$5.0 million**
	Advancing the Goal of Ending the Opioid Crisis	**+$38.0 million**
	Shortages & Supply Chain	**+$21.6 million**
	Predictive Toxicology Roadmap	**+$7.5 million**
	Animal Drug Medical Product Supply Chain	**+$2.3 million**
	Drug Safety Surveillance and Oversight	**+$5.6 million**
	Medical Product Safety Data Modernization	**+$8.6 million**
Investing in Core Operations	**FDA Capacity Building**	**+$59.4 million**
	Office of the Chief Counsel	*+$9.1 million (non-add)*
	Essential Services	*+$43.7million (non-add)*
	Office of Laboratory Safety	*+$6.6 million (non-add)*
	Office of Minority Health and Health Equity	**+$4.7 million**
	Public Health Employee Pay Costs	**+$51.9 million**
	Optimizing Inspectional Activities	**+$33.8 million**
	Reduce Animal Testing through Alternative Methods	**+$5.0 million**
	Enterprise Technology and Data	**+$44.5 million**
Modernizing Infrastructure, Buildings & Facilities	**White Oak Complex**	**+$2.5 million**
	GSA Rent	**-$833,000**
	Other Rent and Rent Related	**+$22.8 million**
	Buildings & Facilities	**+$18.0 million**

PANDEMIC PREPAREDNESS – MANDATORY

The FY 2023 Budget includes FDA's contributions to the Pandemic Preparedness Plan. The Budget proposes a cross-agency effort to carry out priorities for national pandemic preparedness. The FY 2023 Budget Pandemic Preparedness request for FDA proposes $1.63 billion in new mandatory resources for spending over five years. This funding will expand and modernize FDA's regulatory capacity, information technology (IT), laboratory infrastructure, including strengthening the personal protective equipment supply chain by building analytics and creating predictive modeling capabilities. FDA will also focus on evaluation of vaccines and therapeutics that target high-profile viral families and speed development of diagnostics, including expansion of test validation capacity and development of common performance standards. The Budget will also support FDA's work with its international partners to strengthen foreign inspections, harmonize premarket review of therapeutics and diagnostics, and reduce zoonotic pathogen spillover.

LEGISLATIVE PROPOSALS

The FY 2023 Budget includes several legislative proposals that better support agency efforts to protect American consumers and patients, particularly during public health emergencies like the COVID-19 pandemic. The proposals include enhanced authorities related to shortages of drugs, medical devices, and foods (including infant formula); additional tools to allow FDA to continue certain oversight activities when inspections are not feasible; expanded authorities for information sharing with the states; and additional authorities for destruction of products which present a significant public health concern. The Budget also proposes new authorities which would require medical device manufacturers to address cybersecurity issues, ensure that confirmatory studies under the accelerated approval pathway progress in a timely manner, and encourage timely marketing of first generics that leads to cost savings. Finally, the Budget would provide FDA with additional authorities to increase oversight of cosmetics, dietary supplements, and to modernize the tobacco user fee framework to allow for a fair distribution of tobacco user fee assessments to all regulated tobacco products.

FY 2023 DISCRETIONARY REQUEST

The FY 2023 Budget includes $6.8 billion of annual funding, an overall increase of 10 percent or $615.1 million above the FY 2022 Annualized CR level. The request includes $3.7 billion for budget authority – an increase of $458.4 million compared to the FY 2022 Annualized CR – and $3.0 billion for user fees – an increase of $156.7 million compared to the FY 2022 Annualized CR. The Budget invests in new initiatives focused on providing additional resources to address FDA's most urgent public health priorities, strengthen FDA's public health capacity and business operations, advance FDA's agency-wide IT modernization capabilities, and improve FDA's physical infrastructure.

The budget authority (BA) crosswalk in the suite of tables provides full details of the FY 2023 Budget discretionary request. New initiatives are summarized in the following sections by major activity with funding levels identified in parentheses in comparison to an FY 2022 Annualized CR level. 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.

The Budget prioritizes investments that address our underlying infrastructure, including increases to address our physical infrastructure, capacity and business functions within the Office of the Commissioner, and federal public health employee pay costs. The Budget also advances additional special programmatic activities such as advancements to implement the New Era of Smarter Food Safety, including animal food safety oversight, new funding to support crosscutting work to reduce animal testing through new alternative methods, and additional funding to improve health equity through nutrition and reducing exposure to harmful chemicals. The Budget proposes new funding to advance cybersecurity for medical devices, additional funding to optimize and modernize FDA's inspections, and new funding for the Cancer Moonshot.

CANCER MOONSHOT (BA $20.0 MILLION / 5 FTE)

The FY 2023 Budget includes $20.0 million in new, one-time funding[1] for FDA to: advance a variety of research, external collaborations and educational outreach programs, continue to support development and regulation of oncology medical products; and, build upon existing programs to advance Moonshot goals to cut today's age-adjusted death rate from cancer by at least 50 percent over the next 25 years and improve the experience of people and their families living with and surviving cancer. FDA will continue to facilitate and expand internal and external collaborations to expedite the development of oncology and malignant hematology products using an integrated approach to the clinical evaluation of drugs, biologics, and devices for the treatment of patients with cancer.

The agency will focus on initiatives to increase diversity and speed progress against the most deadly and rare cancers, including childhood cancers by investing resources in research, education and activities as well expand programs that address development of diagnostic and therapeutic products to benefit rare cancers and foster development of novel therapeutics for patients with ultra-rare cancers. FDA will enhance efforts to expand resources and collaborations

[1] The $20 million for Cancer Moonshot is captured within the Medical Product Safety totals on page 18.

to improve evidence generation for underrepresented subgroups in oncology clinical trials and support pragmatic and decentralized trials and our source of evidence through patient-generated data and real-world evidence to learn from all patients. FDA will advance the oncology Facilitate Call Center to support patients, caregivers, and survivors, and expand access networks to provide patients with cancer options for receiving novel/investigational therapies when a clinical trial is not available to them.

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

The FY 2023 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 state-of-the-art 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 2023 Budget provides a significant investment to modernize the agency's data infrastructure and put data to work. The FY 2023 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). Through the agency-wide data and technology governance process, FDA Centers and Offices will build on the centralized data investments and strategy and support customization and specific applications. The Enterprise Technology and Data request is included on page 13 and the

resources for this initiative are also reflected in the Food Safety and Medical Product Safety totals and summaries starting on pages 14 and 18.

FOOD SAFETY (BA $1.602 BILLION / 4,874 FTE; UF $17.1 MILLION / 50 FTE)

The FY 2023 Budget provides $1.6 billion for food safety, an increase of $181.3 million compared to the FY 2022 Annualized CR. The request includes $1.6 billion in budget authority – an increase of $181 million compared to the FY 2022 Annualized CR – and $17.1 million for user fees – an increase of $337,000 compared to the FY 2022 Annualized CR. The Budget will enable FDA to strengthen data-driven approaches to protecting consumers, allocating regulatory oversight resources based on risk, and improving FDA's capacity to quickly respond to ongoing and evolving public health challenges through implementation of the New Era of Smarter Food Safety.

The FDA has an immediate need for funding that will allow the agency to more effectively leverage new tools and approaches outlined in the New Era of Smarter Food Safety to address ongoing and emerging food safety issues impacting every U.S. consumer. This effort builds on progress made over the last decade through the Food Safety Modernization Act (FSMA) and other scientific advancements that have allowed the agency to identify more targeted needs and approaches to address the challenges facing our food safety system, while also preparing the agency to manage food safety issues into the future. We are already witnessing rapid changes in the way foods are produced, delivered, and handled and 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 these sweeping changes, potentially putting consumers at risk. Additional funds are also 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.

New Era of Smarter Food Safety (+$51.8 million / 59 FTE)

The FY 2023 Budget provides an increase of $51.8 million above the FY 2022 Annualized CR, for a total of $58.9 million, to enable FDA to continue essential work to achieve the goals of the New Era of Smarter Food Safety[2], as well as the agency's cross-cutting Technology and Data Modernization Act Plans. The 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 attributed to FDA-regulated foods and to protect consumers from other unsafe foods. This approach builds on the modernized food safety regulatory framework created by the FSMA, including investments in animal food safety oversight.

[2] New Era of Smarter Food Safety Blueprint

New Era of Smarter Food Safety:

Data Modernization and Enhanced Technologies and Smarter Food Safety (+$35.4 million / 46 FTE)

The FY 2023 Budget includes an increase of $35.4 million above the Annualized CR, for a total of $39.0 million in FY 2023, across the Center for Food Safety and Applied Nutrition (CFSAN), Center for Veterinary Medicine (CVM), Office of Food Policy and Response (OFPR), National Center for Toxicological Research (NCTR), and Office of Regulatory Affairs (ORA) to advance goals of the New Era of Smarter Food Safety.

The Budget will enable FDA to leverage the latest science on foodborne outbreaks for human and animal food and apply new technologies and data analytics to strengthen prevention of human and animal foodborne illnesses, enable food contamination to be rapidly traced to its source, improve the efficiency and effectiveness of FDA's oversight activities, and better understand food safety challenges. With strengthened traceback capabilities, FDA will incorporate root cause data to develop commodity-specific prevention plans for human food – expanding on our experience with targeted, action-oriented initiatives (i.e. leafy greens) – and improve prevention-oriented food safety practices to better avoid identified risks, including the development of training materials for FDA inspectors and state partners. Using standardized criteria and reports for post-action activities, 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.

FDA will also focus on implementation of the FSMA Food Traceability Rule, which is scheduled to publish in late 2022. Additional funding will make it possible for FDA to conduct industry outreach and provide technical assistance to foster compliance with the rule. FDA will also conduct training for FDA, state, local, and tribal regulatory partners to understand the new rule requirements and facilitate efficient traceback and trace forward investigations during outbreak and recall events. FDA will complete development of a product tracing system to ensure that we can link tracing data to outbreak data as required by the rule and remove problematic foods from the marketplace more quickly, including complementary investments to increase traceback capabilities for animal food. 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.

The FY 2023 Budget will also strengthen data sharing and predictive analytics capabilities to better prevent foodborne illnesses. 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. FDA will also develop standards for identifying and assimilating external sources of data and information, including evaluation of best practices for cloud-based data-sharing. FDA will also expand

the use of information-sharing agreements with regulatory and public health partners, academic institutions, industry, and others, building on lessons learned from COVID-19 response efforts. FDA will develop requirements for user-friendly IT platforms to better analyze and share data with stakeholders, including industry, academia, and regulatory partners. FDA will also continue development of FDA IT systems to further support the science and risk-based standards established by the Food Safety Modernization Act.

In addition, FDA will invest in additional artificial intelligence (AI) methods to replace current manual analysis processes that are time consuming, labor-intensive, and expertise-dependent. For example, 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. With the FY 2023 Budget, FDA will further develop new predictive analytical capabilities to target violative shipments of FDA-regulated products coming across our borders. 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. These investments in predictive analytics and data sharing will improve the agency's intelligence on potentially contaminated food, enabling faster response and more efficient utilization of resources to prevent contaminated food from entering the U.S. market.

Animal Food Safety Oversight (+$16.4 million / 13 FTE)

The FY 2023 Budget requests an increase of $16.4 million, for a total of $20 million across CVM and ORA, to initiate critical work towards the goals of Domestic Mutual Reliance as a critical component of the New Era of Smarter Food Safety. Domestic mutual reliance 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.

Healthy and Safe Food for All (+$13.5 million / 26 FTE)

The FY 2023 Budget includes $13.5 million to improve health equity through nutrition and reducing exposure to harmful chemicals and toxins in food. Proper nutrition and reduced exposure to toxins is critical to ensuring that the foods consumers eat today provide for their healthier tomorrow. In FY 2023, FDA plans to build on its maternal and infant health and nutrition focus requested in the FY 2022 Budget that recognizes a child's lifelong dietary

patterns are influenced by early taste preferences. By applying an approach that integrates nutrition/diet, toxicology, and health across the lifespan, FDA can help ensure that Americans of all ages and backgrounds can reduce their risk of diet-related chronic diseases and continue to have confidence in the food supply.

With additional investments in FY 2023, FDA seeks to make gains in balancing the ongoing efforts of providing safe food with a renewed emphasis on encouraging the increased availability in the marketplace of healthy food options. To meet these goals, FDA needs better tools and greater capacity to generate and analyze real-time information on the food supply's evolving composition. The FY 2023 investments will provide essential information for understanding and addressing population exposures to various food components—both those that are helping consumers reduce their risk to diet-related chronic disease and also those that may be leading to exposures that have chronic health risks.

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

The FY 2023 Budget requests an increase of $18 million above the Annualized CR, for a total of $20.0 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, and FDA is uniquely 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.

Additionally, the U.S. has a high prevalence of obesity and nutrition-related chronic disease and 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 while also reducing dietary exposure to toxic elements.

Emerging Chemical and Toxicology Issues, Food (+$19.7 million / 40 FTE)

The FY 2023 Budget requests $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.

New funding would also support the hiring of staff to develop new compliance policies and coordinate industry compliance and increased enforcement activities related to food allergens,

update IT systems to increase regulatory oversight over cosmetics and increase scientific and regulatory capacity for dietary supplements.

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.

MEDICAL PRODUCT SAFETY (BA $2.023 BILLION / 5,671 FTE; UF $2.198 BILLION / 6,727 FTE)

The FY 2023 Budget for medical product safety and availability is $4.2 billion, an increase of $313.1 million above the FY 2022 Annualized CR. The request includes $2.0 billion for budget authority – an increase of $256.9 million compared to the FY 2022 Annualized CR – and $2.2 billion for user fees – an increase of $56.1 million compared to the FY 2022 Annualized CR.

The Budget requests an increase of $256.9 million above the FY 2022 Annualized CR for medical product safety activities. Of that amount, $113.6 million will support initiatives that advance medical product safety efforts, including $5.0 million for Premarket Animal Drug Reviews, $5.0 million for Medical Device Cybersecurity, $38 million to Advance the Goal of Ending the Opioid Crisis, $21.6 million for Device Shortages and Supply Chain, $7.5 million for Predictive Toxicology Roadmap – Guideline Studies, $5.6 million is for Drug Safety Surveillance and Oversight, $2.3 million for the CVM Medical Product Supply Chain, and $8.6 million for Data Modernization Medical Product Safety efforts.

The Budget funds FDA priorities for medical product safety and availability. FDA's Budget advances the highest priorities 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 and this Budget request takes steps to address high priority programmatic efforts.

Premarket Animal Drug Review Workload ($5.0 million / 21 FTE)

The FY 2023 Budget includes $5.0 million in new budget authority to continue to meet performance commitments, including the reduced review times negotiated as part of the Animal Generic Drug User Fee Amendment (AGDUFA) III. The number of animal drug submissions received have steadily increased over time and therefore more effort is needed to review the additional submissions within agreed upon timeframes. Meeting our performance commitments provides greater regulatory certainty and helps enable industry to 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.

Medical Device Cybersecurity (+$5.0 million / 6 FTE)

The FY 2023 Budget includes $5.5 million, an increase of $5.0 million above the FY 2022 Annualized CR, to develop a more comprehensive Cybersecurity Program for medical devices. Cybersecurity exploits are one of the most substantial threats faced by this nation, and the impact

is particularly harmful for our health care system, where vulnerabilities could compromise entire hospital systems or disrupt manufacturing of countless devices if they are impacted. The cybersecurity threats to medical devices are increasing and can involve nation states. Ultimately, these threats are of national security concern because if they go unchecked, they could cripple healthcare delivery. A funding increase to the program will allow for safer devices and will positively impact national security. The Center for Devices and Radiological Health (CDRH) has used previous funds from Congress to conduct critical activities including serving as the government lead for public private partnerships on legacy devices and vulnerability communications, as well as working to update CDRH guidance and generally supporting incident response activities associated with ongoing legacy and/or fielded device issues that can impact patient safety. As the cybersecurity exploits and other incidents continue to increase, we must also increase our vigilance and adopt a stronger posture.

Advancing the Goal of Ending the Opioid Crisis (+$38.0 million / 40 FTE)

The FY 2023 Budget FDA requests $38 million above the FY 2022 Annualized CR to support activities in the Center for Drug Evaluation and Research (CDER), ORA, and 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 hire 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 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 2023 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. This will be accomplished 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 data analytics for predictive modeling, early signal detection and monitoring, 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 for enhancing resiliency in the medical device supply chain.

Predictive Toxicology Roadmap (+$7.5 million)

The FY 2023 Budget requests $7.5 million for 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.

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

The FY 2023 Budget requests $2.3 million to enable the 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 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.

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

The FY 2023 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.

Data Modernization and Enhanced Technologies – Medical Product Safety (+$8.6 million / 6 FTE)

The FY 2023 Budget requests funding for centralized enterprise technology and data activities and program specific investments aligned with the Data Modernization and Enhanced Technology request. For Medical Product Safety, this includes three programmatic efforts:

Digital Transformation (+$2.8 million)

In FY 2023, 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 (+$900,000)

In FY 2023, FDA requests an increase of $900,000 to support the Center for Biologics Evaluation and Research (CBER) 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.

Modernizing Data Enterprise and Infrastructure (+$10.7 million / 8 FTE)

In FY 2023, 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 evolving regulatory landscape. Of the $10.7 million, $5.8 million is aligned to food safety and $4.9 million is aligned to medical product safety. 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. 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.

CROSSCUTTING (BA $199.3 MILLION / 231 FTE)

The FY 2023 Budget includes $199.3 million above the FY 2022 Annualized CR to support agency-wide crosscutting initiatives that support both Food Safety and Medical Product Safety[3]. FDA's crosscutting initiatives include critically needed investments to optimize inspectional activities and new funding to reduce animal testing through alternative methods. FDA also requests new resources to invest in core agency-wide operations including funding to address public health employee pay costs and bolster FDA's essential business functions.

FDA Capacity Building (+$59.4 million / 78 FTE)

FDA requests $59.4 million to support core operations, including recruitment of HR specialists to ramp up capacity building, updating FDA's records management policies and procedures to comply with federal requirements, providing agency-wide legal services, responding to an increase in FOIA requests, and supporting laboratory safety. In further support of these needs, FDA seeks to invest in essential services through FDA's Working Capital Fund to support agency-wide business functions. The FY 2023 Budget includes investments for the following FDA Capacity Building efforts:

Office of the Chief Counsel (OCC) (+$9.1 million / 34 FTE)

The FY 2023 Budget includes an increase of $9.1 million above the FY 2022 Annualized CR for the Office of Chief Counsel (OCC). As a regulatory agency, it is critical that all of FDA's actions are supported by our legal and regulatory authorities. Accordingly, legal staff are an integral part of our work, including medical product reviews, food safety assessments, enforcement cases, defense of agency decisions, and other high-profile matters involving multiple motivated stakeholders. FDA has identified the lack of adequate legal resources as a risk to agency activities. The FY 2023 Budget increase will support critical OCC recruitment and retention incentives, including student loan repayment for OCC attorneys.

[3] These resources are also captured under food and medical product safety totals for FY 2023.

Essential Services (+$43.7 million / 33 FTE)

The FY 2023 Budget includes $43.7 million for investments in the Essential Services. This new funding will allow FDA to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Budget will improve FDA's recruitment efforts to hire additional specialized and qualified staff such as, microbiologists, chemists, medical reviewers, and investigators, which are particularly acute among highly competitive fields.

The increased capacity will strengthen critical human capital efforts, including training, conflict prevention and resolution, anti-harassment initiatives, and employee and labor relations. These central investments will increase FDA's capacity to support Centers and Offices across the human capital portfolio. The Budget will provide expanded support for FDA's eDiscovery program, in order to support litigation, freedom of information requests, Congressional requests, and investigations inquiries. The Budget supports other vital functions, including technical engineering services to manage and oversee FDA's presence at over 360 buildings across the nation. The increase also bolsters FDA's capacity to conduct critical compliance, oversight, and quality control over the $6 billion in annual funding and $940.5 million in COVID-19 supplemental appropriations.

Office of Laboratory Safety (+$6.6 million / 11 FTE)

The FY 2023 Budget includes an increase of $6.6 million above the FY 2022 Annualized CR 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 Minority Health and Health Equity (+$4.7 million / 3 FTE)

The FY 2023 Budget includes an increase of $4.7 million above the FY 2022 Annualized CR, 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.

Public Health Employee Pay Costs (+$51.9 million)

The FY 2023 Budget includes $51.9 million in funding to partially fund anticipated increases in pay costs associated with the FY 2023 Cost of Living Adjustments (COLA), with an assumed pay increase of 4.6% for Civilian and Military FTE in FY 2023. Approximately 50% of FDA's costs, including both the budget authority discussed here and user fees, fund payroll and benefits for our employees. At the end of FY 2021, FDA's on-board strength was over 19,000 employees, or nearly 18,500 FTE, which is a growth of over 4.7% from the FY 2020 Actuals FTE levels. When program funding remains flat, but the cost of payroll increases, FDA must either reduce the number of staff hired or reduce the contracts and equipment purchases that helps the agency carry out its mission. This critical increase is needed to support and help 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.

Optimizing Inspectional Activities (+$33.8 million / 90 FTE)

The FY 2023 Budget includes $33.8 million for inspections. This initiative supports capacity building towards an advanced, highly trained staff capable of analyzing available data to increase the efficiency and productivity of our operations. Throughout FY 2020 and into FY 2021, the COVID-19 pandemic significantly impacted ORA's in-person inspectional operations, for both medical products and food safety, as well as highlighted the need for a safe and secure medical supply chain. The Budget also will support cross-agency inspection analysis and improvement projects to streamline, improve, and optimize end-to-end inspection processes and improve overall inspections operations for both Food and Medical Product inspections. With additional personnel and tools, FDA will improve its inspectional capacity and build on the efforts to keep pace with a rapidly expanding industry including medical counter measures and advanced manufacturing.

Reducing Animal Testing through Alternative Methods (+$5.0 million / 11 FTE)

The FY 2023 Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them. The New Alternative Methods Program will be centrally coordinated and managed through the Office of the Commissioner/Office of the Chief Scientist, with FDA Centers responsible for specific programmatic objectives, including expansion of capacity to qualify alternative methods and fill information gaps with applied research that will support advancement of new policy and guidance development.

The FY 2023 Budget request will allow FDA to establish a cohesive and comprehensive program that advances the development, qualification, and implementation of new alternative methods for product testing. While animal studies can be critical to evaluating safety and, at times, effectiveness, premarket animal-based assessments are time and resource intensive and do not

always fully predict/detect potential toxicities of FDA-regulated products for proposed uses in humans and animals. New alternative methods have the potential to provide both more timely and more predictive information to accelerate product development and enhance emergency preparedness for the benefit of US patients, consumers, and animals. Additionally, reducing the need for animal testing is a priority for FDA, and implementing the New Alternative Methods Program will demonstrate a clear and strong commitment from FDA to the 3Rs.

Data Modernization and Enhanced Technologies – Enterprise Technology and Data (+$44.5 million / 49 FTE)

As previously noted, the FY 2023 Budget includes an increase of $75.9 million, for a total of $82.9 million, for Data Modernization and Enhanced Technologies efforts. These funds will support FDA's plan for 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.

A central component of this effort is funding to support the agency-wide Enterprise Technology and Data request. The FY 2023 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 2023 Budget builds on these initial steps, incorporates lessons learned, and progresses FDA on a path for the modern era.

INFRASTRUCTURE AND BUILDINGS & FACILITIES (BA +$42.5 MILLION)

The FY 2023 Budget provides a budget authority increase of $42.5 million above the FY 2022 Annualized CR to ensure that FDA's offices and labs across the country and its fully integrated headquarters Campus are optimally functioning and enable FDA to carry out its mission, evaluate food safety and medical products, and respond to emergencies. This will directly support FDA's priorities by providing secure, modern, reliable, and cost-effective office and

laboratory space that empowers FDA's workforce to protect and promote the safety and health of American families.

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. Specific increases are being requested for the Other Rent & Rent Related and White Oak portions of the Infrastructure budget and the Buildings and Facilities budget, with a decrease requested for the GSA Rent portion of the Infrastructure budget.

GSA Rent (-$833,000)

The FY 2023 Budget includes $166.3 million, a decrease of $833,000 below the FY 2022 Annualized CR, to meet FDA's rent obligations. It includes estimates for rent changes associated with continuing occupancies for which renewal rents will reset to market and periods of double rent for laboratory decommissioning projects.

Other Rent & Rent-Related (+$22.8 million)

The FY 2023 Budget includes $107.1 million, an increase of $22.8 million above the FY 2022 Annualized CR, to meet FDA's fixed obligations associated with the Other Rent & Rent-Related (OR&RR) account. The OR&RR account funds rent-related charges that are not part of the GSA Rent account, including costs for operating, maintaining, and securing FDA-owned and FDA-occupied GSA facilities nationwide. Operations and maintenance costs continue to increase as FDA buildings and their equipment and systems age and require more maintenance and repairs to keep site infrastructure and facilities operational. Security costs associated with FDA buildings also continue to increase from the pressures of inflation and expanding needs.

White Oak Campus (+$2.5 million)

The FY 2023 Budget includes $48.4 million, an increase of $2.5 million above the FY 2022 Annualized CR, to support operations at FDA's White Oak Campus, infrastructure improvements above GSA-standard level, and specific support for above-standard infrastructure needs associated with the laboratory-building infrastructure, such as recommissioning and correcting identified deficiencies.

Buildings & Facilities (+$18 million)

The FY 2023 Budget includes $30.8 million, an increase of $18 million above the Annualized CR, to complete projects that will improve the condition of FDA's owned buildings and site infrastructure and meet program mission needs. This increase reflects the funding level that needs to be sustained for a minimum of 10 years to produce a reduction in FDA's backlog of maintenance and repairs sufficient to improve the condition of FDA's mission-critical, owned, site infrastructure and buildings.

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 regulate medical, food, and tobacco products. The current 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 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.

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, 2020, these actions include:

- Conducting over 28,000 retail inspections and issued more than 1,900 warning letters and civil money penalties during the COVID-19 pandemic while working to protect the health and safety of all stakeholders involved in the compliance check process

- Conducting over 230 tobacco manufacturing inspections, investigations, and Remote Regulatory Assessments (RRAs) and over 650 vape shop inspections
- Conducting investigations involving thousands of websites resulting in warning letters to manufacturers, importers, and vape shops for illegally marketing over 130 unauthorized ENDS products
- Issuing over 180 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 companies that received those warning letters have over 17 million products listed with FDA.

In light of the alarming uptick in youth use of disposable e-cigarettes revealed in the 2020 National Youth Tobacco Survey 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 ultimately through the end of that fiscal year. In FY 2021, tobacco manufacturer, vape, and retailer inspections resumed on a limited basis in areas where the spread of COVID-19 was less prevalent, increasing throughout the year.

Applications for premarket review for many e-cigarettes, cigars and other new tobacco products were required to be filed by September 9, 2020. FDA has processed submissions that cover over 8 million products under the Premarket Tobacco Product Application pathway. This includes 1.3 million products that were the subject of applications submitted after September 9, 2020. For companies that submitted timely applications, FDA generally continued 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, unless a negative action was taken by FDA on an application during that time. In addition, FDA has discretion to defer enforcement action against a particular product now that the one-year period for review has come to an end.

On August 9, 2021, FDA issued a Refuse to File (RTF) letter to JD Nova Group LLC notifying the company that their PMTAs for 4.5 million of their products do not meet the filing requirements for new tobacco products seeking marketing orders. As a result of this RTF action, the company must remove these products from the market or risk enforcement action by FDA.

On August 26, 2021, FDA issued the first marketing denial orders (MDOs) for ENDS products after determining the applications for about 55,000 flavored ENDS products lacked sufficient evidence that these products have a benefit to adult smokers sufficient to overcome the public health threat posed by the well-documented alarming levels of youth use of such products. As of November 1, 2021, FDA has issued over 340 MDOs for more than 1.2 million tobacco products. In FY 2023, 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. This additional funding will help FDA bolster compliance and enforcement

efforts for all tobacco products and expand public education campaigns and science and research programs, as it works to address substance use and to protect consumers from the dangers of tobacco use. For public education campaigns and scientific research, CTP has reallocated funds towards ENDS public education and scientific research that would have otherwise been invested toward other activities for various tobacco products, such as cigarettes. In other areas, such as the retailer inspection program, CTP utilized existing programs and funds, to include ENDS products, in addition to other regulated tobacco products. 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.

All-Purpose Table

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Foods	**3,882**	**1,110,471**	**3,882**	**1,111,237**	**4,035**	**1,231,960**	**153**	**120,723**
Budget Authority	***3,838***	***1,099,160***	***3,838***	***1,099,701***	***3,991***	***1,220,193***	***153***	***120,492***
User Fees	***44***	***11,311***	***44***	***11,536***	***44***	***11,767***	***---***	***231***
Center	1,157	344,155	1,157	344,869	1,277	420,833	120	75,964
Budget Authority	1,154	343,289	1,154	343,986	1,274	419,932	120	75,946
User Fees	3	866	3	883	3	901	---	18
Food and Feed Recall	1	253	1	258	1	263	---	5
Voluntary Qualified Importer Program	1	253	1	258	1	263	---	5
Third Party Auditor Program	1	360	1	367	1	375	---	8
Field	2,725	766,316	2,725	766,368	2,758	811,127	33	44,759
Budget Authority	2,684	755,871	2,684	755,715	2,717	800,261	33	44,546
User Fees	41	10,445	41	10,653	41	10,866	---	213
Food and Feed Recall	4	1,040	4	1,061	4	1,082	---	21
Food Reinspection	19	4,760	19	4,855	19	4,952	---	97
Voluntary Qualified Importer Program	18	4,495	18	4,584	18	4,676	---	92
Third Party Auditor Program	---	150	---	153	---	156	---	3
Human Drugs	**6,737**	**1,997,174**	**6,746**	**2,091,393**	**6,873**	**2,219,690**	**127**	**128,297**
Budget Authority	***2,083***	***689,195***	***2,083***	***689,195***	***2,210***	***790,133***	***127***	***100,938***
User Fees	***4,654***	***1,307,979***	***4,663***	***1,402,198***	***4,663***	***1,429,557***	***---***	***27,359***
Center	5,700	1,753,685	5,709	1,844,017	5,772	1,940,854	63	96,837
Budget Authority	1,324	510,226	1,324	510,226	1,387	580,931	63	70,705
User Fees	4,376	1,243,459	4,385	1,333,791	4,385	1,359,923	---	26,132
Prescription Drug (PDUFA)	2,854	800,637	2,863	878,206	2,863	895,565	---	17,359
Generic Drug (GDUFA)	1,410	404,241	1,410	419,210	1,410	427,258	---	8,048
Biosimilars (BsUFA)	110	37,928	110	35,709	110	36,420	---	711
Outsourcing Facility	2	653	2	666	2	680	---	14
Field	1,037	243,489	1,037	247,376	1,101	278,836	64	31,460
Budget Authority	759	178,969	759	178,969	823	209,202	64	30,233
User Fees	278	64,520	278	68,407	278	69,634	---	1,227
Prescription Drug (PDUFA)	43	8,707	43	9,312	43	9,498	---	186
Generic Drug (GDUFA)	226	54,096	226	57,205	226	58,209	---	1,004
Biosimilars (BsUFA)	7	1,322	7	1,487	7	1,516	---	29
Outsourcing Facility	2	395	2	403	2	411	---	8

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Biologics	**1,438**	**437,071**	**1,445**	**450,902**	**1,472**	**475,415**	**27**	**24,513**
Budget Authority	***811***	***254,138***	***811***	***254,138***	***838***	***274,917***	***27***	***20,779***
User Fees	***627***	***182,933***	***634***	***196,764***	***634***	***200,498***	***---***	***3,734***
Center	1,210	393,322	1,217	407,009	1,225	423,565	8	16,556
Budget Authority	590	212,132	590	212,132	598	224,962	8	12,830
User Fees	620	181,190	627	194,877	627	198,603	---	3,726
Prescription Drug (PDUFA)	559	164,951	566	178,620	566	182,112	---	3,492
Medical Device (MDUFA)	56	14,981	56	14,886	56	15,184	---	298
Generic Drug (GDUFA)	4	983	4	1,103	4	1,033	---	-70
Biosimilars (BsUFA)	1	275	1	268	1	274	---	6
Field	228	43,749	228	43,893	247	51,850	19	7,957
Budget Authority	221	42,006	221	42,006	240	49,955	19	7,949
User Fees	7	1,743	7	1,887	7	1,895	---	8
Prescription Drug (PDUFA)	6	1,514	6	1,649	6	1,652	---	3
Medical Device (MDUFA)	1	229	1	238	1	243	---	5
Animal Drugs and Foods	**1,042**	**245,307**	**1,007**	**245,894**	**1,090**	**300,843**	**83**	**54,949**
Budget Authority	***825***	***192,369***	***825***	***192,456***	***898***	***242,360***	***73***	***49,904***
User Fees	***217***	***52,938***	***182***	***53,438***	***192***	***58,483***	***10***	***5,045***
Center	726	175,083	691	175,591	762	211,798	71	36,207
Budget Authority	515	123,599	515	123,646	576	154,882	61	31,236
User Fees	211	51,484	176	51,945	186	56,916	10	4,971
Animal Drug (ADUFA)	138	30,117	115	28,648	115	29,185	---	537
Animal Generic Drug (AGDUFA)	73	21,250	61	23,178	71	27,610	10	4,432
Third Party Auditor Program	---	117	---	119	---	121	---	2
Field	316	70,224	316	70,303	328	89,045	12	18,742
Budget Authority	310	68,770	310	68,810	322	87,478	12	18,668
User Fees	6	1,454	6	1,493	6	1,567	---	74
Animal Drug (ADUFA)	2	390	2	393	2	401	---	8
Animal Generic Drug (AGDUFA)	1	224	1	244	1	292	---	48
Food Reinspection	3	840	3	856	3	874	---	18
Third Party Auditor Program	---	---	---	---	---	---	---	---

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Devices and Radiological Health	**2,345**	**627,664**	**2,345**	**636,136**	**2,393**	**698,245**	**48**	**62,109**
Budget Authority	***1,508***	***408,108***	***1,508***	***408,126***	***1,556***	***465,911***	***48***	***57,785***
User Fees	***837***	***219,556***	***837***	***228,010***	***837***	***232,334***	***---***	***4,324***
Center	1,839	528,784	1,839	536,869	1,871	588,374	32	51,505
Budget Authority	1,022	323,103	1,022	323,103	1,054	370,522	32	47,419
User Fees	817	205,681	817	213,766	817	217,852	---	4,086
Prescription Drug (PDUFA)	15	4,446	15	5,361	15	5,280	---	-81
Medical Device (MDUFA)	774	194,199	774	201,228	774	205,252	---	4,024
Mammography Quality Standards Act (MQSA)	28	7,036	28	7,177	28	7,320	---	143
Field	506	98,880	506	99,267	522	109,871	16	10,604
Budget Authority	486	85,005	486	85,023	502	95,389	16	10,366
User Fees	20	13,875	20	14,244	20	14,482	---	238
Medical Device (MDUFA)	11	2,368	11	2,507	11	2,510	---	3
Mammography Quality Standards Act (MQSA)	9	11,507	9	11,737	9	11,972	---	235
National Center for Toxicological Research (BA Only)	**276**	**66,712**	**276**	**66,761**	**280**	**78,956**	**4**	**12,195**
Tobacco	**1,279**	**681,513**	**1,287**	**679,944**	**1,303**	**777,165**	**16**	**97,221**
Center	**1,190**	**658,906**	**1,202**	**652,459**	**1,218**	**754,671**	**16**	**102,212**
Budget Authority	---	---	---	---	---	---	---	---
User Fees	1,190	658,906	1,202	652,459	1,218	754,671	16	102,212
Family Smoking Prevention and Tobacco Control Act	1,190	658,906	1,202	652,459	1,218	654,671	16	2,212
Expand tobacco products (Proposed)	---	---	---	---	---	100,000	---	100,000
Field	**89**	**22,607**	**85**	**27,485**	**85**	**22,494**	**---**	**-4,991**
Family Smoking Prevention and Tobacco Control Act	89	22,607	85	27,485	85	22,494	---	-4,991
FDA Headquarters	**927**	**319,572**	**925**	**319,374**	**993**	**357,616**	**68**	**38,242**
Budget Authority	514	194,951	514	194,256	580	228,063	66	33,807
User Fees	***413***	***124,621***	***411***	***125,118***	***413***	***129,553***	***2***	***4,435***
Prescription Drug (PDUFA)	215	60,354	215	59,725	215	61,423	---	1,698
Medical Device (MDUFA)	36	10,459	36	10,652	36	10,912	---	260
Generic Drug (GDUFA)	100	34,575	100	35,561	100	36,841	---	1,280
Biosimilars (BsUFA)	8	1,417	8	1,009	8	1,032	---	23
Animal Drug (ADUFA)	4	1,172	4	937	4	957	---	20
Animal Generic Drug (AGDUFA)	3	740	3	788	3	963	---	175
Family Smoking Prevention and Tobacco Control Act	43	14,485	41	14,999	43	15,949	2	950
Mammography Quality Standards Act (MQSA)	---	76	---	77	---	79	---	2
Food and Feed Recall	---	78	---	80	---	81	---	1
Food Reinspection	2	499	2	509	2	519	---	10
Voluntary Qualified Importer Program	1	288	1	294	1	300	---	6
Third Party Auditor Program	---	41	---	41	---	42	---	1
Outsourcing Facility	1	437	1	446	1	455	---	9

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
FDA White Oak Campus	---	**52,944**	---	**53,082**	---	**56,011**	---	**2,929**
Budget Authority	---	45,914	---	45,914	---	48,414	---	2,500
User Fees	---	***7,030***	---	***7,168***	---	***7,597***	---	***429***
Prescription Drug (PDUFA)	---	3,886	---	3,925	---	4,004	---	79
Medical Device (MDUFA)	---	---	---	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	---	3,144	---	3,243	---	3,593	---	350
Other Rent and Rent Related	---	**150,557**	---	**136,862**	---	**161,106**	---	**24,244**
Budget Authority	---	98,262	---	84,262	---	107,095	---	22,833
User Fees	---	***52,295***	---	***52,600***	---	***54,011***	---	***1,411***
Prescription Drug (PDUFA)	---	26,652	---	26,919	---	27,457	---	538
Medical Device (MDUFA)	---	5,344	---	5,398	---	5,506	---	108
Generic Drug (GDUFA)	---	13,338	---	13,472	---	13,741	---	269
Biosimilars (BsUFA)	---	1,092	---	1,102	---	1,125	---	23
Animal Drug (ADUFA)	---	805	---	806	---	822	---	16
Animal Generic Drug (AGDUFA)	---	269	---	272	---	274	---	2
Family Smoking Prevention and Tobacco Control Act	---	4,301	---	4,128	---	4,572	---	444
Food and Feed Recall	---	45	---	46	---	47	---	1
Food Reinspection	---	212	---	216	---	220	---	4
Voluntary Qualified Importer Program	---	177	---	180	---	184	---	4
Third Party Auditor Program	---	25	---	25	---	26	---	1
Outsourcing Facility	---	35	---	36	---	37	---	1
GSA Rental Payments	---	**221,661**	---	**237,390**	---	**238,801**	---	**1,411**
Budget Authority	---	153,119	---	167,119	---	166,286	---	-833
User Fees	---	***68,542***	---	***70,271***	---	***72,515***	---	***2,244***
Prescription Drug (PDUFA)	---	36,052	---	36,412	---	37,141	---	729
Medical Device (MDUFA)	---	8,479	---	8,564	---	8,735	---	171
Generic Drug (GDUFA)	---	12,975	---	13,105	---	13,367	---	262
Biosimilars (BsUFA)	---	460	---	465	---	474	---	9
Animal Drug (ADUFA)	---	856	---	857	---	873	---	16
Animal Generic Drug (AGDUFA)	---	314	---	316	---	320	---	4
Family Smoking Prevention and Tobacco Control Act	---	8,557	---	9,686	---	10,721	---	1,035
Food and Feed Recall	---	76	---	77	---	79	---	2
Food Reinspection	---	362	---	369	---	377	---	8
Voluntary Qualified Importer Program	---	302	---	308	---	314	---	6
Third Party Auditor Program	---	49	---	50	---	51	---	1
Outsourcing Facility	---	60	---	62	---	63	---	1

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Color Certification	37	10,469	37	10,678	37	10,891	---	213
Export Certification	26	4,886	26	4,983	26	5,083	---	100
Export Certification (Proposed)	---	---	---	---	---	4,453	---	4,453
Priority Review Vouchers (PRV) Tropical Disease	---	2,556	---	2,608	---	2,660	---	52
Priority Review Vouchers (PRV) Pediatric Disease	11	7,997	11	8,156	11	8,320	---	164
Priority Review Vouchers (PRV) Medical Countermeasures	---	2,556	---	2,608	---	2,660	---	52
Over the Counter Monograph	---	28,400	---	25,143	---	30,356	---	5,213
Food and Drug Safety -- No Year (P.L. 113-6)	---	---	---	---	---	---	---	---
Food Safety	---	---	---	---	---	---	---	---
Drug Safety	---	---	---	---	---	---	---	---
21st Century Cures (BA Only)	187	70,000	187	50,000	187	50,000	---	---
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	1,000	---	---	---	---	---	---
MCMi - No Year	---	---	---	---	---	---	---	---
Opioids - No Year	---	---	---	---	---	---	---	---
Cancer Moonshot (No-Year)	---	---	---	---	5	20,000	5	20,000
Subtotal, Salaries and Expenses	**18,187**	**6,038,510**	**18,174**	**6,133,151**	**18,705**	**6,730,231**	**531**	**597,080**
Buildings and Facilities (Budget Authority)	**---**	**12,788**	**---**	**12,788**	**---**	**30,788**	**---**	**18,000**
Total Program Level	**18,187**	**6,051,298**	**18,174**	**6,145,939**	**18,705**	**6,761,019**	**531**	**615,080**
Non-Field Activities	*13,099*	*4,297,083*	*13,090*	*4,401,125*	*13,472*	*4,841,090*	*382*	*439,965*
Field Activities	*4,901*	*1,245,265*	*4,897*	*1,254,692*	*5,041*	*1,363,223*	*144*	*108,531*
White Oak, Rent Activities, and B&F	---	*437,950*	---	*440,122*	---	*486,706*	---	*46,584*
Food and Drug Safety -- No Year	---	---	---	---	---	---	---	---
Opioids - No Year	---	---	---	---	---	---	---	---
21st Century Cures	*187*	*70,000*	*187*	*50,000*	*187*	*50,000*	---	---
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	*1,000*	---	---	---	---	---	---
Cancer Moonshot (No-Year)	---	---	---	---	*5*	*20,000*	*5*	*20,000*
User Fees:								
Current Law								
Prescription Drug (PDUFA)	*3,692*	*1,107,199*	*3,708*	*1,200,129*	*3,708*	*1,224,132*	---	*24,003*
Medical Device (MDUFA)	*878*	*236,059*	*878*	*243,473*	*878*	*248,342*	---	*4,869*
Generic Drug (GDUFA)	*1,740*	*520,208*	*1,740*	*539,656*	*1,740*	*550,449*	---	*10,793*
Biosimilars (BsUFA)	*126*	*42,494*	*126*	*40,040*	*126*	*40,841*	---	*801*
Animal Drug (ADUFA)	*144*	*33,340*	*121*	*31,641*	*121*	*32,238*	---	*597*
Animal Generic Drug (AGDUFA)	*77*	*22,797*	*65*	*24,798*	*75*	*29,459*	*10*	*4,661*
Family Smoking Prevention and Tobacco Control Act	*1,322*	*712,000*	*1,328*	*712,000*	*1,346*	*712,000*	*18*	---
Subtotal, Current Law	**7,979**	**2,674,097**	**7,966**	**2,791,737**	**7,994**	**2,837,461**	**28**	**45,724**

(Dollars in Thousands)	FY 2021 Final		FY 2022 Annualized CR		FY 2023 President's Budget		FY 2023 President's Budget +/- FY 2022 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Indefinite								
Mammography Quality Standards Act (MQSA)	*37*	*18,619*	*37*	*18,991*	*37*	*19,371*	---	*380*
Color Certification	*37*	*10,469*	*37*	*10,678*	*37*	*10,891*	---	*213*
Export Certification	*26*	*4,886*	*26*	*4,983*	*26*	*5,083*	---	*100*
Priority Review Vouchers (PRV) Tropical Disease	---	*2,556*	---	*2,608*	---	*2,660*	---	*52*
Priority Review Vouchers (PRV) Pediatric Disease	*11*	*7,997*	*11*	*8,156*	*11*	*8,320*	---	*164*
Priority Review Vouchers (PRV) Medical Countermeasures	---	*2,556*	---	*2,608*	---	*2,660*	---	*52*
Food and Feed Recall	*5*	*1,492*	*5*	*1,522*	*5*	*1,552*	---	*30*
Food Reinspection	*24*	*6,673*	*24*	*6,805*	*24*	*6,942*	---	*137*
Voluntary Qualified Importer Program	*20*	*5,515*	*20*	*5,624*	*20*	*5,737*	---	*113*
Third Party Auditor Program	*1*	*742*	*1*	*755*	*1*	*771*	---	*16*
Outsourcing Facility	*5*	*1,580*	*5*	*1,613*	*5*	*1,646*	---	*33*
Over the Counter Monograph	---	*28,400*	---	*25,143*	---	*30,356*	---	*5,213*
Subtotal, Indefinite	**166**	**91,485**	**166**	**89,486**	**166**	**95,989**	**---**	**6,503**
Proposed								
Export Certification (Proposed)	---	---	---	---	---	*4,453*	---	*4,453*
Expand tobacco products (Proposed)	---	---	---	---	---	*100,000*	---	*100,000*
Subtotal, Proposed	**---**	**---**	**---**	**---**	**---**	***104,453***	**---**	***104,453***
Total User Fees	**8,145**	**2,765,582**	**8,132**	**2,881,223**	**8,160**	**3,037,903**	**28**	**156,680**
Total Budget Authority, Pre-Transfer	**10,042**	**3,285,716**	**10,042**	**3,264,716**	**10,545**	**3,723,116**	**503**	**458,400**
BA, S&E	*9,855*	*3,201,928*	*9,855*	*3,201,928*	*10,353*	*3,622,328*	*498*	*420,400*
BA, B&F	---	*12,788*	---	*12,788*	---	*30,788*	---	*18,000*
Food and Drug Safety -- No Year								
21st Century Cures	*187*	*70,000*	*187*	*50,000*	*187*	*50,000*	---	---
Seafood Safety Studies-GP Sec. 763 (No-Year)	---	*1,000*	---	---	---	---	---	---
Opioids - No Year	---	---	---	---	---	---	---	---
Cancer Moonshot (No-Year)	---	---	---	---	*5*	*20,000*	*5*	*20,000*
Total Program Level, Pre-Transfer	**18,187**	**6,051,298**	**18,174**	**6,145,939**	**18,705**	**6,761,019**	**531**	**615,080**
HHS OIG transfer (BA Only)	**---**	**-1,500**	**---**	**-1,500**	**---**	**-1,500**	**---**	**---**
Total Budget Authority, Post-Transfer	**10,042**	**3,284,216**	**10,042**	**3,263,216**	**10,545**	**3,721,616**	**503**	**458,400**
Total User Fees	**8,145**	**2,765,582**	***8,132***	***2,881,223***	***8,160***	***3,037,903***	***28***	***156,680***
Pandemic Preparedness	**---**	**---**	**---**	**---**	**---**	**1,630,000**	**---**	**1,630,000**
Total Program Level, Post-Transfer	**18,187**	**6,049,798**	**18,174**	**6,144,439**	**18,705**	**8,389,519**	**531**	**2,245,080**
NEF	**---**	**8,000**	**---**	**---**	**---**	**42,570**	**---**	**42,570**

*FY 2021 Actuals do not include $32.05M User Fee refunds; $209.05M COVID Supplemental; $1.43M MQSA upward adjustment from prior FY; $110K Energy Saving

**FY 2021 Actual FTE figures do not include an estimated 77 reimbursable, 1 FOIA, 32 PEPFAR, 4 IDDA, and 42 COVID Supplemental.

***FY 2021 Final total reflects the reallocation from CFSAN to ORA of $500,000, which has been carried out starting in FY 2019, to better align food safety resources.

****Cancer Moonshot funding will support 15 FTE over 3years.

*****User Fees reflect August 2021 FRNs.

******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

(Dollars in Thousands)	FY 2022 Annualized CR		FY 2023 CJ																	
			Infrastructure and B & F		Enhancing Food Safety and Nutrition															
					New Era of Smarter Food Safety								Maternal and Infant Health and Nutrition		Emerging Chemical and Toxicological Issues		Healthy and Safe Food for All		Total 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	FTE	$000
Salaries and Expenses Account:																				
Foods	3,838	1,099,701	---	---	10	13,900	10	6,300	---	---	20	20,200	26	18,000	40	19,500	26	13,500	112	71,200
Center	1,154	343,986	---	---	10	7,300	10	3,550	---	---	20	10,850	26	18,000	40	19,500	26	13,500	112	61,850
Field	2,684	755,715	---	---	---	6,600	---	2,750	---	---	---	9,350	---	---	---	---	---	---	---	9,350
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	192,456	---	---	2	6,387	16	4,600	13	16,400	31	27,387	---	---	---	---	---	---	31	27,387
Center	515	123,646	---	---	2	5,787	16	4,600	5	2,300	23	12,687	---	---	---	---	---	---	23	12,687
Field	310	68,810	---	---	---	600	---	---	8	14,100	8	14,700	---	---	---	---	---	---	8	14,700
Devices and Radiological Health	1,508	408,126	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Center	1,022	323,103	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Field	486	85,023	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
National Center for Toxicological Research	276	66,761	---	---	---	---	2	1,250	---	---	2	1,250	---	---	---	150	---	---	2	1,400
FDA Headquarters	514	194,256	---	---	5	2,500	1	500	---	---	6	3,000	---	---	---	---	---	---	6	3,000
FDA White Oak Complex	---	45,914	---	2,500	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Other Rent and Rent Related	---	84,262	---	22,833	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
GSA Rental Payments	---	167,119	---	-833	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Subtotal, Salaries and Expenses Account	9,855	3,201,928	---	24,500	17	22,787	29	12,650	13	16,400	59	51,837	26	18,000	40	19,650	26	13,500	151	102,987
Buildings and Facilities Account	---	12,788	---	18,000	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Total Budget Authority, Pre-Transfer	9,855	3,214,716	---	42,500	17	22,787	29	12,650	13	16,400	59	51,837	26	18,000	40	19,650	26	13,500	151	102,987
Non-Field Activities	5,395	1,774,110	---	---	17	15,587	29	9,900	5	2,300	51	27,787	26	18,000	40	19,650	26	13,500	143	78,937
Field Activities	4,460	1,130,523	---	---	---	7,200	---	2,750	8	14,100	8	24,050	---	---	---	---	---	---	8	24,050
Rent Activities, B&F, and White Oak	---	310,083	---	42,500	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
21st Century Cures	187	50,000	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Cancer Moonshot (No-Year)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Total Budget Authority with 21st Century Cures	10,042	3,264,716	---	42,500	17	22,787	29	12,650	13	16,400	59	51,837	26	18,000	40	19,650	26	13,500	151	102,987
HHS OIG transfer	---	-1,500	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Total Budget Authority, Post-Transfer	10,042	3,263,216	---	42,500	17	22,787	29	12,650	13	16,400	59	51,837	26	18,000	40	19,650	26	13,500	151	102,987

(Dollars in Thousands)	FY 2023 CJ																	
	Advancing 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		Premarket Animal Drug Review Workload		Medical Device Cybersecurity		Total Medical Product Safety	
	FTE	$000	FTE	$000	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	21	5,000	---	---	34	12,213
Center	---	---	7	2,300	---	---	---	---	---	---	6	4,913	21	5,000	---	---	34	12,213
Field	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Devices and Radiological Health	18	21,600	---	---	---	---	---	2,000	---	---	---	2,800	---	---	6	5,000	24	31,400
Center	18	21,600	---	---	---	---	---	2,000	---	---	---	2,800	---	---	6	5,000	24	31,400
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	21	5,000	6	5,000	116	93,613
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	21	5,000	6	5,000	116	93,613
Non-Field Activities	18	21,600	7	2,300	18	5,600	15	28,000	---	7,500	6	8,613	21	5,000	6	5,000	91	83,613
Field Activities	---	---	---	---	---	---	25	10,000	---	---	---	---	---	---	---	---	25	10,000
Rent Activities, B&F, and White Oak	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
21st Century Cures	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Cancer Moonshot (No-Year)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	5	20,000
Total Budget Authority with 21st Century Cures	18	21,600	7	2,300	18	5,600	40	38,000	---	7,500	6	8,613	21	5,000	6	5,000	121	113,613
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	21	5,000	6	5,000	121	113,613

(Dollars in Thousands)	FY 2023 CJ																				FY 2023 President's Budget	
	Investing in Core Operations - Crosscutting																		Total Changes			
	DMET Enterprise Wide		Inspections		Pay Cost		Office of Minority Health and Health Equity		Capacity Building						Reducing Animal Testing Through Alternative Methods		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	FTE	$000
Salaries and Expenses Account:																						
Foods	10	9,374	20	8,483	---	19,738	---	---	---	---	---	---	9	11,023	2	674	41	49,292	153	120,492	3,991	1,220,193
Center	3	2,992	---	---	---	6,912	---	---	---	---	---	---	3	3,518	2	674	8	14,096	120	75,946	1,274	419,932
Field	7	6,382	20	8,483	---	12,826	---	---	---	---	---	---	6	7,505	---	---	33	35,196	33	44,546	2,717	800,261
Human Drugs	17	15,848	35	12,945	---	11,638	---	---	---	---	---	---	13	17,463	4	1,444	69	59,338	127	100,938	2,210	790,133
Center	15	14,043	---	---	---	8,276	---	---	---	---	---	---	11	15,342	4	1,444	30	39,105	63	70,705	1,387	580,931
Field	2	1,805	35	12,945	---	3,362	---	---	---	---	---	---	2	2,121	---	---	39	20,233	64	30,233	823	209,202
Biologics	6	4,644	18	5,751	---	4,357	---	---	---	---	---	---	3	4,741	---	386	27	19,879	27	20,779	838	274,917
Center	5	4,119	---	---	---	3,302	---	---	---	---	---	---	3	4,123	---	386	8	11,930	8	12,830	598	224,962
Field	1	525	18	5,751	---	1,055	---	---	---	---	---	---	---	618	---	---	19	7,949	19	7,949	240	49,955
Animal Drugs and Foods	2	1,968	3	1,101	---	3,967	---	---	---	---	---	---	1	2,555	2	713	8	10,304	73	49,904	898	242,360
Center	1	1,231	---	---	---	2,703	---	---	---	---	---	---	1	1,689	2	713	4	6,336	61	31,236	576	154,882
Field	1	737	3	1,101	---	1,264	---	---	---	---	---	---	---	866	---	---	4	3,968	12	18,668	322	87,478
Devices and Radiological Health	6	5,975	14	5,520	---	8,053	---	---	---	---	---	---	4	6,260	---	577	24	26,385	48	57,785	1,556	465,911
Center	5	4,820	---	---	---	5,721	---	---	---	---	---	---	3	4,901	---	577	8	16,019	32	47,419	1,054	370,522
Field	1	1,155	14	5,520	---	2,332	---	---	---	---	---	---	1	1,359	---	---	16	10,366	16	10,366	502	95,389
National Center for Toxicological Research	1	515	---	---	---	1,203	---	---	---	---	---	---	---	1,000	1	577	2	3,295	4	12,195	280	78,956
FDA Headquarters	7	6,176	---	---	---	2,944	3	4,700	11	6,600	34	9,100	3	658	2	629	60	30,807	66	33,807	580	228,063
FDA White Oak Complex	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	2,500	---	48,414
Other Rent and Rent Related	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	22,833	---	107,095
GSA Rental Payments	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-833	---	166,286
Subtotal, Salaries and Expenses Account	49	44,500	90	33,800	---	51,900	3	4,700	11	6,600	34	9,100	33	43,700	11	5,000	231	199,300	498	420,400	10,353	3,622,328
Buildings and Facilities Account	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	18,000	---	30,788
Total Budget Authority, Pre-Transfer	49	44,500	90	33,800	---	51,900	3	4,700	11	6,600	34	9,100	33	43,700	11	5,000	231	199,300	498	438,400	10,353	3,653,116
Non-Field Activities	37	33,896	---	---	---	31,061	3	4,700	11	6,600	34	9,100	24	31,231	11	5,000	120	121,588	354	284,138	5,749	2,058,248
Field Activities	12	10,604	90	33,800	---	20,839	---	---	---	---	---	---	9	12,469	---	---	111	77,712	144	111,762	4,604	1,242,285
Rent Activities, B&F, and White Oak	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	42,500	---	352,583
21st Century Cures	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	187	50,000
Cancer Moonshot (No-Year)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	5	20,000	5	20,000
Total Budget Authority with 21st Century Cures	49	44,500	90	33,800	---	51,900	3	4,700	11	6,600	34	9,100	33	43,700	11	5,000	231	199,300	503	458,400	10,545	3,723,116
HHS OIG transfer	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	-1,500
Total Budget Authority, Post-Transfer	49	44,500	90	33,800	---	51,900	3	4,700	11	6,600	34	9,100	33	43,700	11	5,000	231	199,300	503	458,400	10,545	3,721,616

MAJOR ACTIVITIES TABLE

Major Activities																								
(Dollars in Thousands)	FY 2021 Final						FY 2022 Annualized CR						FY 2023 President's Budget						FY 2023 President's Budget +/- FY 2022 Annualized CR					
	Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total	
Programs	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**
Budget Authority:																								
Foods	**3,838**	**1,099,160**	**---**	**---**	**3,838**	**1,099,160**	**3,838**	**1,099,701**	**---**	**---**	**3,838**	**1,099,701**	**3,991**	**1,220,193**	**---**	**---**	**3,991**	**1,220,193**	**153**	**120,492**	**---**	**---**	**153**	**120,492**
Center	1,154	343,289	---	---	1,154	343,289	1,154	343,986	---	---	1,154	343,986	1,274	419,932	---	---	1,274	419,932	120	75,946	---	---	120	75,946
Field	2,684	755,871	---	---	2,684	755,871	2,684	755,715	---	---	2,684	755,715	2,717	800,261	---	---	2,717	800,261	33	44,546	---	---	33	44,546
Human Drugs	**---**	**---**	**2,083**	**689,195**	**2,083**	**689,195**	**---**	**---**	**2,083**	**689,195**	**2,083**	**689,195**	**---**	**---**	**2,210**	**790,133**	**2,210**	**790,133**	**---**	**---**	**127**	**100,938**	**127**	**100,938**
Center	---	---	1,324	510,226	1,324	510,226	---	---	1,324	510,226	1,324	510,226	---	---	1,387	580,931	1,387	580,931	---	---	63	70,705	63	70,705
Field	---	---	759	178,969	759	178,969	---	---	759	178,969	759	178,969	---	---	823	209,202	823	209,202	---	---	64	30,233	64	30,233
Biologics	**---**	**---**	**811**	**254,138**	**811**	**254,138**	**---**	**---**	**811**	**254,138**	**811**	**254,138**	**---**	**---**	**838**	**274,917**	**838**	**274,917**	**---**	**---**	**27**	**20,779**	**27**	**20,779**
Center	---	---	590	212,132	590	212,132	---	---	590	212,132	590	212,132	---	---	598	224,962	598	224,962	---	---	8	12,830	8	12,830
Field	---	---	221	42,006	221	42,006	---	---	221	42,006	221	42,006	---	---	240	49,955	240	49,955	---	---	19	7,949	19	7,949
Animal Drugs and Foods	**618**	**140,003**	**207**	**52,366**	**825**	**192,369**	**618**	**140,072**	**207**	**52,384**	**825**	**192,456**	**655**	**174,919**	**243**	**67,441**	**898**	**242,360**	**37**	**34,847**	**36**	**15,057**	**73**	**49,904**
Center	322	74,146	193	49,453	515	123,599	322	74,176	193	49,470	515	123,646	348	90,775	228	64,107	576	154,882	26	16,599	35	14,637	61	31,236
Field	296	65,857	14	2,913	310	68,770	296	65,896	14	2,914	310	68,810	307	84,144	15	3,334	322	87,478	11	18,248	1	420	12	18,668
Devices and Radiological Health	**---**	**---**	**1,508**	**408,108**	**1,508**	**408,108**	**---**	**---**	**1,508**	**408,126**	**1,508**	**408,126**	**---**	**---**	**1,556**	**465,911**	**1,556**	**465,911**	**---**	**---**	**48**	**57,785**	**48**	**57,785**
Center	---	---	1,022	323,103	1,022	323,103	---	---	1,022	323,103	1,022	323,103	---	---	1,054	370,522	1,054	370,522	---	---	32	47,419	32	47,419
Field	---	---	486	85,005	486	85,005	---	---	486	85,023	486	85,023	---	---	502	95,389	502	95,389	---	---	16	10,366	16	10,366
National Center for Toxicological Research	**21**	**5,087**	**255**	**61,625**	**276**	**66,712**	**21**	**5,091**	**255**	**61,670**	**276**	**66,761**	**23**	**6,656**	**257**	**72,300**	**280**	**78,956**	**2**	**1,565**	**2**	**10,630**	**4**	**12,195**
FDA Headquarters	**179**	**56,239**	**335**	**119,712**	**514**	**194,951**	**179**	**56,011**	**335**	**119,245**	**514**	**194,256**	**205**	**68,927**	**375**	**140,136**	**580**	**228,063**	**26**	**12,916**	**40**	**20,891**	**66**	**33,807**
FDA White Oak Campus	**---**	**---**	**---**	**---**	**---**	**45,914**	**---**	**---**	**---**	**---**	**---**	**45,914**	**---**	**---**	**---**	**---**	**---**	**48,414**	**---**	**---**	**---**	**---**	**---**	**2,500**
Other Rent and Rent Related	**---**	**49,577**	**---**	**48,685**	**---**	**98,262**	**---**	**42,513**	**---**	**41,749**	**---**	**84,262**	**---**	**54,033**	**---**	**53,062**	**---**	**107,095**	**---**	**11,520**	**---**	**11,313**	**---**	**22,833**
GSA Rental Payments	**---**	**71,500**	**---**	**81,619**	**---**	**153,119**	**---**	**78,037**	**---**	**89,082**	**---**	**167,119**	**---**	**77,648**	**---**	**88,638**	**---**	**166,286**	**---**	**-389**	**---**	**-444**	**---**	**-833**
SUBTOTAL, BA Salaries and Expenses	**4,656**	**1,421,566**	**5,199**	**1,715,448**	**9,855**	**3,201,928**	**4,656**	**1,421,425**	**5,199**	**1,715,589**	**9,855**	**3,201,928**	**4,874**	**1,602,376**	**5,479**	**1,952,538**	**10,353**	**3,622,328**	**218**	**180,951**	**280**	**236,949**	**498**	**420,400**
Building and Facilities	**---**	**---**	**---**	**---**	**---**	**12,788**	**---**	**---**	**---**	**---**	**---**	**12,788**	**---**	**---**	**---**	**---**	**---**	**30,788**	**---**	**---**	**---**	**---**	**---**	**18,000**
Non-Field Activities	**1,676**	**478,761**	**3,719**	**1,276,251**	**5,395**	**1,774,012**	**1,676**	**479,264**	**3,719**	**1,275,846**	**5,395**	**1,774,110**	**1,850**	**586,290**	**3,899**	**1,452,958**	**5,749**	**2,058,248**	**174**	**107,026**	**180**	**177,112**	**354**	**284,138**
Field Activities	**2,980**	**821,728**	**1,480**	**308,893**	**4,460**	**1,130,621**	**2,980**	**821,611**	**1,480**	**308,912**	**4,460**	**1,130,523**	**3,024**	**884,405**	**1,580**	**357,880**	**4,604**	**1,242,285**	**44**	**62,794**	**100**	**48,968**	**144**	**111,762**
White Oak, Rent Activities, and B&F	**---**	**121,077**	**---**	**130,304**	**---**	**310,083**	**---**	**120,550**	**---**	**130,831**	**---**	**310,083**	**---**	**131,681**	**---**	**141,700**	**---**	**352,583**	**---**	**11,131**	**---**	**10,869**	**---**	**42,500**
21st Century Cures	**---**	**---**	**187**	**70,000**	**187**	**70,000**	**---**	**---**	**187**	**50,000**	**187**	**50,000**	**---**	**---**	**187**	**50,000**	**187**	**50,000**	**---**	**---**	**---**	**---**	**---**	**---**
Seafood Safety Studies-GP Sec. 763 (No-Year)	**---**	**1,000**	**---**	**---**	**---**	**1,000**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**
Cancer Moonshot (No-Year)							**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**5**	**20,000**	**5**	**20,000**	**---**	**---**	**5**	**20,000**	**5**	**20,000**
Total BA	**4,656**	**1,422,566**	**5,386**	**1,785,448**	**10,042**	**3,285,716**	**4,656**	**1,421,425**	**5,386**	**1,765,589**	**10,042**	**3,264,716**	**4,874**	**1,602,376**	**5,671**	**2,022,538**	**10,545**	**3,723,116**	**218**	**180,951**	**285**	**256,949**	**503**	**458,400**
Total BA, Pre-Transfer	**4,656**	**1,422,566**	**5,386**	**1,785,448**	**10,042**	**3,285,716**	**4,656**	**1,421,425**	**5,386**	**1,765,589**	**10,042**	**3,264,716**	**4,874**	**1,602,376**	**5,671**	**2,022,538**	**10,545**	**3,723,116**	**218**	**180,951**	**285**	**256,949**	**503**	**458,400**

Major Activities

(Dollars in Thousands)	FY 2021 Final						FY 2022 Annualized CR						FY 2023 President's Budget						FY 2023 President's Budget +/- FY 2022 Annualized CR					
	Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total	
Total User Fees	**50**	**16,425**	**6,736**	**2,026,688**	**8,145**	**2,765,582**	**50**	**16,749**	**6,717**	**2,141,796**	**8,132**	**2,881,223**	**50**	**17,086**	**6,727**	**2,197,926**	**8,160**	**3,037,903**	**---**	**337**	**10**	**56,130**	**28**	**156,680**
Current Law																								
Prescription Drug (PDUFA)	---	---	3,692	1,107,199	3,692	1,107,199	---	---	3,708	1,200,129	**3,708**	**1,200,129**	---	---	3,708	1,224,132	**3,708**	**1,224,132**	---	---	---	**24,003**	**---**	**24,003**
Medical Device (MDUFA)	---	---	878	236,059	878	236,059	---	---	878	243,473	**878**	**243,473**	---	---	878	248,342	**878**	**248,342**	---	---	---	**4,869**	**---**	**4,869**
Generic Drug (GDUFA)	---	---	1,740	520,208	1,740	520,208	---	---	1,740	539,656	**1,740**	**539,656**	---	---	1,740	550,449	**1,740**	**550,449**	---	---	---	**10,793**	**---**	**10,793**
Biosimilars (BsUFA)	---	---	126	42,494	126	42,494	---	---	126	40,040	**126**	**40,040**	---	---	126	40,841	**126**	**40,841**	---	---	---	**801**	**---**	**801**
Animal Drug (ADUFA)	---	---	144	33,340	144	33,340	---	---	121	31,641	**121**	**31,641**	---	---	121	32,238	**121**	**32,238**	---	---	---	**597**	**---**	**597**
Animal Generic Drug (AGDUFA)	---	---	77	22,797	77	22,797	---	---	65	24,798	**65**	**24,798**	---	---	75	29,459	**75**	**29,459**	---	---	10	**4,661**	**10**	**4,661**
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	1,322	712,000	---	---	---	---	**1,328**	**712,000**	---	---	---	---	**1,346**	**712,000**	---	---	---	---	**18**	**---**
Mammography Quality Standards Act (MQSA)	---	---	37	18,619	37	18,619	---	---	37	18,991	**37**	**18,991**	---	---	37	19,371	**37**	**19,371**	---	---	---	**380**	**---**	**380**
Color Certification	---	---	---	---	37	10,469	---	---	---	---	**37**	**10,678**	---	---	---	---	**37**	**10,891**	---	---	---	---	**---**	**213**
Export Certification	---	2,003	26	2,883	26	4,886	---	2,043	26	2,940	**26**	**4,983**	---	2,084	26	2,999	**26**	**5,083**	---	41	---	**59**	**---**	**100**
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	2,556	---	2,556	---	---	---	2,608	**---**	**2,608**	---	---	---	2,660	**---**	**2,660**	---	---	---	**52**	**---**	**52**
Priority Review Vouchers (PRV) Pediatric Disease	---	---	11	7,997	11	7,997	---	---	11	8,156	**11**	**8,156**	---	---	11	8,320	**11**	**8,320**	---	---	---	**164**	**---**	**164**
Priority Review Vouchers (PRV) Medical Countermeasures			---	2,556	---	2,556			---	2,608	**---**	**2,608**			---	2,660	**---**	**2,660**	---	---	---	**52**	**---**	**52**
Food and Feed Recall	5	1,492	---	---	5	1,492	5	1,522	---	---	**5**	**1,522**	5	1,552	---	---	**5**	**1,552**	---	30	---	**---**	**---**	**30**
Food Reinspection	24	6,673	---	---	24	6,673	24	6,805	---	---	**24**	**6,805**	24	6,942	---	---	**24**	**6,942**	---	137	---	**---**	**---**	**137**
Voluntary Qualified Importer Program	20	5,515	---	---	20	5,515	20	5,624	---	---	**20**	**5,624**	20	5,737	---	---	**20**	**5,737**	---	113	---	**---**	**---**	**113**
Third Party Auditor Program	1	742	---	---	1	742	1	755	---	---	**1**	**755**	1	771	---	---	**1**	**771**	---	16	---	**---**	**---**	**16**
Outsourcing Facility	---	---	5	1,580	5	1,580			5	1,613	**5**	**1,613**			5	1,646	**5**	**1,646**	---	---	---	**33**	**---**	**33**
Over the Counter Monograph	---	---	---	28,400	---	28,400	---	---	---	25,143	**---**	**25,143**	---	---	---	30,356	**---**	**30,356**	---	---	---	**5,213**	**---**	**5,213**
Proposed					---	---					**---**	**---**					**---**	**---**	---	---	---	**---**	**---**	**---**
Export Certification (Proposed)	---	---	---	---	---	---	---	---	---	---	**---**	**---**	---	---	---	4,453	**---**	**4,453**	---	---	---	**4,453**	**---**	**4,453**
Expand Tobacco Products (Proposed)	---	---	---	---	---	---	---	---	---	---	**---**	**---**	---	---	---	---	**---**	**100,000**	---	---	---	**---**	**---**	**100,000**
Food and Feed additive user fee (Proposed)	---	---	---	---	---	---	---	---	---	---	**---**	**---**	---	---	---	---	**---**	**---**	---	---	---	**---**	**---**	**---**
Cosmetics (Proposed)	---	---	---	---	---	---	---	---	---	---	**---**	**---**	---	---	---	---	**---**	**---**	---	---	---	**---**	**---**	**---**
Total Program Level, Pre-Transfer	**4,706**	**1,438,991**	**12,122**	**3,812,136**	**18,187**	**6,051,298**	**4,706**	**1,438,174**	**12,103**	**3,907,385**	**18,174**	**6,145,939**	**4,924**	**1,619,462**	**12,398**	**4,220,464**	**18,705**	**6,761,019**	**218**	**181,288**	**295**	**313,079**	**531**	**615,080**
HHS OIG transfer	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**-1,500**	**---**	**---**	**---**	**---**	**---**	**---**
Total BA, Post-Transfer	**4,656**	**1,422,566**	**5,386**	**1,785,448**	**10,042**	**3,284,216**	**4,656**	**1,421,425**	**5,386**	**1,765,589**	**10,042**	**3,263,216**	**4,874**	**1,602,376**	**5,671**	**2,022,538**	**10,545**	**3,721,616**	**218**	**180,951**	**285**	**256,949**	**503**	**458,400**
Total Program Level, Post-Transfer	**4,706**	**1,438,991**	**12,122**	**3,812,136**	**18,187**	**6,049,798**	**4,706**	**1,438,174**	**12,103**	**3,907,385**	**18,174**	**6,144,439**	**4,924**	**1,619,462**	**12,398**	**4,220,464**	**18,705**	**6,759,519**	**218**	**181,288**	**295**	**313,079**	**531**	**615,080**

*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

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

BUDGET EXHIBITS

COVID-19 SUPPLEMENTAL FUNDING

Food and Drug Administration
FY 2023 COVID-19 Supplemental Funding
(Dollars in thousands)

COVID-19 Supplemental	Appropriation
Coronavirus Preparedness and Response Supplemental Appropriations Act (P.L. 116-123)	61,000
Coronavirus Aid, Relief, and Economic Security (CARES) Act (P.L. 116-136)	80,000
Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139)/1	22,000
Consolidated Appropriations Act (P.L. 116-260)	55,000
American Rescue Plan Act of 2021, (P.L. 117-2)/2	722,500
Total	**940,500**

1/Provided via direct transfer from HHS.
2/PL 117-2 provided $500M to FDA, and $222.5M was provided via an IDDA from HHS.

APPROPRIATION LANGUAGE

Salaries and Expenses (Including Transfers of Funds)

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; [$6,250,157,000] *$4,416,025,000*: *Provided*, That of the amount provided under this heading, [$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; $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; $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; $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; $33,836,000] *$32,238,000* 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; [$23,137,000] *$29,459,000* shall be derived from generic new animal drug user fees authorized by 21 U.S.C. 379j–21, and shall be credited to this account and remain available until expended; $712,000,000 shall be derived from tobacco product user fees authorized by 21 U.S.C. 387s, and shall be credited to this account and remain available until expended: *Provided further*, That in addition to and notwithstanding any other provision under this heading, amounts collected for [prescription drug user fees, medical device user fees, human generic drug user fees, biosimilar biological product user fees,] animal drug user fees, and generic new animal drug user fees that exceed the respective fiscal year [2021] *2023* 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] *2023* including any such fees collected prior to fiscal year [2021] *2023* but credited for fiscal year [2021] *2023*, shall be subject to the fiscal year [2021] *2023* limitations: *Provided further*, That the Secretary may accept payment during fiscal year [2021] *2023* of user fees specified under this heading and authorized for fiscal year [2022] *2024*, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year [2022] *2024* for which the Secretary accepts payment in fiscal year [2021] *2023* 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 under this heading, $20,000,000 shall be available until September 30, 2025, for the Oncology Center of Excellence to develop and review research, advance regulatory policy, support clinical review of submissions to the Food and Drug Administration related to medical products intended to diagnose or treat cancer, and conduct education and outreach partnerships, in addition to any*

other amounts available for such purposes: 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 Ser vices—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 notification to 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), medical countermeasure priority review voucher user fees authorized by 21 U.S.C. 360bbb–4a, and fees relating to over-the-counter monograph drugs authorized by 21 U.S.C. 379j–72 shall be credited to this account, to remain available until expended.

Salaries and Expenses

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.

In addition, contingent upon the enactment of authorizing legislation, the Secretary shall charge a fee for prescription drug review activities, medical device review activities, biosimilar biological products review activities, and human generic drugs review activities: Provided, That fees of $1,224,132,000 for prescription drug reviews shall be credited to this account and remain available until expended; fees of $248,342,000 for medical device reviews shall be credited to this account and remain available until expended; fees of $550,449,000 for human generic drug reviews shall be credited to this account and remain available until expended; and fees of $40,841,000 for biosimilar biological product reviews shall be credited to this ac-count 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, biosimilar biological product user fees, and human generic drug user fees that exceed the respective fiscal year 2023 limitations are appropriated and shall be credited to this account and remain available until expended: Provided further, That fees derived from prescription drug reviews, medical device reviews, biosimilar biological products reviews, and

human generic drugs reviews for fiscal year 2023 received during fiscal year 2023, including any such fees assessed prior to fiscal year 2023 but credited for fiscal year 2023, shall be subject to the fiscal year 2023 limitations: Provided further, That the Secretary may accept payment during fiscal year 2023 of user fees specified in this paragraph and authorized for fiscal year 2024, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2024 for which the Secretary accepts payment in fiscal year 2023 shall not be included in amounts in this paragraph.

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, $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", $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.

FY 2023 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 [2022] *2023*; 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
Prescription Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for prescription drugs. The additional resources are estimated at $1,224,132,000. This will strengthen and improve the process for the review of human drugs and improve risk management for drugs
Medical Device User Fee	The Administration will propose legislation to allow FDA to collect fees for medical devices. The additional resources are estimated at $248,342,000. This will strengthen the review processes and improve the ability to meet performance goals for the medical device program.
Generic Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for generic drugs. The additional resources are estimated at $550,449,000. This will help bring timely review for human generic drug applications and reduce the backlog of human generic drug
Biosimilar User Fee	The Administration will propose legislation to allow FDA to collect fees for biosimilars. The additional resources are estimated at $40,841,000. This provides a mechanism and structure for the collection of development-phase user fees to support FDA's biosimilar review program activities.
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 $9,536,000. This proposal, and the increased certification fee ceiling it promotes, is necessary to ensure that FDA can efficiently implement the export certification program, while ensuring that other public health programs do not suffer.
Tobacco Control Act Fee Increase	The Administration will propose 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.

AMOUNTS AVAILABLE FOR OBLIGATION

(dollars in thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget
General Fund Discretionary Appropriation:			
Appropriation	3,284,216	3,263,216	3,721,616
Coronavirus Preparedness and Responses Supplemental Appropriations Act (P.L. 116-123)	---	---	---
Coronavirus Aid, Relief, and Economic Security Act (P.L. 116-136)	---	---	---
Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139)	---	---	---
Consolidated Appropriations Act (P.L. 116-260)	55,000	---	---
Total Discretionary Appropriation	**3,339,216**	**3,263,216**	**3,721,616**
Mandatory Appropriation:			
CRADA	2,000	2,000	2,000
American Rescue Plan Act of 2021 (P.L. 117-2)	500,000	222,500	---
Pandemic Preparedness Package	---	---	1,630,000
Total Mandatory Appropriation	**502,000**	**224,500**	**1,632,000**
Offsetting Collections:			
Non-Federal Sources:	2,765,582	2,881,223	3,037,903
Total Offsetting Collections	**2,765,582**	**2,881,223**	**3,037,903**
Total Obligations	**6,606,798**	**6,368,939**	**8,391,519**

*FY 2021, FY 2022 and FY 2023 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

Appropriation Account Title
Summary of Changes
(Dollars in millions)

FY 2022 CR	
Total estimated budget authority	$3,263.216
(Obligations)	
FY 2023 President's Budget	
Total estimated budget authority	$3,721.616
(Obligations)	
Net Change	+$458.400

	FY 2022 CR		FY 2023 President's Budget 1/		FY 2023 +/- FY 2022	
	FTE	BA	FTE	BA	FTE	BA
Increases:						
Built-in:						
Annualization of 2021 commissioned corps pay increase	--	--	--	$3.510	--	+$3.510
Annualization of 2021 civilian pay increase	--	--	--	$48.390	--	+$48.390
Subtotal, Built-in Increases	**--**	**--**	**--**	**$51.900**	**--**	**+$51.900**
Infrastructure and Buildings & Facilities	--	$310.083	--	$352.583	--	+$42.500
Food Safety						
Maternal and Infant Health and Nutrition	--	--	26	$18.000	+26	+$18.000
Emerging Chemical and Toxicological Issues	--	--	40	$19.650	+40	+$19.650
Healthy and Safe Food for All	--	--	26	$13.500	+26	+$13.500
New Era						
DMET Smarter Food Safety	--	--	17	$22.787	+17	+$22.787
Smarter Food Safety	--	--	29	$12.650	+29	+$12.650
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
Advancing the Goal of Ending the Opioid Crisis	14	$75.001	54	$113.001	+40	+$38.000
Predictive Toxicology Roadmap	--	--	--	$7.500	--	+$7.500
DMET Medical Product Safety	--	--	6	$8.613	+6	+$8.613
Premarket Animal Drug Review Workload	--	--	21	$5.000	+21	+$5.000
Medical Device Cybersecurity	--	--	6	$5.000	+6	+$5.000
White House Cancer Moonshot	--	--	5	$20.000	+5	+$20.000
Crosscutting						
DMET Enterprise -Wide	--	--	49	$44.500	+49	+$44.500
Inspections	--	--	90	$33.800	+90	+$33.800
Office of Minority Health and Health Equity	--	--	3	$4.700	+3	+$4.700
Reducing Animal Testing Through Alternative Methods			11	$5.000	+11	+$5.000
Capacity Building:					--	--
Laboratory Safety	--	--	11	$6.600	+11	+$6.600
Office of the Chief Counsel	--	--	34	$9.100	+34	+$9.100
Essential Services	--	--	33	$43.700	+33	+$43.700
Subtotal, Program Increases	**14**	**$385.084**	**517**	**$791.584**	**+503**	**+$406.500**
Total Increases	**14**	**$385.084**	**517**	**$843.484**	**+503**	**+$458.400**
Decreases:						
Subtotal, Program Decreases	**--**	**--**	**--**	**--**	**--**	**--**
Total Decreases	**--**	**--**	**--**	**--**	**--**	**--**
Net Change	**14**	**$385.084**	**517**	**$843.484**	**+503**	**+$458.400**

1/ The FY 2023 President's Budget also includes $156.9 million in user fee increases. Within this amount, $100.0 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.

APPROPRIATIONS HISTORY

Salaries and Expenses

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation*:				
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 /4				
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				
Base	6,343,805,000	6,207,066,000	6,151,625,000	---
Supplemental #6 (P.L. 117-2)	---	---	---	222,500,000
FY 2023				
Base	6,490,145,000			
Pandemic Preparedness Package	1,630,000,000			

* Excludes Indefinite user fees.

1/ 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, $50 million for FY 2022, and $50 million for FY 2023.

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

5/ The Enacted levels 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.

6/ FY 2023 Budget Estimate to Congress does not include $20 million for Cancer Moonshot.

Buildings and Facilities

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation:				
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	21,788,000	15,288,000	---
FY 2023	30,788,000			

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

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget
Salaries and Expenses Account:			
Foods	**1,099,160**	**1,099,701**	**1,220,193**
Center	343,789	343,986	419,932
Field	755,371	755,715	800,261
Human Drugs	**689,195**	**689,195**	**790,133**
Center	510,226	510,226	580,931
Field	178,969	178,969	209,202
Biologics	**254,138**	**254,138**	**274,917**
Center	212,132	212,132	224,962
Field	42,006	42,006	49,955
Animal Drugs and Feeds	**192,369**	**192,456**	**242,360**
Center	123,599	123,646	154,882
Field	68,770	68,810	87,478
Devices and Radiological Health	**408,108**	**408,126**	**465,911**
Center	323,103	323,103	370,522
Field	85,005	85,023	95,389
National Center for Toxicological Research	**66,712**	**66,761**	**78,956**
FDA Headquarters	**194,951**	**194,256**	**228,063**
FDA White Oak Consolidation	**45,914**	**45,914**	**48,414**
Other Rent and Rent Related	**98,262**	**84,262**	**107,095**
GSA Rental Payments	**153,119**	**167,119**	**166,286**
Subtotal, Salaries and Expenses Account	**3,201,928**	**3,201,928**	**3,622,328**
Food and Drug Safety -- No Year (P.L. 113-6)	**---**	**---**	**---**
Food Safety	---	---	---
Drug Safety	---	---	---
21st Century Cures	**70,000**	**50,000**	**50,000**
Seafood Safety Studies-GP Sec. 763 (No Year)	**1,000**	**---**	**---**
Cancer Moonshot	**---**	**---**	**20,000**
Opioids - No Year	**---**	**---**	**---**
Buildings and Facilities Account	**12,788**	**12,788**	**30,788**
Total Budget Authority	**3,285,716**	**3,264,716**	**3,723,116**
HHS OIG Transfer	**-1,500**	**-1,500**	**-1,500**
Total Budget Authority, Post-Transfer	**3,284,216**	**3,263,216**	**3,721,616**
FTE	**10,042**	**10,042**	**10,545**

* FTE figures do not include an estimated 77 reimbursable, 1 FOIA and 32 PEPFAR, 4 IDDA and 42 COVID Supplemental.

LEGISLATIVE PROPOSALS

Amend the 180-Day Exclusivity Provisions to Encourage Timely Marketing of First Generics

In practice, 180-day patent challenge exclusivity is not operating as expected to encourage early generic entry, because this exclusivity is often "parked" by first applicants who either receive approval but do not begin marketing for extended periods of time following approval, or by first applicants who delay receiving final approval of their ANDAs for extended periods of time. This proposal would substantially increase the likelihood that generic versions of patent-protected drugs will come into the market in a timely fashion, and that multiple versions of generic products will be approved quickly (leading to significant cost savings). FDA is proposing to amend sections 505(j)(5)(B)(iv) and (D)(i)-(iii) of the FD&C Act, which govern the 180-day patent challenge exclusivity provisions, to specify that FDA can approve subsequent applications unless a first applicant begins commercial marketing of the drug, at which point approval of subsequent applications would be blocked by 180 days, ensuring that the exclusivity actually lasts 180 days (i.e., from the date of first commercial marketing by a first applicant until 180 days later) rather than for multiple years, as can occur under current law.

Ensuring Feasibility and Timeliness of Confirmatory Studies and Enhancing Withdrawal Procedures for Prescription Drugs Approved through Accelerated Approval

The FD&C Act does not provide FDA with easily implementable legal authorities to help target the problem of accelerated approval confirmatory studies that progress too slowly. A statutory provision would help provide greater assurance at the time of a drug product's accelerated approval that the confirmatory study will progress in a timely manner, and reap high-quality, interpretable results. Enhancing the timeliness and quality of confirmatory studies will help support FDA's regulatory decision-making for drugs approved through the accelerated approval pathway and minimize the time that a product is marketed based on accelerated approval before its clinical benefit can be confirmed. To this end, FDA is seeking to amend the accelerated approval provisions of the FD&C Act to 1) revise section 506(c)(2)(A) of the FD&C Act such that FDA may require, as a condition of a drug product application's acceptance for filing, or as a condition of a drug product's receipt of accelerated approval, that a drug sponsor must first demonstrate that a proposed post-approval (i.e., confirmatory) study is adequately designed to verify and describe clinical benefit and can be completed in a timely manner; and 2) revise section 506(c)(3) so that FDA can follow its dispute resolution procedures for drug applications when withdrawing a drug product's accelerated approval. FDA is also proposing a technical fix to 3) revise the withdrawal standard at FD&C Act 506(c)(3)(C) so that it mirrors the analogous withdrawal standard set forth in section 505(e) for drugs with traditional approvals.

Authority to Require Destruction of Imported Products that Pose a Significant Public Health Risk

FDA is requesting to revise section 801 of the FD&C Act to give FDA the authority to require an owner or consignee to destroy any FDA-regulated product(s) that has been refused and presents a significant public health concern, thus removing their option to export such product under current section 801(a). FDA believes this new authority would prevent the potential re-importation of such products and would deter owners and consignees from offering products they know to pose a significant public health risk for import into the U.S. FDA also believes this

authority would increase efficiency when Customs and Border Protection (CBP) seizes an FDA-regulated product. Under current practice, when CBP seizes an FDA-regulated product, an FDA violation is used to support the seizure. CBP then consults with FDA to confirm that the product seized violates the FD&C or PHS Acts and/or FDA regulations. Additionally, if the seizure is successful, the government will likely end up paying for the destruction. Under this proposal, FDA would order the destruction based on the agency's admissibility review and evaluation of the significant public health concern presented by the products offered for import, thereby reducing the need for CBP consultations with FDA. Moreover, the importer of record would be required to pay the destruction costs up front so FDA and CBP do not have to file legal action to recoup the destruction costs.

Expansion of FDA Tools to Provide Oversight of FDA-Regulated Products

FDA's authority to conduct remote regulatory assessments is limited to requests for records and other information in advance or in lieu of drug inspections and FDA currently lacks authority to require any establishment to participate in remote interactive evaluations. The agency relies on voluntary participation for remote regulatory assessments of non-drug establishments but reliance on voluntary requests is not sufficient to achieve effective and efficient oversight, as firms can refuse to provide records or other information in advance of or in lieu of an inspection or to participate in remote regulatory assessments. This proposal would expand FDA's authority to request records or other information in advance of or in lieu of inspections to include all FDA-regulated products by revising section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to explicitly include medical device, food, tobacco product, and cosmetic establishments, and to clarify applicability for biomedical research monitoring (BIMO) inspections. Additionally, this proposal would add explicit authority to conduct remote regulatory assessments with establishments, which may include remote interactive evaluations such as livestreaming video of operations, teleconferences, and screen sharing, so FDA may interact virtually with an establishment and assess its compliance with applicable laws and regulations. This proposal will promote regulatory compliance and help to protect the public health, particularly during a public health emergency like the COVID-19 pandemic where in-person inspections and investigations were limited, by allowing FDA to conduct certain oversight activities prior to arriving for or instead of an inspection, thus improving the efficiency of FDA resources and reducing FDA's on-site inspectional time, and by allowing the FDA to assess conditions at a facility without going onsite when an in-person visit is not feasible or deemed necessary by FDA.

Medical Device Cybersecurity

Currently there is no statutory requirement (pre- or post-market) that expressly requires medical device manufacturers to address cybersecurity, yet cybersecurity incidents put patients at great risk, and also have the potential to cause supply chain disruptions that can cripple our health care system. This proposal would advance medical device safety by explicitly requiring that medical device manufacturers design cybersecurity into their devices and by ensuring that FDA and the public have certain information about device cybersecurity. Specifically, FDA seeks to have express authority to require: that premarket submissions to FDA include evidence demonstrating reasonable assurance of the device's safety and effectiveness for purposes of cybersecurity; that marketed devices demonstrate a reasonable assurance of the device's safety and effectiveness for purposes of cybersecurity; that devices have the capability to be updated and patched in a timely

manner; that manufacturers provide a device Software Bill of Materials (SBOM) with their devices so users know which components of their devices are or may be subject to cyber threats; and that device manufacturers publicly disclose when they learn of a cybersecurity vulnerability so users know when a device may be vulnerable, and to provide direction to users to reduce their risk. These authorities are critical, as FDA has already seen and responded to several ransomware and other malware incidents within the health care sector. Stronger cybersecurity protections are necessary to ensure we remain prepared to protect patients and our health care workers on the front lines. Enacting FDA's proposal would reduce the likelihood of harm to patients, interrupted access to devices, and loss of market share or market withdrawal for devices for which a vulnerability is identified as a result of cybersecurity incidents.

Medical Device Shortages

The COVID-19 pandemic demonstrated that by the time there is an emergency, it is often too late to prevent or mitigate shortages. Under the CARES Act, FDA received device shortages authority during or in advance of a public health emergency (PHE). While the new authority has been helpful, the tie to public health emergencies limits FDA's ability to respond to any early signs of supply constraints or a potential shortage situation. 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 product recalls and natural disasters, that may not 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; 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; and authorizing 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.

Modernizing the Dietary Supplement Health and Education Act

In the more than 25 years since the Dietary Supplement Health and Education Act of 1994 (DSHEA) was enacted, the dietary supplement market in the U.S. has grown from approximately 4,000 products to somewhere between 50,000 and 80,000 products. FDA is seeking to modernize DSHEA to strengthen FDA's implementation and enforcement of DSHEA and clarify FDA's authorities relating to products marketed as "dietary supplements." Specifically, FDA is seeking to amend DSHEA to: (1) require annual listing with FDA of individual dietary supplement products, including basic information about each unique product; and (2) clarify FDA's authorities over products marketed as dietary supplements to facilitate enforcement against unlawfully marketed products. These amendments would allow FDA to know when new products are introduced, quickly identify dangerous or illegal products on the market, and take appropriate action to protect consumers when necessary.

Update Legislative Authorities and Authorize Registration Fees for Cosmetics

FDA's regulatory authority for cosmetics dates to the 1938 FD&C Act, which gives FDA very limited post-market authority over cosmetic safety. FDA is seeking to update legislative authorities to modernize and enhance the FDA Cosmetic Safety Program. Specifically, FDA proposes that legislation be enacted to: (1) require domestic and foreign cosmetic firms to register their establishments and list their products with FDA; (2) require domestic and foreign cosmetic firms to report serious and frequently occurring adverse events to FDA; (3) provide explicit authority for FDA to promulgate Good Manufacturing Practices regulations; (4) require domestic and foreign cosmetic firms to allow FDA access to records (including consumer complaints and safety data) during a routine or for-cause inspection; (5) provide FDA mandatory recall authority for cosmetics that pose serious risk to the public health; (6) provide explicit authority for requiring listing of known cosmetic allergens in the ingredient list on the product label; and (7) authorize FDA to collect registration fees from the cosmetic industry to provide increased resources for FDA's Cosmetic Safety Program. This new authority would significantly strengthen FDA's post-market surveillance systems and better protect the public health by helping to ensure the safety of cosmetic products and ingredients that are in use in the United States.

Enhancing FDA's Authority to Better Protect Infants and Young Children

FDA is seeking to amend the FD&C Act to grant FDA new authority to establish binding contamination limits in foods, including those consumed by infants and young children, via an administrative order process. Under current law, FDA has limited tools to help reduce exposure to toxic elements in the food supply. This new authority to allow FDA to establish contamination limits in foods, including those consumed by infants and young children, via the administrative order process would improve the efficiency, timeliness, and predictability of issuing binding limits to reduce exposure to toxic elements by these vulnerable populations, and updating limits as new scientific information becomes available.

Product Testing Requirements for Foods Marketed for Consumption by Infants and Young Children

Under current law, industry is not required to test ingredients or final products marketed for consumption by infants and young children to help assess levels of toxic elements in such foods or to measure progress reducing exposure to the lowest possible levels. FDA is seeking to amend the FD&C Act to: (1) require industry to conduct toxic element testing of final products marketed for consumption by infants and young children and maintain such records of these testing results for FDA inspection; and (2) provide FDA with new authority to remotely access records of these test results and to review these test results whenever necessary. This new authority would help FDA understand levels of toxic elements in such products, allow FDA to monitor industry progress in reducing levels of these toxic elements over time, and identify where FDA should devote more time and resources to better protect infants and young children.

Modernizing of Tobacco User Fees Framework

The Federal Food, Drug, & Cosmetic (FD&C) Act, Section 919, authorizes FDA to assess and collect tobacco user fees from domestic manufacturers and importers of six classes of products: cigars, pipe tobacco, cigarettes, snuff, chewing tobacco, and roll-your-own tobacco. Section 919

also authorizes the total amount of tobacco user fees FDA must assess and collect each year. However, because electronic nicotine delivery systems (ENDS) were a relatively new product category when the FD&C Act was amended to include tobacco in 2009, the budgets established by Congress under Section 919 could not have taken into account the resources required for the regulation of ENDS, which are currently the most used tobacco product category by youth. This presents two issues: 1) Manufacturers and importers of regulated tobacco products outside of the six product classes listed above, including ENDS, do not pay tobacco user fees for their regulatory oversight, and 2) FDA has had to reallocate a significant portion of the $712 million in user fees it collects annually from the existing six product classes to properly regulate deemed products, especially ENDS. This proposal seeks to amend Section 919 of the FD&C Act to: authorize the agency to assess user fees on, and collect such fees from, each manufacturer and importer of all products subject to Chapter 9 of the FD&C Act, promoting a fair distribution of tobacco user fee assessments to all regulated tobacco products; increase the current limitation on total tobacco user fee collections by $100 million; and index all future collections to inflation.

Lengthen Expiration Dates to Mitigate Critical Drug Shortages

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

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 with them 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 Federal Food, Drug, and Cosmetic Act (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 in order to keep confidential non-public information provided by FDA (such as confidential commercial information). 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 product 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.

Preventing Food Shortages, Including Infant Formula and Certain Medical Foods

No law requires manufacturers of infant formulas or essential 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 firms to notify FDA of anticipated significant interruptions in the supply of infant formula or essential medical foods for patients with certain inborn errors of metabolism (e.g., phenylketonuria, medium chain acyl-coenzyme A dehydrogenase deficiency). 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 help FDA to take steps to promote the continued availability of these foods. Additionally, FDA is seeking authority to require firms to provide shortage notification for other FDA-designated categories of food during a declared public health emergency. 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.

FDA FY 2023 BUDGET REQUEST FOR PANDEMIC PREPAREDNESS

The FY 2023 Budget includes an effort totaling $81.7 billion in mandatory funding, available over five years, across the Office of the Assistant Secretary for Preparedness and Response (ASPR), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), and Food and Drug Administration (FDA) to support the Administration's plan to transform U.S. capabilities to prepare for and respond rapidly and effectively to future pandemics and other high consequence biological threats. Within this total, the Budget requests $1.63 billion in mandatory funding for FDA to carry out the activities described herein to advance the Administration's vision for pandemic preparedness.

From the start of its COVID-19 response to the present, FDA continues to make decisions guided by science, data, and the best evidence. Now is the time to build on lessons learned and provide significant transformational investments to modernize and innovate the agency and operations for the future. FDA has a unique and central role to the whole-of-government response to protect and promote public health.

The FY 2023 Budget Pandemic Preparedness request for FDA proposes $1.63 billion in new resources for spending over five years. This funding will expand and modernize FDA's regulatory capacity, information technology, and laboratory infrastructure, including strengthening the personal protective equipment supply chain by building analytics and creating predictive modeling capabilities. FDA will also focus on evaluation of vaccines and therapeutics that target high-priority viral families and speed development of diagnostics, including expansion of test validation capacity and development of common performance standards. The Budget will also support FDA's work with its international partners to strengthen foreign inspections, harmonize premarket review of therapeutics and diagnostics, and reduce zoonotic pathogen spillover.

Build Core Capabilities & Focus on Evaluation of Vaccines and Therapeutics ($1.1 billion)

To maintain FDA's gold standard for science-based product review and regulatory decision-making, the FY 2023 Pandemic Preparedness budget includes $1.1 billion to build capabilities and transform medical defenses at FDA. The Budget provides new funds to advance health equity by protecting against existing and emerging threats through an agency-wide effort to develop and implement a set of recommendations to assess, incorporate, and improve health equity related considerations in FDA's pandemic response management.

The Budget also provides critical resources to expand and modernize FDA's regulatory capacity, information technology, and laboratory infrastructure. Through these investments, FDA will modernize applications, tools, and workstreams, as well as improve FDA's public health infrastructure, data exchange, and underlying technology platforms. The modernization is central to improving FDA's ability to respond more swiftly and efficiently when preparing and responding to a pandemic. The Budget also will improve FDA's laboratory facilities so that FDA has modern and safe physical spaces necessary to conduct our regulatory pandemic preparedness and response work.

Given the continued influx of COVID-19 submissions for medical device Emergency Use Authorizations (EUAs), the Budget also provides funding to build FDA's capacity to review critical products including in vitro diagnostic tests, personal protective equipment (PPE), and

ventilators. Additionally, the ability to anticipate, predict and respond to PPE supply chain vulnerabilities and risks is critical for preventing and mitigating impacts caused by shortages to U.S. healthcare workers, patients and the U.S. health care system. The Budget will strengthen the supply chain by building data and visual analytics, creating predictive modeling capabilities, and evaluating new and emerging technologies to monitor the PPE supply chain.

The Budget also includes new funding for the Drug Development and Regulatory Science Pandemic Preparedness Program to accelerate the timeline to research, develop and authorize therapeutics for emerging and future outbreaks. This program will be multi-disciplinary in nature comprised of intramural and extramural components that will focus on human therapeutics needed to respond to public health emergencies, including anti-infectives, oral antivirals, immune modulators and other medical countermeasures (MCM).

The Budget includes funding for FDA to support the "end-to-end" development of MCM building basic science; advanced development, manufacturing, and infrastructure; and real-world safety and effectiveness monitoring that will significantly reduce timelines. The Budget will better position FDA to more effectively respond to newly-emerging outbreaks even as it takes on the regulatory enhancements necessary to strengthen overall preparedness by providing additional capacity for each medical product center. The funds will allow FDA to continue developing a robust surveillance system to facilitate rapid evaluation of safety signals for newly authorized or approved vaccines and work with manufacturers and other partners to modernize the chemistry, manufacturing, and controls of existing vaccines. FDA will leverage additional staff to bolster its reviewer cadre and develop the necessary guidances and regulatory developments to speed vaccine development and global vaccination.

The Budget will allow the agency to develop additional capacity in relevant scientific, analytical, and technical expertise to support execution and program oversight to enable FDA to respond rapidly to pandemics, including effectively bring new therapeutics to patients. The Budget will also support efforts to speed development of diagnostics, including expansion of test validation capacity and development of common performance standards.

Speed Diagnostic Development, Expand Test Validation Capacity, and Develop Common Performance Standards ($355 million)

The Budget includes $355 million to increase the capacity to validate tests on a larger scale, create common performance standards for tests, and build the infrastructure necessary for the post-market surveillance of authorized tests. With these resources, FDA will also more rapidly develop widely available diagnostics to expand resources and capacity to enable thorough review and rapid deployment of diagnostics tests.

Modernize FDA Safety Surveillance and Oversight, Foreign Inspections, Harmonize Premarket Review of Medical Products, and Reduce Zoonotic Pathogen Spillover ($175 million)

The Budget includes $175 million to Modernize FDA Safety Surveillance and Oversight, Foreign Inspections, Harmonize Premarket Review of Medical Products, and Reduce Zoonotic Pathogen Spillover. The Budget will allow FDA to create and implement the 21st Century

Roadmap for modernizing FDA's safety surveillance and oversight program for marketed and authorized drug products to prepare for the next pandemic. This investment will improve the regulatory environment and focus on key areas to leverage the use of existing and emerging technologies and modern approaches. These approaches will strengthen the ways we assess drug safety and address possible drug safety concerns, and will further develop Sentinel as a unique and powerful tool with many potential applications that can serve public health.

The Budget proposes for FDA to expand work with its international partners to strengthen foreign inspections, harmonize premarket review of vaccines, therapeutics, diagnostics and reduce zoonotic pathogen spillover. This includes funding for global inspections expansion and modernization to expand Mutual Reliance operational capabilities with the European Union and United Kingdom and to explore opportunities to negotiate mutual reliance agreements with additional regulatory partners to share inspectional findings that strengthen oversight of human and veterinary drugs areas.

The Budget also provides resources to allow the agency to coordinate and strengthen capacities for the development, manufacturing, and regulatory approval of safe and effective vaccines, human and animal drugs, diagnostics, PPE, and other supplies that can assist FDA to speed future pandemic responses. This funding would support global harmonization efforts such as the development of harmonized regulatory expectations, information technology systems to support international work and building regulatory and manufacturing capacity ultimately leading to better availability of medical products around the world. Finally, FDA will solidify its interdisciplinary and collaborative approaches to solving multifaceted public health challenges by leveraging One Health principles to strengthen and respond to emerging threats and reduce zoonotic pathogen spillover. Funding will allow FDA to develop and implement risk mitigation strategies that leverage One Health principles to help predict, prevent and control infectious diseases and zoonotic pathogen spillover at the intersection of human and animal health.

FOODS

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Foods	**1,110,471**	**1,099,001**	**1,111,237**	**1,231,960**	**120,723**
Budget Authority	***1,099,160***	***1,098,973***	***1,099,701***	***1,220,193***	***120,492***
User Fees	***11,311***	***28***	***11,536***	***11,767***	***231***
Center	344,155	343,289	344,869	420,833	75,964
Budget Authority	343,289	343,289	343,986	419,932	75,946
User Fees	866	---	883	901	18
Food and Feed Recall	*253*	---	*258*	*263*	*5*
Voluntary Qualified Importer Program	*253*	---	*258*	*263*	*5*
Third Party Auditor Program	*360*	---	*367*	*375*	*8*
Innovative Food Products (Proposed)	---	---	---	---	---
Field	766,316	755,712	766,368	811,127	44,759
Budget Authority	755,871	755,684	755,715	800,261	44,546
User Fees	10,445	28	10,653	10,866	213
Food and Feed Recall	*1,040*	---	*1,061*	*1,082*	*21*
Food Reinspection	*4,760*	---	*4,855*	*4,952*	*97*
Voluntary Qualified Importer Program	*4,495*	---	*4,584*	*4,676*	*92*
Third Party Auditor Program	*150*	*28*	*153*	*156*	*3*
FTE	**3,882**	**4,037**	**3,882**	**4,035**	**153**

Figure 1 - Narrative by Activity

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[4]
- 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.[5]

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.[6]

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

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

- Review of infant formula notifications from manufacturers before marketing a new formula

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[4] 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.

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

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

- Premarket regulation of ingredients and packaging, such as review of food additive and color additive petitions
- Postmarket monitoring for chemical contaminants
- Authorization of nutrient content and health claims
- Regulation of dietary supplements
- Cosmetics safety and labeling

The FDA Food Safety Modernization Act

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

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

FDA finalized seven foundational FSMA rules in 2015 and 2016 and is conducting extensive outreach to industry to ensure that stakeholders understand the new requirements. These seven foundational FSMA rules provide a framework for the food industry to implement effective measures to prevent contamination.[7]

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.

In December of 2021, FDA issued a final rule establishing the Laboratory Accreditation for Analyses of Foods (LAAF) program as required by FSMA.[8] Under the LAAF program, FDA will recognize accreditation bodies (ABs) that will accredit food testing laboratories to standards established in the final rule (referred to as LAAF-accredited laboratories).

Currently, food testing, including environmental testing, is largely completed by private laboratories that may conform to a variety of standards and be subject to various levels of oversight. Once the LAAF program is fully implemented, only LAAF-accredited laboratories will be able to conduct food testing in certain circumstances that are defined in the final rule.

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

[8] https://www.fda.gov/food/food-safety-modernization-act-fsma/fsma-final-rule-laboratory-accreditation-analyses-foods-laaf

The LAAF program will cover food testing:

- to support removal of a food from an import alert through successful consecutive testing requirements;
- to support admission of an imported food detained at the border because it is or appears to be in violation of the Federal Food, Drug, and Cosmetic Act;
- required by existing FDA food safety regulations, when applied to address an identified or suspected food safety problem (i.e., certain tests of shell eggs, sprouts, and bottled drinking water);
- required by a directed food laboratory order, a new procedure being implemented in this final rule that will allow the FDA to require use of a LAAF-accredited laboratory to address an identified or suspected food safety problem in certain, rare circumstances; and
- conducted in connection with certain administrative processes such as testing submitted in connection with an appeal of an administrative detention order.

The establishment of the LAAF program will improve FDA's capacity to protect U.S. consumers from unsafe food by improving the accuracy and reliability of certain food testing through the uniformity of standards and enhanced oversight of participating laboratories.

Additionally, in December of 2021, FDA published a proposed rule that would revise subpart E of FSMA's Produce Safety Rule to change certain pre-harvest agricultural water requirements for covered produce other than sprouts.[9]

Under this proposal, farms would be required to conduct annual systems-based agricultural water assessments to determine and guide appropriate measures to minimize potential risks associated with pre-harvest agricultural water. The assessment would include an evaluation of the water system, agricultural water use practices, crop characteristics, environmental conditions, potential impacts on source water by activities conducted on adjacent and nearby land, and other relevant factors, such as the results of optional testing.

This proposal was developed following hundreds of farm visits and meetings with stakeholders, including an Agricultural Water Summit hosted by the Produce Safety Alliance and reflects findings from several recent produce outbreak investigations that offered additional insights into potential routes of contamination. The requirements described in this proposal are intended to be workable across produce farms of all sizes, both domestic and foreign, recognizing the wide variety of water systems, uses, and practices. They also are designed to be adaptable to future advancements in agricultural water quality science and technology.

FDA is committed to engaging with stakeholders on the proposed rule. As such, the agency intends to hold two virtual public meetings to discuss the proposal and hear feedback. In addition, the agency is also developing an online tool to assist farms in evaluating potential risks posed by their water sources and in determining potential management options.

[9] https://www.fda.gov/food/food-safety-modernization-act-fsma/fsma-proposed-rule-agricultural-water

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.[10]

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 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[11]
- Temporary policy regarding certain requirements under the FSMA Accredited Third-Party Certification Program for foreign food entities and their products[12]
- 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[13]
- 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[14]

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

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

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

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

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

- 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[15]

Announced the New Era of Smarter Food Safety Blueprint

In July 2020, FDA released the New Era of Smarter Food Safety blueprint.[16] 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.

In September 2020, FDA announced a proposed rule to establish additional traceability recordkeeping requirements for certain foods.[17] 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.

FDA held additional meeting series in October and November of 2021 to discuss New Era developments and engage with public comments. The first of which was a New Era Summit on E-Commerce held in October titled "Ensuring the Safety of Foods Ordered Online and Delivered Directly to Consumers."[18] The second series, held in November, was titled "Ensuring the Safety of Foods Ordered Online and Delivered Directly to Consumers."[19]

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.[20] 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.

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

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

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

[18] https://www.fda.gov/food/workshops-meetings-webinars-food-and-dietary-supplements/new-era-smarter-food-safety-summit-e-commerce-ensuring-safety-foods-ordered-online-and-delivered

[19] https://www.fda.gov/food/workshops-meetings-webinars-food-and-dietary-supplements/collaborating-culture-new-era-smarter-food-safety-11042021-11042021

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

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)[21] and the Produce Safety rules.[22] 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.[23]

In line with the Blueprint's priorities of increased traceability, improved predictive analytics, rapid response to outbreaks, reduced contamination of food, and fostering the development of stronger food safety cultures, FDA and USDA's Produce Safety Working Group held joint industry webinars on FSMA's Produce Safety Rule (PSR) and Foreign Supplier Verification Program (FSVP) for stakeholders in Latin America. These industry communications are critical given that 46% of all fresh produce consumed in the U.S. is imported from Latin America—the majority of which coming from Mexico.[24] These events give producers and industry leaders the opportunity to ask questions about FSMA rules and ultimately improve transparency. These vital opportunities for communication increase both the agencies' effectiveness in mitigating foodborne illness and help food industry workers to remain compliant with FSMA regulation.

Developed 2020 Leafy Greens STEC Action Plan

Between 2009 and 2018, FDA and 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.

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.

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

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

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

[24] https://www.fda.gov/food/cfsan-constituent-updates/fda-and-usda-collaborate-present-webinars-fsma-produce-safety-rule-produce-exporters-latin-america

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.

Continuing these efforts, in May of 2021, FDA released findings of a year-long sampling assignment from November 2019 through December 2020 that tested raw agricultural commodity romaine lettuce mostly at facilities and on farms in growing regions of the Salinas, California, and Yuma, Arizona for the presence of pathogens Escherichia coli (specifically, Shiga toxin-producing E. coli or STEC) and Salmonella spp.[25]

FDA collected and tested 279 samples for both pathogens. Each sample was made up of 10 subsamples, with each subsample consisting of one or more heads or hearts of romaine lettuce and weighing at least 300 grams. This approach – the collection and testing of samples composed of multiple subsamples – increases the probability of detecting pathogens if present, given that microbial hazards may not be uniformly present.

Although no pathogens were detected during this assignment, maintaining surveillance during the growing/harvesting season is helpful to informing the agency's leafy greens prevention efforts, specifically those outlined in the FDA's Leafy Greens Action Plan.

Conducted Sampling Assignment on Romaine Lettuce

In October 2021, FDA released the findings of a sampling assignment for which FDA collected and tested 504 romaine lettuce samples from commercial coolers in Yuma County, Arizona during February and March 2021. The agency tested the lettuce for Shiga toxin-producing Escherichia coli (STEC), specifically enterohemorrhagic Escherichia coli (EHEC), and Salmonella spp. This assignment was part of the FDA's ongoing surveillance following multistate E. coli O157:H7 outbreaks of foodborne illness in recent years linked to or potentially linked to romaine lettuce.

During the assignment FDA detected E. coli O130:H11 in one sample. The isolate was found to be moderate to high risk and could be capable of causing severe illness in humans, though it was not linked to any known human illnesses, and no product ever reached consumers. The owner of the product did not harvest the remaining crop from the field where it was grown.

In response to the finding, FDA conducted an investigation at the farm to identify possible sources and routes of contamination. The FDA was able to collect romaine lettuce from the field, multiple samples of soil, water, sediment, and animal fecal material. FDA also assessed farm equipment and other surfaces. Only one of the total 24 samples yielded STEC (specifically, E. coli O116:H-). This sample came from the outer leaves of romaine lettuce. The strain was further characterized as low risk to human health, and FDA's analysis indicated the strain was not linked with any past known foodborne illness 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.

[25] https://www.fda.gov/food/sampling-protect-food-supply/microbiological-surveillance-sampling-fy20-fy21-sample-collection-and-analysis-romaine-lettuce-raw

FDA has updated its approach to these issues and has outlined specific actions to address new findings and provide resources for mitigating risk.[26] 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 2021

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.

Date	#	Title	Description
Nov 2021	FDA-2016-D-4484	Guidance for Industry: Temporary Permits for Interstate Shipment of Experimental Packs of Food Varying from the Requirements of Definitions and Standards of Identity	Clarifies, for the food industry, aspects of the application process for temporary marketing permits and highlights a change that simplifies the label review process.
Oct 2021	FDA-2014-D-0055	Guidance for Industry: Voluntary Sodium Reduction Goals	Provides measurable voluntary short-term (2.5-year) goals for sodium content in commercially processed, packaged, and prepared foods to reduce excess population sodium intake, while recognizing and supporting the important roles sodium plays in food technology and food safety.
Sep 2021	FDA-2007-D-0207	Guidance for Industry: Microbiological Considerations for Antimicrobial Agents	Assists submitters of food additive petitions, food contact notifications, generally recognized as safe notices, and threshold of regulation exemption requests

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

Date	#	Title	Description
		Used in Food Applications	in providing data to demonstrate that an antimicrobial agent achieves its intended technical effect in or on food or food contact articles as well as if the agent is safe and effective for its intended use.
July 2021	FDA-2020-D-1456	Guidance for Industry: Use of Recycled Plastics in Food Packaging (Chemistry Considerations)	Highlights the chemistry and potential food contamination issues for which FDA recommends a manufacturer of recycled plastic consider during the manufacturer's evaluation of a recycling process for producing material suitable for food-contact applications.
July 2021	FDA-2019-D-1997	FDA Oversight of Food Products Covered by Systems Recognition Arrangements	Provides guidance related to FDA's regulatory oversight activities for food products covered by a Systems Recognition Arrangement between another country's food safety authority and FDA.

Improved Outbreak Response

The Coordinated Outbreak Response and Evaluation (CORE) Network coordinates the agency's efforts to find, reduce, and work to prevent outbreaks of illness related to food, cosmetics, and dietary supplements. This team coordinates activities across FDA's 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.

On December 9, 2021, FDA released the Foodborne Outbreak Response Improvement Plan (FORIP) to improve the agency's ability to identify the sources and causes of foodborne illness

outbreaks.[27] The plan was informed by an independent review of FDA's capacity to support, participate in, or lead multistate outbreak investigations.[28] The plan is an important step that FDA is taking to enhance the speed, effectiveness, coordination, and communication of outbreak investigations. The plan is focused on multi-state outbreaks that require significant engagement coordinated by FDA's CORE.

FDA has set forth in this plan a series of actions that the agency intends to take to respond more quickly and more efficiently to foodborne outbreaks and reduce the number of foodborne outbreaks that go unsolved in the future. Continued investments throughout FDA and the food safety system will be critical to modernizing and strengthening the response to foodborne outbreaks, as well as to accomplishing the goals stated in the plan.

Additionally, CORE has been engaged in activities related to improvements in outbreak response and coordination, including increasing responsibilities required to address improved detection (WGS, Rep Strains), smarter prevention tools (FSMA implementation), New Era and Outbreak Response Improvement Plan Activities (Traceability, Outbreak Investigation Reports), and increased transparency and communications (Advisories, Articles, Outreach, and the CORE Investigation Table).

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

- Earlier this year, there was an outbreak of acute non-viral hepatitis that affected children, adults, and pets. The "Real Water" Brand Alkaline bottled water was the only common link identified among the cases. Due to the lack of cooperation by this firm, Real Water Inc. agreed to cease operations until they can comply with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and other requirements listed in a consent decree. On June 1, 2021, A U.S. District Judge entered a consent decree of permanent injunction between the U.S. and AffinityLifestyles.com Inc. (which is the majority shareholder of Real Water Inc.), Real Water Inc., and the President and Vice President of Real Water.
- Jule's Cashew Brie, a vegan, or plant-based cheese alternative was found to be the likely source of a *Salmonella* outbreak that consisted of several different serotypes of *Salmonella*: *Salmonella* Typhimurium, *Salmonella* Chester, *Salmonella* Duisburg, and *Salmonella* Urbana. This outbreak prompted public warnings, product recalls, and FDA worked with the cashew supplier associated with Jule's to ensure that potentially contaminated product was removed from the market and that the supplier implemented corrective actions.

[27] https://www.fda.gov/food/new-era-smarter-food-safety/new-era-smarter-food-safety-fdas-foodborne-outbreak-response-improvement-plan

[28] https://www.fda.gov/food/new-era-smarter-food-safety/independent-review-fdas-foodborne-outbreak-response-processes

- In July and August of 2021, FDA, along with federal and state partners, conducted an outbreak response investigation into an outbreak of *Salmonella* Typhimurium linked to packaged leafy greens produced at a Controlled Environment Agriculture (CEA) indoor hydroponic operation in Rochelle, IL. There were 31 cases in four states. This outbreak resulted in an initial recall, and then two subsequent expanded recalls. Although no clear route of contamination was readily identified, FDA is preparing a report to discuss findings and provide information to assist in future prevention efforts.
- In October 2021, FDA released an outbreak advisory warning that whole, fresh onions were found to be linked to a *Salmonella* outbreak resulting in 892 illnesses. These onions were distributed nationwide and resulted in multiple voluntary recalls, including downstream recalls.[29]

All of the outbreaks mentioned above are also included in the CORE Investigation Table, which was released in late 2020.[30] This new tool shares information on FDA's foodborne illness outbreak investigations, even in their early stages and as soon as FDA begins its response to the outbreak. It gives consumers early awareness of developing multistate outbreaks that are occurring across the United States. Although FDA does not have all the information in the early phase of these investigations, this new outbreak information is being shared early and will updated weekly as a demonstration of FDA's commitment to more real-time and transparent communication with stakeholders and consumers about outbreaks that FDA is investigating.

In 2021, FDA released investigation reports sharing findings from two major 2020 outbreaks. The first report detailed the investigation of an outbreak of *Salmonella* Newport in red onions in the U.S. and Canada between June and October 2020, and the second report detailed the investigational findings of an outbreak of *Salmonella* Enteritidis linked to the consumption of peaches during the summer of 2020. These reports provide additional details on the root cause investigation and make these findings, and their implications, available to the public and the affected industry in an effort to help prevent a reoccurrence.

FDA Releases Cyclospora Prevention, Response and Research Action Plan

In July 2021, FDA released a Cyclospora Prevention, Response and Research Action Plan[31] that outlines FDA's strategy for reducing the public health burden of foodborne cyclosporiasis in the United States caused by *Cyclospora cayetanensis* (*C. cayetanensis*) in both domestically grown and imported produce.

Cyclosporiasis is a foodborne intestinal illness caused by the parasite *C. cayetanensis.* The number of reported cases of cyclosporiasis in the US has been rising in recent years, likely due in

[29] https://www.fda.gov/food/outbreaks-foodborne-illness/outbreak-investigation-salmonella-oranienburg-whole-fresh-onions-october-2021

[30] https://www.fda.gov/food/outbreaks-foodborne-illness/investigations-foodborne-illness-outbreaks

[31] https://www.fda.gov/food/foodborne-pathogens/cyclospora-prevention-response-and-research-action-plan

part to better diagnostic testing methods. According to the CDC,[32] there have been roughly 6,000 reported domestically-acquired cases of cyclosporiasis over the last 3 years. The number of reported cases typically rises during the spring and summer.

Historically cyclosporiasis was associated with travel to or consumption of produce from countries where *C. cayetanensis* was endemic. In response to outbreaks of cyclosporiasis, FDA has taken samples of imported produce, inspected foreign farms and created import alerts[33] in response to adverse findings. However, over the last several years *Cyclospora* has been increasingly confirmed in surface water and on food grown in the US. This may be partially attributed to improvements in testing and surveillance tools that are able detect this parasite better than in the past.

Rising case numbers and the emergence of Cyclospora in domestically grown produce prompted the FDA to create the Cyclospora Task Force in 2019. The task force comprises multidisciplinary experts across FDA and CDC with the goal of reducing the public health burden of foodborne illness caused by Cyclospora in produce.

We have continued to see annual outbreaks of cyclosporiasis including as recently as 2020 where an outbreak linked to bagged salads caused more than 700 laboratory confirmed illnesses. To tackle this ongoing public health issue, the *Cyclospora* Task Force developed
The *Cyclospora* Prevention, Response and Research Action Plan. The plan is intended to serve as a strategic guide to reducing the public health burden caused by this parasite through three priority focus areas: improving prevention, enhancing response activities, and filling knowledge gaps.

Bending the curve of foodborne illness is a key focus of the New Era of Smarter Food Safety blueprint, which establishes goals for a more digital, traceable, and safer food system. Key New Era goals will support the *Cyclospora* Prevention, Response and Research Action Plan, including advancing traceability and strengthening root cause analyses and predictive analytics.

Improved Pathogen Detection and Traceability

Figure 2 - GenomeTrakr

In October 2021, FDA published results from an external study which assessed the impact of the Whole Genome Sequencing (WGS) program.[34] The data, covering foodborne illness outbreaks from 1999 to 2019, suggests that for each additional 1,000 WGS isolate sequences added to the

[32] https://www.cdc.gov/parasites/cyclosporiasis/outbreaks/index.html

[33] https://www.fda.gov/industry/actions-enforcement/import-alerts

[34] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0258262

database for a given pathogen, there is a reduction of approximately six illnesses per year associated with that pathogen.

Researchers examined the effect of WGS program isolates collected in the U.S. on outbreak illnesses, compared results with existing literature and conducted an analysis to estimate benefits and costs. The program helped decrease foodborne illness in the U.S. within the first year after launch and the effect of the program on human health shows clear improvements over time, as the WGS database grows. FDA estimates that the program was likely cost effective in its second year of implementation and at current funding levels, the program is generating $100 million to $450 million in net annual health benefits.

The agency initiated the GenomeTrakr network in 2012, which has grown to include federal, state, hospital and other labs in the U.S. and other nations that use WGS for pathogen identification. FDA continues to facilitate opportunities to speed the adoption of WGS by public and private laboratories. WGS and the GenomeTrakr network also have roles in advancing the goals set out in the New Era of Smarter Food Safety Blueprint, which include facilitating opportunities to speed the sequencing of pathogens.

The Network is now in its nineth year and has collected more than 710,000 whole bacterial genome sequences (including more than 390,000 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, further augmenting food safety efforts in the US through enhanced surveillance and genomic epidemiological linkage between clinical and environmental foodborne pathogens.

In 2021, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions totaling more than 110 compliance-related and outbreak response actions for the year. To date, WGS has supported more than 850 cases of product adulteration and

contamination events investigated by the FDA. For example, in 2021, a massive outbreak caused by *Salmonella* Oranionburg was linked to onions grown in Mexico. This event, spanning May to October 2021, was one of the largest Salmonella outbreaks in more than a decade and sickened more than 890 people in 38 states and Puerto Rico. Whole genome sequencing provided a strong linkage between restaurant sample and the clinical cases, establishing a genetic link between onions and the resultant illnesses, and also helping to identify the geographic region of origin. Whole genome sequencing also augmented an outbreak investigation of hydroponically grown salad greens contaminated with *Salmonella* Typhimurium that sickened people across the US. WGS confirmed the actual outbreak strain of *S.* Typhimurium in a pond outside but adjacent to the hydroponics facility.

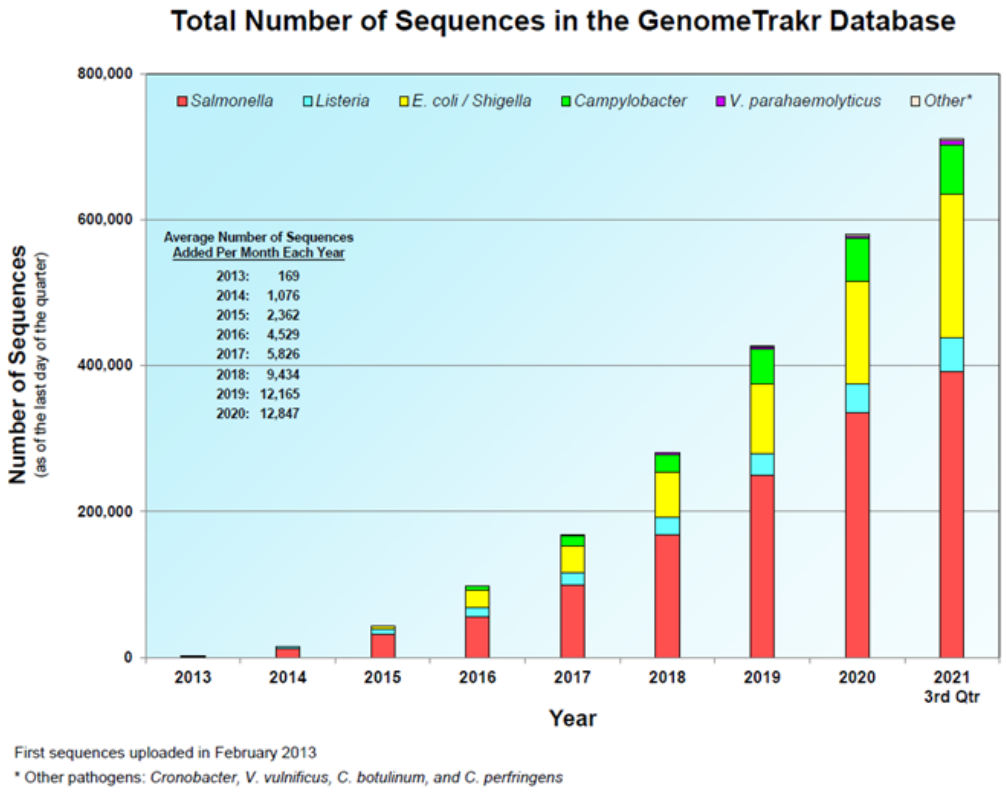

Figure 3 - The Total Number of Sequences in the GenomeTrakr Database

Release of 2019 Annual Report on the Sources of Foodborne Illness by the Interagency Food Safety Analytics Collaboration

In October 2021, the Interagency Food Safety Analytics Collaboration (IFSAC)—a collaboration of CDC, FDA, and USDA-FSIS—released its latest annual report on "Foodborne illness source

attribution estimates for 2019 for *Salmonella*, *Escherichia coli* O157, *Listeria monocytogenes*, and *Campylobacter* using multi-year outbreak surveillance data, United States."[35]

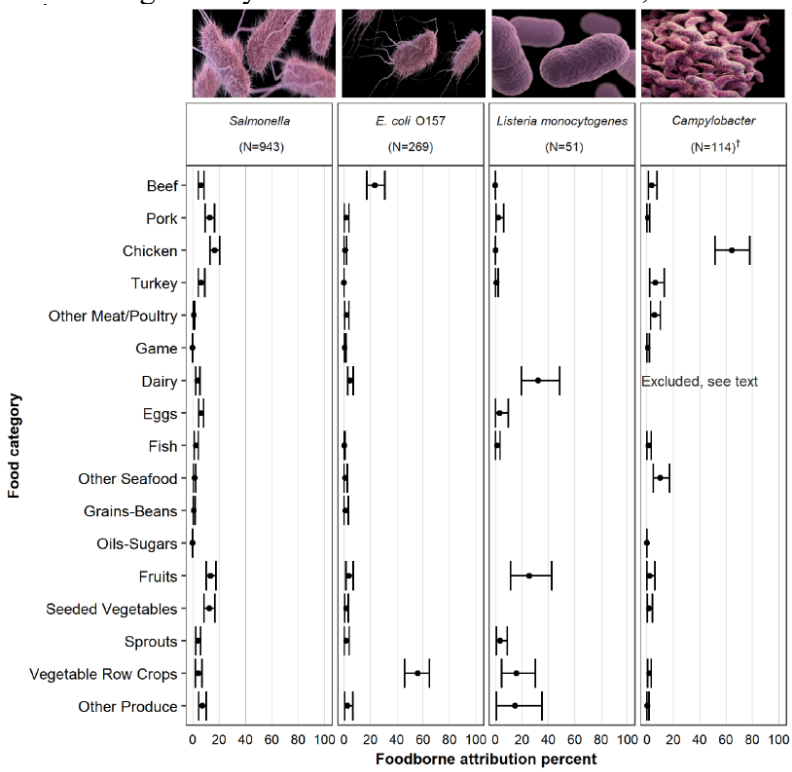

Figure 4 - Estimated Percentage for Foodborne Illnesses Attributed to 17 Food Categories

Figure 4 Description: Estimated percentage (with 90% credibility intervals) for 2019 of foodborne *Salmonella, Escherichia coli* O157*, Listeria monocytogenes* and *Campylobacter* illnesses attributed to 17 food categories, based on multi-year outbreak data, United States. Based on a model using outbreak data that gives equal weight to each of the most recent five years of data (2015-2019), and exponentially less weight to each earlier year (1998-2014). *Campylobacter* estimates exclude results derived from Dairy outbreak data.

In an ongoing effort to understand sources of foodborne illness in the United States, IFSAC collects and analyzes foodborne illness outbreak data for four pathogens - Salmonella, *Escherichia coli* O157, *Listeria monocytogenes*, and *Campylobacter* - and specific foods and food categories that are responsible for foodborne illnesses in the United States. The data are analyzed by calendar year and released in an annual report. The Centers for Disease Control and Prevention (CDC) estimates that, together, these four pathogens cause nearly two million cases of foodborne illnesses in the U.S. each year.

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

[35] https://www.cdc.gov/foodsafety/ifsac/pdf/P19-2019-report-TriAgency-508.pdf

agencies' abilities to assess whether prevention measures are working. The continued efforts of IFSAC improve coordination of federal food safety analytic efforts and address cross-cutting priorities for food safety data collection, analysis, and use.

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 2021, FDA issued eight injunctions and conducted two product seizures 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.

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 2021, FDA issued 398 import alert notices for human food, cosmetic, and dietary supplement products.

Released Results of Talc-Containing Cosmetics Study and Repealed Color Additive Approval for the Use of Lead Acetate in Hair Dyes

In October 2021, FDA released the results of the agency's most recent sampling assignment testing talc-containing cosmetic products for the presence of asbestos. Asbestos fibers were not detected in any of the 50 samples tested in 2021. The testing was conducted using Polarized Light Microscopy (PLM) and Transmission Electron Microscopy (TEM)—the use of highly sophisticated instruments to observe mineral specific optical properties of and identify characteristics of asbestos in air, bulk materials and even finely-processed talc minerals like those found in cosmetics.

Sampled products were selected based on various factors including, type of talc-containing cosmetic product, price range, popular products on social media and in advertisements, products marketed to children, and, if any, third party reports of potential asbestos contamination. Products were then blind-tested by AMA Analytical Services, Inc., awarded the contract for experience and expertise in asbestos testing. To continue this ongoing effort of testing talc-containing cosmetic products, the FDA is planning to test 50 additional samples in 2022 and will post a report when available.

Additionally, in October 2021, FDA announced that it was removing the stay of the final rule Termination of Listing of Color Additives Exempt From Certification; Lead Acetate, effective January 6, 2022. This conclusion is based on the recognition that there is no safe exposure level for lead.[36]

[36] https://www.fda.gov/food/cfsan-constituent-updates/fda-repeal-color-additive-approval-use-lead-acetate-hair-dyes

FDA intends to exercise enforcement discretion for 12 months from the effective date to provide industry with the opportunity to deplete their current stock and reformulate their hair dye products containing lead acetate. Additional details can be found in the Federal Register notice.

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 2021, FDA ensured safe access to the food supply by reviewing two Food Additive or Color Additive Petitions, 66 GRAS notifications, and 78 premarket notifications for Food Contact Substances.

FDA Issues Update on Recent Activities Pertaining to PFAS in Food

In June 2021, FDA released results from recent testing efforts performed to better understand the occurrence of per- and polyfluoroalkyl substances (PFAS) in the food supply. These results showed that all but one of the 94 food samples did not have detectable levels of PFAS. In August 2021, FDA released further results related to the testing of processed foods, including several baby foods. This survey showed that 164 of the 167 foods tested had no detectable levels of the PFAS measured. Three food samples had detectable levels of PFAS: fish sticks (PFOS and PFNA), canned tuna (PFOS and PFDA), and protein powder (PFOS).[37]

Since 2019, the FDA has analyzed 440 Total Diet Study (TDS) samples for PFAS in four collections. The three previously posted TDS survey results were from three regional collections and included foods that are more likely to vary by location or time of year, such as fresh produce, meats, and dairy products. In total, seven of the 440 foods have been found to have detectable levels of PFAS.

The foods tested represent a broad range of foods that are in the general food supply, which the average consumer might eat, and that were not specifically collected from areas of known environmental PFAS contamination. The sample sizes for the specific types of foods are limited

[37] https://www.fda.gov/food/cfsan-constituent-updates/fda-makes-available-pfas-testing-results-first-survey-processed-foods

and therefore cannot be used to draw definitive conclusions, but they do help to inform the agency's approach to future surveillance efforts.

When the FDA finds detectable levels of a chemical contaminant in food, such as PFAS, the agency conducts a safety assessment to evaluate whether the levels present a possible human health concern and warrant further FDA action. The FDA's approach considers a number of factors, including whether there is an established action level or tolerance, how much of the specific food people typically eat, the level of the contaminant detected in that food, and the toxicity of the specific contaminant(s).

One such contaminant, perfluoroalkyl carboxylic acids (PFCAs), has been found in some containers used by food industry workers that are not authorized for food contact use.[38] FDA has issued letters to industry stressing the importance of which fluorinated polyethylene containers are authorized for food contact use. The agency took this step to ensure that manufacturers that produce, distribute, or use these types of containers are aware of FDA's regulation pertaining to the requirements for fluorinating polyethylene containers used with food (21 CFR 177.1615).

As part of the FDA's ongoing effort to use the best available current science to assess the safety of exposure to PFAS from foods, the agency monitors the scientific literature and available toxicological reference values for PFAS and updates the values we use in our evaluations as warranted. Recently, the agency began using the finalized minimal risk levels (MRLs) from the Agency for Toxic Substances and Disease Registry's May 2021 Toxicological Profile for Perfluoroalkyls,[39] along with a new EPA reference dose,[40] also finalized in 2021, in our evaluations of the safety of exposure to certain PFAS detected in foods.

[38] https://www.fda.gov/media/151326/download

[39] https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf

[40] https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf

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

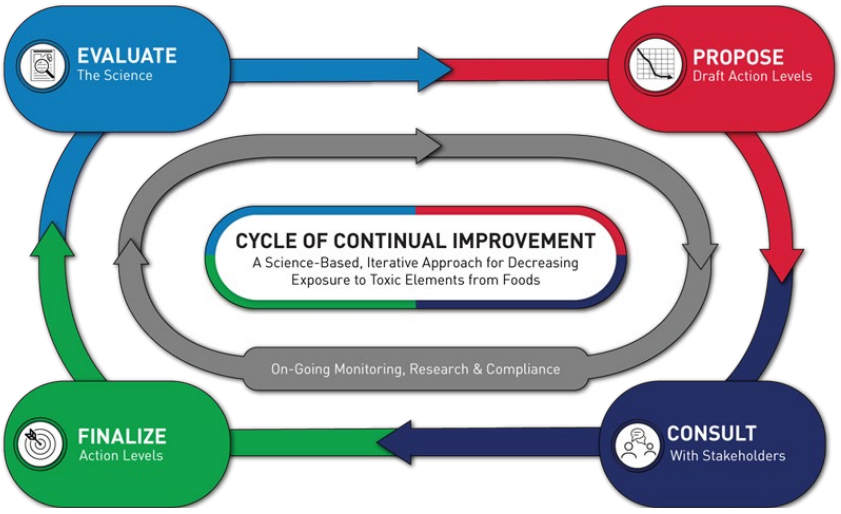

Figure 5 – Closer to Zero Action Plan's Cycle of Continual Improvement.

them of their existing responsibility to consider risks from chemical hazards—including toxic elements—when conducting a hazard analysis.[41] 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[42]" 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.

Consistent with these priorities, in October 2021, FDA—in coordination with EPA—issued updated advice about eating fish and shellfish.[43] Nutrients in fish can support a child's brain and immune system development. In these new guidelines, FDA recommends eating fish as part of a healthy diet, and we encourage children and people who are or might become pregnant or breastfeeding to eat fish that are lower in mercury. This advice can help them choose which fish to eat and how much to eat based on mercury. As a next step, and as a part of the Closer to Zero action plan, FDA plans to evaluate the current research on mercury in food—including fish—consumed by babies and young children, starting in 2022.

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

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

[43] https://www.fda.gov/food/consumers/advice-about-eating-fish

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. FDA held its first of several public meetings to address industry input on November 18, 2021.

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 2021, FDA's operations and oversight, including inspection activities, continued to be impacted by the COVID-19 pandemic. While fewer dietary supplement facility inspections were conducted in FY 2021 as compared with previous years, the agency's overall dietary supplement compliance activity continued and resulted in:

- 111 warning letters
- 1,299 import refusals
- 3 injunctions (filed)
- 1 seizure
- 22 criminal convictions.

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; claims to cure, treat, mitigate, or prevent diabetes, depression and other mental health disorders, and infertility. In addition, FDA also posted 69 public notifications for products that have been found to be tainted with undeclared drugs, many of which are marketed as dietary supplements.

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 2021, FDA responded to 49 NDI notifications. FDA acknowledged 27 of the notifications submitted with no objection. Of the remaining 22 notifications, FDA raised safety or identity concerns with 11, seven were determined to not pertain to a dietary ingredient or dietary supplement, and four were deemed incomplete.

In FY 2021, FDA received more than 2,400 adverse event reports (AERs) related to dietary supplements. The reports are evaluated by clinical reviewers in CFSAN to monitor the safety of consumer products.

Nutrition Innovation Strategy

The multi-year Nutrition Innovation Strategy (NIS) 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.[44]

The NIS's overall focus is on reducing preventable death and disease related to poor nutrition. This new strategy gives consumers easier access to nutritious and affordable foods by providing them with information and by supporting industry innovation towards healthier foods.

Key elements of the strategy include:

- Modernizing health claims
- Modernizing ingredient labels
- Modernizing standards of identity
- Implementing the nutrition facts label and menu labeling
- Reducing sodium

FDA Issues Sodium Reduction Final Guidance

In October 2021, FDA issued final guidance for the food industry that provides voluntary, short-term (2.5 year) sodium reduction targets for a broad range of processed, packaged and prepared foods to help reduce the amount of sodium in the U.S. food supply.[45]

Sodium reduction is a critically important public health issue because Americans consume on average 50% more than the recommended limit for those age 14 years and older. This includes our youngest and most vulnerable populations, with more than 95% of children aged 2 to 13 years old exceeding recommended limits of sodium for their age groups, which could have profound impacts on later health outcomes. Too much sodium can increase the risk for developing hypertension, which, in turn, raises the risk for heart attacks and strokes. In the U.S., diet-related chronic diseases are the leading cause of death and disability. Additionally, these chronic diseases are experienced disproportionately by racial and ethnic minority groups.

The targets in the guidance are designed to support decreasing average daily sodium intake by about 12%—from approximately 3,400 milligrams (mg) to 3,000 mg per day. This reduction is expected to result in tens of thousands of fewer cases of heart disease and stroke and billions saved in healthcare costs. The FDA believes these targets are feasible to achieve in two and a half years and covers both manufactured foods and foods prepared by commercial establishments, such as restaurants. About 70% of the sodium consumed in the U.S. comes from packaged, prepared and restaurant food, so successful sodium reduction depends on reducing sodium broadly and gradually across the food supply.

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

[45] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-voluntary-sodium-reduction-goals

Additionally, in February of 2022, USDA's Food and Nutrition Service issued their final rule on transitional nutrition standards for school-based meals, an action that supports ongoing whole-of-government efforts to improve nutrition, reduce chronic disease and help create a healthier food supply for all.[46]

The USDA rule notes that their transitional sodium standards align with the FDA's short-term voluntary sodium reduction targets, which in turn are anticipated to support a gradual sodium reduction strategy for the National School Lunch Program and the School Breakfast Program. The rule also reflects the importance of the FDA's efforts moving forward to support broad, gradual reduction of sodium intake.

Modernizing Standards of Identity

In June of 2021, in line with its goals to modernize standards of identity, FDA issued a final rule to amend and modernize the standard of identity for yogurt by allowing for greater flexibilities and technological advances in yogurt production.

Under the final rule, lowfat yogurt and nonfat yogurt will be covered under FDA's general definition and standard of identity, which allows nutritionally modified versions of traditional standardized foods.

The final rule expands the allowable ingredients in yogurt, including sweeteners such as agave, and reconstituted forms of basic dairy ingredients. It establishes a minimum amount of live and active cultures yogurt must contain to bear the optional labeling statement "contains live and active cultures" or similar statement and supports the many innovations that have already been made in the yogurt marketplace, including continuing to allow manufacturers to fortify yogurts, such as adding vitamins A and D, as long as they meet fortification requirements. The rule also allows various styles or textures of yogurt as long as they meet requirements in the standard of identity.

The compliance date of this final rule is January 1, 2024, which is the uniform compliance date for final food labeling regulations issued in 2021 and 2022.

Additionally, in November 2021, FDA issued guidance to industry on the Temporary Marketing Permit (TMP) process. The guidance will help clarify, streamline, and improve the efficiency of the TMP application process. TMPs allow manufacturers to market test products that deviate from established Standards of Identity (SOI). TMPs enable manufacturers to conduct research and obtain data that can be used to support a petition to amend a food standard. The guidance is a component of the FDA's work to update food standards of identity (SOIs) and identify new ways to streamline SOI-related processes to provide additional clarity and flexibility to encourage industry to innovate and produce healthier foods.[47]

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[46] https://www.usda.gov/media/press-releases/2022/02/04/usda-helps-schools-build-back-better-issues-transitional-nutrition

[47] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-temporary-permits-interstate-shipment-experimental-packs-food-varying-requirements

Issued Final Rule on Gluten-Free Labeling of Fermented and Hydrolyzed Foods

In August 2021, FDA released a final rule to establish compliance requirements for fermented and hydrolyzed foods, or foods that contain fermented or hydrolyzed ingredients, and bear the "gluten-free" claim.[48] In both fermented and hydrolyzed foods, protein strands have been broken down into smaller strands or individual amino acids. The rule is designed to protect individuals with celiac disease -- a hereditary, chronic inflammatory disorder of the small intestine -- who are advised to avoid all sources of gluten in their diet to protect against adverse health effects associated with consumption of gluten for those with the disease. The compliance date for the rule is August 13, 2021.

[48] https://www.federalregister.gov/documents/2020/08/13/2020-17088/food-labeling-gluten-free-labeling-of-fermented-or-hydrolyzed-foods

Issues Uniform Compliance Date and Resources for Nutrition Facts Labeling Rules

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

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 6 - 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 2019 Actuals	$1,059,926,000	$1,059,926,000	---
FY 2020 Actuals	$1,087,215,000	$1,087,215,000	---
FY 2021 Actuals	$1,099,001,000	$1,098,973,000	$28,000
FY 2022 Annualized CR	$1,111,237,000	$1,099,701,000	$11,536,000
FY 2023 President's Budget	$1,231,960,000	$1,220,193,000	$11,767,000

Figure 5 - Funding History

BUDGET REQUEST

The FY 2023 President's Budget for the Foods Program is $1,231,960,000, of which $1,220,193,000 is budget authority and $11,767,000 is user fees. The budget authority increases $120,492,000 compared to the FY 2022 Annualized CR and User Fees increase by $231,000. The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is $420,833,000. The Office of Regulatory Affairs amount $811,127,000.

BUDGET AUTHORITY

Food Safety (+$71.2 million / 112 FTE)

New Era of Smarter Food Safety (+$20.2 million / 20 FTE)

Center: +$10.9 million / 20 FTE

Field: +$9.4 million

The FY 2023 Budget includes an increase of $10.9 million for CFSAN and $9.4 million for ORA to advance goals of the New Era of Smarter Food Safety Blueprint. The FY 2023 New Era of Smarter Food Safety request builds on the FY 2022 President's Budget to enable FDA to leverage the latest science on foodborne outbreaks and apply new technologies to improve the efficiency and effectiveness of FDA's oversight activities. Of the $20.2 million requested by the Foods program in FY 2023 for New Era of Smarter Food Safety, the request includes $7.3 million for CFSAN and $6.6 million for ORA 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 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.

Root-cause analyses will also provide more robust data for predictive analytics to detect future problems sooner. Working with industry and regulatory partners, FDA will incorporate root cause data to develop commodity-specific prevention plans – expanding on our experience with targeted, action-oriented initiatives (i.e., leafy greens) – and improve prevention-oriented food safety practices to better avoid identified risks. The FY 2023 Budget will also strengthen data sharing and predictive analytics capabilities to better prevent foodborne illnesses.

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. For example, FDA will begin developing requirements for user-friendly IT platforms to better analyze data and better share data with stakeholders, including industry, academia, and regulatory partners.
FDA will adapt our oversight framework to help ensure the safety of foods produced and distributed using new business models (e.g., e-commerce). 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.

Healthy and Safe Food for All (+$13.5 million / 26 FTE)

Center: +$13.5 million / 26 FTE

FDA requires new resources to build on funding requested in FY 2022 to improve health equity through nutrition and reduce exposure to harmful toxins in food. In FY 2023, CFSAN plans to build on its FY 2022 initiative for maternal and infant health and nutrition by applying an approach that integrates nutrition, diet, toxicology, and health across the lifespan. In doing so, the Center will help ensure that Americans of all ages and backgrounds can reduce their risk of diet-related chronic diseases and continue to have confidence in the food supply.

Chronic diseases, such as heart disease and cancer, are the leading cause of death and disability in the United States. Additionally, almost three quarters of the U.S. adult population is obese or overweight and 40% of children and teens are overweight or obese. Poor dietary practices play a central role in chronic and preventable disease. Further, many nutrition-related chronic diseases are experienced disproportionally by racial and ethnic minority populations. For example, more than 4 in 10 American adults have high blood pressure, and that number increases to almost 6 in 10 for African American adults. Many of these disparities have been highlighted during the COVID-19 pandemic. A recent study found that between the second half of 2019 and the second half of 2020, children's obesity rates increased substantially, and that increase was more pronounced in children who were Hispanic, non-Hispanic Black, publicly insured, or lower income. In 2021, CDC issued a report indicating that among children, rates of body mass index (BMI) increases doubled in 2020 compared to rates prior to the pandemic; and further, those already overweight or obese, and younger school-aged children experienced the largest increases.

FDA's Foods Program, in partnership with the agency's Office of Minority Health and Health Equity, has a unique role to play to support federal initiatives that are critically needed to reverse this concerning COVID-related increase in childhood obesity, such as through efforts to encourage industry to reformulate healthier food options for all, including foods provided through public assistance programs to children, and empowering consumers to make decisions that support a healthy diet through more accessible labeling and nutrition education including programs targeted to specific at-risk populations.

With additional resources in FY 2023, FDA will make gains in balancing the ongoing efforts of providing safe food with a renewed emphasis on encouraging the increased availability in the marketplace of healthy food options. This will include an expansion of FDA's nutrition initiatives to support current government-wide nutrition-related priorities—such as modernizing nutrition labeling—which may especially benefit underserved populations. Expanding education and outreach programs to consumers will help to raise awareness and understanding of the labeling updates as well as empower consumers to make healthy choices. Additional resources will also enable FDA to explore opportunities for nutrition labeling in e-commerce. Consumers' use of e-commerce to shop for groceries has dramatically increased in recent years, and further accelerated during the COVID-19 pandemic, making it important for FDA to use our tools to assure that consumers continue to have access to food labeling information on food packages at the point of purchases made through e-commerce. This trend cuts across all demographics, including SNAP participants as USDA expanded the ability to redeem SNAP benefits online in

all states and D.C. in 2020. Additionally, younger consumers, African Americans, and parents tend to grocery shop online more frequently than others.

Increased resources will also enable the agency to make further progress in addressing toxic elements such as lead, arsenic, mercury, and cadmium in food. For example, with funds requested in FY 2022, CFSAN plans to build capacity and work with stakeholders to address the growing concerns related to toxic elements in food commonly consumed by young children—highlighting the Center's crucial role in protecting the nation's food supply as well as the need to address food safety for our youngest consumers through all stages of development. Funds requested in FY 2023 will enable CFSAN to further expand capacity to better mitigate risks posed by chemicals, noting that there may be disparities in exposure to many of these chemicals based on cultural/lifestyle practices. In addition to the outreach for children and parents that FDA plans with FY 2022 funds, FY 2023 funds will allow FDA to extend outreach efforts to other potentially vulnerable populations and produce education materials that integrate information to help consumers make healthy choices that reduce their exposure to toxic elements.

Finally, the requested funding increase will enable FDA to increase scientific and regulatory capacity focused on dietary supplements. Consumers are increasingly seeking out dietary supplements to augment their diet and improve their health. There has been a ten-fold increase in the dietary supplement market since the passage of DSHEA, from $4 billion to $40 billion. This trend has only increased during the COVID-19 pandemic. Yet most dietary supplements can be lawfully introduced to the market without ever notifying FDA. The resources requested will support the legislative proposal to amend the Dietary Supplement Health and Education Act of 1994 (DSHEA) by establishing a product listing requirement and strengthening FDA's enforcement of products marketed as "dietary supplements" that, for example, contain certain drug ingredients. New resources would support this proposal by funding necessary IT system development and new FTE to review additional product data, prioritize FDA investigations, and take compliance actions as needed to ensure that consumers who seek to augment their health with dietary supplements are protected from unsafe or otherwise unlawful products.

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

Center: +18.0 million / 26 FTE

The health and well-being of mothers, infants, and children is critical; yet CFSAN is severely under-resourced in its programs that are best positioned to make progress in this important area. 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, understaffed 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 maintain and carry forward what we have started.

Toxic heavy metals such as lead, arsenic, mercury, and cadmium are naturally present in air, water, and soil and thus a certain amount of contamination in food is unavoidable, but exposure risk for infants and young children from these toxic elements in foods could and should be reduced through agricultural or manufacturing practices. FDA has prioritized babies and young

children because their smaller body sizes and rapid growth and development make them more susceptible to contamination with these metals through the significant impact that these metals can have on children's neurological development. On April 8, 2021, FDA announced its Closer to Zero action plan, which outlines a science-based, transparent, iterative approach for achieving continual improvements over time in reducing the levels of toxic elements in baby food, which would be bolstered with the new funding. FDA wants 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 (1) co-occurrence of contamination with toxic elements in baby foods and impacts on neurodevelopment and (2) 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 healthcare providers and 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 technical assistance education materials for industry which outline requirements for managing and minimizing the presence of toxic elements in their products. FDA will continue working with our federal and state partners in USDA, NIH, and EPA; growers and manufacturers; as well as external scientists and advocacy groups on this important issue. A whole of government approach in conjunction with stakeholders will lead to meaningful and sustainable reductions in exposure to toxic elements from food.

Infant formula is a significant or even the 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 Food, Drug, and Cosmetic 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 and increasing infant formula submission rate, along with the increasing complexity of submissions and the growing number of manufacturers, 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 are legally allowed to 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. Additional review capacity is also needed during outbreak or recall situations involving infant formula, as the subject matter experts supporting response efforts are the same personnel who need to review new submissions and first process submissions to support infant formula supply chains.

Additionally, the U.S. has a strikingly high prevalence of obesity and nutrition-related chronic disease. Nutrition-related diseases such as heart disease and cancer are the leading causes 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 Toxicology Issues, Food (+$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 other food safety programs 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, as well as increasing post-market safety efforts. 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 and ground 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 for 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 underfunded 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 needs 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 (+$49.3 million / 41 FTE)
Capacity Building (+$11 million / 9 FTE)

Center: +$3.5 million / 3 FTE

Field: +$7.5 million / 6 FTE

The FY 2023 President's Budget includes $59.4 million for Capacity Building, including $11 million for the Foods Program. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Public Health Employee Pay Costs (+$19.7 million)

Center: +$6.9 million

Field: +$12.8 million

The FY 2023 President's Budget includes $51.9 million, including $19.7 million within the Foods program, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$8.5 million / 20 FTE)

Field: +$8.5 million / 20 FTE

The FY 2023 President's Budget includes $33.8 million for optimizing inspectional activities, including $8.5 million within CFSAN, to support capacity building towards an advanced, highly trained investigators capable of analyzing available data to increase the efficiency and productivity of our inspection operations.

Reducing Animal Testing Through Alternative Methods (+$674,000 / 2 FTE)

Center: +$674,000 / 2 FTE

The FY 2023 President's Budget includes $5 million, including $674,000 within CFSAN, to implement a cross-agency New Alternative Methods Program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

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

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $9.4 million for the Foods program, 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.

USER FEES

Current Law User Fees (+$231,000 million)

Center: +$18,000

Field: +$213,000

The Foods Program request includes an increase of $231,000 for user fees which will allow FDA to fulfil its mission of promoting and protecting the public health by ensuring safety and efficacy of FDA-regulated products.

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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
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 2021: 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 2021: 880 enrolled Target: 878 enrolled (Target Exceeded)	895	910	+15
212415: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired Shiga toxin-	CY 2020: 3.34 cases/100,000 (Historical baseline)	4.3	4.2	-0.1

Measure	Year and Most Recent Result /Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
producing *Escherichia coli* (STEC) infections. *(Outcome)*				
212416: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired *Listeria monocytogenes* infections. *(Outcome)*	CY 2020: 0.21 cases/100,000 (Historical baseline)	0.25	0.25	Maintain
212417: Foodborne Illness - Reduce the incidence of laboratory-diagnosed, domestically-acquired *Salmonella* infections. *(Outcome)*	CY 2020: 12.80 cases/100,000 (Historical baseline)	14.0	13.7	-0.3
214306: The average number of working days to serotype priority pathogens in food. (Screening Only) *(Output)*	FY 2021: 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 2021: 94.8% 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 2021: 75.3% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2021: 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 2021: 3,200 rad & 2,600 chem Target: 2,500 rad & 2,100 chem (Target Exceeded)	3,200 rad & 2,600 chem	3,200 rad & 2,600 chem	+ 700 rad & 400 chem

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 2021 target of 80% by reviewing and completing 100% of the petitions received within 360 days of receipt, a result consistent with the FY 2019 performance of 100% completed within the same timeframe.

Voluntary National Retail Food Regulatory Program Standards

Strong and effective regulatory programs at the state, local, tribal and territorial (SLTT) 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 2021 actual enrollment number of SLTT in the Retail Program Standards reflects an annual increase of 17 enrollments from the year-end FY 2020 total enrollments (863). 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. The FY 2022 and FY 2023 targets reflect increases in the number of enrollees by 15 above the previous year's actual number of enrollees or target.

Key Pathogens

Consistent with the Healthy People 2030 objectives, FDA is tracking a set of performance measures related to the incidence rates of infection for Shiga toxin-producing *E. coli* (STEC), *Salmonella,* and *Listeria monocytogenes*. These organisms remain significant from a public health perspective in terms of the number and severity of illnesses they cause, and outbreaks are frequently attributed to FDA-regulated products. Therefore, there is a continued need to invest resources into prevention activities to reduce illness caused by these pathogens. In FY 2020, there was a significant decrease in the incidence rate of infection for each of these three pathogens. According to the CDC, there was a 26% decrease in incidence of infections caused by all pathogens transmitted commonly through food during 2020, which was the largest single-year variation in incidence during 25 years of FoodNet surveillance.[52] Widespread public health interventions implemented to prevent SARS-CoV-2 transmission might have contributed to this decrease in detection of illnesses. A higher than usual proportion of infections might have been undetected because factors such as changes in health care-seeking behaviors, and broader use of telehealth might have limited the number of stool specimens tested. Marked decreases in emergency department visits for abdominal pain and other digestive or abdominal signs and

[52] Ray LC, Collins JP, Griffin PM, et al. Decreased Incidence of Infections Caused by Pathogens Transmitted Commonly Through Food During the COVID-19 Pandemic — Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 2017–2020. MMWR Morb Mortal Wkly Rep 2021;70:1332–1336. DOI: http://dx.doi.org/10.15585/mmwr.mm7038a4

symptoms occurred early in the pandemic. The proportion of infections resulting in hospitalization increased slightly; possible explanations include disproportionate decreases in health care-seeking among those with milder illness or delayed health care-seeking during the pandemic resulting in more severe illness at the time of clinical presentation. Public health interventions, such as increased handwashing, to prevent SARS-CoV-2 transmission likely influenced exposures associated with enteric diseases, resulting in real declines in incidence. Continued surveillance might improve the understanding of how the pandemic affected foodborne illness and might help identify prevention measures and strategies that FDA, industry, and other public health partners can use to target particular pathogens and foods. Because of these uncertainties, CFSAN is keeping the original FY 22 and 23 targets consistent with Healthy People 2030 in place for now, and will monitor the potential need to adjust targets going forward.

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 2021, 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 2022 and FY 2023 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.

PROGRAM ACTIVITY DATA

CFSAN Workload and Outputs	FY 2021 Actuals[7]	FY 2022 Estimate[8]	FY 2023 Estimate[8]
Food and Color Additive Petitions			
Petitions Filed [1]	2	10	10
Petitions Reviewed [2]	2	10	10
Premarket Notifications for Food Contact Substances			
Notifications Received	78	94	94
Notifications Reviewed [3]	78	94	94
Infant Formula Notifications			
Notifications Reviews Due to Be Completed [4]	42	45	45
Notification Reviews Completed Within 90 Days of Filing [5]	15	45	45
FDA Review Time	90 days	150 days	150 days
New Dietary Ingredient Notifications			
Notification Reviews Due to Be Completed	46	52	52
Notification Reviews Completed Within 75 Days of Filing [6]	46	52	52
FDA Review Time	75 days	75 days	75 days

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

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

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

[4] A notification may include more than 1 infant formula.

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

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

[7]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.

[8]As of January 19, 2021, the Infant Formula Program began informing those firms providing new infant formula submissions that FDA would need up to an additional 60 days to complete its reviews of those submissions. As of November 19, 2021, this review extension time period changed to 150 days.

Figure 6 - CFSAN Workload and Outputs

Field Foods Program Workload and Outputs	FY 2021 Actuals[5]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***4,657***	***4,320***	***8,000***
Domestic Food Safety Program Inspections	2,629	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.	
Imported and Domestic Cheese Program Inspections	77		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	119		
Domestic Fish & Fishery Products (HACCP) Inspections	357		
Import (Seafood Program Including HACCP) Inspections	58		
Juice HACCP Inspection Program (HACCP)	66		
Interstate Travel Sanitation (ITS) Inspections	244		
Domestic Field Exams/Tests	669	*850*	25,006
Domestic Laboratory Samples Analyzed	7,677	*11,500*	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS[1]	***79***	***50***	***1,400***
All Foreign Inspections	*79*	*50*	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***4,736***	***4,370***	***9,400***
IMPORTS			
Import Field Exams/Tests[2]	*63,640*	*82,500*	168,200
Import Laboratory Samples Analyzed	*11,444*	*12,000*	35,300
Import Physical Exam Subtotal	**75,084**	**94,500**	**203,500**
Import Line Decisions	18,651,210	19,583,771	20,562,959
Percent of Import Lines Physically Examined	0.40%	0.48%	0.99%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***5,940***	***2,500***	***3,000***
State Contract Food Safety (Non HACCP) Inspections	5,276	4,090	5,000
State Contract Domestic Seafood HACCP Inspections	452	327	400
State Contract Juice HACCP	36	29	35
State Contract LACF/Acidified Food Inspections	89	61	75
State Contract Foods Funding	$13,334,560	$13,492,683	$13,627,610
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***10,676***	***6,870***	***12,400***

[1] The FY 2021 actual unique count of foreign inspections includes 77 OGPS inspections (57 for China, 2 for India, & 18 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.

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 7 - Field Foods Program Workload and Outputs

Field Cosmetics Program Workload and Outputs	FY 2021 Actuals[2]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***15***	***20***	100
Domestic Inspections	15	20	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***0***	***0***	0
Foreign Inspections	0	0	0
IMPORTS			
Import Field Exams/Tests[1]	2236	3,300	3,300
Import Laboratory Samples Analyzed	70	215	215
Import Physical Exam Subtotal	**2,306**	**3,515**	**3,515**
Import Line Decisions	3,060,422	3,121,630	3,184,063
Import Line Decisions	0.08%	0.11%	0.11%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***15***	***20***	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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 8 - Field Cosmetics Program Workload and Outputs

HUMAN DRUGS

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Human Drugs	**1,997,174**	**2,006,214**	**2,091,393**	**2,219,690**	**128,297**
Budget Authority	***689,195***	***688,844***	***689,195***	***790,133***	***100,938***
User Fees	***1,307,979***	***1,317,370***	***1,402,198***	***1,429,557***	***27,359***
Center	1,753,685	1,768,212	1,844,017	1,940,854	96,837
Budget Authority	510,226	509,915	510,226	580,931	70,705
User Fees	1,243,459	1,258,297	1,333,791	1,359,923	26,132
Prescription Drug (PDUFA)	*800,637*	*796,722*	*878,206*	*895,565*	17,359
Generic Drug (GDUFA)	*404,241*	*430,627*	*419,210*	*427,258*	8,048
Biosimilars (BsUFA)	*37,928*	*30,047*	*35,709*	*36,420*	711
Outsourcing Facility	*653*	*901*	*666*	*680*	14
Field	243,489	238,002	247,376	278,836	31,460
Budget Authority	178,969	178,929	178,969	209,202	30,233
User Fees	64,520	59,073	68,407	69,634	1,227
Prescription Drug (PDUFA)	*8,707*	*8,763*	*9,312*	*9,498*	186
Generic Drug (GDUFA)	*54,096*	*48,710*	*57,205*	*58,209*	1,004
Biosimilars (BsUFA)	*1,322*	*1,095*	*1,487*	*1,516*	29
Outsourcing Facility	*395*	*505*	*403*	*411*	8
FTE	**6,737**	**6,725**	**6,746**	**6,873**	**127**

Figure 9 - Narrative by Activity

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 DESCRIPTIONS AND ACCOMPLISHMENTS

FDA's Human Drugs Program is responsible for ensuring the safety and efficacy of prescription and over-the-counter (OTC) drug products, including generic drugs, and therapeutic biological products, including biosimilar and interchangeable biosimilar 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 2021, CDER approved 53 novel drugs, of which 25 were first-in-class, which is one indicator of the drug's potential for strong positive impact on public health. In FY 2021, CDER also approved the first interchangeable biosimilar insulin product, and provided new guidance to further enhance the security of prescription drugs in the U.S. supply chain.

This 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 helping to ensure that such treatments 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. CDER continues to explore alternative approaches to inspections of clinical trials, including the use of remote assessments and access to electronic systems and optimizing digital health technologies to facilitate clinical investigations during COVID-19. 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. 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 may be necessary for data reliability and the safety of trial participants and personnel.

Moreover, 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 and reduce the risks of exposure to 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 2023, 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 the postmarket safety of approved drug products, whereas the use of RWE to support effectiveness has been limited. The 21st Century Cures Act requires FDA to evaluate the potential use of RWE to help support the approval of new indications of approved drugs, or to help support or 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 RWE that will advance the development of therapeutic products and strengthen regulatory oversight of medical products across their lifecycle.

Among other drug approvals involving RWE, in July 2021, and based on a non-interventional (observational) study providing key evidence of effectiveness, CDER approved a new indication for Prograf (tacrolimus)—in combination with other immunosuppressant drugs to prevent organ rejection in adult and pediatric patients receiving lung transplantation.[53] The approval reflects how a well-designed, non-interventional study relying on fit-for-purpose RWD, in this case with a suitable control, can be considered adequate and well-controlled under FDA regulations – representing the primary support for a finding of substantial evidence of effectiveness.

In September 2021, FDA issued the draft guidance titled Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products.[54] In October 2021, FDA issued the draft guidance titled Data Standards for Drug and Biological Product Submissions Containing Real-World Data. In November 2021, the

[53] https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-new-use-transplant-drug-based-real-world-evidence

[54] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory?utm_medium=email&utm_source=govdelivery

agency issued the draft guidance titled Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry. In December 2021, FDA issued the draft guidance titled Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products.[55] These draft guidances are part of a series of guidance documents that FDA plans to continue to publish as part of the agency's RWE Program and in support of the 21st Century Cures Act and the Prescription Drug User Fee Act.

FDA also continues to oversee ongoing RWE activities and has launched new research projects to help us better understand how RWD can generate RWE that meets regulatory requirements. In FY 2021, FDA established a five-year Inter-agency Agreement with the Department of Veterans Affairs to support RWD/RWE investigations that are relevant to the safety and effectiveness of FDA-regulated medical products and that also promote a learning healthcare system.

Additional RWE-related activities involved FDA's cooperative agreement with the Duke-Margolis Center for Health Policy and the Reagan Udall Foundation of the FDA. For example, using the convener grant with Duke-Margolis, in February 2021, FDA hosted a two-day public meeting titled *Evaluating RWE from Observational studies in Regulatory Decision-Making: Lessons Learned from Trial Replication Analyses*.[56] In addition, FDA funded new activities in conjunction with the Reagan Udall Foundation to coordinate public webinars aligned with the publication of each of the four RWE guidance documents described above.

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, FDA awarded the third 5-year Sentinel contract to two consortiums led by Harvard Pilgrim Health Care and Deloitte Consulting, which established three distinct coordinating centers: the Sentinel Operations Center, the Sentinel Innovation Center, and the Community Building and Outreach Center. This Sentinel structure widens participation to a broader array of scientific expertise, expands Sentinel's use of electronic health records (EHR) by focusing on emerging technologies including feature engineering, natural language processing, advanced analytics and data interoperability, and cultivates a robust scientific community to uncover novel ways to leverage the system's core capabilities beyond drug safety.

Sentinel maintains and builds upon the core innovations that were responsible for many of the achievements in the prior decade: participation of data partners who bring their knowledge and expertise to the Sentinel network, re-useable analytic tools that use data formatted in the Sentinel Common Data Model, multifaceted data quality and curation processes, 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 capturing approximately 800 million person-years of longitudinal data and more

[55] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-real-world-data-and-real-world-evidence-support-regulatory-decision-making-drug

[56] https://healthpolicy.duke.edu/events/evaluating-rwe-observational-studies-regulatory-decision-making-lessons-learned-trial

than 70 million patients actively accruing new data. Sentinel also includes data on more than 5 million live-birth deliveries with a mother-infant linkage.

This year marked 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 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 congenital cardiac malformations after maternal exposure to armodafinil/modafinil during pregnancy, and Sentinel also evaluated the risk of non-melanoma skin cancer following use of hydrochlorothiazide. In that case, the risk evaluation resulted in a label change to drug products containing hydrochlorothiazide.[57] 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 FDA Catalyst program was launched to leverage the Sentinel infrastructure and supplement it with data from interventions or interactions with health plan members and/or providers. FDA Catalyst is currently being used to provide data linkages to augment a randomized trial that tests whether a commonly used antibiotic can prevent chronic obstructive pulmonary disease (COPD) exacerbations resulting in hospitalization in patients using medical claims data. The FDA Catalyst program was also critical to the development of the FDA MyStudies app that sponsors can use to collect data directly from patients. Currently, the FDA MyStudies app is also supporting two demonstration projects focused on assessing the collection of real-world data in registries as well as the utilization of real-world data in hybrid clinical trials.

Featured below are notable achievements in FY 2021:

- Drug safety analyses conducted in Sentinel informed updates to the labeling[58] of oral anticoagulant products for the risk of clinically significant uterine bleeding and the labeling of parenteral iron products for the risk of severe adverse reactions in pregnant women.
- The Sentinel Innovation Center[59] and the Community Building and Outreach Center[60] separately published their Master Plans, which outline core projects and activities each Center will implement to advance the Sentinel System's strategic aims.
- FDA initiated multiple projects through the Sentinel Innovation Center to advance Sentinel's capabilities to utilize EHR data in areas including natural language processing, machine learning and probabilistic phenotyping.

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[57] https://sentinelinitiative.org/news-events/fda-safety-communications-labeling-changes/fda-label-change-hydrochlorothiazide-and-non

[58] https://sentinelinitiative.org/news-events/fda-safety-communications-labeling-changes

[59] https://www.sentinelinitiative.org/news-events/publications-presentations/innovation-center-ic-master-plan

[60] https://www.sentinelinitiative.org/news-events/publications-presentations/community-building-and-outreach-center-cboc-master-plan

- FDA completed an end-to-end redesign of the Sentinel Initiative website through the Community Building and Outreach Center to improve the usability and findability of information on the site and to better serve the Sentinel community.
- Sentinel has continued supporting FDA's response to the COVID-19 pandemic[61] by expanding and enhancing data infrastructure, launching new scientific studies, and coordinating with other national and international partners. Some key activities include:
    - Developing and maintaining a distributed database with the most current data feasible to support timely FDA studies of the use and performance of therapeutics for COVID-19.
    - Deepening and diversifying partnerships with EHR-based organizations and EHR data aggregators.
    - Monitoring therapeutics authorized by FDA under emergency use authorizations.
    - Evaluating the natural history of coagulopathy among hospitalized COVID-19 patients.
    - Publishing a master protocol designed to use electronic healthcare data to describe COVID-19 clinical characteristics and identify patient factors related to disease progression/prognosis, which is supporting a study addressing questions about the natural history of COVID-19 in pregnancy.
    - Participating in the Reagan-Udall Foundation COVID-19 Evidence Accelerator activities to share insights, compare results, answer key questions about COVID-19, and lead a workstream to evaluate coagulopathy in COVID-19 patients.
    - Collaborating with international regulators through the International Coalition of Medicines Regulatory Agencies[62] on several studies to address key issues in the management of COVID-19.

Overdose Prevention

The agency recognizes that the nation continues to face a drug overdose crisis. While the number of prescription opioids dispensed has steadily declined since 2012, opioid overdose deaths continue to rise. Between October 2020 and September 2021, there were an estimated 78,000 overdose deaths involving legal and illicit opioids. In recent years illicit opioids, largely driven by fentanyl and its analogues, have become key contributors to the overdose crisis. We are additionally aware of other controlled substances – including benzodiazepines and stimulants, particularly methamphetamine – being used in combination with opioids. The complexity of addressing polysubstance use makes our efforts all the more important.

FDA also recognizes the risks of opioids and other controlled substances as well as the benefits of these drugs for patients who need them, including those with debilitating chronic conditions. It will take carefully developed, coordinated, and sustained action by multiple stakeholders to reduce the incidence of drug misuse, abuse, addiction, overdose, and death, while preserving appropriate access to these drugs for patients who need them. Doing our part to ensure the safe use of opioids and other controlled substances and ameliorate the overdose crisis is among

[61] https://www.sentinelinitiative.org/assessments/coronavirus-covid-19

[62] http://icmra.info/drupal/en/covid-19

FDA's highest priorities. FDA is engaging in many ongoing activities aimed at furthering these goals.

In alignment with HHS' new Overdose Prevention Strategy, FDA is focusing our efforts on opioids and other controlled substances in the following four areas:

1. Support primary prevention by reducing unnecessary initial prescription drug exposure and inappropriate prolonged prescribing
2. Encourage harm reduction through innovation and education
3. Advance development of substance use disorder treatments
4. Protect the public from unapproved, diverted, and counterfeit drugs presenting serious overdose risks

FDA has taken the following steps toward its goal to reduce the scope of the overdose crisis:

1) **Primary Prevention**:

- February 2022 - issued draft guidance on the development of non-opioid analgesics for acute pain as part of implementation of SUPPORT Act Section 3001.
- October 2021- collaborated with the Duke-Margolis Center for Health Policy to hold a public workshop to give stakeholders an opportunity to provide input on aspects of the current opioid crisis that could be mitigated in a measurable way by requiring mandatory prescriber education as part of a Risk Evaluation and Mitigation Strategy (REMS).
- July 2021- collaborated with the Duke-Margolis Center for Health Policy to hold a two-day public workshop to gather input related to the safe use of benzodiazepines, including epidemiological and abuse liability data, patient and clinician perspectives and experiences, and gaps in data and understanding.
- December 2020 - convened a public scientific workshop to discuss scientific approaches and develop a path forward for evaluating the effect of the opioid analgesics REMS education program on prescriber behavior and patient outcomes.
- 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). The project is currently underway, and the typical timeframe for guideline development and subsequent adoption ranges from 2-4 years.

2) **Harm Reduction**:

- October 2021 - approved ZIMHI (naloxone hydrochloride), 5 mg injection as an additional option to treat opioid overdose. FDA has previously approved injectable naloxone hydrochloride products in 0.4 mg and 2 mg doses naloxone injectable products.
- October 2021- collaborated with the Reagan-Udall Foundation on two roundtables with clinicians and harm reduction groups to gather input on fentanyl screening and drug checking (testing illegal drugs for the presence of fentanyl) in clinical and community settings. The goal of these roundtables was to inform technology development, research, and practice.
- June 2021 - collaborated with the Duke Margolis Center for Health Policy to facilitate an exchange of information and opinions about consumer-focused disposal options, including in-home disposal options.

- April 2021 - approved a higher dose naloxone nasal spray, KLOXXADO. KLOXXADO is indicated for the emergency treatment of known or suspected opioid overdose. The newly approved product delivers 8 milligrams (mg) of naloxone into the nasal cavity. The FDA had previously approved 2 mg and 4 mg naloxone nasal spray products.
- March 2021 - approved new labeling for opioid analgesics intended for use in the outpatient setting and medicines used to treat opioid use disorder, recommending, among other things, that health care professionals discuss naloxone with all patients when prescribing one of these drugs. In addition, FDA launched a Naloxone Home Study CE Webinar entitled, "An Overview of Naloxone and FDA's Efforts to Expand Access."
- March 2021- issued a white paper which introduces FDA's opioid systems modeling efforts under a cooperative agreement between FDA and research partners. CDER has begun beta-test use of the model to support assessments of policy questions. Additional work is on-going to enhance the model and to integrate the model into an analysis service that can inform policy making.
- 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 medicines for treatment of opioid use disorder and address clinical endpoints acceptable to demonstrate effectiveness of such drugs.
- 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.
- March 2020 – initiated 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. In 2021, CDER implemented prioritized use cases to enable efficient data management, queries, and social media data analyses.

3) **Evidence-Based Treatment**:

- October 2021 - collaborated with the National Institute on Drug Abuse and the Reagan-Udall Foundation to hold a public workshop to discuss a practical research agenda for treatment development for stimulant use disorder, focusing on innovation in clinical trial design and candidate endpoints for the evaluation of potential treatments.
- August 2021 - published a systematic review of literature assessing the amount of patient-reported opioid analgesic used for different acute pain conditions and surgical procedures to provide evidence for the need for take-home disposal options, to help determine useful amounts of opioid analgesics to include in fixed-quantity packaging, and to support evidence-based prescribing guidelines.
- June 2021 - hosted a public scientific workshop to bring stakeholders together to discuss morphine milligram equivalents (MMEs), with the goals of providing an understanding of the science and data underlying existing MME calculations for opioid analgesics, discussing the gaps in these data, and discussing future directions to refine and improve the scientific basis of applications, such as their use in assessing risk of opioid use disorder and overdose.
- June 2020 - submitted a report to Congress on how the agency will support the development of indication-specific, 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.

4) **Other Actions**:

- We are also continuing our rigorous efforts to protect the public from unapproved, diverted, or counterfeit drugs. To date, we have taken the following actions to protect consumers from illegal online sales of controlled substances, including opioids
- September 2021- virtually hosted internet stakeholders, government entities, academia, and other important partners within the internet ecosystem at FDA's third Online Opioid Summit. Discussions at the summit addressed topics including the evolving landscape of online opioid purchasing, such as younger and more vulnerable populations being exposed to these dangerous opioids through social media and other online platforms; ways to enhance cross-industry and global collaboration; successes and novel solutions implemented since prior summits; and new ways to continue to prevent the illegal sale of opioids through internet platforms and services.
- February 2021 - issued a warning letter to the sponsor of Dsuvia regarding disseminated promotional communications that undercut FDA-required conditions on the proper administration of the drug, which requires particular diligence to minimize the risk of serious or even fatal adverse events.
- From August 2020 to September 2021 -issued 21 warning letters to website operators marketing unapproved and misbranded opioids for sale to U.S. consumers. Three of these warning letters cited the sale of unapproved and misbranded opioids and benzodiazepines on the same websites.
- June 2020 - launched a 120-day pilot with the National Telecommunications and Information Administration (NTIA) and three domain name registries to help reduce the availability of unapproved opioids illegally offered for sale online. As the result of the pilot, nearly 30 websites illegally offering opioids for sale became inaccessible to the public. FDA continues to collaborate with registries in a similar manner to protect the American public from dangerous opioids sold online.

FDA recognizes both the risks of opioid and other controlled substances as well as the benefits of these drugs for patients who need them, including those with debilitating chronic conditions. Addressing misuse, abuse, and overdose deaths while maintaining appropriate access to important treatment options remains one of FDA's highest priorities. It will take carefully developed, coordinated, and sustained action by multiple stakeholders to reduce the incidence of addiction, misuse, abuse, 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 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 PFDD through implementation of provisions of the 21st Century Cures Act and related commitments made under the FDA Reauthorization Act of 2017 Title I (PDUFA VI). Work on these initiatives since 2020 has included, but is not limited to, the following accomplishments that were in accordance with the 21st Century Cures Act, Section 3002 and PDUFA VI:

- Issued final 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[63]
- 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[64]
- Entered into a contract to implement an independent third-party assessment of the use of Patient Experience Data in regulatory decision-making to address three key questions regarding FDA's use of patient experience data:
    - How does FDA use patient experience data in regulatory decision-making?
    - How do FDA staff, applicants, and external stakeholders characterize (a) use of patient experience data in regulatory decision-making and (b) FDA communication about use of these data?
    - What good practices and opportunities for improvement exist for (a) use of patient experience data in regulatory decision-making and (b) FDA communication about use of these data?
- FDA posted the resulting study report, "Assessment of the Use of Patient Experience Data in Regulatory-Decision Making," in June 2021[65]
- October 6, 2020 - conducted a public meeting on PFDD for Stimulant Use Disorder[66]
- October 13, 2020 - conducted a public meeting on PFDD for Systemic Sclerosis and published the Voice of the Patient Report in June 2021[67]

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

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

[65] https://www.fda.gov/drugs/development-approval-process-drugs/assessment-use-patient-experience-data-regulatory-decision-making

[66] https://www.fda.gov/drugs/news-events-human-drugs/public-meeting-patient-focused-drug-development-stimulant-use-disorder-10062020-10062020

[67] https://www.fda.gov/drugs/news-events-human-drugs/public-meeting-patient-focused-drug-development-systemic-sclerosis-10132020-10132020

- March 8, 2021 - conducted a public meeting on PFDD for Vitiligo[68]
- CDER staff have supported patient groups in planning and hosting 21 externally-led PFDD meetings.[69]
- Globally led development of a Reflection Paper proposing internationally harmonized regulatory guidelines for PFDD working in collaboration with the European Medicines Agency (EMA) through the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). This Reflection Paper, endorsed by the ICH Assembly in November 2020, was then posted for international public comment and further updated to reflect relevant input.[70]
- In response to a request from an advisory committee meeting, FDA is funding the development of a patient preference study to better understand how people who can become pregnant weigh the risks and benefits when choosing a contraceptive product.
- July 9, 2020 - issued a funding opportunity announcement to solicit applications to develop core sets of clinical outcome assessments and their related endpoints for a specific disease or condition, and on April 29, 2021 made two awards under this announcement.[71] In addition the agency continues to oversee the development of the initial three awards that were funded in FY 2019. These awards provide avenues to advance the use of patient experience data as an important part of drug development that can foster innovation and the availability of safe and effective drugs. The 2021 awards are:
    - Preparing a clinical outcomes assessment (COA) set for nephrotic syndrome to develop and establish a core set of COAs for nephrotic syndrome, with a primary focus on fluid overload.
    - Expanding the Observer-Reported Communication Ability (ORCA) Measure: Measuring the communication ability of individuals with rare neurodevelopmental disorders (NDDs) to expand on the existing measurement tool created to assess caregiver observations of a child's ability for expressive communication in nonverbal patients with Angelman Syndrome.
- FDA finalized a guidance on enhancing the diversity of clinical trial populations that included a section on considerations to make trial participation less burdensome for participants and enhancing enrollment and retention practices that enhance inclusiveness. This guidance was informed by the public workshop on patient engagement in clinical trials.

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[68] https://www.fda.gov/drugs/news-events-human-drugs/public-meeting-patient-focused-drug-development-vitiligo-03082021-03082021

[69] https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings

[70] https://admin.ich.org/sites/default/files/2021-06/ICH_ReflectionPaper_PFDD_FinalRevisedPostConsultation_2021_0602.pdf

[71] https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-21-004.html

- In the Spring-Summer 2021, FDA offered a semester long course to increase reviewer proficiency with psychometric techniques used to analyze the properties and data from Clinical Outcome Assessments.
- On September 2, 2021, FDA launched a project in collaboration with Johns Hopkins University and the University of Maryland to conduct a systematic landscape review of the current state of the science of swallowing measurement as it relates to the mechanisms of swallowing. The study will help inform FDA recommendations on optimal methods for assessing swallowing in clinical trials of rare neurodegenerative and progressive neuromuscular diseases.

Strengthening the Compounding Program

The Drug Quality and Security Act (DQSA), enacted in November 2013, provided FDA with additional responsibilities to oversee compounding and created a category of compounders known as outsourcing facilities. Following the enactment of DQSA, FDA has increased its drug compounding oversight through inspections and enforcement, developed policies regarding the compounding provisions of Federal law, obtained advisory committee input, collaborated and coordinated with state regulators, and conducted stakeholder outreach.

Since enactment of the DQSA, and as of December 31, 2021, 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 870 inspections of compounders, including 85 inspections conducted in CY 2021
- Performed 8 remote regulatory assessments of outsourcing facilities during the COVID-19 pandemic
- Issued over 280 warning letters to compounders
- Issued over 210 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 270 recall events regarding compounded drug products
- Worked with the Department of Justice on civil and criminal enforcement actions, including 14 that resulted in injunctive relief
- Issued 10 compounding risk alerts[72] to inform health care professionals, compounders and consumers about risks associated with compounded drugs, including information on adverse events, outbreaks or product quality

In the same time period, FDA has issued more than 45 total draft, revised draft, and final guidance documents[73] regarding compounding and related activities, including five Federal Register notices related to the development of the list of bulk drug substances (active pharmaceutical ingredients) for which there is a clinical need to be used in compounding under section 503B of the FD&C Act (503B Bulks List). Other policy documents include five proposed rules, three of which have been finalized. In October 2021, FDA published revisions to the draft

[72] https://www.fda.gov/drugs/human-drug-compounding/compounding-risk-alerts

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

guidance on *Hospital and Health System Compounding Under Section 503A of the FD&C Act.* During the COVID-19 pandemic, five temporary policies on compounding and related activities during the COVID-19 pandemic, as well as a guidance on *Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency*. [74] FDA also intends to engage in rulemaking to implement statutory provisions regarding the standard memorandum of understanding between FDA and the states addressing interstate distribution of compounded drugs and complaint investigation by the states.

FDA also continues to convene the Pharmacy Compounding Advisory Committee (PCAC) to provide advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the FD&C Act. FDA has held ten committee meetings since the enactment of DQSA; the most recent was June 9, 2021.

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. Since the enactment of DQSA, FDA has held more than 50 sets of listening sessions for stakeholder sectors involving more than 100 unique organizations and state regulatory entities. As of December 31, 2021, FDA has also held ten intergovernmental working meetings with representatives of the state boards of pharmacy to increase and improve collaborative efforts regarding oversight of compounding throughout the United States.

In September of 2021, FDA held the second annual *Compounding Quality Center of Excellence Virtual Conference: Culture of Quality* with more than 600 registered participants, to engage outsourcing facilities and other stakeholders on key topics and best practices. A third annual conference is slated to take place in 2022. Through the Compounding Quality Center of Excellence, FDA sponsors the delivery of five instructor-led, multi-day courses, each offered multiple times, for outsourcing facilities on topics related to current good manufacturing practices (CGMP). Since inception in 2020 and through the calendar year 20212, these courses attracted over 450 attendees, primarily from outsourcing facilities. FDA also offers nine self-guided web-based trainings on compounding policy and CGMP. During this same time period, the Compounding Quality Center of Excellence web-based trainings have been taken over 1700 times, engaging outsourcing facilities and compounding related stakeholders.

Research at CDER

Research is critical for creating and validating the tools and standards needed to accelerate drug development. These tools also increase quality while reducing inefficiency and costs. 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

[74] https://www.fda.gov/media/147582/download

original biologics license applications (BLAs) received from October 1, 2012, through September 30, 2017. The goals of the Program were to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval. To accomplish these goals, the Program provided new opportunities for communication between applicants and the FDA review team, as well as time during the 60-day filing period for FDA to ensure the application is complete and reviewable before the PDUFA review clock begins.

PDUFA VI contained many enhancements designed to build on the achievements of earlier agreements. The Program is one of the key initiatives continuing under PDUFA VI. From its inception on October 1, 2012 through October 1, 2021, FDA has received 531 applications through the Program, with more communication between the applicant and the FDA review team during review of marketing applications.

FDA dedicates many PDUFA resources to support early and meaningful communication with drug sponsors during drug development, including through the resource-intensive breakthrough therapy designation program, which is one of the FDA's expedited programs intended to support the expedient development of drugs with the promise of addressing unmet medical needs of patients with a serious or life-threatening disease. Of the 53 novel drugs approved in FY 2021, 43 (81 percent) were approved in the United States before any other country. Of the novel drugs approved in FY 2021, 25 (47 percent) were first-in-class, which may be one indicator of the drug's potential for a strong positive impact on the health of the American people. Additionally, 41 (77 percent) of the FY 2021 novel drug approvals were designated in one or more of the following expedited programs: fast track, breakthrough therapy, priority review, and accelerated approval.

During FY 2021, CDER's Office of New Drugs (OND) published 19 guidance documents. Twelve of these guidance documents were considered clinical/medical in nature and included guidance on notable topics such as developing drugs, including biological products, for treatment of COVID-19; cross labeling oncology drugs; and endpoints for demonstrating effectiveness of drugs for treatment of opioid use disorder.

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 real-world evidence 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 21st Century Cures Act, FDA established an updated qualification process for drug development tools (DDTs) including biomarkers, clinical outcome assessments (COAs), animal models for use under the Animal Rule, and other tools 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. [75] The DDT Qualification Programs also developed a new, user-friendly IT support system to enable more efficient and timely review of submissions and facilitate the agency's bi-annual reporting requirements. In addition, in June 2021 to make the agency's public posting of DDT information more user-friendly, the qualification programs launched a searchable web-based tool.

Biomarker Qualification Program

FDA continues to work 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 5 projects in 2019 and 2 in 2020 to assist them with their ongoing development efforts. To communicate FDA's current thinking regarding requirements for qualification of biomarkers, FDA is developing BQP guidances on *Biomarker Qualification: Evidentiary Framework and Analytical Considerations for CDER/CBER Biomarker Qualification Program*. 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 70 submissions related to COA development projects. In total there are 62 independent COA projects under development. FDA awarded 8 grants in 2019, 6 grants in 2020 and 1 grant in 2021 to further the development of COAs.

Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program

In November 2020, FDA initiated the Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program to expand DDT types by encouraging development of DDTs that are out of scope for existing DDT qualification programs but that may still be beneficial for drug development, including artificial intelligence (AI)-based approaches and complex in vitro systems. To date, the ISTAND Pilot has received 12 submissions and has worked with several other potential submitters with interest in the Pilot.

International Harmonization and Regulatory Convergence

International efforts to develop harmonized global pharmaceutical standards are important for realizing the benefits of safe, effective, high-quality and accessible medicines. Global harmonization efforts can also help streamline and make pharmaceutical research development more efficient.

As a founding member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), FDA is continuing to advance harmonization projects. ICH fosters collaboration across regulatory authorities and drug developers in a multilateral venue to develop and implement consistent global standards for drug quality, safety, and effectiveness.

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

In FY 2021, this included leading efforts to revise the ICH E6(R2) Guideline on Good Clinical Practices and finalize revisions to the ICH E8(R1) Guideline on General Considerations for Clinical Studies to address the increasing diversity of study types and data sources, and the use of innovative technologies. These efforts will facilitate therapeutic product development and the generation of evidence that supports regulatory and other health policy review and decision making. In October, ICH regulatory members approved the final E8(R1) guideline, and it was published on ICH's website.

Revisions to the E6(R2) guideline also seek to incorporate lessons and examples from public health emergencies, including leveraging existing healthcare delivery 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 through ICH to promote advanced pharmaceutical manufacturing by developing scientific and regulatory standards for continuous manufacturing (CM). CM enables rapid, efficient, and flexible adjustments to drug manufacturing that can shorten drug development timelines, reduce manufacturing costs, and improve quality over traditional batch manufacturing. CM likely offers significant advantages during public health crises and in minimizing drug shortages. The ICH Q13 guideline, endorsed by the ICH Assembly in June 2021 and published as a draft FDA guidance for public comment in October 2021[76], provides a scientific framework for CM and outlines regulatory expectations to promote its widespread use.

To help provide a more predictable and efficient approach to management of postapproval changes, FDA worked with international regulators to develop *ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecyle Management* and published it as a final FDA guidance in May 2021.[77] Effective implementation of this guidance will provide an opportunity for the FDA to focus attention and resources on higher risk postapproval changes, incentivizing manufacturers with additional flexibilities to continually improve their manufacturing processes, which can reduce the likelihood of quality-related supply disruptions and related drug shortages.

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. Through our work with ICH, we are committed to not only accommodate the use of promising innovations, but to encourage their responsible use to make pharmaceutical development more efficient, and to provide safe and effective therapeutics to those who need them swiftly. 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 global economic framework for drug development and competition.

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[76] https://www.fda.gov/media/153044/download

[77] https://www.fda.gov/media/148476/download

To facilitate a more coordinated global response to the COVID-19 pandemic, FDA has co-chaired bi-weekly COVID-19 policy teleconferences of the International Coalition of Medicine Regulatory Authorities (ICMRA) to promote timely sharing of information and support better alignment of regulators' respective approaches and guidances issued in their regions to address this public health emergency. Additionally, in July 2021, FDA led the planning and conduct of an international ICMRA-Industry workshop on enabling expansion of manufacturing capacity for COVID-19 therapeutics and vaccines to discuss critical factors affecting industry agility to address critical manufacturing and supply chain resilience.

Advanced Manufacturing

Advanced manufacturing is a collective term for new medical product manufacturing technologies that can improve drug quality, address shortages of medicines, and speed time-to-market. Every field has a different set of production techniques that are considered advanced. They often:

- Integrate novel technological approaches
- Use established techniques in a new or innovative way, or
- Apply production methods in a new domain where there are no defined best practices or experience.

Advanced manufacturing is a high priority because CDER believes it will help address significant challenges or issues related to drug development, supply chain, quality, emerging public health issues, and pharmaceutical manufacturing. Not the least of these challenges is the COVID-19 public health emergency. Challenges like this arise quickly and require a rapid response. Current manufacturing technologies and facilities do not provide sufficient flexibility and agility to adequately and timely 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 encourage 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 FY 2021, 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[78] and, in partnership with CBER, led the development of the ICH Q13 guideline on CM of drug substances and drug products. The ICH Q13 guideline has reached Step 2 and has been published as a draft FDA guidance for public comment.[79]
- CDER held over 100 FDA-industry meetings on advanced manufacturing technologies. From this, CDER approved:
    - 6 applications (including a supplement) utilizing CM for finished dosage form manufacturing,
    - 1 supplemental application utilizing CM for a top-selling active pharmaceutical ingredient,
    - 2 supplemental applications utilizing semi-CM technologies for dialysis solution,
    - 1 application using CM for a biological product,
    - 1 using 3-D printing technology,
    - 1 application using advanced process analytical technologies for monitoring and control of a drug substance bioprocess, and
    - 1 supplemental application for the use of a novel glass container closure system for a parenteral drug product.

  Vertex, Janssen, and Lilly use CM to make their cystic fibrosis, HIV/AIDS, and oncology drugs, respectively.[80] Vertex and Sanofi, have built modern manufacturing facilities in the United States incorporating advanced manufacturing technologies.[81]
- Under the Product Development Science Program, CDER funded more than 56 intramural and extramural research projects in advanced manufacturing areas such as precision analytics for complex active drug substances, formulations and dosage forms, novel manufacturing methods (e.g., continuous manufacturing and 3-D printing), process analytical technologies, artificial intelligence (AI) and machine learning (ML), and advanced modeling. More than 100 internal reports and publications were generated to communicate findings internally and externally. The results produced from the intramural and extramural research projects are fundamental to the success of CDER advanced manufacturing initiatives. FDA used these results to evaluate regulatory submissions incorporating advanced manufacturing (e.g., development of regulatory recommendations for the industry to guide its product and technology development under the Emerging Technology Program), provide knowledge necessary to inform new standards, guidances and policies, develop new tools for more effective surveillance of product quality, and develop materials for training of FDA staff in advanced manufacturing.

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

[79] https://www.fda.gov/media/153044/download

[80] https://ispe.org/pharmaceutical-engineering/ispeak/continuous-osd-manufacturing-product-patient-perspective.

[81] https://optimal-ltd.co.uk/vertex-manufacturing; https://www.multivu.com/players/English/8627651-sanofi-new-digital-manufacturing-facility/.

- CDER and CBER formally stood up the Center for the Advancement of Manufacturing Pharmaceuticals and Biopharmaceuticals (CAMPB) by finalizing its charter. The goals of CAMPB are to accelerate the development, implementation, and evaluation of advanced manufacturing by establishing science- and risk-based standards and policies, advancing drug product development science, and training a world-leading regulatory workforce, through strategic partnership, engagement and communication.

Supplemental funding provided to CDER in FY 2020 and FY 2021 continues and further enhances collaboration with CBER and other internal and external stakeholders in facilitating implementation of advanced manufacturing for product development and commercial production, as well as supporting other activities under CDER's existing Product Development Science Program.

Drug Pricing and Access – Biosimilars

In July 2018, FDA released the Biosimilars Action Plan (BAP)[82] 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 biosimilar biological products. The BAP is focused on four key areas:

- Improving the efficiency of the biosimilar and interchangeable biosimilar 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) support 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 product review program activities. As of February 1, 2022, 97 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 47 different reference products. As of February 1, 2022, FDA has licensed (approved) 33 biosimilar products, including the first interchangeable biosimilar insulin product and the first interchangeable biosimilar monoclonal antibody product. These accomplishments help increase treatment options for patients.

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

Recent accomplishments include:

- FDA and the Federal Trade Commission signed a joint statement[83] regarding enhanced collaboration in support of a robust marketplace for biological products and held a public workshop: FDA/FTC Workshop on a Competitive Marketplace for Biosimilars.[84]
- FDA collaborated with the Duke Margolis Center for Health Policy to host a two-day public workshop entitled "Pharmacodynamic Biomarkers for Biosimilar Development and Approval." This public workshop was a forum for regulators, biopharmaceutical developers and academic researchers to discuss the current and future role of pharmacodynamic (PD) biomarkers in improving the efficiency of biosimilar product development and approval.[85]
- FDA issued draft guidance, *Biosimilarity and Interchangeability: Additional Draft Q&As on Biosimilar Development and the BPCI Act.*[86] This draft guidance provides development-related guidance to biosimilar product sponsors and other stakeholders on discrete issues that do not warrant a "full" guidance document. FDA believes that guidance for industry that provides answers to commonly asked questions regarding FDA's interpretation of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) will enhance transparency and facilitate the development and approval of biosimilar and interchangeable biosimilar products.
- FDA issued a final guidance, *Questions and Answers on Biosimilar Development and the BPCI Act (Rev. 2)*.[87] This guidance document provides answers to common questions from prospective applicants and other interested parties regarding the BPCI Act. The question and answer format is intended to inform prospective applicants and facilitate the development of proposed biosimilar and interchangeable biosimilar products, as well as describe FDA's interpretation of certain statutory requirements added by the BPCI Act.
- FDA released a Biosimilar Curriculum Toolkit to help educate students in health care degree programs for medicine, nursing, physician assistants, and pharmacy, as well as practicing professionals, about biosimilar and interchangeable biosimilar products and the regulatory approval pathway in the United States. The materials included in the toolkit were designed to meet a variety of teaching needs and contain foundational and more in-depth information by levels.

In addition, FDA completed the phased release of the enhanced *Purple Book: Database of FDA-Licensed Biological Products* in August 2020.[88] The Purple Book provides the public with an accessible, easy-to-use online search engine for information about FDA-licensed biological

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

[84] https://www.fda.gov/drugs/news-events-human-drugs/public-workshop-fdaftc-workshop-competitive-marketplace-biosimilars-03092020-03092020

[85] https://healthpolicy.duke.edu/events/biosimilar

[86] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/biosimilarity-and-interchangeability-additional-draft-qas-biosimilar-development-and-bpci-act

[87] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/questions-and-answers-biosimilar-development-and-bpci-act-guidance-industry

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

products, including biosimilar and interchangeable biosimilar products. FDA released the updated Purple Book 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 biosimilar products, and their reference products and includes allergenic, cellular and gene therapy, hematologic, and vaccine products regulated by CBER. In June 2021, FDA updated the Purple Book to provide patent information in compliance with the Biological Product Patent Transparency (BPPT) section of the Consolidated Appropriations Act, 2021. FDA also continues to update the Purple Book to increase usability and functionality.

FDA's ongoing educational efforts are aimed at increasing the understanding of biological products, reference products, biosimilar products, and interchangeable biosimilar products, and awareness of FDA's role in the biosimilar product approval process. All the educational materials, including infographics, fact sheets, videos, and other information about biosimilar products, can be found at www.fda.gov/biosimilars. FDA also regularly conducts stakeholder outreach and presents to health care provider, patient, and payor audiences to ensure continued dissemination of the biosimilar product educational materials.

Over the past year, FDA has been testing patient-focused materials to ensure they resonate with intended audiences and is continuing to update its educational materials and develop new materials based on this testing. In July 2021, FDA released three new fact sheets for health care providers. FDA is currently working with Medscape to provide continuing education (CE) content for health care providers, including nurses, pharmacists, and doctors.

Drug Pricing and Access – Generic Drug Review

Many Americans face challenges with access to drug products due to 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, updating informational web pages, and holding workshops;
- Communicated with and assisted generic drug applicants early in the product development phase by establishing the 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 2020 and FY 2021, FDA established policies and took actions under the DCAP to promote generic drug development in areas where there is inadequate competition. In FY 2020 and FY 2021, FDA has published a total of 393 new, revised, and final product-specific drug development guidance documents. Of these, 178 address the development of generic versions of complex, difficult-to-copy, drugs.

FDA also supported prospective generic drug developers by issuing guidances for industry intended to increase transparency into the generic drug review and approval process, as well as guidances intended to maximize scientific and regulatory clarity with respect to complex generic drugs, thereby supporting the development of generic drugs and submission of high quality ANDAs, including the following issued in FY 2021:

- A final guidance for industry, *ANDAs for Certain Highly Purified Synthetic Peptide Drug Products that Refer to Listed Drugs of rDNA Origin*, providing information to potential applicants on how to determine when an application for a synthetic peptide drug product that refers to a specified previously approved peptide drug product of rDNA origin should be submitted as an ANDA [89]

[89] https://www.fda.gov/media/107622/download

- A final guidance for industry, *Referencing Approved Drug Products in ANDA Submissions*, providing information to potential applicants on how to identify a reference listed drug (RLD), reference standard, and the basis of submission in an ANDA[90]
- A final guidance for industry, *Controlled Correspondence Related to Generic Drug Development*, describing the process by which generic drug manufacturers and related industry can submit controlled correspondence to FDA requesting information related to generic drug development [91]
- A final guidance for industry, *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*, describing the enhanced pathway for discussions between FDA and a prospective applicant preparing to submit or who has submitted an ANDA for a complex generic drug product to FDA[92]
- A revised draft guidance for industry, *Bioequivalence Studies with Pharmacokinetic Endpoints for Drug Products Submitted under an ANDA*, providing bioequivalence recommendations to applicants planning to include bioequivalence information in ANDAs and ANDA supplements[93]

In FY 2021, FDA also published two updates to the List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic. This list comprises approved NDA drug products that are no longer protected by patents or exclusivities, and for which 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 entitled *Competitive Generic Therapies*.[94] This guidance lays out recommendations for the use of the competitive generic therapies (CGT) pathway that provides incentives for developing generic versions of drugs that currently face inadequate generic competition. Since 2017, FDA has received more than 700 requests for CGT designation from drug manufacturers. As of September 30, 2021, FDA has approved 105 ANDAs with a CGT designation, with more than half receiving the 180-day period of marketing exclusivity provided for in the FD&C Act. FDA posts a list online of all approved ANDAs for drug products that received a CGT designation.[95] The growing list of approvals on the CGT website demonstrates the impact of the CGT provisions of the FD&C Act on encouraging development of drug products for which there is inadequate generic competition.

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, FDA recently published:

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[90] https://www.fda.gov/media/102360/download

[91] https://www.fda.gov/media/109232/download

[92] https://www.fda.gov/media/107626/download

[93] https://www.fda.gov/media/87219/download

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

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

- A Federal Register notice opening a public docket[96] to solicit comments from stakeholders on the types of patent information that should be included in (or removed from) the Orange Book
- A final guidance for industry, *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act*, which describes the content for the marketing status notifications required by section 506I of the FD&C Act, the recommended format for submitting these notifications to FDA, and the timelines for submission[97]

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

Drug Pricing and Access – Importation of Certain Drugs

FDA is working to implement a statutory pathway for the importation of certain prescription drugs from Canada in order to reduce the cost of these drugs to the American consumer without imposing additional risk to public health and safety. The agency also announced the availability of a final guidance for industry that describes procedures drug manufacturers can follow to facilitate importation of prescription drugs, including biological products, that are FDA-approved, manufactured abroad, authorized for sale in any foreign country, and originally intended for sale in that foreign country.

In July 2021, the Executive Order on Promoting Competition in the American Economy directed FDA to work with States and Indian Tribes that propose to develop Section 804 Importation Programs in accordance with section 804 of the Food, Drug, and Cosmetic Act and the FDA's implementing regulations to reduce the cost of covered products to the American consumer without imposing additional risk to public health and safety.

Drug Pricing and Access – CREATES Implementation

Among the agency's efforts relating to drug pricing and access is FDA's work to implement the Creating and Restoring Equal Access to Equivalent Samples Act, 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. FDA has developed internal processes to ensure that requests for covered product authorizations (CPAs) under the new law are received, reviewed, and responded to within statutory timeframes across CDER. As of February 18, 2022, FDA has issued over 40 CPAs. All CPAs were issued within the 120-day timeline mandated by CREATES; the successful implementation of this new authority has allowed follow-on product developers to more easily obtain the samples that are needed for product development and testing and, ultimately, the submission of applications. In addition, FDA launched an informational web page explaining how product developers can obtain access to samples under the new law.[98]

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

[97] https://www.fda.gov/media/120095/download

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

Drug Pricing and Access - 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 delays in treatment or changes in treatment regimens, such as substituting second-line 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 as such alternatives may be less effective or pose additional risks.

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 provide certain authorities that have enabled FDA to coordinate with manufacturers to help prevent or mitigate drug shortages. Among other things, the FD&C Act (as amended) requires manufacturers to provide advance 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 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 43 new shortages in 2020. FDA also helped to prevent 154 additional shortages in 2019 and 199 during 2020; FDA has continued these important prevention efforts in 2021, however, challenges persist. The COVID-19 public health emergency has exacerbated these challenges and strained the medical supply chain. Moreover, a couple of major drug manufacturers have closed manufacturing facilities for remediation purposes, resulting in the loss of manufacturing capacity needed for supplies of certain drug products. FDA has been working with manufacturers to resume production and has expedited review of new submissions, helping to increase supplies.

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 including sponsor concerns regarding reduced profitability for drugs that are prescribed and used for a relatively brief period of time.

Despite these considerable challenges in developing antibacterial drugs, since the 2012 passage of the Generating Antibiotic Incentives Now (GAIN) provision of FDASIA, FDA has approved 28 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:

- Research focused on evaluating the impact of dosing strategies for beta-lactam antibacterial drugs for serious infections caused by Gram-negative pathogens on development of beta-lactam resistance and patient outcomes
- Research to advance the science of antibacterial susceptibility testing to ensure that up-to-date susceptibility test interpretive criteria (i.e., breakpoints) are available to inform patient care and antimicrobial stewardship
- Research on developing patient reported outcome (PRO) instruments for evaluating results of clinical trials in pulmonary non-tuberculous mycobacterial (NTM) infections and coccidioidomycosis

In addition, CDER has interagency agreements in place to work with other federal agencies to support the development of antibacterial drugs. For example, FDA collaborated and utilized CARB funding to facilitate:

- Research conducted by the HHS Assistant Secretary for Planning and Evaluation to understand the development and use of clinical practice guidelines for infectious disease and develop a dissemination plan to present the findings at a stakeholder meeting and/or in a publication
- Research conducted by the National Institutes of Health to estimate the national market size for novel gram-negative active agents
- Research conducted by the Centers for Disease Control and Prevention to understand the impact of antibacterial drugs on the human 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 Japan's Pharmaceuticals and Medical Devices Agency (PMDA). These projects resulted in publications in peer-reviewed journals and provide an important resource to various stakeholders. In addition, research studies were conducted to evaluate the relationship between pharmacokinetic-pharmacodynamic (PK-PD) measures associated with efficacy and clinical outcome, a project on assessing renal function variations in patients enrolled in phase 3 studies for complicated urinary tract infections, a project on evaluating data from recently completed complicated urinary tract infection (cUTI) trials to assess the degree of discordance between the clinical and microbiologic endpoints, and another project on performing analysis of recently completed antibacterial drug trials to validate ordinal endpoints using the desirability of outcome ranking (DOOR) approach.

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.

Modeling and simulation play a role in integrating diverse data sources and exploring alternative study designs, which can 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, predicting potential drug efficacy, 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 of how CDER uses these tools include:

- Reviewing investigational new drug applications, new drug applications, and biologics license applications - These approaches provide critical evidence to support safe drug dosing strategies, alleviating the need for additional clinical trials. These approaches also help in assessing the 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.
- Supporting the creation of natural history databases for model-informed drug development - FDA is collaborating with other stakeholders to develop natural history models in Alzheimer's disease, Huntington'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.
- Informing clinical trial designs - FDA collaborated with other stakeholders to develop a model-based clinical trial simulation tool to optimize clinical trial enrichment and the design of efficacy evaluation studies in Parkinson's disease. 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 is CDER's use of a cardiac physiology/pharmacology model to predict the risk of a drug to cause abnormal heart rhythms; thus, alleviating the need for certain cardiac safety clinical trials.
- Predicting the binding characteristics of novel opioids, predicting naloxone dosing requirements in the community setting for overdoses of these opioids and informing labeling for reversal agents.

- CDER also uses mechanistic modeling to predict the potential efficacy of new or existing compounds to treat COVID-19 as well as identify optimum approved drug combinations for treatment of viral diseases like influenza and COVID-19.
- Pre-clinical in silico modeling is important for supporting drug repurposing to explore potential new uses of FDA-approved drugs. NCTR and CDER are collaborating on using in silico modeling to identify drugs that may be promising for use in novel indications or diseases where there are serious unmet clinical needs.
- Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer [99]– A PK-based approach relying on population-PK (Pop-PK) modeling and simulation can be applied to support the approval of alternative dosing regimens for a PD-1 or PD-L1 blocking antibody that is already approved based on clinical efficacy and safety trials.

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 implement drug distribution security requirements that go into effect in 2023. The ultimate goal for achieving electronic, interoperable tracing of product at the package level by November 27, 2023 includes:

- 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 2018, manufacturers and repackagers have been encoding unique product identifiers on prescription drug packages and homogenous cases. To achieve electronic tracking of products at the package level 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 will continue to develop policy and recommendations for effective DSCSA implementation of enhanced drug distribution security, including establishing standards for data exchanges and system attributes for package-level product tracing.

[99] https://www.fda.gov/media/151745/download

Licensing: FDA established a database specifically for wholesale drug distributors and third-party logistics providers to comply with annual reporting requirements. On February 4, 2022, FDA proposed 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. These national standards address the storage, handling, and transport of prescription drugs and will improve the oversight of the entities involved in the distribution prescription drugs in the U.S. When final, every wholesale drug distributor and third-party logistics provider facility in the U.S. will be held to these standards through licensure requirements.

Regulatory Documents: Since enactment of the DSCSA, FDA has worked to develop regulations, standards, policies, and programs to implement the law.[100] As of February 18, 2022, FDA has issued 12 draft guidance documents and 10 final guidances. These efforts included four guidances issued in June 2021 that provided stakeholder clarity of product identifier and verification requirements and specifically our proposed recommendations related to enhanced drug distribution security requirements that go into effect in 2023. As part of FDA's COVID-19 response, we issued one final guidance in April 2020 that clarified an exemption and exclusion from certain supply chain security requirements during the COVID-19 public health emergency. FDA also 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.

Stakeholder Engagement: FDA continues stakeholder engagement and outreach through activities such as public meetings and conference participation to increase awareness of the upcoming DSCSA requirements. To support DSCSA implementation, FDA held public meetings in November 2021 and December 2020 to discuss enhanced drug distribution security requirements that go into effect in 2023. In addition, FDA's DSCSA Pilot Project Program provided a means to explore and evaluate methods to enhance the safety and security of the drug supply chain focusing on the enhanced requirements that go into effect in 2023. Twenty pilot projects were completed in June 2020 under the program. The agency is working to share the results and lessons learned in a public program report.

FDA continues to refine the long-term schedule for implementing the DSCSA's statutory requirements to ensure long-term operation success of DSCSA implementation. FDA is focusing on enhanced drug distribution security requirements that go into effect in November 2023 which includes enhanced product tracing and verification and development of methods to communicate with trading partners for specific DSCSA information when investigating suspect or illegitimate products or in the event of a recall. FDA will continue to engage supply chain stakeholders during this time to facilitate the successful and efficient implementation of these requirements.

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100 https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/default.htm

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.

  FDA expanded earlier solutions and implemented new ones in 2021 that support study data management, drug safety tracking, generic drug correspondence and labeling review, and product quality review.
- 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. CDER's consolidated platform was launched in 2021 with reports and dashboards supporting analytics related to COVID-19, regulatory review, pharmaceutical quality, pharmacovigilance, and manufacturing compliance.
- 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 processes. Additional expansions and modernization of CDER's financial and administrative operations systems were completed over the last year. These solutions are available Center-wide with initial capability focusing on financial planning and human resources business processes.
- 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. CDER aligns its Cloud Infrastructure strategy with FDA's Cloud Forward initiative that prioritizes and facilitates cloud-based hosting and operations in the FDA GovCloud secure environment. CDER has taken advantage of IT Automation for its application development and deployment through FDA's DevSecOps cloud-based model. CDER has also strengthened its security posture through gradual implementation of Zero Trust architecture principles.

COVID-19 Pandemic Response Activities

This past year, CDER expanded its proactive, multi-pronged approach to address the COVID-19 public health emergency by building on the Center's robust response structure established early in the pandemic. Working closely with our Federal colleagues within and outside of the Department of Health and Human Services, CDER's multidisciplinary teams helped ensure that

the most promising treatments for COVID-19 were made available to patients as quickly as possible; sparked innovations to generate new treatments; closely monitored the drug supply chain to prevent and mitigate shortages; protected the public from potentially dangerous products and false claims; and supported CDER's everyday mission of improving access to safe, effective, high-quality treatment options for myriad non-COVID diseases.

CDER's role is integral to the whole-of-government COVID-19 response effort. This has included the Center's evaluation of multiple types of potential therapeutics, such as antivirals and monoclonal antibody therapies. As of January 31, 2022, CDER had reviewed more than 360 trials of potential therapies for COVID-19 and there were more than 640 drug development programs in planning stages. CDER's response efforts also include:

- As of January 21, 2022 currently authorized 13 treatments for emergency use to treat COVID-19, or a serious or life-threatening disease or condition caused by COVID-19 and approving 1 treatment
- Approving more than 1,000 original and supplemental generic applications for COVID-19-related treatments and supportive therapies
- Increasing transparency by disclosing CDER scientific memoranda supporting the issuance, revision, or revocation of authorizations and posting the relevant documents on the CDER website
- Regularly reviewing the appropriateness and circumstances of each Emergency Use Authorization (EUA), including the impact of circulating viral variants of SARS-CoV-2 on the authorized therapeutic
- Optimizing use of CDER's Coronavirus Treatment Acceleration Program (CTAP)[101] by reassigning staff to review the many requests from companies, scientists, and doctors working to develop treatments; and helping to ensure that such treatments are evaluated in diverse populations, including those most vulnerable to COVID-19 by offering guidance about eligibility criteria, enrollment practices, and trial designs, and encouraging broad representation in COVID-19 clinical trials
- Preventing and mitigating drug shortages by expanding supply chain surveillance; establishing the Emergency Event Notification Portal to provide FDA a mechanism to request information from manufacturers on potential drug shortages resulting from supply chain challenges on COVID-related or other emerging events; working with manufacturers of critical COVID-19 therapeutics to increase production/supply; conducting outreach to more than 180 manufacturers related to manufacturing capacity and supply chain; 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. In addition to the efforts described above, FDA works closely with healthcare and pharmacy systems, hospitals, providers, and others on the frontlines of COVID-19 patient care, as well as other stakeholders, to identify potential current or emerging regional and national trends in usage of critical care drugs to treat patients with COVID-19. In response to EO14017, FDA worked closely with HHS to

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

develop policy recommendations to address vulnerabilities in U.S. pharmaceutical supply chains.

- Per Executive Order 13944, published a list of hundreds of "essential medicines" for the United States, setting the stage for onshoring pharmaceutical manufacturing, increasing supply chain resiliency, reducing shortages, and preparing the U.S. government to stand ready to protect the American public during public health emergencies
- Proactively issuing temporary policies to address the pandemic including for certain drugs compounded for hospitalized patients with COVID-19 when FDA-approved drugs are not available.
- Protecting the American public from fraudulent products that claim to diagnose, prevent, treat, or cure COVID-19 - CDER sent more than 128 warning letters to sellers of unproven COVID-19 products
- Taking action against firms marketing hand sanitizer products in the United States that contain dangerous ingredients, such as methanol, 1-propanol, benzene, acetaldehyde, or acetal, by detaining many of these products at the U.S. border, broadly disseminating information about the associated dangers, including publishing a list of more than 250 hand sanitizers that consumers should not use, requesting that manufacturers recall such products, providing testing protocols for stakeholders to use to detect impurities in these products, issuing warning letters, and placing firms on import alert. FDA also placed all alcohol-based hand sanitizers from Mexico on a countrywide import alert to help stop products from entering the U.S. that appear to be in violation until the agency is able to review the products. That action marked the first time the FDA has issued a countrywide import alert for any category of drug product. Removing contaminated hand sanitizer products from the marketplace also led to providing policy for testing pharmaceutical alcohol used in all drug manufacturing for the presence of methanol.
- Collaborating across the USG to guide clinical trial design/conduct and optimize use of clinical trial capacity; consulting on treatment guidelines; establishing new data source partnerships; and ensuring consistent USG communications to stakeholders
- Promptly releasing a guidance document at the onset of the pandemic, *FDA Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Public Health Emergency* to address concerns about completion of clinical trials in general during the pandemic and the safety of patients in such trials. FDA has since released multiple updates to this guidance including updating a Q&A appendix as clinical trial sponsors, investigators, and others posed new questions.[102] FDA also held meetings with trial sponsors and produced public webinars to explain FDA policies outlined in the guidance and to learn about challenges sponsors were facing. In addition, FDA established a dedicated mailbox[103] for stakeholders to contact the agency with questions on clinical trial conduct during the COVID-19 pandemic. As of the end of January 2021, FDA has responded to more than 630 inquiries submitted to the mailbox.
- Making FDA's MyStudies app available to investigators as a free platform (as the COVID MyStudies app) to obtain informed consent securely from patients for eligible

[102] https://www.fda.gov/media/136238/download

[103] Clinicaltrialconduct-COVID19@fda.hhs.gov

clinical trials when face-to-face contact is not possible or practical due to COVID-19 control measures
- Evaluating complaints and referrals of non-compliance related to the conduct of COVID-19 clinical trials and taking appropriate action to ensure the rights, safety, and welfare of trial participants are protected
- Continuing to prioritize mission-critical inspections and conduct inspections as resources are available to meet user fee dates. For all inspections, the safety of personnel (FDA and industry) is paramount. CDER continues to successfully use alternative tools and approaches when inspections are not feasible, including remote interactive evaluations (e.g., remote livestreaming video of operations, teleconferences, or screen sharing), requesting records from regulated establishments, and leveraging information from trusted regulatory partners. These alternative approaches have been useful in assessing certain applications for marketing approval and in assessing the risk of manufacturing facilities currently manufacturing drugs for the U.S. market.
- Strengthening import operations to ensure drug products needed for COVID-19 response are facilitated entry as well as applying extra scrutiny to imported drugs to ensure drug quality and prevent illicit entries
- Communicating with industry and publishing a guidance, Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency, Questions and Answers to respond to frequently asked questions on the impact of travel restrictions on application review, provide general insight into use of alternative tools for inspections, and address other supply chain and inspection topics[104]

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 the 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.

[104] https://www.fda.gov/media/141312/download

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

New Product Approvals

Below are some of CDER's FY 2021 new product approvals. This list does not represent any degree of importance or priority ranking of products.[105]

Product Category	Approved	Product Name	FDA-Approved Use as of Approval Date
Autoimmune Disease	July 2021	Saphnelo	To treat moderate-to severe systemic lupus erythematosus along with standard therapy
Cancer	September 2021	Tivdak	To treat recurrent or metastatic cervical cancer with disease progression on or after chemotherapy
Cardiovascular Disease	January 2021	Verquvo	To mitigate the risk of cardiovascular death and hospitalization for chronic heart failure
Infectious Diseases	July 2021	fexinidazole	To treat human African trypanosomiasis caused by the parasite *Trypanosoma brucei gambiense*
Genetic Disorders	October 2021	Scemblix	To treat Philadelphia chromosome-positive chronic myeloid leukemia with disease that meets certain criteria

[105] Novel Drug Approvals for 2021 | FDA

Generic Product Approvals

Below are some of CDER's FY 2021 generic product approvals. This list does not represent any degree of importance or priority ranking of products.[106]

Product Category	Approved	Product Name	FDA - Approved Use as of Approval Date
Irritable bowel syndrome	February 2021	Linaclotide Capsules (generic of Linzess)	For the treatment of irritable bowel syndrome with constipation and chronic idiopathic constipation
Plaque Psoriasis	February 2021	Apremilast Tablets (generic of Otezla)	For the treatment of adult patients with moderate to severe plaque psoriasis
Lymphoma	March 2021	Ibrutinib Capsules (generic of Imbruvica)	For the treatment of adult patients with mantle cell lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, Waldenström's macroglobulinemia, marginal zone lymphoma, or chronic graft versus host disease
Prostate Cancer	May 2021	Enzalutamide Capsules, 40 mg (generic of Xtandi)	For the treatment of patients with castration-resistant prostate cancer
Type 2 Diabetes	August 2021	Linagliptin Tablets (generic of Tradjenta)	Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus

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

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$1,851,609,000	$662,892,000	$1,188,717,000
FY 2020 Actuals	$1,995,820,000	$682,861,000	$1,312,959,000
FY 2021 Actuals	$2,006,214,000	$688,844,000	$1,317,370,000
FY 2022 Annualized CR	$2,091,393,000	$689,195,000	$1,402,198,000
FY 2023 President's Budget	$2,219,690,000	$790,133,000	$1,429,557,000

Figure 10 - Funding History

BUDGET REQUEST

The FY 2023 Budget for the Human Drugs Program is $2,219,690,000, of which $790,133,000 is budget authority and $1,429,557,000 is user fees. The budget authority is increased by $100,938,000 compared to the FY 2022 Annualized CR and user fees increased by $27,359,000. The Center for Drug Evaluation and Research (CDER) amount in the request is $1,940,854,000. The Office of Regulatory Affairs amount is $278,836,000.

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 program will continue to advance its mission and strategic efforts to further strengthen our programmatic foundation. These efforts accompanied by the necessary funding, will allow the FDA to further our goal to help 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 FY 2023 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 will continue efforts to support one of its highest priorities—the goal of ending the opioids crisis—and will 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 is responsible for the thoughtful regulation of the drugs and devices used in the treatment of pain, as well as the treatment of opioid use disorder (OUD) and overdose, and aims to ensure that the actions it takes are in the best interest of public health and support the nation's response to the opioid 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 OUD. The FY 2023 Budget also 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. With the FY 2023 Budget, FDA will continue collaborative efforts with internal and external stakeholders to support the development and regulation of oncology medical products to advance the Moonshot goals, including supporting the Oncology Center of Excellence's cross-center regulatory approach to enhance coordination of clinical review across oncology-related drugs. In addition, the FY 2023 Budget will provide FDA with resources to spur the development and qualification of new alternative methods for product safety and efficacy testing; methods that have the potential to provide both more timely and more predictive information to accelerate product development and enhance emergency preparedness for the benefit of US patients, consumers, and animals.

BUDGET AUTHORITY

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

Advancing the Goal of Ending the Opioid Crisis (+$36.0 million / 40 FTE)

Center: +$26.0 million / 15 FTE

Field: +$10.0 million / 25 FTE

CDER 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.
The FY 2023 Budget will support 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. 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.

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

The FY 2023 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[107], 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 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

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

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.

Crosscutting (+$59.3 million / 69 FTE)
Capacity Building (+$17.5 million / 13 FTE)

Center: +$15.4 million / 11 FTE

Field: +$2.1 million / 2 FTE

The FY 2023 President's Budget includes $59.4 million Capacity Building, including $17.5 million within the Human Drugs program. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Federal Employee Pay Costs (+$11.6 million)

Center: +$8.3 million

Field: +$3.4 million

The FY 2023 President's Budget includes $51.9 million, including $11.6 million within the Human Drugs Program, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$12.9 million / 35 FTE)

Field: +$12.9 million / 35 FTE

The FY 2023 President's Budget includes $33.8 million for optimizing inspectional activities, including $12.9 million within the Human Drugs Program, to support capacity building towards an advanced, highly trained investigators capable of analyzing available data to increase the efficiency and productivity of our inspection operations.

Reducing Animal Testing Through Alternative Methods (+$1.4 million / 4 FTE)
Center: +$1.4 million / 4 FTE

The FY 2023 President's Budget includes $5 million, including $1.4 million within the Human Drugs Program, to implement a cross-agency New Alternative Methods Program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development

of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

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

Center: +$14.0 million / 15 FTE

Field: +$1.8 million / 2 FTE

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $15.8 million for the Human Drugs Program, 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.

USER FEES

Current Law User Fees (+$27.3 million)

Center: +$26.1 million

Field: +$1.2 million

The Human Drugs Program request includes an increase of $27.4 million for user fees which will allow FDA to fulfil its mission of promoting and protecting the public health by ensuring safety and efficacy of FDA-regulated products.

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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
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 2020: 82% Target: 90% (Target Not Met)	90%	90%	Maintain
223211: Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60-day filing date. (*Output*)	FY 2020: 96% Target: 90% (Target Exceeded)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
223212: Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt. *(Output)*	FY 2020: 95% 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 2020: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
223215: Review and act on 90 percent of standard original Abbreviated New Drug Application (ANDA) submissions within 10 months of receipt. *(Output)*	FY 2020: 95% 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 2020: 97% 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 2021: 90.0% Target: 80% (Target Exceeded)	90%	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 2021: 57.8% Target: 55% (Target Exceeded)	58%	55%	Maintain
292203: Number of medical product analyses conducted through FDA's Sentinel Initiative. *(Output)*	FY 2021: 86 Target: 60 (Target Exceeded)	65	65	Maintain

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

Review Goals

New Drug Review

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. Although the agency met three out of the four PDUFA performance goals, the agency fell slightly short on the measure to review and act on 90 percent of standard NME NDA and original BLA submissions within 10 months of the 60-day filing date. Five FY 2020 standard NME/BLA applications missed the user fee goal date due to COVID travel restrictions impacting the ability to inspect facilities, and challenges arising from the late scheduling of Advisory Committee meetings. The agency will continually work to meet or exceed the review performance goals when possible moving forward.

Generic Drug Review

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 is FDA's active surveillance program that enables the FDA to evaluate the safety of regulated medical products and informs regulatory decision making. To date, the Sentinel Initiative has provided vital information to patients and providers about the safety of drugs and vaccines by contributing to multiple drug safety communications and labeling changes, supporting FDA Advisory Committee Meetings, highlighting potential ways to intervene in the opioid crisis, and influencing numerous regulatory decisions. The Sentinel Initiative is comprised of multiple components including the Sentinel System, and its Active Risk Identification and Analysis (ARIA) program, FDA Catalyst, and the Biologics Effectiveness and Safety System. In 2021, FDA continued to leverage Sentinel as part of a multi-layered response to the COVID-19 pandemic. Some of these activities include near real-time drug monitoring to inform the potential for drug shortages, estimating the prevalence of medicines used among pregnant women with COVID-19, and assessing coagulopathy and its risk factors among hospitalized COVID-19 patients. 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.

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

CDER Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	166	168	169
Efficacy Supplements	248	244	244
Manufacturing Supplements	2,250	2,398	2,536
Commercial INDs (Drugs and Biologics) with Activity	8,847	9,542	10,069
Sponsor Requests: IND-Phase Formal Meetings	3,546	3,546	3,546
Sponsor Requests: Review of Special Study Protocols	151	151	151
Submissions of Promotional Materials	136,000	140,000	147,000
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	69	69	69
Reviews: Standard NDA/BLA	133	133	133
Approvals: Priority NDA/BLA	53	53	53
Approvals: Standard NDA/BLA	61	61	61
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	9	9	9
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	21	21	21
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	8	8	8
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	12	12	12
Reviews: NDA Supplemental	3,104	3,104	3,104
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	8,713	9,323	9,976
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	343	343	343
Receipts: IND/IDE Amendments (Biologics Only)	30,643	30,643	30,643
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	24	24	24
Approvals: PLA/BLA	15	15	15
Reviews: License Supplement (PLA/ELA/BLA)	587	587	587
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	809	850	850
Outputs – Reviews/Approvals			
Actions – ANDA	3,012	2,800	2,800
Approval Actions - ANDA (both Tentative and Full Approvals)	836	825	825
Median Review Time from ANDA Receipt to Approval (months)	25	26	26
Actions - ANDA Supplementals (Labeling and Manufacturing)	10,408	10,600	10,600
Over-the-Counter Drug Review[1]			
OTC Monographs Under Development	25	26	14
OTC Monographs Published	8	17	7
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information	22	20	20
New Written Requests Issued	13	15	15
Pediatric Exclusivity Determinations made	16	13	14
Post Exclusivity Safety Report	5	6	6
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	2,353,126	2,523,378	2,705,818
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	24,234	26,000	28,000
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,115	7,250	7,388
Number of drugs with Risk Communications	125	150	160
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	15	20	33
Number of FOI Requests	2,141	2,500	2,500
Number of FOI Requests Processed	1,933	2,525	2,525
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	70	87	87
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	143	168	168
Number of Citizen Petitions Completed (excluding suitability petitions and OTC monograph-related petitions)[2]	102	107	107

[1] *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. Data beginning in FY 2021 reflect this change; and include OTC monographs deemed by Congress in the CARES Act and subsequently posted by FDA.*

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

Figure 11 - CDER Workload and Outputs

Field Human Drugs Program Workload and Outputs	FY 2021 Actuals[4]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***857***	***810***	***1,695***
Pre-Approval Inspections (NDA)	53	60	100
Pre-Approval Inspections (ANDA)	33	18	90
Bioresearch Monitoring Program Inspections	456	415	600
Drug Processing (GMP) Program Inspections	238	325	650
Compressed Medical Gas Manufacturers Inspections	8	15	50
Adverse Drug Events Project Inspections	28	25	88
OTC Monograph Project and Health Fraud Project Inspections	11	3	70
Compounding Inspections[1]	62	55	127
Domestic Laboratory Samples Analyzed	959	825	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***94***	***90***	***1300***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	23	11	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	18	16	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	34	24	255
Foreign Drug Processing (GMP) Program Inspections	22	44	900
Foreign Adverse Drug Events Project Inspections	0	1	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***951***	***900***	***3,055***
IMPORTS			
Import Field Exams/Tests	4,822	7,100	10,000
Import Laboratory Samples Analyzed	479	850	620
Import Physical Exam Subtotal	**5,301**	**7,950**	**10,620**
Import Line Decisions	1,003,661	1,023,734	1,044,209
Percent of Import Lines Physically Examined	0.53%	0.78%	1.10%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS [5]	***951***	***900***	***3055***

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

[2] The FY 2021 actual unique count of foreign inspections includes 34 OGPS inspections (25 for China, 9 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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

[5] Count of "Third Party" Foreign Inspections 28 (not included in Overall counts above)

Figure 12 - Field Human Drugs Program Workload and Outputs

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
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…….....	42	42	42	42	---

Figure 13 - Narrative by Activity

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

Orphan Product Clinical Trial Grants Program[108]

The Orphan Drug Act created the Orphan Product Clinical Trial Grants Program, to stimulate the development of promising products for rare diseases. HQ continues to administer approximately 70 clinical studies of promising therapies for rare diseases and has awarded 11 new clinical trial grants in FY 2021. In addition, in FY 2021, due to the challenges and increased costs for clinical trials from the COVID-19 pandemic, HQ provided existing grantees with additional funding to implement necessary steps to allow their research to continue, ensure subject safety, maintain compliance with good clinical practice, and minimize risks to trial integrity. However, FDA appropriated grant funds, which are significantly less than the $30.0 million congressionally authorized amounts, are covering less and less of total costs for conducting clinical trials due to the rising study costs.

Recognizing the importance of information about the natural history of disease for prevention and intervention strategies, HQ is funding 8 natural history grants to inform medical product development by better understanding how specific rare diseases progress over time. Examples include studies to follow patients with medullary thyroid cancer and cardiac disease in Duchenne muscular dystrophy.

FDA HQ continues to implement Section 305 of the Pediatric Medical Device Safety and Improvement Act of 2007 (part of the 2007 FDAAA legislation) which mandates demonstration grants for improving pediatric device availability through pediatric device consortia. In FY 2021 FDA HQ provided funding for 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.

[108] FY 2021 includes $1.2 million of OCPP funds to support Orphan Product Grants

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$33,257,000	$29,099,000	$4,158,000
FY 2020 Actuals	$33,257,000	$29,099,000	$4,158,000
FY 2021 Actuals	$33,257,000	$29,099,000	$4,158,000
FY 2022 Annualized CR	$33,257,000	$29,099,000	$4,158,000
FY 2023 President's Budget	$33,257,000	$29,099,000	$4,158,000

Figure 14 - Funding History

BUDGET REQUEST

The FY 2023 Budget 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, pending the availability of funds, FDA HQ plans to continue to fund approximately 5-7 natural history grants targeted on expediting the development of products for these rare conditions.

BIOLOGICS

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Biologics	**437,071**	**441,809**	**450,902**	**475,415**	**24,513**
Budget Authority	***254,138***	***254,031***	***254,138***	***274,917***	***20,779***
User Fees	***182,933***	***187,778***	***196,764***	***200,498***	***3,734***
Center	393,322	399,304	407,009	423,565	16,556
Budget Authority	212,132	212,026	212,132	224,962	12,830
User Fees	181,190	187,278	194,877	198,603	3,726
Prescription Drug (PDUFA)	*164,951*	*173,611*	*178,620*	*182,112*	*3,492*
Medical Device (MDUFA)	*14,981*	*13,529*	*14,886*	*15,184*	*298*
Generic Drug (GDUFA)	*983*	*118*	*1,103*	*1,033*	*-70*
Biosimilars (BsUFA)	*275*	*20*	*268*	*274*	*6*
Field	43,749	42,505	43,893	51,850	7,957
Budget Authority	42,006	42,005	42,006	49,955	7,949
User Fees	1,743	500	1,887	1,895	8
Prescription Drug (PDUFA)	*1,514*	*464*	*1,649*	*1,652*	*3*
Medical Device (MDUFA)	*229*	*36*	*238*	*243*	*5*
FTE	**1,438**	**1,503**	**1,445**	**1,472**	**27**

Figure 15 - Narrative by Activity

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.

CBER's mission 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 2021-2025 strategic plan outlines the goals, objectives, and strategies designed to further its mission and vision during the term of the strategic plan. It aligns with Department of Health and Human Services (HHS) and FDA priorities and new authorities provided through the 21st Century Cures Act and sets forth the Center's four goals:

- 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.[109] These accomplishments align with the Department of Health and Human Services and CBER's strategic plan,[110] and reflect implementation of legislative mandates.

The Biologics Program's recent accomplishments demonstrate an ongoing commitment to facilitating development of biological products and providing oversight throughout the product life cycle:

- Continued COVID-19 pandemic response to help speed the availability of safe and effective vaccines to the American public, including continued monitoring of all available scientific data on the safety and efficacy of these products in collaboration with our domestic and international partners;
- Fostering innovation for continued development of innovative technologies and processes, including advanced manufacturing and cell and gene therapies; and

Fostering 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

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

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

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."[111]

Addressing *Coronavirus* Disease 2019 (COVID-19)

One of the highest priorities at FDA is protecting and advancing public health by ensuring access to safe and effective COVID-19 vaccines and other medical products. FDA protects the public health by making decisions based on a rigorous evaluation of current data and scientific evidence. CBER uses every tool available to the agency to help patients gain timely access to promising safe and effective biological products while facilitating research to evaluate their safety, effectiveness, and manufacturing processes.

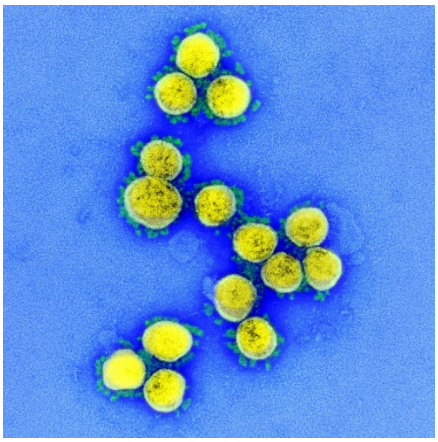

Figure 16 - Transmission electron microscope image of SARS-CoV-2 virus. NIAID-RML

COVID-19 Vaccine Approval

Achieving a major milestone in the battle against COVID-19, in August 2021, FDA licensed the first COVID-19 vaccine. Comirnaty (COVID-19 Vaccine, mRNA) is approved for the prevention of COVID-19 in individuals 16 years of age and older. The biologics license application (BLA) for Comirnaty received Priority Review and Fast Track designation, and FDA completed its review in three months from receipt of the full application, five months before the PDUFA goal date. The BLA built upon the extensive data and information previously submitted that supported the Pfizer-BioNTech Emergency Use Authorization (EUA), including preclinical and clinical data and information, details of the manufacturing process, vaccine testing results to ensure vaccine quality, and inspections of vaccine production sites. FDA licensed a second COVID-19 vaccine, Spikevax (COVID-19 Vaccine, mRNA), in January 2022. Spikevax is manufactured by ModernaTX for the prevention of COVID-19 in individuals 18 years of age and older.

COVID-19 EUAs and Amendments

During a public health emergency, FDA may issue an EUA to authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions. Prior to EUA submissions for the COVID-19 vaccines, FDA had early and frequent interactions with each vaccine manufacturer, providing scientific and regulatory advice and convened its Vaccines and Related Biological Products Advisory Committee (VRBPAC) to discuss, in general, the development, authorization, and/or licensure of vaccines to prevent COVID-19. Since the beginning of the public health emergency, CBER issued EUAs for three vaccines for the prevention of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Pfizer-BioNTech (December 2020), Moderna (December 2020), and Janssen (February 2021) COVID-19 vaccines. FDA convened the VRBPAC to advise the agency on the data to

[111] See Center for Biologics Evaluation and Research 2021 - 2025 Strategic Plan, p. 1, available at https://www.fda.gov/media/81152/download.

support authorization of these vaccines. FDA completed its evaluation of the data and granted authorization for each of the three vaccines within days of receiving recommendations from the VRBPAC.

After the initial authorizations, FDA continued working to lessen the public health burden caused by the COVID-19 pandemic by first convening the VRBPAC to obtain general advice on authorization for pediatric populations, and later expanding the EUA for the Pfizer-BioNTech COVID-19 Vaccine for use in younger populations. In May 2021, FDA authorized the Pfizer-BioNTech COVID-19 Vaccine for use in individuals 12 through 15 years of age, and in October 2021 for use in individuals 5 through 11 years of age. FDA received input from the VRBPAC on the October authorization for use in children 5 through 11 years of age. The VRBPAC overwhelmingly voted in favor of making the vaccine available to children in this age group. Both authorizations were based on the FDA's comprehensive and rigorous evaluation of the totality of scientific evidence pertaining to the vaccine's safety and effectiveness.

FDA also identified situations where additional doses of vaccine would provide benefit to vaccinees and to public health and authorized additional doses for this purpose. FDA initially amended the Pfizer-BioNTech (12 years and older) and Moderna (18 years and older) COVID-19 vaccines EUAs to allow for use of a third primary series dose of the vaccines to certain immunocompromised individuals in August 2021. FDA subsequently authorized the use of a single booster dose of the Pfizer-BioNTech and Moderna COVID-19 vaccine in eligible populations in September and October 2021, respectively. These individuals included those 65 years of age and older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2. The EUA for the Janssen COVID-19 Vaccine was also amended in October 2021 to allow for a single booster dose that may be administered at least 2 months after completion of the single-dose primary regimen to individuals 18 years of age and older. Additionally, FDA authorized the use of each of the available COVID-19 vaccines as a heterologous ("mix and match") booster dose in eligible individuals following completion of primary vaccination with a different FDA-authorized or approved COVID-19 vaccine. FDA convened the VRBPAC to provide input on the use of booster doses for high-risk individuals and the use of heterologous booster doses.

In November 2021, FDA analyzed immune response data and reviewed additional real-world data to reassess the benefits and risks of a single booster dose of the Pfizer-BioNTech and Moderna COVID-19 vaccines following completion of primary vaccination to provide continued protection against COVID-19 and the associated serious consequences. FDA amended the EUAs for both the Moderna and Pfizer-BioNTech COVID-19 vaccine authorizing use of a single booster dose for all individuals 18 years of age and older after completion of primary vaccination with any FDA-authorized or approved COVID-19 vaccine. FDA determined that the currently available data supported expanding the eligibility of a single booster dose to all individuals 18 years of age and older.

COVID-19 Vaccine Surveillance

Real world data from both passive and active safety surveillance systems are crucial to monitoring the safety of authorized and approved COVID-19 vaccines. The FDA and the Centers for Disease Control and Prevention (CDC) have systems in place to ensure that safety concerns are identified and evaluated in a timely manner. The Vaccine Adverse Event Reporting System (VAERS) is a passive reporting database administered by FDA and CDC that relies on

healthcare providers, vaccine recipients, and parents of vaccine recipients to send in reports of their experiences. VAERS is useful for detecting unusual or unexpected patterns of adverse event reporting that might indicate a possible safety problem with a vaccine. VAERS can provide FDA with valuable information that additional evaluation may be necessary to further assess a possible safety concern.

FDA collaborates closely with CDC on safety monitoring, including on collection and analysis of adverse events reported through VAERS and the other systems used by each agency that complement one another. FDA's extensive vaccine safety monitoring system for the COVID-19 vaccines is working as intended. For example, as a result of ongoing safety monitoring, FDA and CDC recommended a temporary pause in the use of Janssen COVID-19 Vaccine, due to reports of a serious and rare type of blood clot in combination with low blood platelets, known as thrombosis thrombocytopenia syndrome, on April 13, 2021. After a thorough review of the available data, where FDA concluded that the known and potential benefits of the Janssen COVID-19 Vaccine outweigh its known and potential risks in individuals 18 years of age and older, the agencies lifted the pause. When the pause was lifted, the vaccine recipient and vaccination provider fact sheets were revised to provide further information about the risk of the syndrome. In addition, safety surveillance suggests an increased risk of Guillain Barré syndrome, within 42 days following receipt of the Janssen COVID-19 Vaccine which led to revisions to the vaccine recipient and vaccination provider fact sheets for the Janssen COVID-19 Vaccine to include information pertaining to an observed increased risk. Additionally, FDA has conducted a rigorous evaluation of post-authorization safety data pertaining to myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine and Moderna COVID-19 Vaccine and has determined that the data demonstrate increased risks, particularly within the seven days following the second dose. The fact sheets were updated to include these risks.

FDA's active surveillance involves proactively obtaining and rapidly analyzing information occurring in millions of individuals recorded in large healthcare data systems to further investigate safety signals identified through passive surveillance or to detect additional safety signals that may not have been reported as adverse events to passive surveillance systems. CBER conducts surveillance using the Sentinel Biologics Effectiveness and Safety (BEST) System, the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA), and other academic and large non-government healthcare data systems. CBER has issued six COVID-19 protocols for vaccine safety monitoring and convalescent plasma surveillance. In July 2021, FDA issued a public communication accompanying one of the protocols where near real-time surveillance detected four potential adverse events of interest (AEIs) (pulmonary embolism, acute myocardial infarction, immune thrombocytopenia, and disseminated intravascular coagulation) in the Medicare healthcare claims database of persons aged 65 years and older who had received the Pfizer-BioNTech COVID-19 Vaccine.[112] FDA shared the initial findings of this safety study in the spirit of transparency but does not believe there is a cause for concern. FDA continues to closely monitor the safety of the COVID-19 vaccines and is investigating these findings by conducting more rigorous epidemiological

[112] Please see https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/initial-results-near-real-time-safety-monitoring-covid-19-vaccines-persons-aged-65-years-and-older

studies. In addition, CBER participates in ongoing international pharmacovigilance efforts, including those organized by the International Coalition of Medicines Regulatory Authorities (ICMRA) and the World Health Organization (WHO).

COVID-19 Research

CBER scientists are conducting research studies to facilitate the evaluation of vaccines, treatments, and diagnostics in response to the COVID-19 pandemic, which include:

- Studying immune responses to inform vaccine development and evaluation;
- Developing a Syrian hamster model of SARS-CoV-2 to aid safety and efficacy evaluations of COVID-19 vaccines and human intravenous immunoglobulin products;
- Developing methods, reagents, antibodies, cell lines, assays, and libraries being used in various SARS-CoV-2 research projects, including a nucleic acid test reference panel to provide standards for nucleic acid-based *in vitro* diagnostics with the Center for Devices and Radiological Health (CDRH);
- Participating in a multi-center international collaborative study to evaluate candidate preparations for the WHO International Standard (IS) for SARS-CoV-2 RNA. The IS will be used for the calibration and control of nucleic acid amplification techniques, which are considered the gold standard method for accurate diagnosis of infection; and
- Actively assessing the impact of new strains (variants) of SARS-CoV-2 on authorized or approved products and working with its international partners to evaluate the impacts.

As part of these efforts, CBER facilitated research collaboration and data sharing through 30 publications and 24 posters/presentations on CBER's COVID-19 related research. Additionally, CBER awarded several grants to support research projects specifically related to enhancing innovations in advanced manufacturing techniques for vaccines such as: integrated and continuous vaccine manufacturing; manufacturing and characterizing potent mRNA lipid nanoparticle vaccines at multiple scales; developing novel 3D printing for advanced manufacturing of complex vaccine formulations; and developing modular platforms for rapid virus-like particle vaccine development.

Updated COVID-19 Guidances

Additionally, CBER issued or updated seven guidances related to COVID-19. For example, CBER updated the guidance for industry entitled "Emergency Use Authorization for Vaccines to Prevent COVID-19," to include a new section that clarifies how the agency intends to prioritize review of EUA requests for the remainder of the current pandemic in May 2021.[113]

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.

[113] For more information, please see Emergency Use Authorization for Vaccines to Prevent COVID-19 | FDA.

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 the end of FY 2021, CBER granted 55 Breakthrough Therapy designations, with 30 of the products being for rare diseases (Orphan designated). FDA granted 64 Regenerative Medicine Advanced Therapy (RMAT) Designations since program inception in December 2016 with 32 being for rare diseases.

CBER approved the first three RMAT-designated products in 2021. In February 2021, CBER approved 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. This approval represents another milestone in the rapidly progressing field of gene therapy by providing an additional treatment option for adults with certain types of cancer affecting blood, bone marrow and lymph nodes. FDA granted Breyanzi Priority Review, Orphan Drug and Breakthrough Therapy designations. CBER approved the second product, StrataGraft, in July 2021. StrataGraft is indicated for the treatment of adult patients with thermal burns containing intact dermal elements (remaining deep skin layers) for which surgical intervention is clinically indicated (also referred to as deep partial thickness burns). StrataGraft can help avoid or decrease the amount of healthy skin needed for grafting and improve the quality of life for burn patients, providing a novel way to treat burn wounds. The FDA granted StrataGraft Priority Review and Orphan Drug designations. In October 2021, CBER approved Rethymic for the treatment of pediatric patients with congenital athymia. Congenital athymia is a rare immune disorder in which a child is born without a thymus – an organ that plays a critical role in helping the body learn to fight infections. Children impacted by this disease typically die within the first two years of life. Rethymic is the first thymus tissue product approved in the U.S. Rethymic was granted Breakthrough Therapy, Rare Pediatric Disease, and Orphan Drug designations.

CBER also approved other innovative therapies to address previously unmet medical needs for children affected by rare pediatric diseases in 2021. For example, in June, CBER approved Ryplazim (plasminogen, human-tvmh), the first treatment for patients with plasminogen deficiency type 1, a disorder that can impair normal tissue and organ function and may lead to blindness. FDA granted Ryplazim Fast Track designation and Priority Review.

FDA continued to engage with stakeholders on topics on the cutting edge of medicine and drug development. Regenerative medicine and 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. In May 2021, CBER held a patient engagement workshop to bring together patients, caregivers, advocates, and other stakeholders to discuss ways for patients and their advocates to help advance regenerative medicine. In August 2021, CBER and the NIH, National Institute of Allergy and Infectious Diseases (NIAID) cohosted a public workshop entitled “Science and Regulation of Bacteriophage Therapy” to exchange information with the medical and scientific community about the regulatory and scientific issues associated with bacteriophage therapy. In June 2021, in collaboration with the Center for Drug Evaluation and Development (CDER), CBER held a workshop called “Model Informed Drug Development

Approaches for Immunogenicity Assessments." This workshop focused on discussing best practices and future directions of quantitative methods for predicting immunogenicity of biological products.

CBER is developing a regulatory program for individualized (bespoke) therapies and fostering global regulatory convergence for cell and gene therapies. FDA will continue to work with stakeholders to facilitate end-to-end solutions for key issues limited the development and application of gene therapies, including manufacturing challenges that make these therapies cost-prohibitive and presently not commercially viable. In October 2021, FDA, NIH, 10 pharmaceutical companies, and five non-profit organizations partnered to accelerate development of gene therapies for the 30 million Americans who suffer from a rare disease by launching the Bespoke Gene Therapy Consortium (BGTC).

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 2021, CBER awarded grants 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. CBER also awarded a contract for a study to enable continuous manufacturing of recombinant adeno-associated virus vectors. These grants and contracts aim to address knowledge and experience gaps identified for emerging manufacturing technologies and support the development and adoption of such technologies in the biological product sector.

Strengthen Science And Efficient Risk-Based Decision Making

To continually modernize its regulatory toolbox, FDA conducts research to develop new tools, standards, and approaches to assess the safety, effectiveness, quality, and performance of FDA-regulated products. It also enables the FDA to understand and assess risk, prepare for, and respond to public health emergencies, such as emerging infectious diseases, and help ensure the safety of products used by patients. FDA is committed to exploring the use of real-world evidence (RWE) in regulatory decision-making, including its ability to provide clinically meaningful information about the safety and effectiveness of medical products and to support labeling changes.

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.

Innovation and Regulatory Science

CBER plays a critical role in the development of biological products that are at the cutting edge of 21st century medicine. CBER's research focuses on creating new knowledge in the fields of diagnostic and therapeutic biological product innovations and the regulatory science needed to ensure those products are safe, effective, and available to the public. This research broadens FDA's knowledge of fundamental biological processes and provides a robust scientific base for regulatory review. CBER scientists also evaluate potential methods for improving ongoing monitoring of the safety of products that CBER has approved for use.

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 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. To support the development of innovative products, FDA's regulatory science program addresses knowledge gaps and improves familiarity with how new science and technology are applied to FDA-regulated products. Research is a critical component to advancing CBER's individualized therapies, advanced manufacturing, pathogen reduction, microbiome, and preparedness initiatives to bring needed treatments and preventative measures to patients.

Reducing Incidence of Infectious Disease

The WHO recognizes vaccine hesitancy as one of the top 10 threats to global health. 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 U.S. due to the use of effective vaccines.[114]

International engagements are an important component of how FDA carries out its regulatory responsibilities. Many of the products that FDA regulates address global infectious disease threats. Over the past year, FDA participated in several International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) meetings. ICH is a unique harmonization project where regulator and industry representatives work to improve the efficiency of new drug development processes, promote public health, prevent duplication of clinical trials in humans, and minimize the use of animal testing without compromising safety and effectiveness.

FDA provided expert advice to the WHO on many important topics, both related to COVID-19 and to other health priorities. For example, FDA research staff contributed to development and implementation of WHO's global research program on COVID-19, which facilitated the development and authorization of vaccines around the world. In addition, FDA participated in meetings of WHO's Global Advisory for Vaccine Safety and WHO's Strategic Advisory Group of Experts on Immunization to address issues that could interfere with confidence in vaccines. CBER collaborated with WHO and other national regulatory authorities to provide input into a revised WHO guideline on quality, safety, and efficacy of DNA vaccines. FDA also participated in the Coalition for Epidemic Preparedness Innovation (CEPI) meetings. CBER took a leadership role in the International Coalition of Medicines Regulatory Authorities (ICMRA) to facilitate global alignment regarding COVID-19 vaccine development and data required for regulatory decision-making. CBER 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.

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[114] 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).
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://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp?mmwr_year=2018

Influenza is an example of an infectious disease caused by constantly changing viruses. The best way to prevent influenza, its complications, and transmission to others is vaccination. The FDA, WHO, CDC, and other public health experts collaborate to review influenza disease surveillance and laboratory data collected internationally to identify strains that may cause the most illness. Annual influenza vaccination can help avoid influenza-associated healthcare visits and hospitalizations, preserving healthcare resources for patients with other diseases and medical conditions. FDA selects the influenza strains that manufacturers should include in their annual vaccines for the U.S. population. In March 2021, the VRBPAC recommended the strains for inclusion in the influenza vaccines for the 2021-2022 U.S influenza season. The VRBPAC met again in September 2021 to recommend the strains for the 2021-2022 southern hemisphere influenza season.

Blood products are critical to public health and offer potentially life-saving benefits for a variety of acute and chronic conditions. Although donor screening and testing can mitigate the risk of transfusion transmission of infectious diseases, they do not eliminate the risk entirely. Pathogen reduction technologies can address the infectious risk from viral, bacterial, and parasitic pathogens, potentially covering emerging infectious diseases as well as the known transfusion transmitted infections which are of concern for the blood supply. Given the importance of blood safety and availability to public health, CBER is working with a variety of different partners to support innovative pathogen reduction technologies and related reagents for blood safety from infectious disease-causing pathogens. In FY 2021, CBER made new awards to support development of new technologies for pathogen reduction in Whole Blood and made continued investments to develop an internal pathogen reduction research program.

Compliance and Oversight

FDA ensures the quality of products regulated by CBER over their entire lifecycle through pre-market review and inspection, and post-market review, surveillance, inspection, outreach, and compliance. CBER monitors the safety, purity, and potency of biological products through review of product deviation reports and 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 that the biologics industry continuously reviews the quality standards of its manufacturing operations to maintain 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 2021, CBER documented three resolved shortages, two new product shortages, 14 prevented shortages, five ongoing shortages, and 32 notifications from 21 different manufacturers. CBER uses regulatory flexibility and expedited reviews to prevent or mitigate shortages when appropriate. For example, CBER resolved an Immune Globulin (IG) product shortage in August 2021 by 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 human cells, tissues, and cellular and tissue-based products (HCT/Ps). FDA's regenerative medicine framework clarifies how it interprets existing regulatory definitions and describes FDA's compliance and enforcement policy.

Compliance actions on HCT/P manufacturers taken by FDA in FY 2021 include the issuance of:

- One Warning Letter for unapproved and/or adulterated regenerative medicine products to treat various diseases or conditions; and
- 12 Untitled Letters for marketing of unapproved regenerative medicine products to treat numerous diseases or conditions, including some that are serious or life threatening.

FDA also issued a Warning Letter for an unapproved and misbranded influenza vaccine and five Untitled Letters related to:

- Marketing of unapproved allergenic extracts intended for sublingual immunotherapy;
- Violating regulations governing the proper conduct of clinical studies involving investigational new drugs; and
- Marketing unapproved cellular products to treat diseases or conditions including leukemia.

Real-World Evidence to Evaluate Effectiveness and Safety

Real World Evidence represents the clinical evidence for the usage and potential benefits or risks of a medical product derived from the analysis of Real-World Data (RWD). CBER is exploring the potential use of RWD and RWE to inform the discovery of new therapies for patients, the risks and benefits in practice, and to inform which therapies are best for which patients. RWD comes from a variety of sources including electronic health records (EHRs), claims and billing activities, product and disease registries, and other patient-generated data. CBER leverages a variety of data partners and systems to build postmarket safety and effectiveness systems for vaccines and therapeutics.

CBER's 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 100 million claims to conduct robust, rapid safety and effectiveness studies of biological products. 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 to improve FDA's ability to identify cases of serious, life-threatening adverse effects.

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, gathers and uses RWD to help ensure the continued safety of the U.S. blood supply and monitor the effects of FDA's policy changes regarding donor deferral. TTIMS monitors approximately 60 percent of the U.S. blood supply for HIV, hepatitis B virus, and hepatitis C virus incidence and prevalence. FDA is committed to ongoing evaluation of deferral policies based on available scientific evidence. FDA is sponsoring the ADVANCE Study, an ongoing

pilot study to provide FDA with evidence by which to consider potential changes in the donor deferral policy while maintaining the safety of the blood supply.[115]

The 21st Century Cures Act directs the FDA to establish a program to evaluate the potential use of RWE to support the approval of a new indication for a drug approved by FDA and to support or satisfy post-approval study requirements. FDA published draft guidance for industry, entitled "Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products" (September 2021), which describes considerations when proposing to use EHRs or medical claims data in clinical studies to support a regulatory decision on effectiveness or safety. Also, as called for in the 21st Century Cures Act, FDA published the draft guidance for industry entitled "Benefit-Risk Assessment for New Drug and Biological Products." This guidance articulates important considerations that factor into CDER and CBER's benefit-risk assessments for drug products, including how patient experience data may be used to inform benefit-risk assessment. It concludes with additional considerations on benefit-risk assessments that inform regulatory decision making that occurs in the postmarket setting.

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.[116] 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, and not discussed elsewhere in the Biologics Program Description and Accomplishments.

Date	#	Title	Description
Nov 2021	FDA-2017-D-6784	Final Guidance for Industry: Manufacture of Blood Components Using a Pathogen Reduction Device in Blood Establishments: Questions and Answers	Provides recommendations for implementing a pathogen reduction device for the manufacture of pathogen reduced blood components.
Sept 2021	FDA-2019-D-5392	Final Guidance for Industry: Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations	Intended to assist stakeholders who seek orphan-drug designation and orphan-drug exclusivity.
Sept 2021	FDA-2021-D-0776	Draft Guidance for Industry: Studying Multiple Versions of a Cellular or Gene Therapy Product in an Early-Phase Clinical Trial	Provides recommendations to sponsors interested in studying multiple versions of a cellular or gene therapy product in an early-

[115] https://advancestudy.org

[116] Complete information on CBER guidances can be found at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances

			phase clinical trial for a single disease.
June 2021	FDA-1995-D-0288	Final Guidance for Industry: Chemistry, Manufacturing, and Controls Changes to an Approved Application: Certain Biological Products	Assists applicants and manufacturers of certain licensed biological products in determining appropriate reporting category for a change in chemistry, manufacturing, and controls (CMC).
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.

In addition to the above guidance documents issued by CBER, the center also has worked with the other medical product centers on the issuance of numerous joint guidance documents.

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
Aug 2021	Ticovac/*Tick-Born encephalitis vaccine*	For active immunization to prevent tick-borne encephalitis (TBE) in individuals 1 year of age and older.
Jul 2021	Vaxneuvance (Pneumococcal 15-valent Conjugate Vaccine)	For the prevention of invasive disease caused by 15 *Streptococcus pneumoniae* serotypes in adults 18 years of age and older.
Jul 2021	Shingrix/Zoster vaccine Recombinant, adjuvanted	Expanded indication in adults aged 18 years or older who are or will be at increased risk of Herpes Zoster due to immunodeficiency or immunosuppression caused by known disease or therapy.
Jul 2021	Immune Globulin Intravenous (Human)	Expanded indication to include treatment of dermatomyositis in adults.
Mar 2021	Abecma/*idecabtagene vicleucel*	Indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$408,610,000	$240,133,000	$168,477,000
FY 2020 Actuals	$426,027,000	$252,128,000	$173,899,000
FY 2021 Actuals	$441,809,000	$254,031,000	$187,778,000
FY 2022 Annualized CR	$450,902,000	$254,138,000	$196,764,000
FY 2023 President's Budget	$475,415,000	$274,917,000	$200,498,000

Figure 17 - Funding History

BUDGET REQUEST

The FY 2023 Budget Request for the Biologics Program is $475,415,000, of which $274,917,000 is budget authority and $200,498,000 is user fees. The budget authority increases by $20,779,000 compared to the FY 2022 Presidents Budget. User Fees increase by $3,734,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is $423,565,000. The Office of Regulatory Affairs amount is $51,850,000.

The FY 2023 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 2023 as necessary. CBER facilitates the development and availability of safe and effective medical products through the integration of advances in science and technology through enhanced FDA-sponsor communications in its user fee programs, the continued use of its expedited programs, and streamlined regulatory pathways. CBER is developing a regulatory program for individualized (bespoke) therapies and fostering global regulatory convergence for cell and gene therapies. 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. CBER will continue to facilitate the development of innovation oncology products including immunotherapies, chimeric antigen receptor T cells (CAR-T) therapies, and cancer vaccines such as the HPV vaccine.

CBER will protect public health from infectious diseases by facilitating the availability of safe and effective vaccines and by working to reduce the risk of transmission through blood or tissues. CBER monitors the impact of disease on the safety and availability of the blood supply and is working to advance pathogen reduction technologies. 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 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 threats and emerging disease

through the development of new countermeasures. 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. 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 vectors for gene therapies, vaccines for emerging infectious disease, and influenza.

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. FDA will continue to initiate regulatory action to address non-compliance with relevant statues and regulations, including those manufacturers, clinics, or health care providers who may be offering unapproved regenerative medical products. CBER continues to use real world data and real world evidence monitor postmarket safety, life-threatening adverse events, and regulatory decisions, such as informing donor blood eligibility or assessing the safety and effectiveness of preventative vaccines. 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 (+$900,000)

Data Modernization and Enhanced Technologies: Regulatory Information Management Modernization (+$900,000)

Center: +$900,000

The FY 2023 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, $900,000 is requested 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 (+$19.9 million / 27 FTE)

Capacity Building (+$4.7 million / 3 FTE)

Center: +$4.1 million / 3 FTE

Field: +$618,000

The FY 2023 President's Budget includes $59.4 million for Capacity Building, including $4.7 million for the Biologics program. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Public Health Employee Pay Costs (+$4.4 million)

Center: +$3.3 million

Field: +$1.1 million

The FY 2023 President's Budget includes $51.9 million, including $4.4 million within the Biologics program, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$5.8 million / 18 FTE)

Field: +$5.8 million / 18 FTE

The FY 2023 President's Budget includes $33.8 million for optimizing inspectional activities, including $5.8 million within Biologics Field, to support capacity building towards an advanced, highly trained investigators capable of analyzing available data to increase the efficiency and productivity of our inspection operations.

Reducing Animal Testing Through Alternative Methods (+$386,000)

Center: +$386,000

The FY 2023 President's Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program, including $386,000 for the Biologics program, to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the

development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

CBER will conduct targeted regulatory science research to further evaluate applicable methods and assays that refine or replace animal use, such as evaluating approaches to using *in-silico* models to predict adverse safety events to therapeutic proteins; approaches using 3D microphysiological systems to detect vaccine-induced pathologies; and approaches that will reduce or replace the use of higher species animals in favor of lower species animals or biomarkers.

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 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies efforts, including $4.6 million for Enterprise Technology and Data within the Biologics program, 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.

USER FEES

Current Law User Fees (+$3.7 million)

Center: +$3.7 million

Field: +8,000

The Biologics Program request includes an increase of $3.7 million for user fees which will allow FDA to fulfil its mission of promoting and protecting the public health by ensuring safety and efficacy of FDA-regulated products.

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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
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 2020: 100% Target 90% (Target Exceeded)	90%	90%	Maintain
233208: Review and act on priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. *(Output)*	FY 2020:67% Target 90% (Target Not Met)	90%	90%	Maintain
233205: Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. *(Output)*	FY 2020: 100% Target 100% (Target Exceeded)	90%	90%	Maintain
233206: Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. *(Output)*	FY 2020: 99.7% 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 2020: 67% Target: 60% (Target Exceeded)	60%	60%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
234101: Increase manufacturing diversity and capacity for influenza vaccine production. *(Output)*	FY 2021: Continued evaluation of new methods to produce high-yield influenza vaccine reference strains. (Target Met)	Continue evaluation of new methods to produce more stable high-yield influenza vaccine reference strains and improve current manufacturing processes	Continue evaluation of new methods to produce more stable high-yield influenza vaccine reference strains and improve current manufacturing processes	Maintain
231301: Percentage of Lot Distribution Reports that were entered into the Regulatory Management System - Biologics License Applications (RMS-BLA) within 7 Days.	FY 2020: 98% 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 compliance. (Outcome)	FY 2020: 77.8% Target: 65% (Target Exceeded)	65%	65%	Maintain

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

Premarket Review - Priority BLA Performance Measure

Although CBER routinely meets its PDFUA performance goals, CBER fell slightly short on the FY 2020 target to review and act on 90 percent of the Priority NME NDA and original BLA submissions within 6 months of the 60-day filing date. Two of the Priority BLA applications missed the user fee goal date due to COVID travel restrictions that impacted the ability to inspect facilities in time. CBER will strive to meet the target of 90%, as established in the PDUFA commitment letter.

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 2021, FDA met the target to continue evaluation of new methods to produce high-yield influenza vaccine reference strains. Activities to meet this target included the following:

- FDA continued efforts to develop new methods for determining influenza vaccine potency, an important component in the evaluation of high-yield influenza vaccine viruses. A new international collaborative study was designed to compare several alternative potency methods and evaluate their potential to quantify sub-potent vaccine using a variety of stress methods. Study materials were prepared in FY 2021 and the study will be conducted in the first half of FY 2022.
- Generated and distributed an H5N8 candidate vaccine virus for a recently identified H5N8 influenza virus with pandemic potential
- Continued efforts to evaluate the impact of including neuraminidase (NA) in candidate vaccines. A candidate vaccine virus that has increased NA antigen content was developed and demonstrated to elicit a more balanced protective NA and hemagglutinin (HA) response. Established collaborations with the NIH Vaccine Research Center to assist in producing recombinant NA for vaccines and for measuring NA responses from individuals in clinical trials.
- New methods were developed to purify and quantify NA in vaccine candidates. A 3-step method was established for purifying soluble NA vaccine antigens produced using insect cells without the need of additional domains for purification. In addition, a more accurate method for measuring inhibitory antibody responses to NA was developed.

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 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
Original Biologics License Applications (BLA)			
Workload [1]	17	17	17
Total Decisions [2]	18	18	18
Approved	13	13	13
BLA Efficacy Supplements			
Workload [1]	17	17	17
Total Decisions [2]	23	23	23
Approved	14	14	14
BLA Manufacturing Supplements			
Workload [1]	1,396	1,396	1,396
Total Decisions [2]	1,484	1,484	1,484
Approved	1,390	1,390	1,390
BLA Labeling Supplements			
Workload [1]	154	154	154
Total Decisions [2]	142	142	142
Approved	12	128	128
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]	19	19	19
Total Decisions [2]	20	20	20
Approved	20	20	20
NDA Labeling Supplements			
Workload [1]	3	3	3
Total Decisions [2]	0	0	0
Approved	0	0	0
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

Figure 18 - CBER Workload and Outputs ½

CBER Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
ANDA Manufacturing Supplements			
Workload [1]	8	8	8
Total Decisions [2]	7	7	7
Approved	7	7	7
ANDA Labeling Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
Device 510Ks			
Workload [1]	45	45	45
Total Decisions [2]	45	45	45
Final Decision - SE	36	36	36
Device Premarket Applications (PMA)[6]			
Workload [1]	0	0	0
Total Decisions [2]	3	3	3
Approved	3	3	3
Device Premarket Applications (PMA) Supplements [7]			
Workload [1]	76	76	76
Total Decisions [2]	82	82	82
Approved	38	38	38
Investigational New Drugs (IND)			
Receipts: IND (new)	791	791	791
Receipts: IND Amendments	15,795	15,795	15,795
Total Active IND [3]	3,846	3,846	3,846
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	25	25	25
Receipts: IDE Amendments	342	342	342
Total Active IDE [3]	103	103	103
Patient Safety			
Adverse Event Reports Received [4]	812,147	850,000	850,000
Biological Deviation Reports Received	14,566	14,500	14,500
Sponsor Assistance Outreach			
Meetings	756	756	756
Final Guidance Documents [5]	40	45	45
Admin/Management Support			
Advisory Committee Meetings Held	11	15	12
FOI Requests Processed	326	375	425

[1] Workload includes applications received and filed.

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

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

[4] Includes MedWatch, Foreign reports and VAERS reports. Does not include Fatality Reports for blood tansfusions or blood collection (under 21CFR606.170) or Medical Device Reports for CBER-regulated medical devices.

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

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

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

Figure 19 - CBER Workload and Outputs 2/2

Field Biologics Program Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***480***	***650***	***1,892***
Bioresearch Monitoring Program Inspections	96	75	100
Blood Bank Inspections	111	900	900
Source Plasma Inspections	78	115	190
Pre-License, Pre-Market Inspections	16	50	55
GMP Inspections	18	20	28
GMP (Device) Inspections	0	5	7
Human Tissue Inspections	161	300	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***2***	***15***	***47***
Bioresearch Monitoring Program Inspections	0	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	0	7	7
Pre-License, Pre-market Inspections	2	7	7
GMP Inspections (Biologics & Device)	0	5	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***482***	***665***	***1,939***
IMPORTS			
Import Field Exams/Tests	53	45	45
Import Line Decisions	177,977	181,537	185,167
Percent of Import Lines Physically Examined	0.03%	0.02%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***482***	***800***	***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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 20 - Field Biologics Program Workload and Outputs

ANIMAL DRUGS AND FOODS

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Animal Drugs and Foods	**245,307**	**238,847**	**245,894**	**300,843**	**54,949**
Budget Authority	***192,369***	***192,352***	***192,456***	***242,360***	***49,904***
User Fees	***52,938***	***46,495***	***53,438***	***58,483***	***5,045***
Center	175,083	169,707	175,591	211,798	36,207
Budget Authority	123,599	123,599	123,646	154,882	31,236
User Fees	51,484	46,108	51,945	56,916	4,971
Animal Drug (ADUFA)	*30,117*	*26,592*	*28,648*	*29,185*	*537*
Animal Generic Drug (AGDUFA)	*21,250*	*19,486*	*23,178*	*27,610*	*4,432*
Third Party Auditor Program	*117*	*30*	*119*	*121*	*2*
Field	70,224	69,140	70,303	89,045	18,742
Budget Authority	68,770	68,753	68,810	87,478	18,668
User Fees	1,454	387	1,493	1,567	74
Animal Drug (ADUFA)	*390*	*387*	*393*	*401*	*8*
Animal Generic Drug (AGDUFA)	*224*	---	*244*	*292*	*48*
Food Reinspection	*840*	---	*856*	*874*	*18*
FTE	**1,042**	**1,061**	**1,007**	**1,090**	**83**

Figure 21 - Narrative by Activity

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 and animal food. The Program is administered by the Center for Veterinary Medicine (CVM) and the Office of Regulatory Affairs (ORA) to protect and promote the health of humans and animals from a One Health perspective by ensuring:

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

Specifically, CVM:

- evaluates new animal drug applications for safety, effectiveness, and manufacturing quality

- monitors animal drugs, animal foods, and animal devices for safety and takes appropriate action to mitigate unsafe or 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 Center 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, honeybees, and pheasants, and for minor uses (infrequent and limited) in the major species (cattle, pigs, chickens, dogs, cats, horses, and turkeys).

In April 2021, CVM posted new and enhanced performance measure dashboards highlighting its accomplishments towards protecting human and animal health. There are now five new dashboards covering the Center's work on animal food safety; compounded animal drugs; emerging technologies; pre-market drug review; and post-market drug safety, effectiveness, and quality. The new dashboards join existing dashboards on antimicrobial stewardship in veterinary settings, as well as the Center's performance on animal drug review timelines agreed upon in the Animal Drug and Animal Generic Drug User Fee Amendments of 2018.

CVM utilizes budget authority and user fees to help meet its mission of protecting human and animal health. Animal Drug User Fee Act (ADUFA) and Animal Generic Drug User Fee Act (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 performed to establish and administer the accredited third-party certification program.

Responding to COVID-19 Public Health Emergency

CVM is facilitating the incorporation of a One Health approach, recognizing that the health of humans, animals, and the environment are intertwined. Approximately 75 percent of recently emerging infectious diseases affecting humans, including HIV, Ebola, and influenza, are zoonotic (i.e., spread from animals to humans).[117] It is also clear that humans are also transmitting diseases to animals in what is often referred to as "reverse zoonoses." As February 15, 2022 there are 356 animals in the United States (companion animals, animals in zoos and wildlife), identified as being infected with COVID-19. Additionally, 458 mink farms around the world, including 17in the US, involving large numbers of mink have been identified as having COVID positive mink. The finding of COVID-19 in white tailed deer raises concerns about a silent reservoir of COVID in our wildlife environment.

[117] 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).

CVM's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) supported the response to the COVID-19 pandemic by facilitating two inter-laboratory comparison exercises to help veterinary diagnostic laboratories ensure that their tests for the novel SARS-CoV-2 virus are reliable for use in animals, as well as to evaluate:

- sensitivity (level of detection) of methods in participating laboratories to detect SARS-CoV-2
- the ability of participants' methods to detect emerging SARS-CoV-2 variants
- specificity of participant methods; namely, to evaluate if participants report any false positives due to presence of non-SARS-CoV-2 animal coronavirus(es)

A large number of participating veterinary diagnostic laboratories were enlisted to test either human samples or both animal and human samples. Method evaluations completed during an inter-laboratory comparison exercise help the laboratories seeking Clinical Laboratory Improvement Amendment (CLIA) certification to conduct human testing for SARS-CoV-2.

In response to the COVID-19 pandemic and disruptions of supply chains that are leading to shortages of animal drugs, in May 2020, CVM published *GFI #271 Reporting and Mitigating Animal Drug Shortages During COVID-19 Public Health Emergency* to assist animal drug sponsors in providing CVM with timely, informative notifications about changes in the production of animal drugs. Early notification is critical in order to help the Center in its efforts to prevent or mitigate shortages of these products. While CVM does not have authority to require mandatory reporting of shortages, during the COVID-19 outbreak the Center continues to monitor the animal drug supply chain and voluntarily solicit information from animal drug sponsors to ascertain, as early as possible, any 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 January 2022, 103 potential product shortages were reported, excluding those we are monitoring or that are still pending, and shortages were averted 84 percent of the time.

CVM also leveraged supplemental COVID-19 funding to begin 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. Once this Information Technology (IT) system is in place, we will be in a better position to quickly identify and address critical facilities and animal drugs impacted by emerging diseases or natural disasters and help to identify approaches to help mitigate potential drug shortages. The system will also include animal drug sales information that will support the identification of shortage situations and directing any subsequent regulatory response.

As part of our COVID-19 Pandemic response, CVM initiated a surveillance and regulatory strategy to support the agency's efforts to mitigate health fraud related to COVID-19 products. To combat fraudulent and dangerous COVID-19 products from entering the market, the Center formed a Health Fraud Team focused on website monitoring and industry surveillance to ensure that individuals and firms were not using the pandemic as an opportunity to take advantage of the public by offering unapproved and fraudulent products for use to treat or prevent COVID-19 in humans or animals. Since this effort began in 2020, CVM's Health Fraud Team worked with numerous third-party distributor websites to remove 287 fraudulent products from the market. Many of these products were unapproved new animal drugs; and other

products were intended for use in both humans and animals, with a few being marketed solely for human use.

Once the drug 'hydroxychloroquine' became widely known as a potential treatment for COVID-19 in humans, the Health Fraud Team began looking at animal drugs with similar components. CVM became aware of an Arizona couple that ingested a similar drug ingredient 'chloroquine phosphate' (which is an unapproved animal drug used in aquaculture), in an attempt to protect themselves from COVID-19. Unfortunately, one of those individuals died from ingesting this product and the Center took efforts to remove all veterinary products from the marketplace that contained this active ingredient. Since 2020, five warning letters were issued specifically to firms marketing chloroquine phosphate. The Center received 100 percent voluntary compliance, as all firms that were issued letters have ceased marketing this product.

Poison control centers across the United States have seen a sharp spike in reports of people suffering adverse health effects after taking the animal drug ivermectin. Various highly concentrated animal ivermectin formulations such as "pour-on," injectable, paste, and "drench" intended for horses, cattle, and sheep, are being purchased and taken by people which has led to adverse events in people.

Once the drug ivermectin became widely disseminated as a potential treatment for COVID-19, CVM became aware of dangerous misuse of over-the-counter animal ivermectin drug products in people. To date, CVM has directly received 22 reports of exposure to ivermectin that have resulted in adverse drug events. The outcome of most cases was either recovery or unknown, however there was one human death reported. It is unclear if the death was definitely related to ivermectin exposure.

CVM has continued concerns that there are people using formulations of the drug ivermectin that are intended for animals, to treat or prevent COVID-19 in humans. Due to these concerns, FDA has issued letters to veterinarians, sponsors, retailers and provided posters, consumer updates, FAQ documents and health advisories in an effort to educate the public on the dangers of misuse of animal ivermectin drug products in people.

Animal Drug Review

CVM 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 evaluations are supported by CVM's Office of Research as it conducts method trials and develops alternative models to replace, reduce or refine (3Rs) the need for animal testing. 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 (and animals) to eat.

CVM exceeded the ADUFA and AGDUFA performance goals for FY 2020 and met performance goals for all FY 2021 cohort submissions reviewed by September 30, 2020. The Center completed reviews of almost 7,000 new animal drug applications (NADAs) and abbreviated new animal drug applications (ANADAs), supplements, and related investigational submissions in FY 2021.

As part of the ADUFA reauthorization in 2018, Congress expanded CVM'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. As of January 31, 2022, CVM has received 26 requests for expanded conditional approval eligibility. On January 14, 2021, CVM 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.

CVM also continues to contribute to FDA-wide efforts to strengthen international harmonization and collaboration with international organizations, other countries' regulatory agencies and related industry. As of January 31, 2021, 50 internationally harmonized guidelines for animal drugs were implemented, with work currently ongoing to revise 19 guidelines and develop five new harmonized guidelines. The Center also simultaneously reviewed and approved 15 applications and is currently reviewing 16 additional applications through the United States-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

In September 2021, FDA and the United Kingdom's Veterinary Medicines Directorate (VMD) announced their decision to expand the US-UK Mutual Recognition Agreement (MRA) to include Good Manufacturing Practice (GMP) inspections for animal drugs. The goal of this MRA is to produce greater efficiencies for both regulatory systems and provide a more practical means for both the FDA and the VMD to oversee the facilities that manufacture animal drugs in these locations. By utilizing each other's inspection reports and related information, an MRA can ultimately enable the FDA and VMD to avoid duplication of some animal drug inspections and enable regulators to devote more resources to other areas where there may be greater risk.

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 CVM with the opportunity to foster a risk-based, and science-based program that provides flexibility in the regulatory process to support the development of significant and beneficial technology, while safeguarding human and animal health.

In October 2021, CVM announced the availability of four final guidance documents that will help encourage animal drug sponsors to use innovative approaches as they prepare data submissions for evaluation and review as part of the new animal drug approval process:

- *Final 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

- *Final 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 (including ongoing surveillance activities, observational studies, and registry data) into proposed clinical investigation protocols and applications for new animal drugs
- *Final GFI #267 Biomarkers and Surrogate Endpoints in Clinical Studies to Support Effectiveness 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
- *Final 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

In September 2021, CVM issued two draft guidances that, if finalized, are intended to assist manufacturers by providing product-specific recommendations that will help developers of Animal Cells, Tissues, and Cell-and Tissue-Based Products (ACTPs) meet FDA manufacturing standards. The Center also published a webinar to provide information and examples on current good manufacturing practices related to preserving cellular function and integrity, ensuring consistency of the process and product, preventing contamination, selecting appropriate donors, and preventing transmission of disease. CVM 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. CVM scientists developed a completely synthetic tissue culture media that, for the first-time, allows consistent production of veterinary stem cells that are then used for therapeutic needs in veterinary patients. This development will result in a more consistent product among all veterinary stem cell manufacturers.

As of January 31 2021, there are 46 products enrolled in the Veterinary Innovation Program (VIP), 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. Promising new technologies such as animal biotechnology, including techniques to intentionally alter the genomes of animals, have the potential to improve human and animal health, animal welfare, and food safety and security. For example, it is reported that intentional genomic alterations (IGAs) are being developed to make animals less susceptible to disease, such as diseases known to significantly impact swine production (e.g. African swine fever and porcine reproductive and respiratory syndrome) and zoonotic diseases such as avian influenza. Additionally, developers of IGAs have stated that they are working on traits that aim to reduce the environmental footprint of animal agriculture, such as IGAs intended to increase thermotolerance in certain breeds of cattle, thereby reducing the resource requirements for producing meat and milk in warmer climates. Developers are also working to address the global organ shortage by developing IGAs in pigs that reduce immunogenicity (such as those that alter the expression of cell surface markers like the IGA in GalSafe Pigs approved on December 14, 2020) for use as sources of tissues and organs for xenotransplantation.

In July 2021, the Center held a virtual animal biotechnology outreach session to collect feedback from stakeholders in order to enhance the predictability, transparency, and efficiency of the review process for IGAs. At the session, the Center shared its science- and risk-based approach for IGAs and also provided a brief overview of the risk analysis and review process. These

outreach sessions are part of a series of animal biotechnology stakeholder outreach initiatives. The Center also continues to meet with stakeholders in virtual meetings and has plans for in-person meetings with farmers and producers in agricultural regions of the United States once travel can safely resume post COVID-19.

Minor Use Minor Species

The Minor Use and Minor Species (MUMS) Animal Health Act created 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 legal options for 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 FDA approval.

As an alternative to seeking full drug approval for non-food-producing minor species, MUMS established "The Index of Legally Marketed New Unapproved Animal Drugs for Minor Species" (the Index). The Index), provides a faster and less resource intensive way to obtain legal marketing status for eligible products. This process benefits animals such as zoo animals, pet birds, and ornamental fish. Indexing is needed to make products available for use in species that are too rare or too varied to be the subject of the adequate and well controlled studies needed to support drug approvals. As of January 2022, the Index includes 14 animal drugs. In order to expand the impact of indexing, CVM requested and received feedback on its policy for determining the eligibility of unapproved animal drugs to be added to the Index. Changing the scope of the current indexing policy for eligibility could help promote legal drug availability for additional underserved animal populations. The Center is reviewing this feedback to determine whether and how expansion of eligibility could be accomplished without compromising human or animal health.

In support of minor use and minor species drug approval, the MUMS "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. Over the last 15 years, FDA has granted 160 MUMS drug "designations" to support drug development for minor uses and minor species. This has contributed to the approval of drugs ranging from antiparasitic drugs for sheep and goats, to drugs to treat heartworm disease in ferrets. As of January 22, CVM has provided more than $6.1 million in grant funding in support of 63 MUMS studies.

Information about drug residues and pharmacokinetic parameters in aquatic species is relatively sparse and it is difficult to rapidly compare data between studies due to differences in experimental conditions, such as water temperatures and salinity. To facilitate the study of aquatic species drug metabolism, CVM's Office of Research constructed a Fish Drug and Chemical Analysis Phish-Pharm database. This database was updated in 2021 to contain over 700 articles that include data from 191 aquatic species (fish and shellfish) and is a valuable resource to investigators of drug metabolism in aquatic species as well as government and private organizations involved in the drug approval process for aquatic species.

Compounded Animal Drugs

Animal drugs compounded from bulk drug substances are used by veterinarians in the United States to treat the wide diversity of animals and disease conditions of their patients, even though these products have not met the FDA's standards for safety and effectiveness and are of

unknown quality or labeling. These compounded drugs have posed some safety issues for animals and potential safety issues for humans, especially when used in food-producing animals through the potential for unsafe drug residues in their edible tissues.

In FY 2021, there were 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 14 inspections of compounders of human and animal drugs
- oversaw 2 recalls regarding compounded animal drug products
- reviewed 17 voluntary animal drug compounding Adverse Drug Event reports
- completed 1 injunction against a compounder of human and animal drugs, in collaboration with the Human Drugs Program

In November 2019, draft *GFI #256 Compounding Animal Drugs from Bulk Drug Substances* was published to solicit input on proposed conditions under which CVM generally would not take action against compounded animal drugs. The comment period was open for more than 10 months and in October 2020 the Center began to review more than 2,200 comments to determine next steps. Since then, CVM has been working to finalize the guidance based on those comments. Although current law does not permit compounding of animal drugs from bulk drug substances, the Center recognizes that there are circumstances when there is no approved, or conditionally approved or indexed drug that can be used or modified through compounding to treat a particular animal with a particular condition. In these situations, FDA does not intend to take action for certain violations of the Food, Drug, and Cosmetic Act's requirements (e.g., approval requirements, requirements for adequate directions for use, and current good manufacturing practices requirements).

Product Approvals

Below are some of CVM's animal drug product approvals in 2021. This list does not represent any priority ranking of products.

Species	Date	Product Name	Purpose or Benefit
Cats	Jan 2022	Zorbium (buprenorphine transdermal solution)	For the control of postoperative pain associated with surgical procedures in cats
Cats	Jan 2022	Solensia (frunevetmab injection)	For the control of pain associated with osteoarthritis in cats
Dogs	Dec 2021	Canalevia – CA1 (Crofelemer delayed-release tablets)	Conditionally approved for the treatment of chemotherapy-induced diarrhea in dogs
Dogs	Jul 2021	Tanovea (rabacfosadine)	For the treatment of lymphoma (first full approval of a previously conditionally approved product in a terrestrial species and first fully approved product for lymphoma in dogs)
Horses	Mar 2021	KetoMed (ketoprofen)	Alleviate inflammation and pain associated with musculoskeletal disorders
Dogs	Jan 2021	KBroVet-CA1 (potassium bromide)	Conditionally approved to control seizures associated with idiopathic epilepsy (first conditional approval for a major use in a major species)

Animal Food Safety

The animal food ingredient industry is rapidly evolving, and submissions of innovative new animal food ingredients are more complex and have more data in their submissions. For example, the Center evaluated a Generally Recognized as Safe (GRAS) notice for a source of protein in aquaculture diets derived from microbes to replace the use of fish meal which is becoming scarcer due to reduced stocks of wild fish. It also reviewed the safety and usefulness of black soldier fly larvae 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 dogs, pigs, poultry, and salmon.

In FY 2020, CVM significantly increased its capacity, through hires from new budget authority, to complete pre-market review of complex and innovative new animal food ingredients. The Center is better positioned to advance greater predictability and timeliness for animal ingredient reviews and to support bringing safe, innovative ingredients to the animal food market. Subsequently, CVM has embarked on a review of its Policy and Procedures Manual (PPM) Guide 1240.3605, Regulating Animal Foods with Drug Claims, to keep pace with innovative uses of substances and the underlying science of how these substances may provide nutrients for

animals. Further discussions of what an animal eats and its impact on human food safety, the environment, and how it impacts the microbiome of the animal are ongoing.

Animals generally eat a very limited and defined diet as their sole ration for their whole lifetime. CVM review of new animal food ingredients allows 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), 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 animal 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 September 2021, CVM hosted a virtual listening session on its oversight of pet food to provide consumers, industry, interest groups, academia, and other stakeholders with the opportunity to share information and feedback that they feel is relevant to pet food oversight. The Center sought information to better understand various perspectives on topics such as the oversight of pet food labeling, ingredients, contaminants, and safety and to help inform resource allocation and any potential future policy development.

In December 2020, CVM published *final GFI #262 Pre-Submission Consultation Process for Animal Food Additive Petitions or Generally Recognized as Safe (GRAS) Notices* , which describes the recommended types of information stakeholders (industry, academia, other organizations, or an individual) should consider including in consultations with CVM. This guidance is being utilized by stakeholders as they prepare information to be submitted to CVM, and the quality of these submissions has increased. This has led to an increase in the efficiency of review by CVM, thus allowing safe and innovative new products to enter the market in a more expeditious manner.

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, the Blueprint for a New Era of Smarter Food Safety was released to build on the modernized food safety regulatory framework created via the Food Safety Modernization Act (FSMA) by leveraging the use of new and emerging technologies to speed outbreak response and accelerate prevention.

In February 2021, CVM released a Compliance Program update outlining a comprehensive inspection model, which is intended to modernize animal food safety inspections by including

the new FSMA regulations as well as other long-established 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 the Center, ORA, and state inspection partners, who it 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.

CVM created a progressive training curriculum that would better prepare investigators to perform comprehensive inspections and to adapt the material and content to current training delivery methods. The Center began offering these courses under the new curriculum in the fall of 2021. This strengthened curriculum will ensure investigators have the foundational skills and knowledge they need to complete comprehensive animal food inspections. The sequential order of the curriculum reduces redundancy in the training courses and ensures the investigators knowledge builds through the progression through the curriculum.

In October 2021, CVM ranked the animal food inventory by risk (high and non-high) based on common risk criteria. This risk-ranked inventory will

- provide the ability to plan surveillance inspections across the entire inventory based on common risk-factors
- create efficiencies in work planning process as surveillance inspection priorities were previously determined through a manual process
- assist with planning and coordinating work with our state regulatory partners to provide greater coverage of the domestic animal food inventory

In FY 2020, FDA received $3.2 million to fund cooperative agreements to support 13 States in implementing the recommendations of the National Association of State Departments of Agriculture (NASDA) PCAF Framework. This 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.

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 both humans and animals. Exposure to improperly formulated, contaminated, mislabeled, or adulterated animal foods, whether intentional or not, can cause illness or death in animals. 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 contaminated animal food, such as pet food, that 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 CVM has to be prepared to quickly respond to ensure the protection of the food supply. Between October 1, 2020 and October 30, 2021, CVM received a wide variety of adverse event reports for a single manufacturer and involving more than 500 cats and dogs potentially related to exposure to aflatoxin contaminated pet food. 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. CVM received reports that indicated more than 170 animals may have died from this incident, although confirmation of aflatoxin exposure was not possible in most of them. CVM's Vet-LIRN, a network of 46 State and university veterinary diagnostic laboratories, had a key role in the investigation of multiple canine illnesses and deaths of dogs exposed to a commercial dog food with suspected aflatoxin contamination, which ultimately led to a large-scale recall in January 2021. In August 2021, the Center issued a corporate-wide warning letter to a company after inspections at multiple manufacturing sites for the firm revealed evidence of violations that were shared across the sites.

Leveraging Real World Adverse Event Data

The public depends on CVM to actively monitor animal food and drug products marketed in the United States for potential safety issues, and to quickly identify, analyze and mitigate any serious issues that may result in harm to humans or animals. The Center monitors the safety of animal food and drugs, human user safety, and the effectiveness of approved animal drugs by leveraging the largest animal drug adverse event database in the world; it contains 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 94,000,000 food animals, and approximately 941,000 companion animals.

Post-market adverse event reporting has transformed from a data-entry heavy, paper-based process to a more efficient electronic process. Manufacturers of approved animal drug products are required by regulation to submit adverse event reports to CVM. In FY 2021, 100 percent of these mandatory adverse event reports were received electronically. Electronic message exchange is based on an internationally harmonized adverse event message and uses standardized data elements and terminology. This evolution improves the efficiency of adverse event reporting for both CVM and industry and enables inter-agency and inter-governmental collaboration on potential safety concerns. CVM also utilizes adverse event signal detection (data mining) and management strategies to improve how the Center identifies, monitors, and learns from problems experienced with animal health products.

Combating Antimicrobial Resistance

CVM 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.

The Center collaborated with key stakeholders in recent years to make significant public health progress to ensure that 96 percent of medically important antimicrobials (i.e., antimicrobials also important for treating human disease) sold or distributed for use in food-producing animals are under veterinary oversight. In June 2021, CVM published *GFI #263 Recommendations for Sponsors of Medically Important Antimicrobial Drugs Approved for Use in Animals to Voluntarily Bring Under Veterinary Oversight All Products That Continue to Be Over-the-Counter* to help bring the remaining drugs under veterinary oversight.

In January 2021, CVM 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 important antimicrobial drugs and establish defined durations of use. Over 31,000 comments were received on the potential framework. The Center is in the process of accessing the feedback received and exploring additional opportunities for obtaining input from interested stakeholders on this issue.

During FY 2021, CVM researchers, in collaboration with Vet-LIRN laboratories, initiated a project to utilize United States and foreign fish health and veterinary diagnostic laboratories to produce fish pathogen antimicrobial susceptibility data. After these data are analyzed and testing interpretive criteria are generated, these laboratories will be able to better interpret future susceptibility data which will inform the selection and use of antimicrobials judiciously.

In December 2020, CVM 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 antimicrobial sales, use, and resistance to monitor the effectiveness of these actions to slow the development of resistance

In October 2020, CVM announced a potential revised process and criteria for ranking antimicrobial drugs based on their importance in human medicine in a Concept Paper: Potential Approach for Ranking of Antimicrobial Drugs According to Their Importance in Human Medicine: A Risk Management Tool for Antimicrobial New Animal Drugs. The Center hosted a public meeting and issued a Request for Comments in the *Federal Register* to obtain feedback on the content of the paper. The public comment period was open until March 2021. The Center is now assessing the comments and considering adjustments to its approach based on the feedback. CVM 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 activities related to managing antimicrobial resistance risks associated with antimicrobial use in animals.

Antimicrobial Drug Sales

In December 2021, CVM published the 2020 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 27% from 2011 through 2020
- decreased by 38% from 2015 (the year of peak sales) through 2019
- decreased by 3% from 2019 through 2020

Sales decreased in 2020, and there was a substantial reduction in the quantity of these drugs sold or distributed in 2020 as compared with peak sales in 2015. This demonstrates that ongoing stewardship efforts, including those initiated by the Center 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 CVM-funded cooperative agreements 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. The Center 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 and additional summary reports are expected in FY 2022. This information will help inform efforts for long-term antimicrobial use data collection.

In August 2020, the Center also began funding two grants for the collection of data on antimicrobial use in dogs and cats. While the 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 grantees are utilizing natural language processing methods to analyze large amounts of antimicrobial use data and have made progress during the first year in recruiting veterinary practices to participate, as well as information technology developments to mine data from veterinary health records while maintaining confidentiality of participants.

The National Antimicrobial Resistance Monitoring System (NARMS)

The National Antimicrobial Resistance Monitoring System (NARMS) monitors antimicrobial resistance in enteric (intestinal) foodborne bacteria. This information is gathered from a wide variety of food and animal sources by partners across the country and is compared with bacteria causing human and animal illnesses. CVM uses data from NARMS and other sources to estimate the overall risk of antimicrobial resistance when determining whether to approve a 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 FY 2021, NARMS hosted a public meeting to review and discuss the recently published NARMS Strategic Plan: 2021 – 2025. CVM, 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.

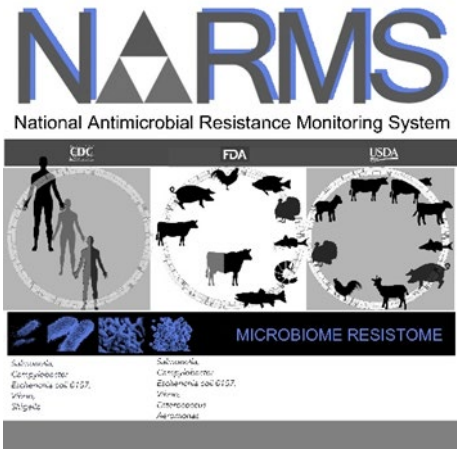

Figure 22 - NARMS Strategic Plan

NARMS partnered with the EPA to begin planning 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 and other genes relevant to food safety, as well as serving as a method to compare bacteria from different sources in an outbreak. In FY2020, CVM enabled all NARMS food laboratories to upload WGS data to the public database at NIH, where software algorithms apply predictive resistance and tabulate the results for access by stakeholders, greatly reducing the time from sample collection to results.

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 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 DNA sequence data, which allows the Center to share NARMS findings publicly via NARMS Now every week, greatly shortening the time for public health response. These data displays include enhanced animal pathogen monitoring from Vet-LIRN.

Guidances

Below are other notable guidances recently issued by CVM. This list does not represent any priority ranking among the guidances.

Issued	Docket #	Title	Description
Sept 2021	FDA-2021-D-0399	CVM Draft GFI #253 Good Manufacturing Practices for Animal Cells, Tissues, and Cell- and Tissue-Based Products	Provides establishments that manufacture animal cells, tissues, and cell- and tissue-based products meeting the definition of a new animal drug (ACTPs) with recommendations for meeting current good manufacturing practices (CGMPs) requirements.
Sept 2021	FDA-2021-D-0401	CVM Draft GFI #254 Donor Eligibility for Animal Cells, Tissues and Cell- and Tissue-Based Products	For sponsors, firms, individuals, and establishments that participate in the manufacture of, or perform any aspect of the donor eligibility determination for animal cells, tissues, and cell- and tissue-based products (ACTPs) that meet the definition of a new animal drug.
July 2021	FDA-2019-D-3361	CVM GFI #261 Eligibility Criteria for Expanded Conditional Approval of New Animal Drugs	To assist sponsors who are interest in pursuing conditional approval of animal drugs for serious or life-threatening conditions or unmet health needs when a demonstration of effectiveness would require a complex or particularly difficult study.
June 2021	FDA-2019-D-3614	CVM GFI #263 Recommendations for Sponsors of Medically Important Antimicrobial Drugs Approved for Use in Animals to Voluntarily Bring Under Veterinary Oversight All Products That Continue to be Available Over the Counter	To assist sponsors in transitioning from over-the-counter to prescription marketing status for approved applications and abbreviated applications for dosage form animal drugs containing medically important antimicrobials
May 2021	FDA-2019-D-3764	CVM GFI #171 Demonstrating Bioequivalence for Soluble Powder Oral Dosage Form Products and Type A Medicated Articles Containing Active Pharmaceutical Ingredients to Be Soluble in Aqueous Media	To describe how the Center will evaluate requests for biowaivers for animal drugs administered orally as soluble powders or as Type A medicated articles manufactured from water-soluble active pharmaceutical ingredients.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$216,949,000	$178,928,000	$38,021,000
FY 2020 Actuals	$234,507,000	$190,854,000	$43,653,000
FY 2021 Actuals	$238,847,000	$192,352,000	$46,495,000
FY 2022 Annualized CR	$245,894,000	$192,456,000	$53,438,000
FY 2023 President's Budget	$300,843,000	$242,360,000	$58,483,000

Figure 23 - Funding History

BUDGET REQUEST

The FY 2023 President's Budget for the Animal Drugs and Foods Program is $300,843,000, of which $242,360,000 is budget authority and $58,483,000 is user fees. The budget authority increases by $49,904,000 compared to the FY 2022 Annualized CR and User Fees increase by $5,045,000. The CVM amount in this request is $211,798,000 and the ORA amount is $89,045,000.

CVM protects and promotes the health of humans and animals by employing a One Health approach to help 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 Center is responsible for all stages of the total product lifecycle, including:

- evaluating new animal drugs for safety, effectiveness, and manufacturing quality
- monitoring animal drugs, animal foods, and animal devices for safety and taking appropriate action to mitigate unsafe or violative products on the market
- evaluating animal food additives for safety and utility
- conducting applied research to further scientific understanding and support data-based decision making to protect human and animal health
- working to prevent and respond to human and animal health emergencies
- developing and implementing policies to combat antimicrobial resistance

CVM's performance measure dashboards highlight accomplishments towards protecting human and animal health. There are dashboards covering the Center's work on animal food safety; compounded animal drugs; emerging technologies; pre-market drug review; and post-market drug safety, effectiveness, and quality; and antimicrobial stewardship in veterinary settings, as well as the Center's performance on animal drug review timelines agreed upon in the Animal Drug and Animal Generic Drug User Fee Amendments of 2018.

These activities and the initiatives requested in the FY 2023 Budget Request support mission critical activities, and Presidential, HHS, and FDA human and animal health priorities.

BUDGET AUTHORITY

Food Safety (+$27.4 million / 31 FTE)

Animal Food Safety Oversight (+$16.4 million / 13 FTE)

Center: +$2.3 million / 5 FTE

Field: +$14.1 million / 8 FTE

The FY 2023 Budget will provide additional 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 the Preventive Control for Animal Food framework. FDA will also expand inspection and enforcement programs, develop outreach and training initiatives, and devote additional resources to the analysis of controls for expected and 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 $3.2 million 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.

Smarter Food Safety (+$4.6 million / 16 FTE)

Center: +$4.6 million / 16 FTE

With this increase, CVM will increase its foundational capacity for root cause analysis and predictive analytics, while advancing traceability and mutual reliance efforts to strengthen response when contaminated animal food is identified. Findings of root cause analyses can be an important step in helping industry modify practices to avoid identified risks and can provide more robust data for predictive analytics. New approaches will help FDA prevent and detect food safety problems efficiently by reducing the time it takes to trace the origin of contaminated 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.

Data Modernization and Enhanced Technologies: Smarter Food Safety (+$6.4 million / 2 FTE)

Center: +$5.8 million / 2 FTE

Field: +$600,000

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, of which $13.3 million is identified for the Animal Drugs and Foods program across Food Safety, Medical Product Safety and Crosscutting.

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 to our IT infrastructure 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, the $600,000 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.

Medical Product Safety (+$12.2 million / 34 FTE)

Pre-Market Animal Drug Review Workload (+$5.0 million / 21 FTE)

Center: +$5.0 million / 21 FTE

With this increase, CVM will hire the additional FTE needed to keep pace with the steady increase in pre-market animal drug review workload. The number of animal drug submissions received have steadily increased over time and therefore more effort is needed to review the additional submissions within agreed upon timeframes. CVM does not have the FTEs needed to keep up with the workload. This budget authority increase will provide the resources needed to continue to meet performance commitments, including the reduced review times negotiated as part of the Animal Generic Drug User Fee Amendment III. Meeting our performance commitments provides greater regulatory certainty and helps enable industry to 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.

CVM 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 COVID-19 inspectional delays, while continuing to monitor for the presence of fraudulent and harmful products on the market.

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

Center: +$4.9 million / 6 FTE

Within CVM, $10.7 million ($4.9 million for 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 to our IT infrastructure 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.

Crosscutting (+$10.3 million / 8 FTE)

Capacity Building (+$2.6 million / 1 FTE)

Center: +$1.7 million / 1 FTE

Field: +$866,000

The FY 2023 President's Budget includes $59.4 million Capacity Building, including $2.6 million for the Animal Drugs and Food program. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Public Health Employee Pay Costs (+$4.0 million)

Center: +$2.7 million

Field: +$1.3 million

The FY 2023 President's Budget includes $51.9 million, including $4.0 for the Animal Drugs and Food program, to partially fund salary and benefits increases which include a 4.6% Cost of

Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$1.1 million / 3 FTE)

Field: +$1.1 million / 3 FTE

The FY 2023 President's Budget includes $33.8 million for optimizing inspectional activities, including $1.1 million within Animal Drugs and Foods Field, to support capacity building towards an advanced, highly trained investigators capable of analyzing available data to increase the efficiency and productivity of our inspection operations.

Reducing Animal Testing Through Alternative Methods (+$713,000 / 2 FTE)

Center: +$713,000 / 2 FTE

The FY 2023 President's Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program, including $713,000 within the Animal Drugs and Foods program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

Data Modernization and Enhanced Technologies: Enterprise Technology and Data (+$2.0 million / 2 FTE)

Center: +$1.2 million / 1 FTE

Field: +$737,000 / 1 FTE

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $2.0 million for Enterprise Technology and Data within the Animal Drugs and Foods program 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.

USER FEES

Current Law User Fees (+$5.0 million / 10 FTE)

Center: +$4.9 million/ 10 FTE

Field: +$74,000

The Animal Drugs and Foods Program request includes an increase of $5.0 million for user fees which will allow FDA to fulfill its mission of promoting and protecting the human and animal health by ensuring safety and efficacy of FDA-regulated 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 in-depth case investigations for detection and response, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
243201: Complete review and action on Non-administrative original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. (Output)	FY 2020[118]: 100% w/in 180 days Target: 90% w/in 180 days (Target Exceeded)	90% w/in 180 days	90% w/in 180 days	Maintain
243202: Complete review and action on Non-administrative original Abbreviated New Animal Drug Applications (ANADAs) and reactivations of such applications received during the fiscal year. (Output)	FY 2020[2]: 100% w/in 240 days Target: 90% w/in 240 days (Target Exceeded)	90% w/in 240 days	90% w/in 240 days	Maintain
244204: Complete review and action on warning letters to better safeguard U.S. consumers by alerting firms to identified deviations in order to become compliant. (Output)	FY 2021: 69% w/in 25 working days Target: 50% w/in 25 working days (Target Exceeded)	50% w/in 25 working days	50% w/in 25 working days	Maintain
244302: Respond to consumer complaints by initiating in-depth Vet-LIRN investigations. within 30 days of receipt. (Output)	FY 2021: 100% 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 2021: 94.8% Target: 80% (Target Exceeded)	80%	80%	Maintain
224221: Percentage of Human and Animal Drug significant inspection	FY 2021: 90.0% Target: 80%	80%	80%	Maintain

[118] Represents FDA's preliminary performance for FY 2020 cohort submissions. Final performance will be available via the FY 2021 ADUFA and AGDUFA performance reports

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
violations which receive appropriate follow-up after regulatory action was taken. (Output)	(Target Exceeded)			
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 2021: 75.3% 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 2021: 57.8% Target: 55% (Target Exceeded)	55%	55%	Maintain

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

New Animal Drug Application Review

In FY 2020, CVM completed review and action on 100 percent of non-administrative original NADAs and reactivations within the timeframes specified. CVM also completed review and action on 100 percent of non-administrative original ANADAs and reactivations within the timeframes specified.

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 involve extremely sensitive and novel legal and policy issues that require coordination and clearance across the agency and a long time to process. In FY 2021, CVM exceeded the performance target for completing 50% of warning letter package reviews for tissue residue and unapproved drug cases within 25 days.

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

CVM Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
New Animal Drug Applications (NADAs) [1]			
Received	7	16	18
Completed	14	16	18
Approved	11	13	16
Pending [2]	13	13	13
New Animal Drug Application Supplements [1, 3]			
Received	557	620	645
Completed	589	620	645
Approved	482	545	570
Pending [2]	197	197	197
Abbreviated New Animal Drug Applications (ANADAs) [1]			
Received	22	25	30
Completed	22	23	30
Approved	21	16	24
Pending [2]	12	14	14
Abbreviated New Animal Drug Application Supplements [1, 3]			
Received	290	350	360
Completed	306	325	335
Approved	233	225	235
Pending [2]	168	193	218
Investigational New Animal Drug (INAD) Files [4]			
Received	3,037	3,000	3,100
Completed	2,973	3,000	3,100
Pending [2]	431	431	431
Generic Investigational New Animal Drug (JINAD) Files [4]			
Received	1,034	975	1,000
Completed	1,010	975	1,000
Pending [2]	156	156	156
Food (Animal) Additive Petitions Completed	48	50	50
Investigational Food Additive Petitions Completed	85	90	90
Adverse Drug Event (ADE) [5]			
ADE Reports Received	93,433	100,000	104,000
Post-Approval ADE Data Reviews	428	350	350

[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).

Figure 24 - CVM Workload and Outputs

Field Animal Drugs and Foods Program Workload and Outputs	FY 2021 Actuals[5]			FY 2022 Estimate			FY 2023 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 FOODS ESTABLISHMENT INSPECTIONS	***336***	***43***	***293***	***305***	***25***	***280***	***1,696***	***298***	***1,398***
Pre-Approval /BIMO Inspections	18	18	0	0	0	0	79	79	0
Drug Process and New ADF Program Inspections	26	26	0	55	55	0	175	175	0
BSE Inspections	59	0	59	105	0	105	1,205	0	1,205
Feed Contaminant Inspections	2	0	2	0	0	0	25	0	25
Illegal Residue Program Inspections	41	0	41	125	0	125	450	0	450
Feed Manufacturing Program Inspections	44	0	44	60	0	60	200	0	200
Domestic Laboratory Samples Analyzed	395	0	395	495	20	475	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FOODS ESTABLISHMENT INSPECTIONS1	***5***	***3***	***2***	***5***	***3***	***2***	***31***	***26***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	1	1	0	3	3	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	2	2	0	6	6	0	33	33	0
Foreign Feed Inspections	0	0	0	0	0	0	5	0	5
BSE Inspections	0	0	0	1	0	1	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FOODS ESTABLISHMENT INSPECTIONS	***344***	***46***	***298***	***310***	***28***	***282***	***1,727***	***324***	***1,403***
IMPORTS									
Import Field Exams/Tests	1,507	268	1239	1,500	500	1000	3,795	495	3,300
Import Laboratory Samples Analyzed	362	0	362	400	0	400	867	2	865
Import Physical Exam Subtotal	**1,869**	**268**	**1,601**	**1,900**	**500**	**1,400**	**4,662**	**497**	**4,165**
Import Line Decisions	550,811	79,275	471,536	578,352	83,239	495,113	607,269	87,401	519,868
Percent of Import Lines Physically Examined	0.34%	0.34%	0.34%	0.33%	0.60%	0.28%	0.77%	0.57%	0.80%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***1,000***	***0***	***1,000***	***1,000***	***0***	***1,000***	***3,924***	***0***	***3,924***
State Contract Inspections: BSE	599	0	599	650	0	650	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	331	0	331	400	0	400	620	0	620
State Contract Inspections: Illegal Tissue Residue	0	0	0	0	0	0	0	0	0
State Contract Animal Feeds Funding	$2,689,277	0	$2,689,277	$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	0	$0
Total State Funding	**$2,689,277**	**$0**	**$2,689,277**	**$3,200,000**	**$0**	**$3,200,000**	**$3,296,000**	**$0**	**$3,296,000**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,344***	***46***	***1,298***	***1,310***	***28***	***1,282***	***5,651***	***324***	***5,327***

[1] The FY 2021 actual unique count of foreign inspections includes 4 OGPS inspections (4 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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 25 - Field Animal Drugs and Foods Program Workload and Outputs

DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Devices and Radiological Health	**627,664**	**642,791**	**636,136**	**698,245**	**62,109**
Budget Authority	***408,108***	***408,108***	***408,126***	***465,911***	***57,785***
User Fees	***219,556***	***234,683***	***228,010***	***232,334***	***4,324***
Center	528,784	542,939	536,869	588,374	51,505
Budget Authority	323,103	323,103	323,103	370,522	47,419
User Fees	205,681	219,836	213,766	217,852	4,086
Prescription Drug (PDUFA)	*4,446*	*2,667*	*5,361*	*5,280*	*-81*
Medical Device (MDUFA)	*194,199*	*211,603*	*201,228*	*205,252*	*4,024*
Mammography Quality Standards Act (MQSA)	*7,036*	*5,566*	*7,177*	*7,320*	*143*
Field	98,880	99,852	99,267	109,871	10,604
Budget Authority	85,005	85,005	85,023	95,389	10,366
User Fees	13,875	14,847	14,244	14,482	238
Medical Device (MDUFA)	*2,368*	*1,994*	*2,507*	*2,510*	*3*
Mammography Quality Standards Act (MQSA)	*11,507*	*12,853*	*11,737*	*11,972*	*235*
FTE	**2,345**	**2,437**	**2,345**	**2,393**	**48**

Figure 26 - Narrative by Activity

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 timely access to less-invasive treatments possible and new options for 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.[119]

[119] 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.

There are 233,000 different types of medical devices on the U.S. market, manufactured at 27,000 facilities worldwide. FDA's Center for Devices and Radiological Health (CDRH) handles 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. 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 include complex instruments that we rely on to 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/machine learning 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 can help diagnose multiple conditions and help determine which treatments patients should pursue based on their individual genetic makeup.

The Devices Program also 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. To make the best use of its resources, the Devices Program tailors its oversight of medical devices according to the degree of risk presented, so it can focus on those products that pose the most risks to patients.

FDA's Devices Program 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 FDA has also been a world leader in harmonizing review and oversight practices to spur development of higher quality devices all over the world - engaging heavily with international counterparts to share information about potential safety concerns with medical devices, and to identify and take action to protect patients and the public health where possible.

Figure 27 - 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 that consumers can rely on the devices they are using.

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.

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

- Approved, cleared, or authorized ("authorized") a record high of 132 novel medical devices in 2020, surpassing the 40-year high mark set in 2018 (a marked increase from the 29 novel devices FDA authorized in 2010).
- Granted over 500 breakthrough designation requests, and approved, authorized, or cleared 23 breakthrough devices through the Premarket Approval (PMA), De Novo classification request ("De Novo"), or premarket notification (510(k)) pathways.
- 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 2015 and remained at 30 days each subsequent year through FY 2020.
- The number of approved early feasibility studies in the United States, where devices are evaluated early in development, more than doubled – from 21 in FY 2014 to 49 in FY 2020.
- 62 percent of novel technology manufacturers intend to bring their devices to the United States first or in parallel with other major markets.
- Conducted timely review of more than 2 million medical device adverse event reports and completed other pivotal work activities such as addressing supply chain shortages and counterfeit products related to COVID-19.

Devices are being introduced to the market more quickly, an increasing number of 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.

It is also important to note that the need for medical devices to respond to the COVID-19 pandemic has far exceeded what has been experienced in any prior Public Health Emergency (PHE). The first EUAs issued for the COVID-19 PHE were for medical devices, and the volume of EUA requests quickly surpassed (by two orders of magnitude) that of any prior PHE or other situation, and emergency use requests included submissions for devices that FDA had never received EUA requests for during prior PHEs. This included ventilators and novel devices such as extracorporeal blood purification devices, as well as novel indications for devices such as continuous renal replacement therapy devices. Since the start of the pandemic, FDA has issued EUAs or granted marketing authorization to over 1,700 medical devices for COVID-19-related uses. FDA also rigorously monitored safety signals and medical device reports, using the information to publish 22 letters to healthcare providers and 7 safety communications, and completed other pivotal work activities such as addressing supply chain shortages and counterfeit products related to COVID-19.

Breakthrough Devices Program

FDA's Breakthrough Devices Program has delivered important advancements for patients since it was established in late 2016 by the 21st Century Cures Act. 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 breakthrough devices will occur more efficiently. At the end of FY 2021, the total number of designated

Breakthrough Devices exceeded 560, increasing by 206 devices since FY 2020 and more than doubling since FY 2019.

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 2021, through the Breakthrough Devices Program, FDA approved the first in the world non-surgical heart valve to treat pediatric and adult patients with a native or surgically-repaired right ventricular outflow tract. The use of this less invasive treatment option may delay the time before a patient needs additional open-heart surgery, as well as potentially reduce the total number of open-heart surgeries required over an individual's lifetime.

In FY 2021, the Devices Program also granted a De Novo request for a Breakthrough Device that utilizes a brain-computer interface to facilitate muscle rehabilitation in chronic stroke patients with upper extremity disability (i.e., hand, wrist, and arm). This novel device offers an additional treatment option for these patients to assist with muscle re-education and maintaining or increasing range of motion, and fills an unmet need for patients who may not have access to home-based stroke rehabilitation technologies.

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 16 collaborators with records on over 161 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.

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. 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. Incorporating UDI as a standard in electronic health records (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 Devices Program has received more than 400 modified submissions for manufacturing changes as part of the program. This volume shows a higher rate of manufacturing improvements, new equipment investment, and process optimizations implemented by participating manufacturing sites. These sites have also demonstrated product quality improvements, 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. Due to the improvements implemented through VIP, one of the participants enrolled in the program since 2018 has been voted best place to work in their state 3 years in a row, increasing the company's domestic manufacturing capacity.

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. VIP participant sites in their 3rd year who focused on supplier management practices reported minimal to no disruption in supply during the COVID-19 pandemic, due to improvements and investments implemented in collaboration with their suppliers.

The Devices Program has taken learnings from the VIP program and initiated a broad improvement of the corrective and preventive action system across the medical device industry and the Accelerate Sustainable Capability (ASC) pilot, which assists struggling manufacturers in improving their systems. Manufacturing sites piloting the Corrective and Preventive Actions (CAPA) improvement framework have reported a 433 percent improvement in quality issues being resolved in less than 30 days, resulting in 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. Manufacturing improvements are being implemented 78 percent faster at participating sites.

Coronavirus (COVID-19)

Diagnostic tests are the first line of defense in an outbreak, and FDA plays an important role to ensure they work through EUA review. The EUA pathway expedites access to accurate diagnostic tests during emergencies, when information gaps and false results may adversely affect individual patient care and public health decision making. EUAs enable molecular diagnostic tests to be developed, validated, authorized, and deployed within weeks rather than several months to over a year, as is typical for test development and traditional premarket submissions. The FDA has employed its EUA authorities to facilitate availability of tests in each PHE or threat situation since 2009, when the Secretary of HHS declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics. In PHEs, FDA is generally open to receiving and reviewing EUA requests for tests from any developer, including commercial kit manufacturers and laboratories.

FDA sought to facilitate COVID-19 test evaluation and authorization through the development and availability of templates. The templates provide recommendations for test validation and a

fill-in-the-blank form to streamline the paperwork and make it easier for developers to provide information in support of a request for emergency use authorization. Since providing the first template in January 2020, FDA has been in daily contact with test developers to answer questions and help them through the EUA process. This has proven to be a helpful tool for many. FDA has now made nine templates available for a variety of test types. As of October 8, 2021, these templates have received over 510,725 hits from those visiting FDA's website. FDA also supported test developers through establishment of a dedicated mailbox, 24/7 toll-free hotline that ran until July 2020, the posting of over 100 frequently asked questions on our website, and by hosting weekly virtual town halls for test developers. The FDA has worked with over 1,000 test developers since January 2020.

The FDA also prioritizes review of EUA requests for at-home rapid antigen tests and is actively engaging with test developers to increase their availability. The agency first announced prioritization of point of care (POC) and at-home tests in April 2020, during weekly virtual Town Halls on COVID-19 tests, due to their potential impact on test accessibility and public health. On July 29, 2020, FDA posted a template for at-home diagnostic tests. This template includes recommendations for validating over-the-counter (OTC) tests for screening asymptomatic individuals with performance expectations that are lower than for lab-based tests. In September 2020, FDA's leadership on tests published an op-ed in The Hill explaining that "FDA is always open to alternative proposals from developers and will continue to consider those.

More significant trade-offs in test accuracy may be appropriate where the need for availability and fast results is not being met. Yet, even in those circumstances, steps can be taken to protect consumers, including strategies to increase accuracy. For example, strategies for serial testing with less sensitive tests, such as 70 percent sensitivity, could increase overall sensitivity and be considered cumulatively rather than based on one-time testing. We welcome developers with alternative proposals to come to talk with us." The agency adopted this position to increase test availability since OTC tests, particularly rapid antigen tests, tend to be less sensitive than lab-based tests. FDA authorized the first home test on November 17, 2020; this was the Lucira molecular test for prescription home use. The first antigen over-the-counter home test was authorized on December 15, 2020.

Throughout the pandemic, FDA has also monitored evolving circumstances and growing scientific knowledge and made adjustments when appropriate to help streamline and expedite the path to market for these and other tests to the extent possible, while assuring they are supported by sound science. In March 2021, FDA obtained results from an NIH-sponsored study that supported further streamlining of FDA's at-home test recommendations. Based on these data, on March 16, 2021, FDA updated the recommendations for manufacturers of tests with at least 80 percent sensitivity in symptomatic individuals, with sensitivity falling in a range as low as 70 percent, to request authorization of their test for OTC serial screening use without additional data collection in certain cases. Multiple tests were authorized under this approach within weeks.

On October 4, 2021, the agency authorized the ACON Laboratories Flowflex COVID-19 Home Test, which the agency expects to significantly increase the availability of rapid, at-home tests. By the end of 2021, the manufacturer plans to produce more than 100 million tests per month, and this number will rise to 200 million per month by February 2022, which we expect to double

rapid at-home testing capacity in the U.S. This authorization added to the growing list of tests that can be used at home without a prescription in the U.S.

FDA further streamlined the regulatory pathway for manufacturers developing OTC at-home tests on October 25, 2021, by providing recommendations for labeling updates to facilitate OTC single-use testing for symptomatic individuals for tests currently authorized only for serial testing. The developers of those tests should now be able to request authorization to add single-use testing for symptomatic individuals without submitting additional data. For example, right now when people go to a pharmacy to buy an over-the-counter test, they are sold in two-packs. This change would allow tests to be sold in singles, meaning more individual tests for sale. In line with the new update to its regulatory pathway, FDA also reauthorized the Quidel QuickVue at-home test to add over-the-counter single-use testing for symptomatic adults and children.[120]

Going forward, the Devices Program continues to take steps to increase access to reliable, accurate rapid antigen tests. This includes continuing to prioritize review of EUA requests for at-home diagnostic tests, and increasing staffing on the antigen test review team as resources permit. FDA is actively working to increase the pipeline of at-home tests by engaging with companies to obtain data that can be used to support their EUA, encouraging developers with authorized POC tests to add at-home test claims, continuing engagement with RADx and international regulators, and conducting targeted outreach to manufacturers of home tests in non-US markets. As part of these efforts, FDA is supporting The National Institutes of Health/NIBIB's new Independent Test Assessment Program (ITAP), which will establish an accelerated pathway to support FDA evaluation of tests with potential for large-scale manufacturing. FDA's authorizations as of November 2021 alone may result in up to 400 million more OTC tests available monthly to American consumers by early 2022.

As of November 2021, 421 tests and sample collection devices are authorized by the FDA under EUAs. These include 292 molecular tests and sample collection devices, 90 antibody and other immune response tests and 39 antigen tests. Among these are 17 EUAs for diagnostic tests that can be run at home (4 molecular and 13 antigen tests), 13 of which do not require a prescription. The Devices Program also authorized 27 tests for serial screening programs (18 antigen and 9 molecular). The volume and variety of available tests is a testament to FDA's support of innovative test design and our commitment to public health.

Since early 2020, FDA has adopted agile, interactive, and innovative approaches to EUA review for all types of devices. For example, FDA developed the umbrella EUA approach to efficiently authorize multiple devices of the same type meeting the same criteria. The agency has also issued 28 guidance documents (including 17 revisions) outlining policies to help expand the availability of medical devices needed in response to COVID-19. Further, FDA made several improvements to our EUA review processes to make the most efficient use of our resources, including establishing a front-end triage process to identify devices that would have the greatest impact on the public health. These improvements incorporate the latest information on device availability and shortages, prioritizing novel or critical devices not yet available on the market or those that would address significant device shortages.

[120] https://www.fda.gov/media/147247/download

FDA has authorized a wide variety of other medical devices for use in combating the pandemic, including a wide range of personal protective equipment (PPE), ventilators, and other therapeutic devices. As of June 29, 2021, FDA has authorized 254 PPE devices including 36 surgical masks, and authorized 205 filtering facepiece respirators (FFRs), and 13 systems for PPE decontamination or bioburden reduction at the time there was a need for these types of devices due to PPE shortages.[121] In addition to granting EUAs, FDA has also cleared, through its premarket notification pathway, over 250 PPE 510(k)s.

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 manual, 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 Supply Chain shortages and disruptions, 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 evaluate, assess, and mitigate medical device shortages. This information helped direct efforts to secure alternate manufacturers and production capability where it was needed.
- Hired experts in supply chain management and funded 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 impacts 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 supply chain disruptions to include but not limited to: geopolitical, weather, and recalls. FDA aims to expand our shortage capabilities to be more proactive, preventing future disruptions and shortages.

The Devices Program supply chain and shortage program will enhance FDA's capacity to enable rapid intervention to prevent and mitigate supply chain interruptions through 1) proactive

[121] https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products

regulatory measures and partnerships with industry, health care providers, patients, and others, 2) development and application of state-of-the-art supply chain intelligence for predictive modeling, 3) early signal detection and continuous surveillance, and 4) fostering a more resilient domestic supply chain through investments in preventive measures that help to avert shortages before they occur. A permanent device shortages program at the FDA is critical to decrease or eliminate the risk of medical device supply chain shortages, and part of the agency's overall investment in core FDA safety programs. These efforts will help ensure U.S. patients and health care providers have access to the critical medical devices they need and help reduce U.S. dependence on devices from other nations.

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 percent 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. Additional improvements through VIP resulted in $20 million of medical product inventory released faster, increasing access for patients and $10 million in savings that the company reinvested into a new innovation program at their U.S. headquarters.

In addition, the Devices Program is developing an advanced manufacturing clearinghouse which will provide a collaborative and independent third party that identifies and evaluates promising advanced manufacturing technologies used in the medical device or other industries. The clearinghouse will provide non-confidential information about these technologies, strategies for successful implementation, and publish assessments of the technology to facilitate adoption of more effective and efficient means of manufacturing. Overtime, these improvements will enable the adoption of advanced methods and technologies in U.S. manufacturing to increase production capacity, improve quality, and reduce costs. A collaborative evaluation project with an industry partner implementing digital technology in manufacturing showed an 85 percent reduction in quality control processing time with a 40 percent decrease in production defects and non-conformances, improving yield and product availability.

Mammography Quality Standards Act Program

As part of FDA's mammography program, FDA and its state partners annually inspect more than 8,700 certified mammography facilities in the U.S. to ensure compliance with national quality standards for mammography. An additional 18 inspectors from 15 states were trained in FY 2021. Likewise in FY 2021, over 88 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. As of November 2021, there were 8,705 certified MQSA facilities, helping to provide over 38 million mammography procedures for U.S. patients.

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 and external stakeholders 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.

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.

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 24 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 2021, 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 used to measure how patients feel and function, potentially 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. FDA integrated the PEAC recommendations into a draft guidance on the ways patients can engage as advisors in the design of clinical studies.

FDA launched the Digital Health Center of Excellence (DHCoE) 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 (DHT) 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. DHTs have the potential to promote health equity.

The DHCoE 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 DHCoE 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.

The DHCoE is focused in multiple areas including artificial intelligence (AI) and machine learning (ML). Artificial intelligence and machine learning 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. To advance efforts in AI/ML, FDA released the Artificial Intelligence/Machine Learning (AI/ML) Based Software as part of the Medical Device Action Plan in January 2021, which highlights five main priority areas. The five areas include drafting guidance on pre-determined change control plans, advancing good machine learning practices, ensuring patient-centricity of the devices through transparency, advancing regulatory science, and conducting real world performance pilots. The DHCoE has built on the AI/ML Action Plan and held a workshop on understanding what transparency means for AI/ML-enabled medical devices to stakeholders, including patients and providers.

The DHCoE is working to harmonize internationally through multiple efforts including IMDRF. The DHCoE with Health Canada and UK's MHRA put out a document on guiding principles for Good Machine Learning Practice for AI/ML-enabled devices. DHCoE is also active on the IMDRF AI/ML working group. Additionally, the DHCoE is collaborating with a group of smaller international regulators on think tanks to scope broader IMDRF efforts.

To foster internal and external collaborations, the Digital Health Center of Excellence has launched an FDA Digital Health Advisory Board to coordinate and collaborate in areas of common interest within FDA, including AI/ML and DHTs. The DHCoE continues to develop training for internal and external stakeholders, including partnering with the Patient Science and Engagement program in clarifying device pathways for digital health stakeholders. Externally, the DHCoE is a member of multiple collaborative communities focused on health equity, AI/ML, and wearable technology. The DHCoE is also collaborating with MDIC's newly launched Digital Health Initiative to focus on developing regulatory science tools to assess DHTs. In collaborations with the Centers of Excellence in Regulatory Science and Innovation, the Digital Health Center of Excellence is engaged in regulatory science research in areas including assessing bias in AI/ML-enabled devices, transparency of AI/ML-enabled devices, and patient outcomes for wearable devices.

Cybersecurity

Medical devices are increasingly connected to the Internet, hospital networks, and other medical devices to provide features that improve health care and increase the ability of health care providers to treat patients. These same features also increase potential cybersecurity risks. Medical devices, like other computer systems, can be vulnerable to security breaches, potentially impacting the safety and effectiveness of the device.

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.

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, developed 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.
- Collaborated with the MITRE Corporation to develop a supplemental rubric for the Common Vulnerability Scoring System (CVSS) that may be used and recognized as a medical device development tool (MDDT) by industry to characterize and assess the severity of 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.
- Collaborating with industry on cybersecurity challenges such as legacy medical devices and vulnerability communications via the Healthcare and Public Health Sector Coordinating Council (HSCC) public-private partnership.
- Aiding in the amplification and convergence of international cybersecurity best practices as co-chair of the International Medical Device Regulators Forum.

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 Federal Trade Commission (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, patch ability of Internet of Things (IoT) devices, and software transparency. Further, FDA is engaging with the National Institutes of Standards and Technology (NIST) and other federal agencies on the President's Executive Order (EO) on Improving the Cybersecurity of the Federal Government (EO 14028).

Personalized Medicine

The Devices Program has a unique role in advancing precision medicine. 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. In October 2021, the FDA granted recognition to the Memorial Sloan Kettering Cancer Center's Oncology Knowledgebase (OncoKB) as the first tumor mutation database that can serve as a source of valid scientific evidence 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.

On 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. FDA has posted two updates to the table since its publication.

In addition, in April 2020, FDA published a guidance to facilitate on the development and labeling of companion diagnostics for a specific group of oncology therapeutic products rather than an individual therapeutic product to support the use of multiple personalized medicine cancer tests and 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. Following the first approved group labeling claim in 2020 for a companion diagnostic intended to identify non-small cell lung cancer patients eligible for treatment with a group of targeted cancer therapies, approval of a second group labeling claim is expected by the end of 2021 for a companion diagnostic intended to identify

melanoma patients for treatment with another group of targeted cancer therapies. Transparency into group labeling continues to be provided through FDA's List of Cleared or Approved Companion Diagnostic Devices.

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, FNIH ctDNA Quality Control Materials Project, and the Sequencing Quality Control Consortium, and the International Organizations for Standardization (ISO) working groups. Some of our contributions to these efforts include the revision of Nucleic Acid Sequencing Methods in Diagnostic Laboratory Medicine. The Devices Program also actively participates as a member in various collaborative communities such as the International Liquid Biopsy Standardization Alliance (ILSA) and the Standardizing Laboratory Practices in Pharmacogenomics Initiative (STRIPE) Collaborative Community 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.[122] 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
Sep 2021	FDA-2021-D-0872	Electronic Submission Template for Medical Device 510(k) Submissions	Draft guidance to introduce submitters of premarket notification (510(k)) submissions to the current resources and associated content developed and made publicly available to support 510(k) electronic submissions to FDA.
Jun 2021	FDA-2018-N-3741	Remanufacturing of Medical Devices	This guidance is intended to help clarify whether activities performed on devices are likely "remanufacturing." Such clarification is intended to help provide consistency and better understanding of applicable statutory and regulatory requirements.
May 2021	FDA-2011-D-0514	Postmarket Surveillance Under Section 522 of the	This guidance document is intended increase transparency to stakeholders on FDA's approach to the issuance and tracking of 522 postmarket

[122] https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products

		Federal Food, Drug, and Cosmetic Act	surveillance orders, and expectations for timely study completion.
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.
Sep 2021	FDA-2021-D-0872	Electronic Submission Template for Medical Device 510(k) Submissions	Draft guidance to introduce submitters of premarket notification (510(k)) submissions to the current resources and associated content developed and made publicly available to support 510(k) electronic submissions to FDA.

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.[123]

Date	Product Name	Description
Oct 2021	ACON Laboratories Flowflex COVID-19 Home Test	An over-the-counter COVID-19 antigen test that will help increase the availability of rapid, at-home tests available for U.S. patients.
Jun 2021	The Cognoa ASD Diagnosis Aid	The Cognoa ASD Diagnosis Aid is a machine learning-based software intended to help health care providers diagnose autism spectrum disorder (ASD) in children 18 months through 5 years of age.
Apr 2021	EPi-Sense Guided Coagulation System	A device used to treat long-standing persistent atrial fibrillation, an abnormal heart rhythm (arrythmia) that lasts for more than 12 months.
Apr 2021	TheraSpher	TheraSphere is a radiation treatment for people who have a specific type of liver cancer called unresectable hepatocellular carcinoma (HCC).

[123] https://www.fda.gov/medical-devices/products-and-medical-procedures/device-approvals-denials-and-clearances

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.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$521,951,000	$386,733,000	$135,218,000
FY 2020 Actuals	$587,305,000	$395,142,000	$192,163,000
FY 2021 Actuals	$642,791,000	$408,108,000	$234,683,000
FY 2022 Annualized CR	$636,136,000	$408,126,000	$228,010,000
FY 2023 President's Budget	$698,245,000	$465,911,000	$232,334,000

Figure 28 - Funding History

BUDGET REQUEST

The FY 2023 Budget for the Devices Program is $698,245,000, of which $465,911,000 is budget authority and $232,334,000 is user fees. The budget authority increases by $57,785,000 compared to the FY 2022 Annualized CR and User Fees increase by $4,324,000. The CDRH amount in this request is $588,374,000 and the ORA amount is $109,871,000.

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 2023 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 2023 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 (+$31.4 million / 24 FTE)

Medical Device Cybersecurity (+$5.0 million / 6 FTE)

Center: +$5.0 million / 6 FTE

The FY 2023 Budget includes $5.5 million, an increase of $5.0 million above the FY 2022 Annualized CR, to begin development of a comprehensive Cybersecurity Program for medical devices within the FDA to improve the safety and security of medical devices, help address risks with legacy devices and rapidly address new medical device cybersecurity vulnerabilities. The cybersecurity threats to medical devices are increasing and can involve nation states. Ultimately, these threats are of national security concern because if they go unchecked, they could cripple healthcare delivery. For example, 2017's WannaCry ransomware attack affected England's National Health Service, resulting in thousands of medical appointments being cancelled or rescheduled and potentially delaying care. When these incidents happen, patients, industry, and all segments of the ecosystem – including healthcare delivery organizations and researchers, depend on FDA to help assess the scope of threat and harm to patients, coordinate mitigations, and support our entire health care system to help prevent harm from coming to patients. A funding increase to the program will help support medical device safety and strengthen our national security.

Medical devices from insulin pumps to implantable cardiac pacemakers are becoming more automated and interconnected. This can lead to improvements in these technologies, as well as providing new options that allow devices to be used in people's homes and other settings outside of the traditional health care settings. However, like computers and the networks they operate in, these devices can be vulnerable to security breaches, and exploitation of a device vulnerability has already threatened the health and safety of patients and ultimately national security. Moreover, exploitation of device vulnerabilities or other vulnerabilities present in systems used to deliver healthcare can and have led to significant patient care impacts and patient safety concerns.

For example, in April 2021, the ransomware infection of a single medical device manufacturer led to the unavailability of radiation therapy treatment for cancer patients for an extended period of time. Shortly afterwards, the ransomware infection of a single hospital in the San Diego area caused significant regional spillover effects to care availability and quality, as testified to Congress by one emergency physician. Both incidents were proceeded by a joint-seal alert from HHS, the FBI, and CISA, warning of a credible heightened threat to the healthcare sector from cybercriminals. Most recently, Blackberry has posted notice of a vulnerability in its software, which is used in medical devices from the premarket through the production phases. If exploited, the vulnerability could result in a denial of service or execution of arbitrary code on affected devices which can impact the device functionality and ultimately patient safety.

Cybersecurity incidents also have the potential to cause domestic supply chain disruptions that could cripple our health care system, and would be particularly devastating in the case of a Public Health Emergency (PHE) when supplies are limited. All of these situations can result in a serious national security risk and entice nation states to interfere with, and undermine, the U.S. healthcare system. These threats can impact access to specific devices or to health care services, potentially on a broad scale. To prevent, detect, and respond to such threats and actual attacks, FDA needs to build on its cybersecurity efforts to promote a multi- stakeholder, multi-faceted approach of vigilance, responsiveness, recovery, and resilience that applies throughout the lifecycle of relevant devices.

There is widespread recognition of the need for strong cybersecurity across all sectors. The Administration issued an Executive Order on Improving the Nation's Cybersecurity in May 2021 to address cybersecurity risks, and the medical device industry recognizes the value of securing devices. FDA is helping drive this cyber protection with robust evaluation of security of medical devices through a total product lifecycle approach.

The FY 2023 Budget will allow FDA to hire 6 FTE to increase its internal capabilities through the recruitment and development of cyber experts to support the review of medical devices and assure that they are highly resistant to security breaches before being marketed. FDA will also be able to administer grants and contracts to develop infrastructure geared towards addressing emerging challenges in order to strengthen cybersecurity resilience in the medical device ecosystem, such as tools to track vulnerabilities associated with devices. This request aligns with and provides funding necessary for FDA's A-19 legislative proposal that seeks additional authorities across the lifecycle of the device and includes elements such as a software bill of materials.

Cybersecurity incident prevention, as with disease, is difficult to measure and needs to be tracked over an extended time to discern improved outcomes. Nevertheless, by being proactive in setting up test beds that would enable earlier identification and remediation of vulnerabilities in a safe environment, removed from patients, FDA can work to establish tangible measures, such as time from vulnerability identification to remediation, that impact medical devices directly.

Device Shortages and Supply Chain (+$21.6 million / 18 FTE)

Center: +$21.6 million / 18 FTE

The FY 2023 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.

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 timelier patient access to innovative, safe, effective, high-quality devices.

Crosscutting (+$26.4 million / 24 FTE)

Capacity Building (+$6.3 million / 4 FTE)

Center: +$4.9 million / 3 FTE

Field: +$1.4 million / 1 FTE

The FY 2023 President's Budget includes $59.4 million for Capacity Building, including $6.3 million for the Devices program. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Pay Costs (+$8.1 million)

Center: +$5.7 million

Field: +$2.3 million

The FY 2023 President's Budget includes $51.9 million, including $8.1 million within the Devices program, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$5.5 million / 14 FTE)

Field: +$5.5 million / 14 FTE

The FY 2023 President's Budget includes $33.8 million, including $5.5 million within Devices Field, to support capacity building towards an advanced, highly trained investigators capable of analyzing available data to increase the efficiency and productivity of our inspection operations.

Reducing Animal Testing Through Alternative Methods (+$577,000)

Center: +$577,000

The FY 2023 President's Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program, including $577,000 within the Devices program, to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

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 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $6.0 million for Enterprise Technology and Data within the Foods program, 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.

USER FEES

Current Law User Fees (+$4.3 million / 0 FTE)

Center: +$4.1 million / 0 FTE

Field: +$238,000 / 0 FTE

The Devices Program request includes an increase of $4.3 million for user fees which will allow FDA to fulfil its mission of promoting and protecting the public health by ensuring safety and efficacy of FDA-regulated products.

PERFORMANCE

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

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
253203: Percentage of received Original Premarket Approval (PMA), Panel-track PMA Supplement, and Premarket Report Submissions reviewed and decided upon. (Outcome)	FY 2019: 90.75% 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 2019: 96.8% 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 2019: 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 2019: 77% in 150 days Target: 55% in 150 days (Target Exceeded)	70% in 150 days	70% in 150 days	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
253221: Percentage of Bioresearch Monitoring (BIMO) follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2021: 100.0% Target: 65% (Target Exceeded)	65%	65%	Maintain
252223: Percent of total received Code Blue MDRs reviewed within 10 days during the year. *(Output)*	FY 2021: 81% Target: 80% (New Measure Historical Baseline)	82%	85%	+3%
254203: Percentage of time CDRH meets the targeted deadlines for on-time recall classification (Output)	FY 2021: 97% Target: 85% (Target Exceeded)	85%	85%	Maintain
253207: Number of technical reviews of new applications and data supporting requests for premarket approvals. (Output)	FY 2021: 3,441 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 2021: 99.4% 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 2021: 91.8% 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 2021: 81.3% 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.

Code Blue MDR Review

Code Blue MDR reports represent the most serious adverse events received, and starting in FY 2021, the agency plans to read 80% of all Code Blue MDRs within 10 calendar days of receipt. The target increases to 82% in FY 2022 and 85% in FY 2023.

ORA Field Performance Measures

ORA's performance goals measure topics such as our commitment to follow-up on firms receiving significant inspection violations, as well as measurements related to ORA regulatory impact on violators, and are tracked on a 3-year rolling basis. Due to the nature of regulatory actions and subsequent follow-up conducted by FDA, the duration of these events can vary considerably. After regulatory action, FDA also works to schedule follow-up after a reasonable time has passed to allow the firm to correct for the original violations. A 3-year rolling timeline also ensures tracking of all significant violations that require attention and allows for a more robust analysis.

PROGRAM ACTIVITY DATA

CDRH Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
Original PMAs and Panel-Track Supplements (without Advisory Committee input)			
Workload [1]	73	74	74
Total Decisions [2]	57	63	63
Approved [3]	45	52	52
Original PMAs and Panel-Track Supplements (with Advisory Committee input)			
Workload	2	3	3
Total Decisions [2]	5	3	3
Approved	4	2	2
Modular PMAs			
Workload	76	74	74
Actions [4]	72	65	65
180-day PMA Supplements			
Workload	203	195	195
Total Decisions [5]	163	172	172
Approved	154	159	159
Real Time PMA Supplements			
Workload	287	325	325
Total Decisions [6]	326	338	338
Approved	315	327	327
510(k) Premarket Notifications			
Workload	4,120	4,045	4,045
Total Decisions [7] (SE & NSE)	3,102	3,336	3,336
Cleared [9] (SE)	2,982	3,184	3,184
Humanitarian Device Exemptions (HDE)			
Workload	4	3	3
Total Decisions [2]	3	2	2
Approved	3	2	2
Investigational Device Exemptions (IDE)			
Workload	392	392	392
Total Decisions [8]	405	405	405
Approved	204	204	204
Investigational Device Exemption Supplements			
Workload	1,913	1,913	1,913
Closures [10]	1,875	1,875	1,875
Pre-Submissions			
Workload	3,173	3,115	3,265
Closures [11]	3,115	3,173	3,328
De Novo			
Workload	63	70	70
Total Decisions [14]	55	55	55
Granted	29	30	30
Standards			
Total Standards Recognized for Application Review	1,481	1,534	1,587
Medical Device Reports (MDRs) [12]			
Reports Received	2,828,248	3,393,897	4,072,677
Analysis Consults [13]	577	577	577

Figure 29 - CDRH Workload and Outputs

Field Devices and Radiological Health Program Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***786***	***900***	***2,546***
Bioresearch Monitoring Program Inspections	72	70	300
Pre-Market Inspections	28	4	60
Post-Market Audit Inspections	18	2	60
GMP Inspections	342	75	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	350	37	750
Domestic Radiological Health Inspections	12	4	50
Domestic Field Exams/Tests	0	2	100
Domestic Laboratory Samples Analyzed	124	72	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***6***	***5***	***613***
Foreign Bioresearch Monitoring Inspections	0	0	14
Foreign Pre-Market Inspections	1	0	30
Foreign Post-Market Audit Inspections	0	0	20
Foreign GMP Inspections	6	5	550
Foreign MQSA Inspections	0	0	14
Foreign Radiological Health Inspections	0	0	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***792***	***905***	***3,159***
Import Field Exams/Tests	7,076	16,650	19,800
Import Laboratory Samples Analyzed	82	310	670
Import Physical Exam Subtotal	**7,158**	**17,000**	**20,470**
Import Line Decisions	24,471,343	24,716,056	24,963,217
Percent of Import Lines Physically Examined	0.03%	0.08%	0.07%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS [2]	***7,914***	***7,020***	***7,880***
Inspections (MQSA) by State Contract	7,097	7,000	6,800
GMP Inspections by State Contract	31	20	20
State Contract Devices Funding	$80,850	$286,443	$286,443
State Contract Mammography Funding	$11,488,198	$11,240,003	$11,240,003
Total State Funding	**$11,569,048**	**$11,526,446**	**$11,526,446**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***8,706***	***7,925***	***11,039***

[1] The FY 2021 actual unique count of foreign inspections includes 6 OGPS inspections (6 for China)

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

3 Domestic MQSA Non-VHA and VHA Inpsections have been combined into one output line.

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

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

[6] Count of "Third Party" Device Inspections (not included in Overall counts above) Foreign 4 and Domestic 3

Figure 30 - Field Devices and Radiological Health Program Workload and Outputs

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
National Center for Taxological Research (Budget Authority).....	66,712	66,634	66,761	78,956	12,195
FTE…….....	276	308	276	280	4

Figure 31 - Narrative by Activity

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, NCTR enhances FDA's basis for science-based regulatory decisions by conducting collaborative research to:

- Expedite the translation of laboratory findings to clinical and regulatory applications.
- Use biomarkers—biological indicators of disease—to foster precision medicine.
- Provide FDA with data to support the agency's COVID-19 response.
- 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 human pregnancy, neonates, and children.
- Provide strategies to reduce and rapidly detect contaminants in FDA-regulated products.
- Identify adverse effects earlier in product development and understand the risks and benefits of nanomaterials used in FDA-regulated products.

The following selected accomplishments demonstrate NCTR's delivery of its regulatory and public health responsibilities within the context of current priorities[124]. NCTR generates an extremely large amount of data to support the FDA product centers and its scientists are committed to harnessing 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 the United States of America and around the world.

[124] Please visit www.FDA.gov for additional program information and detailed news items.

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[125] and Guidance[126]) were taken to address and combat the epidemic. Since the epidemic began, NCTR has taken many actions to support FDA's regulatory role, some of which were funded by FDA's COVID-19 Supplemental Funding[127] issued by Congress. Below are a few examples of NCTR's COVID-19 response:

NCTR has published seven peer-reviewed COVID-19-related articles since the pandemic began, providing data to aid FDA and the public in addressing the challenges associated with COVID-19. In addition, NCTR currently has 16 active COVID-19-related projects with 13 additional projects in various phases of development. Below is a list of NCTR's COVID-19-related publications:

- "Identification of Epidemiological Traits by Analysis of SARS-CoV-2 Sequences." *Viruses* (2021).
- "Biochemical features and mutations of key proteins in SARS-CoV-2 and their impacts on RNA therapeutics." *Biochemical Pharmacology* (2021).
- "Elucidating Interactions Between SARS-CoV-2 Trimeric Spike Protein and ACE2 Using Homology Modeling and Molecular Dynamics Simulations." *Frontiers in Chemistry* (2021).
- "Informing selection of drugs for COVID-19 treatment through adverse events analysis." *Nature Scientific Reports* (2021).
- "Can SARS-CoV-2 infect the central nervous system via the olfactory bulb or the blood-brain barrier?" *Brain, Behavior, and Immunity* (2021).
- "Conformational Changes of the Receptor Binding Domain of SARS-CoV-2 Spike Protein and Prediction of a B-Cell Antigenic Epitope Using Structural Data." *Frontiers in Artificial Intelligence* (2021).
- "Pericytes Within A Pulmonary Neurovascular Unit in Coronavirus Disease 2019 Elicited Pathological Changes." *Current Neurovascular Research* (2020).

At the onset of the COVID-19 pandemic, NCTR's Division of Microbiology initiated a project to develop an approach to rapidly indicate effectiveness of COVID-19 therapeutics. A manuscript describing the initial findings of this study can be found in *Frontiers in Artificial Intelligence*[128]. An additional manuscript for this research is expected by the end of FY 2022.

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[125] For more information, please visit: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covid19euas

[126] For more information, please visit: www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19#eua

[127] For more information, please visit: www.fda.gov/news-events/press-announcements/fda-signing-covid-19-emergency-relief-bill-including-landmark-over-counter-drug-reform-and-user-fee

[128] For more information, please visit: Frontiers | Conformational Changes of the Receptor Binding Domain of SARS-CoV-2 Spike Protein and Prediction of a B-Cell Antigenic Epitope Using Structural Data | Artificial Intelligence (frontiersin.org)

NCTR scientists developed a method to detect SARS-CoV-2 RNA in wastewater and are applying it to selected metropolitan areas in Arkansas. This method, which was recently optimized to detect the Delta variant, can help estimate viral spread at the community level without individual testing and may serve as an early warning tool for increased circulation of the virus. Presentations for this research were given at the NCTR Science Advisory Board (SAB) annual meeting, the 2021 FDA Scientific Forum, and the American Society for Virology's 40th Annual Meeting in 2021. Scientists are collaborating with the Arkansas Department of Health and the University of Arkansas for Medical Sciences to apply these methods to the local public health system.

In addition, NCTR is collaborating and supporting two Broad Agency Agreements (BAAs) to help conduct COVID-19-related research:

- BAA with the University of Tennessee Health Science Center to support the "Evaluation of Small Animal Models for COVID-19 and their Application in Nonclinical Safety and Efficacy Studies of Investigational Therapeutics."
- BAA with the Georgia Institute of Technology to support "Quantitative, Label-Free Chemical Imagining for Mechanistic Discovery, Identification and Stratification of Disease."

Artificial Intelligence and Machine Learning (AL/ML)

AI/ML 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.

Figure 32 - 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.

Support for research and development of AI technologies at FDA can be found in FDA's Artificial Intelligence/Machine Learning Action Plan[129] and in Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS)[130]. 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.

[129] For more information, please visit: www.fda.gov/news-events/press-announcements/fda-releases-artificial-intelligencemachine-learning-action-plan

[130] For more information, please visit: www.fda.gov/media/145001/download

Applications or research areas of AI include, but are not limited to:

- 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

A current AI-related study is ongoing in collaboration with the FDA Office of Women's Health (OWH). This project aims 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. A publication related to this research can be found in *Current Opinion in Toxicology*[131].

NCTR also is conducting AI projects which will provide data and tools to combat COVID-19. In FY 2021, NCTR initiated an AI project in collaboration with the FDA Office of the Chief Scientist (OCS), Medical Countermeasures Initiative (MCMi) to support efforts to effectively treat COVID-19 patients. 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 will extend into FY 2023. Another FY 2021 project, in collaboration with the Center for Drug Evaluation and Research (CDER), will develop an AI-powered network pharmacology approach to comprehensively explore the potential of existing drugs to treat COVID-19 with over 3 million data points utilized. Recently, the repurposing candidates were further prioritized for treating COVID-19 patients with different severity based on the COVID-19 patients' genomics profiles.

Beginning in FY 2022, NCTR will support the Office of Food Policy and Response via AI-related research efforts. The AI work being done at NCTR will support the Smarter Tools & Approaches section of the New Era Blueprint. The AI/ML tools being developed by NCTR will significantly reduce review time and variation introduced by humans. Investing in completion of AI/ML tools will accelerate the translation, access, and availability of data to improve the agency's operation of food safety regulation. In collaboration with regulatory Centers and the Office of Regulatory Affairs (ORA), NCTR has already shown the benefits of AI tools which are being used now across FDA and in the public sector.

One project that supports the New Era Blueprint is in collaboration with ORA. NCTR and ORA scientists worked together to develop methods that are accurate in detecting food contaminants such as insect pests (aka pantry beetles). By applying Deep Learning (DL), which is arguably the most promising computational method of machine learning and artificial intelligence, they developed an AI model to identify the exact species of pantry beetles based on the patterns on

[131] For more information, please visit: www.sciencedirect.com/science/article/pii/S2468202020300176

their elytra (hardened fore-wings). This mission-critical project offers a new way of managing and detecting food contamination as some species are more harmful than others. This method can be extended to allow automation of the whole food screening process in the future. A paper describing this work was published in *Scientific Reports*[132].

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[133] (FD&C Act) and that may put the health and safety of consumers at risk[134]. For example, FDA has sent several warning letters to various companies who claim unsubstantiated benefits for cannabis-derived products[135]. FDA has also approved a cannabis-derived product 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[136]. 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.

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 vapor, 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 vapor and cigarette smoke. This research assisted CDER's regulatory decision-making by providing the quality information needed for incoming cannabis-drug master files (DMFs) and will provide a framework for the quality considerations of INDs. This research was completed, and a final report was submitted in FY 2021.

In collaboration with OCS, researchers in NCTR's Division of Neurotoxicology (DNT) 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

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[132] For more information, please visit: https://www.nature.com/articles/s41598-021-86643-y

[133] For more information, please visit: www.fda.gov/regulatory-information/laws-enforced-fda/federal-food-drug-and-cosmetic-act-fdc-act

[134] For more information, please visit: www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd

[135] For more information, please visit: www.fda.gov/news-events/public-health-focus/warning-letters-and-test-results-cannabidiol-related-products

[136] For more information, please visit: www.fda.gov/news-events/press-announcements/fda-approves-first-drug-comprised-active-ingredient-derived-marijuana-treat-rare-severe-forms

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. In FY 2022, DNT, in collaboration with CDER, will start an in vitro study to define CBD doses that cause neurotoxic effects to neural cells and compare the vulnerability of different neural cell types to CBD using human neural stem-cell models.

NCTR is also performing CBD research in collaboration with the Center for Food Safety and Applied Nutrition (CFSAN) and the Center for Veterinary Medicine (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
- Immunomodulating effects of developmental CBD 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)[137]. The FDA Opioid Action Plan[138] provides comprehensive guidance for reestablishing safe-use standards for these products. In support of these efforts, NCTR is conducting research related to opioid addiction and toxicity potential.

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 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 may 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 2021 publication can be found in the *Journal of Molecular Structure*[139].

An innovative opioid-related project will use 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

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[137] National Vital Statistics System. Atlanta, GA: CDC, National Center for Health Statistics; 2017. Available at: https://www.cdc.gov/injury/wisqars/LeadingCauses.html

[138] For more information, please visit: https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm

[139] For more information, please visit: https://doi.org/10.1016/j.molstruc.2021.131589

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 2021 paper outlining this method entitled: "Predictive Models to Identify Small Molecules Activators and Inhibitors of Opioid Receptors" was published in *Journal of Chemical Information and Modeling*[140].

Babies born to mothers who used opioids during pregnancy may have brain damage and respiratory problems. Replacing illicit opioid use during pregnancy with methadone or buprenorphine, or medication-assisted treatment (MAT), is considered best practice for the mother and the baby. These drugs decrease withdrawal symptoms in the pregnant woman and often lead to better health outcomes for the infants, but they still carry risks for the developing fetus. A flood of illicit synthetic opioids has been seen during the pandemic and has exacerbated the opioid crisis in the US. Anticipating a large population of adolescents with a history of perinatal exposure to methadone or buprenorphine, there is an unmet need to understand the long-term effects of perinatal MAT. Therefore, NCTR plans to initiate research regarding the long-term brain effects that may occur due to methadone or buprenorphine exposure during vulnerable periods of development.

A closely related opioids study recently began, in which NCTR scientists will initiate a study entitled: "Assessing the effects of methadone or buprenorphine and their combined use with cannabinoids on human neural stem cells." This study will describe the molecular, cellular, and electrophysiological changes caused by each drug and their combinations. It will also determine the time-course and dose-dependent effects of each drug, therefore supporting development of strategies to guide the safe use of the drugs during pregnancy.

Advancing Alternative Methods

In FY 2022, FDA requested funding for NCTR to support The FDA Predictive Toxicology Roadmap[141]. The Roadmap articulates a regulatory framework where the agency decision-making process is progressively informed by novel non-animal testing methods that have the potential to provide faster and more human-relevant data than that generated by current animal-based guideline testing. To ensure that novel methods can be relied upon for both product development and regulatory decision-making, a side-by-side evaluation of the merits and challenges of the current guideline testing processes and novel methods is required. This process will guarantee a smooth transition while protecting public health.

International regulatory agencies, including FDA, have long relied on guideline animal studies (e.g., rodent toxicological assays) to assess the safety of the products they regulate. However, in most instances, the extent to which these non-animal testing processes can replace, reduce, or refine guideline animal experimentation has not been assessed. A critical step to enable FDA, and other regulatory agencies, to make this determination is the comparative assessment of in vivo guideline and in vitro/in silico alternative testing procedures to ascertain their relative strengths and weaknesses to inform the regulatory process. This research will ensure that FDA has the guideline-study data required to support its decision-making process and remove the

[140] For more information, please visit: https://pubs.acs.org/doi/pdf/10.1021/acs.jcim.1c00439

[141] https://www.fda.gov/science-research/about-science-research-fda/fdas-predictive-toxicology-roadmap

precarious position that FDA could encounter where the agency does not have statutory authority to request the data it needs from the product sponsors.

Except for a few contract research organizations, only NCTR has the infrastructure and expertise in the U.S. to conduct large-scale guideline rodent assays, including developmental and reproductive toxicity studies. NCTR research in support of the Predictive Toxicology Roadmap is essential to providing FDA with the guideline testing required to make an informed transition to alternative testing paradigms. This will be accomplished by implementing a testing strategy where, as possible and in close collaboration with the FDA product centers, animal experimentation and alternative testing methodologies are conducted in parallel. This side-by-side assessment of the value and challenges of each approach in a well-framed regulatory context can expedite the formulation of an optimized future strategy for toxicological testing to improve human and animal health.

Perinatal Health Center of Excellence (PHCE), 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 the perinatal period (the period-of-time including pregnancy, childbirth, 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, the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiological Health (CDRH), CFSAN, CVM, and NCTR. A recently completed PHCE-funded study was a collaboration between CFSAN and NCTR scientists that examined polyfluorinated alkyl substance (PFAS)-based 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*[142].

A PHCE-related poster entitled: "Evaluation of maternal toxicity in CF-1 mice following gestational opioid exposure" was presented at the 2021 FDA Science Forum in May 2021. The poster summarized work highlighted from a current PHCE-funded project. To examine if maternal toxicity may contribute, mice were exposed to opioids during pregnancy and assessed for hypoxia (low oxygen levels in bodily tissues). Some physiological changes indicative of maternal hypoxia were observed, which may be useful supplemental data regarding opioid risks during pregnancy.

Other PHCE research topics include, but are not limited to:

- Neonatal immune responses to vaccines
- Computer-based pregnancy models

[142] For more information, please visit: https://pubmed.ncbi.nlm.nih.gov/31923437/

- COVID-19 effects on pregnancy, prenatal, and postnatal development
- Drug labeling associated with pregnancy

Many drugs and other medical products provided to pregnant women, neonates, and infants are used off-label. For this reason, PHCE research is designed to stimulate robust efforts to provide faster, less expensive, and more predictive approaches and models; thus, leading the way to improved safety and/or efficacy of FDA-regulated products in these susceptible populations. One current PHCE study examines 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 expedite the development of safer anesthesia regimens for use in a clinical setting.

Read more information about the PHCE and its progress.

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 140,000 human prescriptions, biological, over-the-counter (OTC), and animal-drug labeling documents. FDALabel can be used to inform drug repurposing and precision medicine applications. Recent publications related to FDALabel can be found in *Nature Biotechnology*[143] and *Drug Discovery Today*[144].

Differences in a person's genes can make someone more or less likely to benefit from a drug, suffer side effects, or require a dose that is different from another individual. 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

[143] For more information, please visit: https://www.nature.com/articles/s41587-020-00751-0

[144] For more information, please visit: www.sciencedirect.com/science/article/pii/S1359644620300490?via%3Dihub

Pharmacogenomic Information in Ethnic Minority Populations (dbPGxEMP). A paper describing this work can be found in *Pharmaceutics*[145].

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 the agency 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 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 970 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.

With OCS Nanotechnology Collaborative Opportunity for Research Excellence in Science (CORES) grant support, NCTR is conducting multiple projects, including the immunotoxicity evaluation of nanomaterial generated from prosthetic implants after radiation exposure, nanocrystalline drug effects on gastrointestinal tract microbiome and function, and epigenetic effects of nanomaterial on human cells. Office of Women's Health (OWH) supported project on sex-based differences for immunotoxicity of nanomaterial is in progress.

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

[145] For more information, please visit: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7693750/

involvement from government agencies, academia, and industry. NCTR is developing documentary standards to include nanomaterial-characterization methods to ascertain product quality, consistency, and in vitro safety. These standards are identified by FDA and international regulatory agencies as a priority and are developed through the ASTM International E56 subcommittee on Nanotechnology and ISO Technical Committee 229. Four documentary test methods have become international standards, three liposome standards are in the final stages of approval with two other work items related to nanotechnology are under development at the NanoCore for quality assurance and robustness testing and are going through the consensus-standard process at ASTM International.

The FDA Nanotechnology Task Force, chaired by Dr. Anil Patri, Director of the NCTR Nanocore, organized FDA's Nano Day Internal Virtual Research Symposium on October 8, 2021, to showcase progress and research at FDA. Through the National Nanotechnology Initiative, Nanoscale Science Engineering and Technology (NSET) sub-committee, an inter-agency 'interest group on nanoplastics' is formed to share information, minimize redundancies, and coordinate across US government. This group has 100 members from 20 US government agencies and is chaired by Dr. Patri. Through sponsorship from Asia Pacific Economic Cooperation (APEC), Oceans and Fisheries Working Group (OFWG), an international workshop on 'Nanoplastics in Marine Debris in APEC Region' is scheduled to be held from December 13-15th, 2021. These activities will inform future collaborative work on micro nanoplastics at FDA.

Read more about nanotechnology at NCTR and nanotechnology at FDA.

Global Summit on Regulatory Science (GSRS)

The NCTR-established Global Summit on Regulatory Science is now in its 12th year. The GSRS is internationally recognized and consistently proving the importance for international regulators, policy makers, and scientists to exchange views on how to develop and implement innovative research methodologies into regulatory assessments. The GSRS is led by the Global Coalition for Regulatory Science Research, which is comprised of regulatory-science leaders from around the world. The goal of the GSRS is to engage the global research 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.

Figure 33 - Global Summit on Regulatory Science 2021

The 11th Global Summit on Regulatory Science (GSRS21) was held virtually October 4-6, 2021. NCTR's Director serves as the co-chair of the Coalition's executive committee and works with the Coalition to promote global interaction. This year's virtual Global Summit was co-hosted by NCTR. The theme for GSRS21 was "Regulatory Sciences for Food/Drug Safety with Real-World Data and Artificial Intelligence (AI)." There were presentations and workshops, with presentations from Brazil, Canada, EU, India, Italy, Japan, Switzerland, Singapore, and the United States. GSRS21 highlights include, but are not limited to:

- Opening remarks by the FDA Acting Commissioner, Janet Woodcock.
- Two keynote presentations by government-agency senior leadership from US and EU:
- Frank Yiannas (Deputy Commissioner for Food Policy and Response, FDA)
- Stephen Quest (General Director at Joint Research Center, EU)

- Platform presentations from scientists representing nine countries world-wide.
- A live debate on the topic, "Is Regulatory Science Ready for AI?".
- A special workshop to showcase data-science tools currently in regulatory use by Food and Drug Administration (FDA), European Medicine Agency (EMA), and Swiss Agency for Therapeutic Products (Swissmedic).

In addition, a paper summarizing the activities of the GSRS20 has been accepted for publication (https://journals.sagepub.com/eprint/UXVVZA5WQC8P7INFEHC3/full) and is expected to be in print by January 2022.

For more information on the Global Summit, please visit https://www.fda.gov/about-fda/science-research-nctr/global-summit-regulatory-science.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$66,712,000	$66,712,000	---
FY 2020 Actuals	$66,702,000	$66,702,000	---
FY 2021 Actuals	$66,634,000	$66,634,000	---
FY 2022 Annualized CR	$66,761,000	$66,761,000	---
FY 2023 President's Budget	$78,956,000	$78,956,000	---

Figure 34 - Funding History

BUDGET REQUEST

The FY 2023 President's Budget is $78,956,000 for NCTR, which is all Budget Authority. The Budget Authority is an increase of $12,195,000 compared to the FY 2022 Annualized CR. The FY 2023 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 clinical and regulatory applications.
- Use biomarkers—biological indicators of disease—to foster precision medicine.
- Provide FDA with data to support the agency's COVID-19 response.
- 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 human pregnancy, neonates, and children.
- Provide strategies to reduce and rapidly detect contaminants in FDA-regulated products.
- Identify adverse effects earlier in product development and understand the risks and benefits of nanomaterials used in FDA-regulated products.

These research areas include but are not limited to: COVID-19 Response, Artificial Intelligence and Machine Learning (AI/ML), Cannabis and Cannabis-Derived Products such as Cannabidiol, Opioids, Advancing Alternative Methods, Perinatal Health Center of Excellence, Pediatric Medicine, and Maternal Medicine, Bioinformatics, Nanotechnology, and the Global Summit on Regulatory Science. 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 (+$1.4 million / 2 FTE)

New Era of Smarter Food Safety (+$1.2 million / 2 FTE)

Center: +$1.2 million / 2 FTE

The FY 2023 Budget provides $1.4 million to support the Office of Food Policy and Response via AI-related research efforts. The AI research to be conducted at NCTR will support the Smarter Tools & Approaches section of the New Era Blueprint. The AI/ML (Machine Learning) tools being developed by NCTR will significantly reduce review time and variation introduced by humans. Investing in completion of an AI/ML tools will accelerate the translation, access, and availability of data to improve the agency's operation of food safety regulation. In collaboration with regulatory Centers and ORA, NCTR has already shown the benefits of AI tools which are being used now across FDA and in the public sector.

Emerging Chemical and Toxicology Issues, Food (+$150,000)

Center: +$150,000

The FY 2023 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 ($7.5 million)

Toxicology Roadmap – Guideline Studies ($7.5 million)

Center: +$7.5 million

The FY 2023 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.

Crosscutting (+$3.3 million / 2 FTE)

Capacity Building (+$1.0 million)

Center: +$1.0 million

The FY 2023 President's Budget includes $59.4 million for Capacity Building, including $1.0 million within NCTR. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Public Health Employee Pay Costs (+$1.2 million)

Center: +$1.2 million

The FY 2023 President's Budget includes $51.9 million, including $1.2 million within NCTR, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Reducing Animal Testing Through Alternative Methods (+$577,000 / 1 FTE)

Center: +$577,000 / 0 FTE

The FY 2023 President's Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program, including $577,000 within NCTR, to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them.

Data Modernization and Enhanced Technologies: Enterprise Technology and Data (+$515,000 / 1 FTE)

Center: +$515,000 / 1 FTE

The FY 2023 Budget an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $515,000 for Enterprise Technology and Data within NCTR, 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.

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 discovery of perinatal and maternal therapeutic 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 2022 Target	FY 2023 Target
263103: Conduct translational and regulatory research to advance the safety of products that FDA regulates. (Output)	FY 2021: Preliminary results showed that inorganic arsenic (commonly found in water, soil, or foods such as rice) may induce developmental toxicity in zebrafish at high exposure levels. These results were presented at the EPA/FDA Workshop on May 5, 2021. (Target Met) FY 2021: A manuscript regarding 3D modeling of opioids was published in *Archives of Toxicology*. A second manuscript entitled "Identification of Structural Factors that Affect Binding to Cannabinoid Receptor Type 1" was recently accepted for publication in the *Journal of Molecular Structure*. (Target Met)	In collaboration with the FDA Office of the Chief Scientist, provide preliminary data on CBD exposure in the developing brain.	Support CDER compounding efforts by characterizing compounded triamcinolone-moxifloxacin. Draft a manuscript on the effects of drug toxicity using a microphysiological human-placental barrier model.
263201: Develop science base for supporting FDA regulatory review of new and emerging technologies. (Output)	FY 2021: In collaboration with CFSAN, CDRH, and Emulate a CRADA was executed with Emulate Inc. to collaborate and provide Alzheimer's disease-on-a-chip technology. This research may provide a screening	Initiate the development of a virtual pregnant-woman modeling suite to support regulatory decisions using bioinformatics and artificial intelligence.	In collaboration with CBER, report findings associated with Zika virus utilizing a microphysiological system.

Measure	Most Recent Result / Target for Recent Result	FY 2022 Target	FY 2023 Target
	platform for assessing the potential neurotoxic effects of any FDA-approved drug, biologic, or medical device for the treatment of CNS-related disorders. (Target Met)	Report preliminary findings related to COVID-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 2021: NCTR scientists have developed preliminary data to better assess immunotoxicity associated with FDA products containing nanomaterials. (Target Met)	Perform research to identify potential biomarkers for the onset of prostate cancer.	In collaboration with CDER, improve minimally invasive MRI biomarkers to modernize drug neurotoxicity testing which may ensure that safer drugs reach the market faster. In collaboration with OWH and CDER, report preliminary preclinical data, which may advance detection and treatment strategies for women with Alzheimer's disease.
264101: Develop risk assessment methods and build biological dose-response models in support of food protection. (Output)	FY 2021: A manuscript describing the biology of a specific type of plasmid (IncI1 plasmid) was published in *Microbiology and Molecular Biology Reviews*. These plasmids are known to carry antimicrobial resistance genes and potentially genes that contribute to increased pathogenicity. (Target Met)	Report preliminary findings regarding nanomaterial interaction with the gastrointestinal tract	Report preliminary findings on evaluating the virulence potential of bacterial pathogens using 3D tissue-culture model systems.

Measure	Most Recent Result / Target for Recent Result	FY 2022 Target	FY 2023 Target
263104: Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates. (Output)	FY 2021: In collaboration with CBER, NCTR scientists 1) acquired lipidomics data and 2) developed proteomics methods to research newborn susceptibility to vaccines. (Target Met)	Construct a database of opioid agonists/antagonists to assist the review and development of alternative pain-management products.	Support CBER improvement of pediatric vaccines by studying whether maternal obesity impacts vaccine outcomes.
263102: Develop computer-based models and infrastructure to predict the health risk of biologically active products. (Output)	FY 2021: Four papers describing the development of a predictive model for detecting drug induced liver injury (DILI) were published in the *Journal of Hepatology*, *Environmental Research and Public Health*, *Scientific Reports*, and *Archives of Toxicology*. (Target Met)	Provide initial data on a study to benchmark and compare computational and genomic predictive methods for toxicity for drug-induced-liver injury (DILI) using AI-based methods.	Report findings associated with DeepDILI which will compare computational and genomic predictive methods for drug-induced liver injury (DILI).

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 the FDA regulates. In FY 2021, NCTR researchers finalized data regarding 3D molecular modeling of opioids and other chemicals. A manuscript regarding 3D modeling of opioids was published in *Archives of Toxicology* and a second manuscript was recently accepted for publication in the *Journal of Molecular Structure*. In FY 2022, researchers will provide preliminary data on cannabidiol, better known as CBD, exposure in the developing brain. In FY 2023, NCTR will support CDER compounding efforts by characterizing compounded triamcinolone-moxifloxacin as well as drafting a manuscript on the effects of drug toxicity using a microphysiological human placental barrier model.

Science Base for Alternative Assays

NCTR continues to develop a science base to promote the FDA's move towards alternative assays. These efforts look to replace animal models with in vitro (i.e., cellular) or in silico (computer-based) models. In FY 2021, in collaboration with CFSAN, CDRH, and Emulate, a CRADA was executed with Emulate Inc. to collaborate and provide Alzheimer's disease-on-a-chip technology. This research may provide a screening platform for assessing the potential

neurotoxic effects of drugs, biologics, or medical devices for the treatment of central nervous system (CNS)-related disorders. Plans for FY 2022 include, initiating the development of a virtual pregnant-woman modeling suite to support regulatory decisions using bioinformatics and AI. The proposed pregnant-woman modeling suite will be the first-of-its-kind in the field of biological modeling, pregnancy health, and regulatory science. In FY 2023, NCTR scientists, in collaboration with CBER, will report findings associated with Zika virus utilizing a microphysiological system.

Maternal and Perinatal Medicine

Scientific expertise in perinatal and maternal health has long been a strength and focus of the NCTR. In FY 2019, NCTR began the Perinatal Health Center of Excellence to focus on this vastly understudied area of regulatory science. The PHCE focuses on the perinatal period (the period-of-time including pregnancy, childbirth, and infant/child development) and covers a broad range of research 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, NCTR scientists conducted research to determine the neurotoxic effects of inorganic arsenic (commonly found in water, soil, or foods such as rice). Preliminary results showed that inorganic arsenic may induce developmental toxicity and neurotoxicity in a zebrafish model at high levels of exposure. These results were presented at the EPA/FDA Workshop on May 5, 2021. 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. Finally, in FY 2023, NCTR will support CBER with improvement of pediatric vaccines by studying whether maternal obesity impacts vaccine outcomes.

PROGRAM ACTIVITY DATA

Program Workload and Outputs	FY 2021 Actual	FY 2022 Estimate	FY 2023 Estimate
Research Outputs			
Research Publications	143	166	170
Research Presentations	145	150	160
Patents (Industry)	14	14	14
Leveraged Research			
Federal Agencies (Interagency Agreements)	5	5	5
Nongovernmental Organizations	83	78	48

Figure 35 – NCTR Program Workload and Outputs

OFFICE OF REGULATORY AFFAIRS - FIELD ACTIVITIES

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Office of Regulatory Affairs	**1,245,265**	**1,224,098**	**1,254,692**	**1,363,223**	**108,531**
Budget Authority	***1,130,621***	***1,130,376***	***1,130,523***	***1,242,285***	***111,762***
User Fees	***114,644***	***93,722***	***124,169***	***120,938***	***-3,231***
Prescription Drug (PDUFA)	*10,221*	*9,227*	*10,961*	*11,150*	*189*
Medical Device (MDUFA)	*2,597*	*2,030*	*2,745*	*2,753*	*8*
Generic Drug (GDUFA)	*54,096*	*48,710*	*57,205*	*58,209*	*1,004*
Biosimilars (BsUFA)	*1,322*	*1,095*	*1,487*	*1,516*	*29*
Animal Drug (ADUFA)	*390*	*387*	*393*	*401*	*8*
Animal Generic Drug (AGDUFA)	*224*	*---*	*244*	*292*	*48*
Family Smoking Prevention and Tobacco Control Act	*22,607*	*18,887*	*27,485*	*22,494*	*-4,991*
Mammography Quality Standards Act (MQSA)	*11,507*	*12,853*	*11,737*	*11,972*	*235*
Food and Feed Recall	*1,040*	*---*	*1,061*	*1,082*	*21*
Food Reinspection	*5,600*	*---*	*5,711*	*5,826*	*115*
Voluntary Qualified Importer Program	*4,495*	*---*	*4,584*	*4,676*	*92*
Third Party Auditor Program	*150*	*28*	*153*	*156*	*3*
Outsourcing Facility	*395*	*505*	*403*	*411*	*8*
FTE	**4,901**	**5,205**	**4,897**	**5,041**	**144**

Figure 36: Narrative by Activity

Authorizing Legislation: Filled Milk Act (21 U.S.C. §§ 61-63); Federal Meat Inspection Act (21 U.S.C. § 679(b)); Federal Import Milk Act (21 U.S.C. § 141, et seq.); Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301, et seq.); The Office of Criminal Investigations (OCI) of ORA conducts criminal investigations and executes search warrants as permitted by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 372), the Public Health Service Act (42 U.S.C. 262) and the Federal Anti-Tampering Act (18 U.S.C. 1365); Poultry Products Inspection Act (21 U.S.C. § 467f(b)); Small Business Act (15 U.S.C. § 638); The Fair Packaging and Labeling Act (15 U.S.C. 1451, et seq.); Executive Order 11490, § 1103; Comprehensive Drug Abuse Prevention and Control Act of 1970 (84 Stat. 1241); Controlled Substances Act (21 U.S.C. § 801, et seq.); Lead-Based Paint Poisoning Prevention Act (42 U.S.C. § 4831(a)); Federal Advisory Committee Act (5 U.S.C. Appx. 2); Federal Caustic Poison Act (44 Stat. 1406); Egg Products Inspection Act (21 U.S.C. § 1031, et seq.); Stevenson-Wydler Technology Innovation Act of 1980 (15 U.S.C. § 3701, et seq.) and Executive Order 12591; Equal Access to Justice Act (5 U.S.C. § 504); Consumer-Patient Radiation Health and Safety Act of 1981 (42 U.S.C. §§ 10007 and 10008); Patent Term Extension (35 U.S.C. § 156); Pesticide Monitoring Improvements Act of 1988 (21 U.S.C. §§ 1401-1403); Food, Agriculture, Conservation, and Trade Act of 1990 (7 U.S.C. §138a); Effective Medication Guides of the Agriculture, Rural Development, Food and Drug Administration (FDA), and Related Agencies Appropriations Act of 1997 (Public Law 104-180); Best Pharmaceuticals for Children Act (Public Law 107-108), as amended by Pediatric Research Equity Act of 2003 (Section 3(b)(2) of Public Law 108-155); Drug Quality and Security Act of 2013; Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

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 federal, state and local partnerships, and
- Information sharing with domestic and international regulatory and mutual reliance partners.

ORA activities support the Fiscal Year (FY) 2022 – FY 2026 HHS strategic plan goal: Safeguard and Improve National and Global Health Conditions and Outcomes. ORA works to improve its capabilities to predict, prepare for, and respond to public health emergencies and threats in the nation and across the globe by strengthening its network of regulatory partners and applying shared data and knowledge in the application of surveillance and enforcement activities. By targeting the products that pose the greatest risk, American patients and consumers can have added confidence and timely access to safe foods and medical products.

Recent Accomplishments

Three of ORA's most significant accomplishments from the past year are described below.

Supporting the Opioid Initiative

ORA has taken multiple steps to address the opioid public health crisis. ORA has fully implemented the 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. Additionally, ORA has prioritized support to increase personnel, improve space, analytical detection tools, and information technology (IT) infrastructure at the nine International Mail Facilities (IMF).

FDA's IMF staff work diligently to examine and document suspicious mail parcels; however FDA investigators are only able to inspect a fraction of the incoming international mail packages. It is estimated that FDA staff at IMFs are only able to physically inspect less than 0.06 percent of the packages that are presumed to contain drug products. Recognizing these hurdles, FDA is increasing existing resources, increasing efficiencies, and identifying innovative ways to expand the impact of its efforts. In FY 2021, FDA reviewed over 95,000 products, almost double the number of products processed in FY 2020. The number of products reviewed should continue to increase as the FDA continues to increase staff, add space, and make IT improvements.

In October of 2020, FDA and Customs and Border Protection (CBP) signed a Memorandum of Understanding (MOU). The MOU addresses the areas of cooperation outlined in the SUPPORT Act, including information sharing, operational coordination for better targeting of higher risk parcels, facility improvements at IMFs, and collaborative strategies designed to integrate each agency's respective regulatory enforcement requirements. Under this MOU, FDA will be collaborating and sharing information with CBP in FY 2022 to target opioids and unapproved drugs.

The establishment of permanent spaces at the IMFs for analytical equipment and laboratory analysts to conduct expedited analytical field testing is in progress. The first of these satellite laboratories was established at the Chicago O'Hare IMF. Plans are underway to establish satellite laboratories at additional selected IMF locations, with Miami anticipated to be operational early in 2022. The success of the satellite lab effort is directly connected with the increased inspections by FDA's import investigators and improved communications with CBP. Efforts at the mail facilities have continued throughout the COVID-19 pandemic.

Initiating a New Era of Smarter Food Safety

The New Era of Smarter Food Safety (New Era) represents a new approach to food safety, leveraging technology and other tools to create a safer and more digital, traceable food system. In FY 2021, ORA has made strides to advance the New Era foundational pillars including Smarter Tools and Approaches for Prevention and Outbreak Response through the use of new remote activities including virtual engagement during outbreak investigations and voluntary remote regulatory activities.

ORA implemented the first ever use of technology for virtual subject matter experts (SMEs) participation during an onsite investigation into a foodborne outbreak. Use of the virtual technology allowed experts to remain in different locations throughout the investigation and mitigated potential limitations in participation due to travel restrictions under COVID-19. agency SMEs were able to view in real time, what the investigation team was 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 locations of interest and used Center SMEs for a small but necessary window during the investigation rather than monopolizing the SME for an entire week.

ORA implemented the first ever Remote Regulatory Assessment (RRA) pilot in the human foods program. Using the RRA pilot, the agency was able to maintain a level of regulatory oversight of industry while allowing the activities to be performed remotely. Firms provided requested information that allowed the agency to determine if previously corrected actions had been implemented. In one instance the agency was able to determine that an immediate onsite inspection was needed, which was performed and found the inspection to be classified as Official Action Indicated. Both industry and the agency acknowledge that while these remote regulatory activities are not a replacement for in person inspections, they do provide the agency with important information that helps maintain a level of regulatory oversight and is also beneficial to more efficient work planning for future years.

ORA was a key participant in the October 2021 FDA New Era of Smarter Food Safety Summit on E-Commerce: Ensuring the Safety of Foods Ordered Online and Delivered Directly to Consumers. The summit, designed to help the agency improve its understanding of how human and animal foods are sold through Business to Consumer e-commerce models across the U.S. and globally was an opportunity for FDA to further our collaboration on food safety with our federal, state, local and tribal regulatory partners and a broad array of stakeholders including industry, consumers, consumer and public health organizations, academia and foreign regulatory counterparts. ORA's participation in this summit supported discussions surrounding the safety risks associated with foods sold through business to consumer e-commerce, including challenges and gaps in regulatory approaches that need to be addressed.

Expanding FDA Medical Product Safety

ORA has advanced two key initiatives in medical product safety, both domestic and international. First, ORA supports FDA's Compounding Quality Center of Excellence. 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 practices) to protect patient health. Outsourcing facilities are intended to produce a reliable supply of compounded drugs needed by hospitals, clinics, and other health care providers. It is important that this sector meets health care provider needs for compounded drugs distributed without patient-specific prescriptions. The Compounding Quality Center of Excellence is designed to 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. The Compounding Quality Center of Excellence has provided both instructor-led virtual training, as well as, web-based training during the past year and continues to refine and update courses as necessary.

The second initiative that ORA continues to advance, in collaboration with FDA's centers, is the Mutual Recognition Agreement (MRA). The amended Pharmaceutical Annex of the 1998 United States and 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; FDA is currently conducting capability assessments of E.U. veterinary agencies. To date, 13 of the 23 E.U. member state assessments (11 dual competence authorities and 2 single veterinary only authorities) have been completed. This exceeds the goal of nine dual competency authority assessments. An additional five single veterinary only authority assessments are on track to be completed by the end of the calendar year. In addition, efforts are underway for exploring a MRA with Switzerland.

Ongoing Field Accomplishments

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, local 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 193 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.

The agency is currently limited in the information it can provide its domestic partners (local, state, tribal, and territorial), requiring extensive review, redaction, and valuable time. Although an OMB Circular A-19 legislative proposal to expand information sharing was submitted in FY 2019 with a limited scope of foods and pharmacy compounding, it was requested that ORA expand it to cover all commodities, and the recent COVID-19 pandemic highlighted the need to collaborate with regulatory partners on devices. In FY 2020, ORA submitted for the Department of Health and Human Services (HHS) clearance an expanded proposal to amend the FD&C Act, section 708, to allow sharing of trade secrets in all commodities and resubmitted the proposal in FY 2021.

ORA continues to expand its Non-Contract Inspection program which allows the agency to obtain state inspection findings from non-contract state accomplished inspections for those states that voluntarily choose to participate in the program. The agency utilizes the information obtained from the states to aid in more informed work planning to obtain efficiencies in workforce planning and to expand the agency understanding of our regulated industry. In addition to FDA obtaining state inspection data, the agency is also sharing findings from ORA inspections with the states to help expand the state datasets and understanding of their local regulated industry. To date the agency has received inspection findings for more than 500 firms from participating states and has leveraged the data received for a more robust understanding of the inventory and utilization of the data for more efficient resource planning within ORA.

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.

To accomplish this objective, FDA has 192 cooperative agreement programs (CAPs) and/or grants with 50 states and 9 associations. In FY 2021, ORA provided $109.5 million to its SLTT regulatory partners to ensure oversight of the nation's domestic food supply and executed 86 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.

FDA works collaboratively with its public health/regulatory association partners to develop, revise, and promote conformance with regulatory program standards 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 jurisdictions enrolled in the regulatory program standards are taking steps to ensure they have the regulatory foundation and framework necessary to protect public health. As of September 2021, a total of 880 SLTT jurisdictions were enrolled in the VNRFRPS, 44 in the MFRPS, and 23 in the AFRPS. The ERPS are being released and launched in FY 2022 with two states enrolled under an egg inspection contract option with FDA.

FDA continues to take modernized approaches in new and existing resources. ORA continues to integrate outbreak response by developing rapid response teams (RRTs) with state partners. Since 2009, the RRT program has grown from 9 to 24 states in 2021, three of which participate in the program voluntarily (outside of the funded cooperative agreement). ORA also entered into three Partnership Agreements in FY 2021 to facilitate a coordinated effort between the FDA and individual states with goals to reduce duplication of regulatory oversight and increase public health protection by focusing on areas of higher risk. Examples of these efforts include improved information sharing, inventory reconciliation activities, and establishing the Non-Contract Inspection (NCI) program which leverages both FDA and state non-contract inspectional data to support and inform regulatory oversight. In FY 2020 and FY 2021 combined, the agency accepted data for more than 500 inspection reports.

In FY 2021, FDA awarded 55 cooperative agreements to state labs under a new Laboratory Flexible Funding Model CAP. The Laboratory Flexible Funding Model (LFFM) allows laboratories from state governments and universities to increase their testing capability and capacity. From September 2020 - June 2021, these laboratories analyzed over 18,000 human and animal food samples. As a result of this testing, there were 11 voluntary recalls of products and 1 state consumer advisory. In FY 2021, FDA awarded 47 State Produce Safety Cooperative Agreement to states to support state produce safety programs focused on outreach as well as implementing and enforcing the Produce Safety Rule.

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.

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. Under the BIMO Program, ORA conducts more than 1,100 domestic and 315 foreign inspections on average each fiscal year.

These BIMO inspections and data audits are integral to ensuring the safety and effectiveness of new medicines, medical devices, food and color additives, veterinary products, and the safety of new tobacco products, during the FDA preapproval process. For example, on March 22, 2021, a Florida medical doctor was sentenced to 63 months in prison after pleading guilty to her role to falsify pediatric clinical trial data. The doctor admitted to participating in a scheme to defraud a pharmaceutical company by fabricating data and participation of subjects in the clinical trial.

Records were falsified to make it appear as though the pediatric subjects made scheduled visits, took study drugs as required, and received checks as payment. Additionally, three employees were held accountable for their participation in the scheme including charges of wire fraud and making false statements to an FDA investigator.

Post-market Surveillance 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.

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.

During the pandemic, ORA has developed and successfully launched a Remote Regulatory Assessment (RRA) process to subsidize surveillance efforts. This process was launched in February 2021 for assessment of medical device manufacturers and as of the end of the FY 2021, ORA has preannounced 283 firms with 151 RRAs completed. ORA's use of RRAs in support of drug work has led to the issuance of Warning letters, Import Alerts and approval of applications, and was expanded to pharmacy outsourcer 503B facilities. ORA has completed over 1,000 requests for records to human and animal drug manufacturers. Additionally, ORA received surveillance reports for foreign work from MRA and PIC/S inspectorates.

Outreach

Aside from regulatory and enforcement activities, ORA participates, in collaboration with the FDA centers, in outreach activities such as meetings and publications. A few examples of FY 2021 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.
- ORA launched a communications campaign with industry stakeholders demonstrating and emphasizing value and importance of medical device inspections. The presentation "Uncovering and Maximizing the Value of FDA Inspections" included messaging on the business value and patient impact of inspections, and information to connect stakeholders to additional important regulatory information on ORA's medical device website (link: Working Together - Keeping Informed: FDA Medical Device Virtual Conference 2021 - 06/23/2021 - 06/23/2021 | FDA). This information was presented at three conferences, reaching over 500 industry participants.

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.

IMPORT LINES BY PROGRAM AREA
FY 2016-FY 2024 (Est.)

Program Area	2016	2017	2018	2019	2020	2021	5 Yr Actual Percent Growth*	2020 Percent of Total Lines	Estimate 2022	Estimate 2023	Estimate 2024
Foods	13,952,537	15,251,687	16,859,790	17,722,742	16,983,686	16,651,210	2%	29.64%	17,483,771	17,483,771	18,357,959
Cosmetics	2,939,034	2,625,555	2,729,584	2,762,411	2,350,216	3,060,422	4%	5.45%	3,213,443	3,374,115	3,542,821
Human Drugs	739,309	789,853	871,212	838,267	959,585	1,003,661	5%	1.79%	967,604	967,604	967,604
Animal Drugs & Feeds	434,384	426,484	456,684	410,237	493,192	550,811	6%	0.98%	578,352	607,269	607,269
Biologics	151,911	157,080	170,575	181,328	152,158	177,977	3%	0.32%	197,462	197,642	197,642
Medical Devices & Rad Health	18,757,725	20,584,138	22,291,902	22,967,758	22,512,049	34,471,343	12%	61.35%	27,308,539	27,308,539	27,308,539
Tobacco Products	32,972	199,066	281,097	280,901	275,261	271,621	8%	0.48%	285,202	299,462	314,435
Total	37,007,872	40,033,863	43,660,844	45,163,644	43,726,147	56,187,045	8%	100.00%	50,034,373	50,238,402	51,296,269

*Percent growth based on a five-year average of actuals from FY 2016 - FY 2021

Figure 37 - Number of Import Lines by Program Area: FY 2015 through FY 2023 (Est.)

ORA has continued oversight of food importers through establishment of the remote inspection protocol for Foreign Supplier Verification Programs (FSVP) Inspections. The FSVP rule specifically authorizes remote inspections of FSVP Importers. As of November 8, 2021, in FY 2021, ORA has conducted 1674 FSVP Inspections. Of these 1674 FY 2021 FSVP Inspections, 1609 were conducted remotely and 65 were performed onsite. Additionally, two of the inspections in FY 2021 were inspections of FSVP importers of product from foreign suppliers whose foreign inspection was postponed due to the COVID-19 pandemic.

ORA continues implementation of the Voluntary Qualified Importer Program (VQIP). On January 1, 2021, the VQIP application portal became available on www.fda.gov and remained open to accept completed VQIP applications through May 31, 2021. This year, FDA received four VQIP applications for FY 2022 benefits, including extensions from the three approved applicants from FY 2021. The associated information for all importers approved for participation in this program may be found in the FDA Data Dashboard under 'Approved VQIP Importers. The VQIP Application portal will be open between January 1 and 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 commodity specialized laboratory programs at 13 distinct locations across the United States and Puerto Rico and is in the process of establishing satellite laboratories at selected International Mail Facilities (IMF).

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 unapproved pharmaceuticals and chemical contaminants in a vast variety of products including human and animal foods, vaping liquids, and pharmaceutical drugs. ORA laboratories adhere to a strict quality system and regulatory standards 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 current and future threats.

Compliance, Enforcement, and Criminal Investigation Activities

ORA continues to investigate unlawfully marketed products that claim (but are not proven) to prevent, treat, or cure diseases or other health condition. In addition, ORA works with agency programs and in certain instances, the Federal Trade Commission (FTC) to act against companies marketing fraudulent products. For example, in May 2021, FDA and the FTC issued warning letters to five companies for illegally selling dietary supplements that claim to cure, treat, mitigate, or prevent infertility and other reproductive health disorders in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act). ORA's Health Fraud Branch was integral in the investigation of the companies which was in response to numerous reports, including a report from the Centers for Science in the Public Interest (CSPI) which detailed a host of illegally marketed treatments for infertility and related reproductive conditions. ORA conducted active surveillance and worked with FDA counterparts to develop consumer education and outreach materials. The initiative was extremely well-received by media, patient and consumer groups, with 120 different outlets providing coverage that was seen by as many as 72 million individuals.

ORA, through the Office of Criminal Investigations (OCI), has the primary responsibility for criminal investigations conducted by FDA and for all law enforcement and intelligence issues pertaining to threats against FDA-regulated products and industries. In FY 2021, criminal investigations led to 189 arrests and more than $450 million in forfeitures and seizures.

A series of events impacting public health in FY 2021 have underscored the importance of FDA's criminal investigations. The COVID-19 pandemic brought with it an illicit market full of fraudsters and profiteers seeking to take advantage of the public health crisis. ORA has opened approximately 138 criminal cases involving fraudulent COVID-19 products and obtained indictments in several of these cases. Many cases involve imported medical products, including unapproved drugs that are touted as "cures", bogus test kits, and substandard medical equipment.

The opioid crisis, which has taken countless lives, continues to be a major concern to the agency. 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.

A recent case involving a nurse highlights ORA's investigations to tackle the serious crime of tampering with opioids intended for patient use by health care professionals. In that case, the nurse took vials of fentanyl, used a syringe to withdraw the narcotics from the vials, and reinjected saline into vials so that it would appear as if none of the narcotics were missing. The nurse knew that the adulterated vials of fentanyl she replaced would be used in surgical procedures, and that the absence of an anesthetic during an outpatient procedure may cause serious bodily injury to the patient. Numerous victims submitted letters to the judge describing physical pain they experienced during their procedures at the clinic during this time period.

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:

- international engagement to ensure the safety of the FDA-regulated supply chain;
- combating cybercrime on the surface net and dark nets; and
- import operations to detect and seize violative products prior to their entering domestic markets

Two examples of the intersection of these three pivotal areas are 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.

Enhancing Opioids Enforcement

In October 2020, leadership from FDA, Customs Border Protection (CBP), and the U.S. Immigration and Customs Enforcement, Homeland Security Investigations (ICE-HSI) signed an MOU to stop harmful products that pose a threat to public health and attempt to enter the United States through International Mail Facilities (IMFs). To further the collaboration and information sharing in the IMF, FDA and CBP have agreed upon a National Opioid Strategy (NOS) which will launch in FY 2022 and target unapproved drugs and illegal opioids in the IMF and courier environment.

The SUPPORT Act added a section to the FD&C Act, giving FDA authority to treat an FDA-regulated article as a drug if it is or contains an API in an approved drug or licensed biologic or an active pharmaceutical ingredient (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." FDA has updated and will continue to update the API list, using an established review process. This has granted FDA with more authority in limiting the domestic distribution and importation of violative drug products. The implementation of 801(u) is an unquestioned success. ORA increased the overall destruction rate from 77% of refused drug products in FY 2020 to more than 86% of violative refused drug products in FY2021.

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 United States 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.

ORA also continues to make an impact online with the Cybercrime Investigation Unit which targets illegal online marketplaces and manufacturers that sell counterfeit opioid products. ORA's Operation Cyberpharma has thus far led to the arrest of 48 darknet vendors, the takedown of a major darknet marketplace, and the seizure of drug counterfeiting tools and $7 million in virtual currencies and other assets. Further arrests and seizures are anticipated in this on-going operation.

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 50 inspections of domestic tobacco product manufacturers and 189 investigations in FY 2021. In response to evidence of increasing youth use of Electronic Nicotine Delivery Systems (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 10 foreign and 12 domestic Premarket Tobacco Application (PMTA) records assessments via the Remote Regulatory Assessment procedures.

In January 2020, FDA published the guidance for industry, Enforcement Priorities for 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. Since January 2020, the heightened surveillance of indicated ENDS products has led to a yearly average increase compared to the year prior to publication of the enforcement priorities. Since implementation, this has resulted in over 2000 lines of ENDS products being examined by FDA, with over 900 (44%) found to be in violation. FDA had 59 violative product lines in FY 2021 resulting in refusal of admission and continues to work with CBP to prevent violative ENDS products from reaching the consumer. There were over 160 CBP seizures of ENDS products per fiscal year in FY 2020 and FY 2021, providing evidence of the continued collaboration between CBP and FDA when interdicting potentially harmful ENDS products at the border

Data Modernization and Enhanced Technologies

ORA is committed to supporting expanded regulatory authorities, increasing productivity, and maintaining program integrity through its information technology systems and initiatives. ORA continues to make progress to enhance and modernize its IT portfolio and expand functionality to encompass and support new regulatory requirements and business initiatives described in the accomplishments above.

In FY 2021, FDA and ORA made technological advancements using novel technology to engage subject matter expertise located remotely during an investigation in real-time. Use of the technology allowed experts in FDA's 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. This was an instrumental step in advancing field operations, created great efficiencies in the investigation, and saved the agency human and financial resources.

ORA also enhanced its operational systems and external information sharing and management capability with internal and external partners. Some examples include:

- Modernized the Recall Enterprise System providing a new interface to users. The modern framework allows for improved implementation of user requested enhancements, extensibility options such as better interfacing with other systems, easier maintenance, and improved security.
- Created new inspection capabilities to include new work assignment features, delivered three new Inspection Protocols enabling targeted inspection data collection, and delivered new Remote Regulatory Assessment capabilities.
- In the ORA Data Exchange program supporting the IFSS, ORA onboarded 41 total new State partners including 7 State labs expanding State inspection and sample collection/analysis/sharing via the Data Exchange.
- Progressed toward replacing the legacy systems for the Import program by replacing legacy functionality for entry review via the System for Entry Review and Import Operations. ORA also enhanced its capabilities at the IMFs by implementing label scanning technology which will reduce time to collect and input data from mail packages.
- Improved availability of center registration/listing data to field users by providing data through a mobile application.
- Supported development of FDA/center analytical platforms by providing data management, reporting and other business intelligence capabilities to support CDER's CDEROne initiative, CFSAN's Enterprise Information Repository for Research and Analytics (CEIRRA) and OFPR's big data initiatives to support high priority analytical work.

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 and retain 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, Title-21 Cures, and COVID-19 and Consumer Safety Officer Direct Hire Authority. As a result, ORA has continued its positive hiring trajectory by increasing its overall Full Time Equivalent Employee (FTE) count from

4,527 in FY 2019 to 4,910 as of July of FY 2021. ORA's hiring goal for FY 2021 was to hire 438 FTEs overall, and is at 90% of the hiring goal with two months remaining in the year. ORA maintains a 5.54% attrition rate which is below FDA's average attrition rate.

Training and development of ORA staff is critical. To date in FY 2021, ORA has held 186 vILT courses with 4,425 students in attendance. In FY 2021, ORA has laid the foundation to build commodity specific course curriculums in the areas of Human and Animal Foods, Medical Products, Laboratory, Produce, and Cooperative Programs including Retail, Milk and Shellfish.

Coronavirus (COVID-19) Pandemic

ORA is on the forefront of the COVID-19 pandemic response and has adapted regulatory work to meet the challenges created by the pandemic. ORA has conducted domestic/foreign inspections of clinical investigators and sponsors, emergency use authorization (EUA) investigations and inspections of viable manufacturers, pre-market/post-market inspections, and import activities (such as screenings and entry review). To support efforts related to the COVID-19 pandemic, ORA has:

- Developed and implemented remote regulatory activities to maintain oversight and engagement with regulated industry.
- Adjusted entry screening to provide greater oversight of products imported from foreign firms where travel restrictions have postponed inspections.
- Facilitated entry of necessary personal protective equipment, by working with FDA centers to streamline the entry process for products meeting EUA and immediately-in-effect (IIE) enforcement guidance documents.
- Answered over 19,000 COVID-19 import related inquiries and facilitated over 1,300 COVID relief shipments (previously referred to as OWS).
- Coordinated with CBP to increase screening to address substandard and dangerous hand sanitizers and increase testing in ORA's Medical Products Laboratories. As a result, 71 foreign suppliers have been added to import alert 66-78, "Detention Without Physical Examination of Drugs, Based Upon Analytic Test Results" to deny future shipments from entering the United States.
- Migrated 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.
- Expanded long-standing information sharing with the Securities Exchange Commission (SEC) during the COVID-19 pandemic to mitigate risk of fraudulent products. This 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.
- Established an EUA investigation program in March 2021 to allow for rapid information gathering and feedback for products under EUA consideration.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$1,143,329,000	$1,063,123,000	$80,206,000
FY 2020 Actuals	$1,224,332,000	$1,123,417,000	$100,915,000
FY 2021 Actuals	$1,224,098,000	$1,130,376,000	$93,722,000
FY 2022 Annualized CR	$1,254,692,000	$1,130,523,000	$124,169,000
FY 2023 President's Budget	$1,363,223,000	$1,242,285,000	$120,938,000

Figure 38: Funding History

BUDGET REQUEST

The FY 2023 President's Budget for the Office of Regulatory Affairs Program is $1,363,223,000, of which $1,242,285,000 is budget authority and $120,938,000 is user fees. The budget authority is increased by $111,762,000 compared to the FY 2022 Annualized CR and User Fees decreased by $3,231,000. The FY 2023 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

Food Safety (+$24.1 million / 8 FTE)

Field: +$24.1 million / 8 FTE

The FY 2023 Budget Request includes an increase of $24.1 million to Enhance Food Safety and Nutrition, ensuring that the nation's food and feed supply is safe, sanitary, wholesome, and properly labeled, and that cosmetic products are safe and properly labeled. This mission becomes more challenging every year as globalization, advances in science and technology, and shifts in consumer expectations drive change throughout the food system.

New Era of Smarter Food Safety (+$2.8 million)

Field: +$2.8 million

The FY 2023 Budget will also strengthen data sharing and predictive analytics capabilities to support human and animal food safety. 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 also make investments to lay the foundations for improvements in data and information sharing with stakeholders including industry, academia, and regulatory partners with a vision towards user-friendly IT platforms for sharing and analyzing information.

Animal Food Safety Oversight (+$14.1 million / 8 FTE)

Field: +$14.1 million / 8 FTE (Field Animal Drugs and 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. FDA will also update inspection and enforcement programs, develop outreach and training initiatives, and devote resources to the analysis of expected and unknown animal food hazards. Animals have died and humans have been sickened because animal food has been contaminated by preventable hazards. FDA historically relied on states to conduct 80% of animal food safety inspections.

Data Modernization and Enhanced Technologies: Smarter Food Safety ($7.2 million)

Field: +7.2 million

FDA requires additional resources in FY 2023 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 predictive 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.

Medical Product Safety (+$10.0 million / 25 FTE)

Advancing the Goal of Ending the Opioid Crisis (+$10.0 million / 25 FTE)

Field: +$10.0 million / 25 FTE

ORA is requesting funding to expand the current 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. Under the 2018 Omnibus Spending Bill FDA did hire additional compliance officers, but the increased volume has taxed our compliance staff to a greater extent than anticipated, and this requested increase would lessen the burden on the compliance officers, who are also responsible for compliance and enforcement action for other types of imported products and FSVP Inspections.

Under the current IMF initiative, ORA has multiple laboratory supported subcomponents, inclusive of unapproved foreign drugs, counterfeit pharmaceuticals, health fraud, opioid testing, establishment of IMF mobile laboratories, field deployable toolkit development, training and deployment, and sample analyses related to criminal investigations. As the program matures, additional resources will be required to meet the increased volume and complexity of the samples. Additional resources are required for management and support of new or existing analytical tools deployed for field use, development of new analytical methods or strategies, 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 opioid and opioid products. This expanded investigation has involved tracking and tracing supply chain 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. These same resources could assist in label review and subject matter assistance at the IMFs.

Crosscutting (+$77.7 million / 111 FTE)

Capacity Building (+$12.5 million / 9 FTE)

Field: +$12.5 million / 9 FTE

The FY 2023 President's Budget includes $59.4 million Capacity Building, including $12.5 million for Field. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Public Health Employee Pay Costs (+$20.8 million)

Field: +$20.8 million

The FY 2023 President's Budget includes $51.9 million, including $20.8 million for Field, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Optimizing Inspectional Activities (+$33.8 million / 90 FTE)

Field: +$33.8 million / 90 FTE

The FY 2023 Budget includes $33.8 million in dedicated budget authority for inspections. With the expanding global market and complex supply chains there has been an increased need for foreign inspections of both food and medical products. As the US drug market shifted toward lower-priced generic drugs, manufacturers came under increasing cost pressures and found these efficiencies compelling reasons to locate more of their facilities overseas particularly in

developing parts of the world. ORA is the lead for the agency on foreign inspections and has been significant in those areas.

FDA's drug inspection program shifted from one focused heavily on U.S. based facilities through the early 2000s to a program that, since 2015, has conducted more foreign than domestic drug inspections. FDA's drug inspection program is now risk-based, and FDA prioritizes inspections for facilities deemed higher risk-based on specific, defined criteria. FDA achieves this foreign coverage by using a mixed investigator work force consisting of U.S. based investigators who perform both domestic and foreign inspections; a dedicated foreign cadre of U.S. based investigators who conduct foreign inspections exclusively; foreign office-based investigators who inspect facilities manufacturing drugs. The majority of foreign inspections are performed by domestic based staff. The increase in staffing will allow for increased inspectional oversight of facilities shipping to the U.S.

The request also includes funding to better position ORA to take advantage of technological advances in mobile platforms and analytics to support its inspectional operations. The technology investment includes modernization of its inspection platform to improve mobile data capture and automated report generation. The investment also includes hiring staff to manage and implement Artificial Intelligence (AI) and machine learning tools to identify the most significant public health risks requiring attention through unplanned work.

Data Modernization and Enhanced Technologies (+$10.6 million / 12 FTE)

Field: +$10.6 million / 12 FTE

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $10.6 million for Enterprise Technology and Data within the Field programs, 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.

USER FEES

Current Law User Fees: -$3.2 million

Field Foods: $213,000

Field Human Drugs: $1.2 million

Field Biologics: $8,000

Field Animal Drugs and Foods: $74,000

Field Devices: $238,000

Field Center for Tobacco: -$4.9 million

The Office of Regulatory Affairs Program request includes a decrease of $3.2 million for current law user fees authorized.

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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
214221: Percentage of Human and Animal Food significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2021: 94.8% 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 2021: 90.0% Target: 80% (Target Exceeded)	80%	80%	Maintain
234221: Percentage of Biologics significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2021: 86.7% Target: 70% (Target Exceeded)	70%	70%	Maintain
254221: Percentage of Medical Device and Radiological Health significant inspection violations which receive appropriate follow-up after regulatory action was taken. (Output)	FY 2021: 91.8% 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 2021: 75.3% Target: 65% (Target Exceeded)	65%	65%	Maintain
224222: Percentage of Human and Animal Drug follow-up inspections conducted due to	FY 2021: 57.8% Target: 55%	55%	55%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
regulatory action on significant inspection violations that moved toward compliance. (Outcome)	(Target Exceeded)			
234222: Percentage of Biologics follow-up inspections conducted due to regulatory action on significant inspection violations that moved toward compliance. (Outcome)	FY 2021: 80.0% 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 2021: 81.3% 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 2021: 100.0% Target: 65% (Target Exceeded)	65%	65%	Maintain
214206: Maintain accreditation for ORA labs. (Outcome)	FY 2021: 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 2021: 3,200 rad & 2,600 chem Target: 2,500 rad & 2,100 chem (Target Exceeded)	3,200 rad & 2,600 chem	3,200 rad & 2,600 chem	+ 700 rad & 400 chem

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

While COVID-19 continued to impact inspection activities throughout FY 2021, FDA did continue mission critical and prioritized inspections through July 2021. After July 2021, FDA resumed standard operations through the remainder of FY 2021 allowing FDA to meet and/or exceed the identified performance goals.

PROGRAM ACTIVITY DATA

Field Foods Program Workload and Outputs	FY 2021 Actuals[5]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***4,657***	***4,320***	***8,000***
Domestic Food Safety Program Inspections	2,629	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.	
Imported and Domestic Cheese Program Inspections	77		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	119		
Domestic Fish & Fishery Products (HACCP) Inspections	357		
Import (Seafood Program Including HACCP) Inspections	58		
Juice HACCP Inspection Program (HACCP)	66		
Interstate Travel Sanitation (ITS) Inspections	244		
Domestic Field Exams/Tests	669	*850*	25,006
Domestic Laboratory Samples Analyzed	7,677	*11,500*	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS[1]	***79***	***50***	***1,400***
All Foreign Inspections	*79*	*50*	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***4,736***	***4,370***	***9,400***
IMPORTS			
Import Field Exams/Tests[2]	*63,640*	*82,500*	168,200
Import Laboratory Samples Analyzed	*11,444*	*12,000*	35,300
Import Physical Exam Subtotal	**75,084**	**94,500**	**203,500**
Import Line Decisions	18,651,210	19,583,771	20,562,959
Percent of Import Lines Physically Examined	0.40%	0.48%	0.99%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***5,940***	***2,500***	***3,000***
State Contract Food Safety (Non HACCP) Inspections	5,276	4,090	5,000
State Contract Domestic Seafood HACCP Inspections	452	327	400
State Contract Juice HACCP	36	29	35
State Contract LACF/Acidified Food Inspections	89	61	75
State Contract Foods Funding	$13,334,560	$13,492,683	$13,627,610
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***10,676***	***6,870***	***12,400***

[1] The FY 2021 actual unique count of foreign inspections includes 77 OGPS inspections (57 for China, 2 for India, & 18 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.

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 39 - Field Foods Program Workload and Outputs

Field Cosmetics Program Workload and Outputs	FY 2021 Actuals[2]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***15***	***20***	***100***
Domestic Inspections	15	20	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***0***	***0***	***0***
Foreign Inspections	0	0	0
IMPORTS			
Import Field Exams/Tests[1]	2236	3,300	3,300
Import Laboratory Samples Analyzed	70	215	215
Import Physical Exam Subtotal	**2,306**	**3,515**	**3,515**
Import Line Decisions	3,060,422	3,121,630	3,184,063
Import Line Decisions	0.08%	0.11%	0.11%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***15***	***20***	***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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 40 - Field Cosmetics Program Workload and Outputs

Field Human Drugs Program Workload and Outputs	FY 2021 Actuals[4]	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***857***	***810***	***1,695***
Pre-Approval Inspections (NDA)	53	60	100
Pre-Approval Inspections (ANDA)	33	18	90
Bioresearch Monitoring Program Inspections	456	415	600
Drug Processing (GMP) Program Inspections	238	325	650
Compressed Medical Gas Manufacturers Inspections	8	15	50
Adverse Drug Events Project Inspections	28	25	88
OTC Monograph Project and Health Fraud Project Inspections	11	3	70
Compounding Inspections[1]	62	55	127
Domestic Laboratory Samples Analyzed	959	825	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***94***	***90***	***1300***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	23	11	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	18	16	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	34	24	255
Foreign Drug Processing (GMP) Program Inspections	22	44	900
Foreign Adverse Drug Events Project Inspections	0	1	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***951***	***900***	***3,055***
IMPORTS			
Import Field Exams/Tests	4,822	7,100	10,000
Import Laboratory Samples Analyzed	479	850	620
Import Physical Exam Subtotal	**5,301**	**7,950**	**10,620**
Import Line Decisions	1,003,661	1,023,734	1,044,209
Percent of Import Lines Physically Examined	0.53%	0.78%	1.10%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS [5]	***951***	***900***	***3055***

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

[2] The FY 2021 actual unique count of foreign inspections includes 34 OGPS inspections (25 for China, 9 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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

[5] Count of "Third Party" Foreign Inspections 28 (not included in Overall counts above)

Figure 41 - Field Human Drugs Program Workload and Outputs

Field Biologics Program Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***480***	***650***	***1,892***
Bioresearch Monitoring Program Inspections	96	75	100
Blood Bank Inspections	111	900	900
Source Plasma Inspections	78	115	190
Pre-License, Pre-Market Inspections	16	50	55
GMP Inspections	18	20	28
GMP (Device) Inspections	0	5	7
Human Tissue Inspections	161	300	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***2***	***15***	***47***
Bioresearch Monitoring Program Inspections	0	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	0	7	7
Pre-License, Pre-market Inspections	2	7	7
GMP Inspections (Biologics & Device)	0	5	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***482***	***665***	***1,939***
IMPORTS			
Import Field Exams/Tests	53	45	45
Import Line Decisions	177,977	181,537	185,167
Percent of Import Lines Physically Examined	0.03%	0.02%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***482***	***800***	***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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 42 - Field Biologics Program Workload and Outputs

Field Animal Drugs and Foods Program Workload and Outputs	FY 2021 Actuals[5]			FY 2022 Estimate			FY 2023 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 FOODS ESTABLISHMENT INSPECTIONS	***336***	***43***	***293***	***305***	***25***	***280***	***1,696***	***298***	***1,398***
Pre-Approval /BIMO Inspections	18	18	0	0	0	0	79	79	0
Drug Process and New ADF Program Inspections	26	26	0	55	55	0	175	175	0
BSE Inspections	59	0	59	105	0	105	1,205	0	1,205
Feed Contaminant Inspections	2	0	2	0	0	0	25	0	25
Illegal Residue Program Inspections	41	0	41	125	0	125	450	0	450
Feed Manufacturing Program Inspections	44	0	44	60	0	60	200	0	200
Domestic Laboratory Samples Analyzed	395	0	395	495	20	475	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FOODS ESTABLISHMENT INSPECTIONS1	***5***	***3***	***2***	***5***	***3***	***2***	***31***	***26***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	1	1	0	3	3	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	2	2	0	6	6	0	33	33	0
Foreign Feed Inspections	0	0	0	0	0	0	5	0	5
BSE Inspections	0	0	0	1	0	1	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FOODS ESTABLISHMENT INSPECTIONS	***344***	***46***	***298***	***310***	***28***	***282***	***1,727***	***324***	***1,403***
IMPORTS									
Import Field Exams/Tests	1,507	268	1239	1,500	500	1000	3,795	495	3,300
Import Laboratory Samples Analyzed	362	0	362	400	0	400	867	2	865
Import Physical Exam Subtotal	**1,869**	**268**	**1,601**	**1,900**	**500**	**1,400**	**4,662**	**497**	**4,165**
Import Line Decisions	550,811	79,275	471,536	578,352	83,239	495,113	607,269	87,401	519,868
Percent of Import Lines Physically Examined	0.34%	0.34%	0.34%	0.33%	0.60%	0.28%	0.77%	0.57%	0.80%
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***1,000***	***0***	***1,000***	***1,000***	***0***	***1,000***	***3,924***	***0***	***3,924***
State Contract Inspections: BSE	599	0	599	650	0	650	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	331	0	331	400	0	400	620	0	620
State Contract Inspections: Illegal Tissue Residue	0	0	0	0	0	0	0	0	0
State Contract Animal Feeds Funding	$2,689,277	0	$2,689,277	$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	0	$0
Total State Funding	**$2,689,277**	**$0**	**$2,689,277**	**$3,200,000**	**$0**	**$3,200,000**	**$3,296,000**	**$0**	**$3,296,000**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,344***	***46***	***1,298***	***1,310***	***28***	***1,282***	***5,651***	***324***	***5,327***

[1] The FY 2021 actual unique count of foreign inspections includes 4 OGPS inspections (4 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 scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

Figure 43 - Field Animal Drugs and Foods Program Workload and Outputs

Field Devices and Radiological Health Program Workload and Outputs	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***786***	***900***	***2,546***
Bioresearch Monitoring Program Inspections	72	70	300
Pre-Market Inspections	28	4	60
Post-Market Audit Inspections	18	2	60
GMP Inspections	342	75	1,400
Inspections (MQSA) FDA Domestic (non-VHA and VHA)	350	37	750
Domestic Radiological Health Inspections	12	4	50
Domestic Field Exams/Tests	0	2	100
Domestic Laboratory Samples Analyzed	124	72	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***6***	***5***	***613***
Foreign Bioresearch Monitoring Inspections	0	0	14
Foreign Pre-Market Inspections	1	0	30
Foreign Post-Market Audit Inspections	0	0	20
Foreign GMP Inspections	6	5	550
Foreign MQSA Inspections	0	0	14
Foreign Radiological Health Inspections	0	0	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***792***	***905***	***3,159***
Import Field Exams/Tests	7,076	16,650	19,800
Import Laboratory Samples Analyzed	82	310	670
Import Physical Exam Subtotal	**7,158**	**17,000**	**20,470**
Import Line Decisions	24,471,343	24,716,056	24,963,217
Percent of Import Lines Physically Examined	0.03%	0.08%	0.07%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS [2]	***7,914***	***7,020***	***7,880***
Inspections (MQSA) by State Contract	7,097	7,000	6,800
GMP Inspections by State Contract	31	20	20
State Contract Devices Funding	$80,850	$286,443	$286,443
State Contract Mammography Funding	$11,488,198	$11,240,003	$11,240,003
Total State Funding	**$11,569,048**	**$11,526,446**	**$11,526,446**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***8,706***	***7,925***	***11,039***

[1] The FY 2021 actual unique count of foreign inspections includes 6 OGPS inspections (6 for China)

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

3 Domestic MQSA Non-VHA and VHA Inpsections have been combined into one output line.

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

[5] In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA scaled back foreign and domestic inspection work and target its resources on the highest- risk facilities and industries during FY20 and FY21. ORA will continue to monitor progress throughout FY22.

[6] Count of "Third Party" Device Inspections (not included in Overall counts above) Foreign 4 and Domestic 3

Figure 44 - Field Devices and Radiological Health Program Workload and Outputs

TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Tobacco	**681,513**	**765,697**	**679,944**	**777,165**	**97,221**
Center	658,906	746,810	652,459	754,671	102,212
User Fees	658,906	746,810	652,459	754,671	102,212
Family Smoking Prevention and Tobacco Control Act	*658,906*	*746,810*	*652,459*	*654,671*	*2,212*
Expand tobacco products (Proposed)	---	---	---	*100,000*	*100,000*
Field	22,607	18,887	27,485	22,494	-4,991
Family Smoking Prevention and Tobacco Control Act	*22,607*	*18,887*	*27,485*	*22,494*	*-4,991*
FTE	**1,279**	**1,228**	**1,287**	**1,303**	**16**

Figure 45: Narrative by Activity

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,[146] and nearly 1,500 youth aged 12 to 17 smoke their first cigarette every day in the United States.[147] 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.

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.

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[146] 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.

[147] 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/

Figure 46 - Tobacco products and devices

Following publication of the final deeming rule, FDA announced an enforcement policy with staggered timeframes. Some of the requirements, such as the Federal minimum age of sale, were enforced immediately when the deeming rule took effect on August 8, 2016, while through an exercise of enforcement discretion, FDA temporarily deferred enforcement of other provisions such as premarket review of "new" tobacco products. FDA announced a new plan for tobacco and nicotine regulation in 2017, which included publication of a new compliance policy, which extended the compliance period for premarket review of deemed new tobacco products (that were on the market on August 8, 2016) to August 2021 and August 2022 (depending on the type of product). 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.[148] The 2019 National Youth Tobacco Survey (NYTS) results on e-cigarette use showed that 4.11 million high school and 1.24 million middle school students were current e-cigarette users (having used within the last 30 days) – with a majority reporting

[148] 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

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.[149] Published 2019 NYTS data in the *Journal of the American Medical Association (JAMA)*[150] showed that e-cigarettes remained 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, showed a decline in current e-cigarette use: 19.6 percent of high school students and 4.7 percent of middle school students were current e-cigarette users. According to the NYTS, in 2020, 1.73 million fewer U.S. youth used tobacco products compared to 2019. Despite the decline in current use, approximately 3.6 million U.S. youth 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 (from 2.4 to 26.5 percent among high school current e-cigarette users and from 3.0 percent to 15.2 percent among middle school current e-cigarette users).[151] The 2021 NYTS was fully conducted amid the continuing COVID-19 pandemic. Because of the changes in the way the survey was conducted, the results of the 2021 NYTS cannot be compared to findings from previous surveys. According to published data from the 2021 NYTS, approximately 2.06 million U.S. middle and high school students were estimated to be current e-cigarette users in 2021. Among current youth e-cigarette users, 84.7 percent used flavored e-cigarettes, and disposable e-cigarettes (53.7 percent) were the most commonly used device type.[152]

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.

The 2017 compliance policy for premarket review of deemed new tobacco products became the subject of litigation and in May 2019, the U.S. District Court for the District of Maryland vacated FDA's August 2017 compliance policy. In July 2019, the court issued a further order directing FDA to require applications for deemed new tobacco products such as e-cigarettes and other ENDS, cigars, pipe tobacco, and hookah that were on the market as of August 8, 2016, be

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[149] 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

[150] 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

[151] 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

[152] Park-Lee E, Ren C, Sawdey MD, et al. Notes from the Field: E-Cigarette Use Among Middle and High School Students - National Youth Tobacco Survey, United States, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(39):1387-1389

filed with FDA no later than 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 has taken action on 99 percent of the applications submitted by the September 9, 2020 deadline. FDA will continue working to review all pending and incoming applications of premarket applications for e-cigarettes and other new tobacco products.

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.

FDA remains committed to tackling the epidemic of youth vaping using a comprehensive approach which includes regulatory policy, compliance and enforcement, premarket review of new products, and public education. 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."[153] 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.

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

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 continued to exercise enforcement discretion for up to one year pending FDA review of the application, unless there was a negative action by FDA on such application. In addition, FDA has discretion to defer enforcement action against a particular product now that the one-year period for review has come to an end.

Since September 9, 2020, FDA is also prioritizing enforcement against ENDS products that are illegally marketed in the U.S. and not the subject of a pending premarket application. This includes products for which no application was submitted and those with a Marketing Denial Order.

Importantly, FDA's enforcement priorities are not a "ban" on flavored or cartridge-based ENDS. FDA has already accepted and taken action on 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.

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 finalized two 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. On October 5, 2021, FDA's final rules regarding Premarket Tobacco Product Applications (PMTA)[154] and the content and format of Substantial Equivalence (SE) Reports[155] published in the Federal Register. The finalization of these rules helps ensure that all future submissions contain the basic information needed to determine whether the new tobacco products meet the relevant premarket requirements to efficiently and effectively implement the Family Smoking Prevention and Tobacco Control Act. In addition, as described in the Unified Agenda, FDA is working towards a proposed rule regarding requiring manufacturers to establish tobacco product manufacturing practices.

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[154] https://www.federalregister.gov/documents/2021/10/05/2021-21011/premarket-tobacco-product-applications-and-recordkeeping-requirements

[155] https://www.federalregister.gov/documents/2021/10/05/2021-21009/content-and-format-of-substantial-equivalence-reports-food-and-drug-administration-actions-on

On April 29, 2021, FDA announced[156] 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 by the end of April 2022 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. These two tobacco product standards will help to significantly reduce youth initiation, increase the chances of smoking cessation among current smokers, and address health disparities experienced by communities of color, low-income populations, and LGBTQ+ individuals, all of whom are far more likely to use these tobacco products. Characterizing flavors in tobacco products, including menthol, enhance taste and make them easier to use. Menthol in particular masks the harshness and irritation of tobacco smoke and reduces initial aversive responses to smoking, particularly for young people.

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 percent smoke menthol cigarettes, compared to 30 percent 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.

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 percent 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 percent of cigarillo users and 56 percent 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 requires FDA to issue regulations requiring color graphics depicting the negative health consequences of smoking to accompany new textual warning statements on cigarette packages and in cigarette advertisements. On March 17, 2020, FDA issued a final rule[157] 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.

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[156] https://www.fda.gov/news-events/press-announcements/fda-commits-evidence-based-actions-aimed-saving-lives-and-preventing-future-generations-smokers

[157] https://www.federalregister.gov/documents/2020/03/18/2020-05223/tobacco-products-required-warnings-for-cigarette-packages-and-advertisements

The 11 finalized cigarette health warnings represent the most significant change to cigarette labels in more than 35 years and will considerably increase public understanding of the negative health consequences of smoking. In addition, FDA has issued a guidance to accompany the final rule. The "Required Warnings for Cigarette Packages and Advertisements: Small Entity Compliance Guide"[158] 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 are submitted for FDA review under one of these three marketing pathways:

- Premarket tobacco product application (PMTA)
- Report demonstrating substantial equivalence (SE Report) to an eligible predicate tobacco product
- Request for exemption from demonstrating substantial equivalence (EX REQ)

FDA continues to take steps to strengthen and educate the public on the tobacco product review process. This includes holding public meetings, issuing regulations and guidance, and providing other information to assist the public in understanding the process.

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).

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 Products," 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

[158] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/required-warnings-cigarette-packages-and-advertisements-small-entity-compliance-guide-revised

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.

On June 11, 2021, CTP hosted a live, virtual meeting about the general scientific review of applications submitted by September 9, 2020. The meeting focused on the application intake process, review progress, and allocation of review resources, and included time for audience questions.

In October 2021, FDA issued a final rule to set forth requirements related to the content, format, and review of PMTAs as part of the agency's continued commitment to its oversight of e-cigarettes and other tobacco products.[159] This final rule published in the Federal Register on October 5, 2021, with an effective date of November 4, 2021. The final rule helps to ensure that PMTAs contain sufficient information for evaluation such as details regarding the characteristics of a tobacco product and information on the product's potential public health benefits and harms. This rule also formalizes the general procedures the FDA follows when evaluating PMTAs, including application acceptance, application filing and inspections. It also outlines, among other things, requirements for submitting application amendments, the time for review, withdrawal of applications, postmarket reporting requirements for applicants that receive marketing granted orders, requirements for manufacturers to maintain records related to the legal marketing status of their tobacco products, the FDA's communications with an applicant and the FDA's disclosure procedures and electronic submission requirements. The final rule also explains how applicants may submit a supplemental PMTA or a resubmission, which would improve efficiency in certain situations by not requiring applicants to resubmit duplicative information.

To provide more clarity to applicants and support efficient and predictable review of SE Reports, FDA issued a final rule in October 2021, entitled "Content and Format of Substantial Equivalence Reports; Food and Drug Administration Actions on Substantial Equivalence Reports."[160] The final rule published in the Federal Register on October 5, 2021, with an effective date of November 4, 2021. The SE final rule provides additional information on the requirements for the content and format of SE Reports, allowing for greater predictability and efficiency for all stakeholders by providing applicants with a better understanding of the level of detail that an SE Report must contain for the FDA to evaluate the comparison of the new tobacco product to a predicate tobacco product. Additionally, the SE final rule establishes the general procedures FDA intends to follow when evaluating SE Reports. It also addresses the FDA's communications with the applicant, the retention of records that support the SE Report, confidentiality of an SE Report, how an applicant can amend or withdraw an SE Report, how an applicant may transfer ownership of an SE Report to a new applicant and electronic submission of the SE Report and amendments.

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[159] https://www.federalregister.gov/documents/2021/10/05/2021-21011/premarket-tobacco-product-applications-and-recordkeeping-requirements

[160] https://www.federalregister.gov/documents/2021/10/05/2021-21009/content-and-format-of-substantial-equivalence-reports-food-and-drug-administration-actions-on

Similarly, FDA intends to issue a proposed rule that would establish basic content and format requirements for modified risk tobacco product applications (MRTPAs). The proposed rule would help to ensure that MRTPAs contain sufficient information for FDA to determine whether it should issue an order for a modified risk tobacco product (MRTP).

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 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 placed stringent restrictions on how the products are marketed – particularly via websites and through social media platforms.

On December 7, 2020, FDA announced it authorized the marketing of an updated version of the non-combusted tobacco heat stick system holder and charger that complemented the earlier authorized non-combusted cigarette products that had been issued marketing granted orders in April 2019.

On October 12, 2021, FDA announced it authorized the marketing of three new tobacco products, marking the first set of ENDS products ever to be authorized by the FDA. Following FDA's robust, scientific premarket evaluation, it was determined that marketing these tobacco-flavored products is appropriate for the protection of the public health because, among several key considerations, the agency determined that study participants who used only the authorized products were exposed to fewer harmful and potentially harmful constituents from aerosols compared to users of combusted cigarettes. The toxicological assessment also found the authorized products' aerosols are significantly less toxic than combusted cigarettes based on available data comparisons and results of nonclinical studies. Additionally, FDA determined that the potential benefit to smokers who switch completely or significantly reduce their cigarette use, would outweigh the risk to youth, provided the applicant follows post-marketing requirements aimed at reducing youth exposure and access to the products. This authorization imposes strict marketing restrictions on the company, including digital advertising restrictions as well as radio

and television advertising restrictions, to greatly reduce the potential for youth exposure to tobacco advertising for these products.

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[161] 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 an order permitting the product to be legally marketed in the United States.

In FY2019, 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 FY2019. These performance measures are similar to those used for Regular SE Reports but are tailored for the unique circumstances of provisional SE reports.

In FY2020, FDA met the performance goals for statutory tobacco products to issue Acknowledgement (ACK), Refuse-to-Accept (RTA), or Withdrawal ACK letter within 21 days for Regular SE Reports and Exemption Requests. FDA did not meet the performance goals to review and act on Regular SE Reports within 90 days, Provisional SE Reports within 120 days, or EX Requests within 60 days as resources were redirected to preparations for the influx of PMTA, SE, and EX submissions that were expected to be submitted in September of 2020. In FY2020 and FY2021, FDA received and reviewed an unprecedented number of applications that cover more than 8 million tobacco products. FDA issued final actions in FY2021 for 7.6 million tobacco products through the PMTA pathway (far exceeding the almost 400 final actions from FY2020 under this pathway), for over 1,000 tobacco products through the EX pathway (2x increase over FY2020) and over 2,300 tobacco products through the SE pathway (nearly 5x increase over FY2020).

FDA regularly provides premarket review metrics on the agency's website at: https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/tobacco-product-applications-metrics-reporting.

161 http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm

FDA continues scientific review of provisional SE Reports.[162] 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 comprehensive manual for manufacturers preparing or anticipating review of a tobacco product application, these documents can serve as a resource to manufacturers.

Modified Risk Tobacco 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. A MRTP is any tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products.

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 limit 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

[162] 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.

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, PMTAs and MRTPAs through October 31, 2021. Due to the large volume of PMTAs received, the numbers for PMTAs are expected to change as FDA continues to process applications submitted after September 9, 2020. FDA has processed submissions that cover over 8 million products under the PMTA pathway. This figure includes 1.3 million products that were the subject of PMTA applications submitted after September 9, 2020.

On August 9, 2021, FDA issued a Refuse to File (RTF) letter to JD Nova Group LLC notifying the company that their PMTAs for 4.5 million of their products do not meet the filing requirements for new tobacco products seeking marketing orders. As a result of this RTF action, the company must remove these products from the market or risk enforcement action by FDA.

On August 26, 2021, FDA issued the first marketing denial orders (MDOs) for ENDS products after determining the applications for about 55,000 flavored ENDS products lacked sufficient evidence that these products have a benefit to adult smokers sufficient to overcome the public health threat posed by the well-documented alarming levels of youth use of such products.

As of November 1, 2021, FDA has issued over 340 MDOs for more than 1.2 million tobacco products.

FDA is posting expanded data on its 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, FDA is 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 with each update, more details will be provided on the agency's progress on reviewing premarket applications. The new website includes the following:

- 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 [163]	Cumulative through 10/31/2021				
		Exemption Requests	Regular SE Reports	Provisional SE Reports	Premarket Tobacco Product Applications	Modified Risk Tobacco Product Applications
Received	Cigarettes	1,043	1,532	2,392	18	18
	Roll-Your-Own	27	1,180	646	4	0
	Smokeless	62	511	589	14	19
	ENDS	0	2	18	8,056,566	14
	Cigars	347	3,283	0	15	0
	Pipe Tobacco Products	6	1,820	0	12	0
	Waterpipe Tobacco Products	1,693	2,828	0	75	0
	Other	0	3	0	679	0
	Total	3,178	11,159	3,645	8,057,383	51
Open	Cigarettes	212	168	394	5	6
	Roll-Your-Own	2	131	13	0	0
	Smokeless	7	94	76	0	7
	ENDS	0	0	0	293,176	0
	Cigars	165	2,913	0	10	0
	Pipe Tobacco Products	6	1,418	0	12	0
	Waterpipe Tobacco Products	968	876	0	0	0
	Other	0	1	0	213	0
	Total	1,360	5,601	483	293,416	13
Closed [164]	Cigarettes	831	1,364	1,998	13	12
	Roll-Your-Own	25	1,049	633	4	0
	Smokeless	55	417	513	14	12

[163] Other includes tobacco products that are not defined (e.g., nicotine gel, dissolvable products from extracts, tobacco-derived nicotine discs) and products not under CTP jurisdiction.

[164] 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.

Application Status	Product Class[163]	Cumulative through 10/31/2021				
	ENDS	0	2	18	7,763,390	14
	Cigars	182	370	0	5	0
	Pipe Tobacco Products	0	402	0	0	0
	Waterpipe Tobacco Products	725	1,952	0	75	0
	Other	0	2	0	466	0
	Total	1,818	5,558	3,162	7,763,967	38

Research

FDA invests in research to inform regulatory actions by addressing scientific knowledge gaps and adding to the evidence-based knowledge. The regulatory research informs FDA's tobacco regulatory activities and helps FDA better understand tobacco use and associated risks which supports FDA's mandate to reduce the public health burden of tobacco product use in the United States. In FY2021, FDA invested more than $234.0 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 or switch to tobacco products that are potentially less harmful. Research priorities address the following Scientific Domains:

- Chemistry and Engineering: understanding the chemical 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.

NIH Tobacco Regulatory Science Program (TRSP)

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 FY2021, FDA funded more than 120 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 from use of tobacco products
- Varying nicotine levels and other constituents' effects on initiation, dependence, and quitting
- Studying the impact of flavors 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[165] 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.

[165] 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 47 Population Assessment of Tobacco and Health logo

Data are 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 FY2017 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 11,000 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 9,000 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 6 data collection launched March 2021 and is scheduled to be completed by the end of 2021. Wave 7 is scheduled to launch in 2022.

Wave 5 questionnaire data were released to researchers February 2021 and to the public October 2021. Initial Wave 4 biomarker data were released to researchers in August 2020 with additional biomarker data released June 2021. Data from Special Collection Wave 5.5 and the PATH-ATS are scheduled for release to researchers Spring 2022 and to the public Fall 2022.

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 including chemical and physical testing of tobacco filler, e-liquid, smoke, and aerosol. Additional specialized tobacco testing support activities have also been established at the Winchester Engineering and Analytical Center, which supports engineering and battery safety testing for electronic nicotine delivery device and endotoxin testing in e-liquids, and at the Forensic Chemistry Center, which supports tobacco product testing for counterfeit markers, both chemical and physical, specialized method development (e.g. synthetic nicotine), as well as testing associated with adverse events and emergency responses (i.e., EVALI).

CTP partners with FDA's National Center for Toxicological Research (NCTR) and the Center for Drug Evaluation and Research (CDER) to understand the toxicity of tobacco product exposure (i.e., e-cigarettes) via cell culture and animal models.

In addition, CTP funds research contracts to understand the physical and chemical characteristics of regulated products (i.e., chemical characteristics of e-cigarettes aerosols by device type).

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. NYTS survey data allows FDA to monitor youth awareness of, susceptibility to, experimentation with, and use of, a wide range of tobacco products. 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[166]. On November 5, 2019, data from this survey were published in the *Journal of the American Medical Association (JAMA)*[167] 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.[168] On October 1, 2021, findings from the 2021 NYTS, fully conducted amid the ongoing COVID-19 pandemic, were published and indicated that an estimated 2.06 million U.S. middle and high school students reported currently using e-cigarettes in 2021. The majority of current youth e-cigarette users reported flavored e-cigarette use (84.7 percent) and disposables were the most often used device type (53.7 percent); in addition, among current e-cigarette users, 39.4 percent reported frequent e-cigarette use (≥20 days) and 24.6 percent reported daily use during the past 30 days.[169]

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

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[166] 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

[167] 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

[168] 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

[169] Park-Lee E, Ren C, Sawdey MD, et al. Notes from the Field: E-Cigarette Use Among Middle and High School Students - National Youth Tobacco Survey, United States, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(39):1387-1389

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 the National Death Index 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 with health expenditure data from the Centers for Medicare and Medicaid Services (CMS) and cancer incidence data from NCI's Surveillance, Epidemiology, and End Results 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 shop inspections ultimately through the end of that fiscal year.

In FY 2021, tobacco manufacturer, vape, and retailer inspections resumed on a limited basis in areas where the spread of COVID-19 was less prevalent, increasing throughout the year. To guide this work, FDA activated the Base-Case Scenario: Gradual Transition to Standard Operations detailed in the agency's Resiliency Roadmap. 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, 2020, 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:

- Conducted over 28,000 retail inspections and issued more than 1,900 warning letters and civil money penalties during the COVID-19 pandemic while working to protect the health and safety of all stakeholders involved in the compliance check process
- Conducted over 230 tobacco manufacturing inspections, investigations and Remote Regulatory Assessments (RRAs) and over 650 vape shop inspections
- Conducted investigations involving thousands of websites resulting in warning letters to manufacturers, importers, and vape shops for illegally marketing over 130 unauthorized ENDS products
- Issued over 180 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 companies that received those warning letters have over 17 million products listed with FDA
- Issued warning letters to more than 40 companies for continuing to unlawfully market ENDS products that received negative marketing orders from FDA (i.e., Marketing Denial Orders, Refuse to Accept, and/or Refuse to File)

- Refused admission into the U.S. over 100 shipments of ENDS products, including disposables, worth tens of thousands of dollars, for violations of the FD&C Act
- In collaboration with U.S. Customs and Border Protection, seized more than $1.5 million worth of unauthorized ENDS products coming from China.

Figure 48 - Examples of unauthorized ENDS products targeted to minors.

In March 2021, FDA also sent official requests to four e-cigarette companies – 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.

Tobacco Retailer Inspection Program

As of October 31, 2021, FDA has contracts for tobacco retailer compliance check inspections in 56 states and territories. As mentioned above, a partial stop work order was in place from March through September 2020 as a safety measure due to the COVID-19 pandemic. In FY 2021, retailer inspections resumed on a limited basis in areas where the spread of COVID-19 was less prevalent and increased throughout the fiscal year. 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 utilizes approximately 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 2021 Actuals	FY 2022 (as of 10/31/2021)	Total Since the Program's Inception (as of 10/31/2021)
Retailer Inspections	28,803	5,915	1,235,992
Total Warning Letters	1,902	1,115	101,036
Warning Letters Resulting from the Sale of ENDS Products to Minors	1,028	522	13,112
Total Civil Money Penalties	11	0	25,831
Civil Money Penalties Resulting from the Sale of ENDS Products to Minors	2	0	2,057
No-Tobacco-Sale-Orders	1	0	220

Figure 49 - The number of Civil Money Penalty Complaints filed by the Center for Tobacco Products in FY 2021

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 (CCI) Notice, which quickly informs the retailer that a potentially violative inspection occurred at the establishment. FDA will review the evidence obtained during the inspection to determine whether there was a violation of federal law. If a violation occurred, the retailer will be notified of the violation(s) and be provided further information and instructions. In addition, FDA conducts undercover online inspections to determine whether online retailers are in compliance with the law. Violation(s) may result in an advisory or enforcement action such as a Warning Letter or Civil Money Penalty.

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.[170] 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 January 2021, CTP added a new poster and "This Is Our Watch"-branded stickers, featuring the new federal minimum age of 21, to CTP's Exchange Lab for retailers to order for their stores.

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 through CTP's coordination with ORA. FDA also facilitates inspections at vape shops using contracted inspectors. Since the inception of the Tobacco Program's manufacturer inspection activities through October 31, 2021, CTP has overseen the completion of more than 2,600 inspections of vape shops to verify whether they were engaged in manufacturing activities, and ORA has completed over 950 routine biennial inspections and 25 RRAs of tobacco product manufacturers. As mentioned above, in March 2020, FDA temporarily postponed manufacturing inspections, including tobacco product manufacturers, due to the COVID-19 pandemic and the related partial stop work order for inspection contracts impacted 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, or RRAs, 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 October 31, 2021, FDA has issued over 1,000 warning letters as a result of these surveillance activities. This includes issuance of 115 warning letters in FY 2021. FDA also conducts investigations of events where free samples of tobacco products are distributed and events sponsored by the tobacco industry to ensure compliance with the Tobacco Control Act.

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[170] https://digitalmedia.hhs.gov/tobacco/print_materials/search.protocol=https?page=1&tag=This+Is+Our+Watch

Office of Small Business Assistance (OSBA)

CTP's OSBA informs small businesses of existing guidances, regulations, and submission pathways through publications and online webinars. CTP has produced more than 80 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

Public education campaigns are a proven, evidence-based component to a comprehensive tobacco control effort. Under the Tobacco Control Act, FDA has the authority to educate the public about the dangers of using tobacco products and has implemented multiple public education efforts designed to reduce tobacco initiation, disrupt progression to sustained use and encourage cessation by focusing on key populations who remained vulnerable to using tobacco in all its forms.

Since FDA launched its first public education effort to prevent smoking among youth in 2014, the tobacco landscape has changed dramatically with the introduction of e-cigarettes and the escalating rates of youth e-cigarette use over time. National data showed alarming increases of youth use of e-cigarettes and increases of youth use of cigars, cigarillos, and little cigars as well as historic decreases of youth use of cigarettes. In response to shifting patterns of use, FDA has aligned our public education efforts to address the tobacco products most used by youth, beginning e-cigarette prevention education in late 2017 while continuing to educate youth on the harms of cigarette use – which accounts for a large share of the preventable disease and death in the United States.

"The Real Cost" cigarette prevention campaign has been proven to prevent up to 587,000 teens from initiating smoking, thereby saving the country more than $53.0 billion in future smoking-related costs. The campaign realized a cost savings of $180 for every dollar of the nearly $250.0 million invested in the first two years of the effort. However, in order to replicate comparable levels paid media in a mass-market effort that is needed to effectively reach all teens and drive down youth vaping rates, FDA has sunset four of our original public education efforts targeting discrete audiences and different types of tobacco product usage - "The Real Cost" Smokeless, "Fresh Empire," "This Free Life," and "Every Try Counts" campaigns. Given our current budget levels, we were not able to achieve optimal paid media reach levels across all our efforts and therefore prioritized youth vaping prevention as our main public education goal. Should additional funding be provided in the future to address initiation and cessation of various types of combustible and non-combustible products, FDA would be able to again target unique, vulnerable populations to prevent initiation, address addiction and encourage cessation, via evidence-based efforts designed to change knowledge, attitudes, and beliefs about using tobacco products.

FDA remains committed to decreasing the harmful effects of tobacco products among at-risk populations. The agency will continue to provide free prevention and cessation resources to stakeholders and conduct foundational research on other tobacco products that pose particular

risk to vulnerable populations and have shown recent increases in youth use, such as little cigars and cigarillos.

FDA's tobacco public education campaigns:

Campaigns	Date of Implementation	Description
"The Real Cost" Cigarette Campaign	February 2014-Current	Educates at-risk youth aged 12 to 17 about the harmful effects of cigarette use.
"The Real Cost" Smokeless Campaign	April 2016-December 2020	Educated 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-Current	Educates at-risk youth aged 12 to 17 about the harmful effects of e-cigarette use.
"Fresh Empire" Campaign	May 2015-June 2020	Educated at-risk African American, Hispanic, and Asian American/ Pacific Islander youth ages 12 to 17 about the harmful effects of cigarette use.
"This Free Life" Campaign	May 2016-February 2020	Educated Lesbian, Gay, Bisexual, and Transgender (LGBT) young adults aged 18 to 24 about the harmful effects of cigarette use.
"Every Try Counts" Campaign	January 2018-April 2020	Encouraged cigarette smokers to quit through messages of support that underscore the health benefits of quitting. Targeted smokers ages 25 to 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. FDA began e-cigarette messaging in late 2017.

Figure 50 - "The Real Cost" Campaign logo

In September 2018, FDA launched "The Real Cost" E-Cigarette Campaign to prevent youth e-cigarette use and continues to be FDA's highest public education priority. 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.

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 16 billion views from teen exposure to paid media messages and high online engagement. Across social media platforms, FDA has engaged teen audiences with more than 4.2 million likes, over 368,000 shares, and over 94,000 comments. Additionally, on the campaign's social media channels approximately 10 percent 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 co-developed two vaping cessation resources for teens to be added on the Teen.SmokeFree.gov website. The first resource was cessation content that focused on comprehensive behavioral techniques to help teens deal with cravings or stress, navigate peer pressure, prepare to quit, and make it through their quit day. Since the content launched in July 2019, there have been over 2 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 second resource was a vaping quit plan builder; an interactive, mobile-optimized tool designed to help teens develop a comprehensive, personalized "road map" for quitting e-cigarettes. Since the tool launched in July 2020, 25 percent of the 34,000 completed vaping quit plans were directly attributed to promotion from "The Real Cost."

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. FDA continues to provide national paid media messages through digital media platforms such as YouTube, while 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 and plans to test new messages during the fall of 2021.

Since its launch, "The Real Cost" Cigarettes Prevention Campaign has shown positive results for reach and engagement. Over the past eight years, the campaign has reached up to 85 percent of teenagers nationwide and has generated over 22 billion teen views from the paid media. Across social media platforms, the FDA has engaged teen audiences with more than 4.5 million likes, over 1 million shares, and over 407,000 comments.

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.

This effort is one of the four campaigns that was sunset, and FDA will continue to provide smokeless tobacco prevention messaging and resources for stakeholders. 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.

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 launched in May 2015 and sunset in June 2020. The campaign was designed to educate 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 addiction caused by cigarette smoking.

Figure 51 – "Fresh Empire" Campaign logo

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. Paid media efforts for "Fresh Empire" have ended and no additional metrics will be reported for this effort in the

future. 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 vulnerable sub-populations for future prevention efforts.

This Free Life

The "This Free Life" campaign was launched in May 2016 and sunset in February 2020. Lesbian, Gay, Bisexual, and Transgender (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 52 – "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.

This campaign has ended, and no additional metrics will be reported for this effort. 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 use.

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 "Every Try Counts" campaign was launched in January 2018 and sunset in 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

Figure 53 – "Every Try Counts" Campaign logo

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. This campaign has ended, and no additional metrics will be reported for "Every Try Counts."

While there will be no continued paid media efforts for "Every Try Counts", FDA plans to continue to develop a range of education materials for adults that message on the benefits of cessation and address nicotine misperceptions. The materials will include cessation messages for young adult and adult smokers and feature tailored content to reach LGBTQ+ audiences who remain at higher risk for tobacco use. Materials will be available in English and Spanish, and 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.

Cigarette cessation materials are available for use via CTP's content sharing platform, the Exchange Lab. The Exchange Lab provides access to cessation free 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.

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.

"The Real Cost" (E-cigarettes & Cigarettes)

FDA implements 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, beliefs, intentions, and behaviors.

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 $53.0 billion by reducing smoking-related costs like early loss of life, costly medical care, lost wages, lower productivity, and increased disability.

The latest wave of outcome evaluation results assessing the impact of "The Real Cost" E-cigarette and "The Real Cost" cigarette prevention campaign is promising, indicating that increased exposure to The Real Cost ads would increase population-level shifts in youth's negative beliefs about e-cigarettes and cigarettes. In addition, recent outcome evaluation data showed that approximately 79 percent of youth were aware of at least one campaign ad from

"The Real Cost" E-Cigarette Campaign and 75 percent 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.

The FDA will continue to assess the impact of "The Real Cost" on key outcomes, including increasing perceptions of risk and knowledge of the harms caused by e-cigarette use.

"The Real Cost" (Smokeless)

To evaluate the impact of "The Real Cost" Smokeless campaign, FDA implemented a 3-year randomized controlled longitudinal study. The study included a baseline survey, with four waves of data over a 4-year period. Data were collected from males aged 11 to 16 years old at baseline targeted by the campaign who lived in the rural segments of 30 media markets (15 treatment markets and 15 control).

Outcome evaluation results demonstrate significant success. "The Real Cost" Smokeless campaign influenced beliefs and attitudes among older boys in the 15 treatment media markets, increasing understanding of the harms of smokeless tobacco use. Changes in campaign-targeted beliefs and attitudes have historically been shown to be predictive of downstream behavior change. In addition, study results show that "The Real Cost" Smokeless campaign attained high levels of ad awareness and those who had increased exposure to the campaign had increased agreement with selected campaign-targeted attitudes and beliefs with negative attitudes toward smokeless tobacco.

"Fresh Empire"

FDA designed and implemented a repeated cross-sectional survey to evaluate the "Fresh Empire" campaign. The study involved 6 waves of data collection with youth surveyed approximately every 6 months over a 4-year period. Data were collected from youth aged 12 to 18 targeted by the campaign who lived in one of the 30 evaluation markets, a subset of the 36 campaign markets.

Outcome evaluation study results show that "Fresh Empire" was successful in reaching a high level of youth within the campaign target and was very well received by those youth. Brand awareness increased significantly over time and brand equity was consistently high throughout the campaign. Awareness of "Fresh Empire" video ads was also consistently high throughout the campaign. The campaign had a modest effect on changing tobacco-related attitudes and beliefs among the campaign-target audience. The FDA intends to build on the successes of "Fresh Empire" to inform future public education efforts aimed at preventing and reducing tobacco use among black, Hispanic, and Asian-American youth.

"This Free Life"

To evaluate the impact of "This Free Life," FDA implemented a market-level treatment-control study in 2016 that included a baseline survey, with six follow-up surveys conducted approximately 6 months apart over the course of the 3-year campaign. All evaluation participants self-identified as lesbian, gay, bisexual and transgender (LGBT) and lived in one of

24 designated market areas (12 campaign, 12 control) with a high prevalence of LGBT young adults who are occasional smokers.

Outcome evaluation study results show that "This Free Life" was successful in reaching a high-level of LGBT young adults and was very well received by the audience. Brand and ad awareness peaked in treatment markets approximately 2.5 years into the 3- year campaign and were significantly higher in treatment than control markets. Brand equity and ad receptivity were generally high and similar across LGBT subgroups. The campaign had a modest effect on changing tobacco-related attitudes and beliefs among the campaign-target audience. "This Free Life" was unique as the first large-scale LGBT focused tobacco public education campaign and demonstrated significant success in FDA's ability to reach and appeal to a discrete and vulnerable sub-population with historically higher rates of tobacco use in comparison to their heterosexual/straight peers.

Collaboration with 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 each year to more than 1.3 million educators and have reached an estimated 5.7 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. The e-cigarette prevention poster content surpassed expectations by receiving nearly 7,000 entries from middle and high school students. The winners included four middle school and four high school students from across the U.S. FDA continues to identify ways in which to work with Scholastic to provide free educational resources to middle and high school teachers about the harms associated with e-cigarette use.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$686,991,000	---	$686,991,000
FY 2020 Actuals	$752,921,000	---	$752,921,000
FY 2021 Actuals	$765,697,000	---	$765,697,000
FY 2022 Annualized CR	$679,944,000	---	$679,944,000
FY 2023 President's Budget	$777,165,000	---	$777,165,000

Figure 54: Funding History

BUDGET REQUEST

The FY 2023 Budget Request is $777,165,000 all from user fees. This amount is $100,000,000 above the FY 2023 level authorized in the Tobacco Control Act less the amounts for GSA Rent, FDA Headquarters, FDA White Oak Campus, and Other Rent and Rent Related, which are

shown in their own sections of the budget request. This amount is $97,221,000 above the FY 2022 Annualized CR. The Center for Tobacco Products amount in this request is $754,671,000.

Currently, the Tobacco Control Act does not provide a means for FDA calculation of user fees for ENDS products – which include e-cigarettes - and certain other deemed products. These products represent an increasing share of 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 help FDA bolster compliance and enforcement efforts for all tobacco products and expand public education campaigns and science and research programs, as it works to address substance use and to protect consumers from the dangers of tobacco use. For public education campaigns and scientific research, CTP has reallocated funds towards ENDS public education and scientific research that would have otherwise been invested toward other activities for various tobacco products, such as cigarettes. In other areas, such as the retailer inspection program, CTP utilized existing programs and funds, to include ENDS products, in addition to other regulated tobacco products.

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 2023, CTP will continue to take action to protect American families, charting a new course for comprehensive change, and continue to focus on the Center's six strategic priorities:

- Comprehensive Nicotine 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:

- 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 tobacco product manufacturing practices and MRTPs
- Working toward issuing proposed product standards to ban menthol as a characterizing flavor in cigarettes and ban all characterizing flavors (including menthol) in cigars.

Comprehensive Nicotine 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[171] tobacco products:

- By demonstrating they are appropriate for protection of the public health, or
- By demonstrating substantial equivalence[172] to eligible 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 issued final rules on Premarket Tobacco Product Applications[173] and the content and format of Substantial Equivalence Reports.[174] The effective date for both rules was November 4, 2021. Work also continues on other foundational rules such as a proposed rule that would address tobacco product manufacturing practices and a proposed rule that would establish content and format requirements for Modified Risk Tobacco Product Applications. Also, FDA has issued draft guidance entitled "Tobacco Products: Principles for Designing and Conducting Tobacco

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[171] 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.

[172] 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.

[173] https://www.federalregister.gov/documents/2021/10/05/2021-21011/premarket-tobacco-product-applications-and-recordkeeping-requirements

[174] https://www.federalregister.gov/documents/2021/10/05/2021-21009/content-and-format-of-substantial-equivalence-reports-food-and-drug-administration-actions-on

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.

In addition to developing rules and guidances, 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. Based on this authority, FDA is working towards issuing proposed product standards to ban menthol as a characterizing flavor in cigarettes and ban all characterizing flavors (including menthol) in cigars.

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 susceptible to use. FDA began prevention efforts to address youth use of vaping products in 2017 through "The Real Cost" campaign and prioritizes 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 at-risk and vulnerable populations 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 2023, FDA will continue to:

- Implement campaigns designed to reach at-risk and vulnerable populations – especially young people – with messages about the dangers of using tobacco products
- Continue 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 formative research and outcome evaluation studies
- Develop interactive digital communication technologies and products such as CTP's content sharing platform
- 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 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 received a negative marketing order from the agency
- Prioritizing the enforcement of unauthorized ENDS on the market to prevent youth use of these products
- Utilizing the Base-Case Scenario: Gradual Transition to Standard Operations detailed in the agency's Resiliency Roadmap to guide inspection work
- Continuing inspections and investigations at brick and mortar locations, to the extent possible
- Closely investigating manufacturers' internet storefronts and distribution practices and taking enforcement actions if violations of the restrictions, including online sales to minors, are found
- Conducting inspections of tobacco manufacturing facilities to the extent possible and remote regulatory assessments when necessary
- Inspecting vape shops to ensure that they are in compliance with the requirements of the FD&C Act and regulations
- Enforcing sales, distribution, marketing, promotion, advertising, and labeling requirements
- Investigating whether manufacturers claiming to use synthetic nicotine may be marketing violative products, and exploring how to best address the growing number of products where the jurisdiction is under review due to the source of nicotine
- 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. FDA is committed to diversity, equity, inclusion, and accessibility to cultivate an engaged workforce that reflects the country it serves.

Additional Support Activities

FDA will continue to:

- Partner with other agencies and centers, 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 through 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
- Examine the prevalence of tobacco product use among middle and high school students and the prevalence of e-cigarette use among youth, supporting the Commissioner's Youth

Tobacco Prevention Plan, a key component of the agency's Comprehensive Plan for Tobacco and Nicotine Regulation

- 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, along with research and administrative activities to improve management and analysis of scientific 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 in an evolving marketplace.

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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
280005: Total number of compliance check inspections of retail establishments in States under contract. (Outcome)	FY 2021: 28,803 Target: 10,000 (Target Exceeded)	75,000	90,000	+15,000
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 2020: 56% Target: 80% (Target Not Met) see "Regular SE Reports" section below for explanation	80%	80%	Maintain
280007: Educate at-risk youth (12-17 year olds) about the harmful effects of tobacco use. (Output)	FY 2021: 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. Prior to FY 2020, FDA consistently conducted well over 100,000 inspections each fiscal year. In response to the COVID-19 pandemic, a partial stop work order for retailer inspections was put in place from March through September 2020. In FY 2021, FDA lowered its target to 10,000, and resumed retailer inspections on a limited basis in areas where the spread of COVID-19 was less prevalent and was able to perform 28,803 retailer inspections. In FY 2022 and 2023, FDA expects jurisdictions and private entities to continue to contract with FDA to conduct inspections. However, while FDA has increased the FY 2022 and FY 2023 targets, we anticipate that some contractors may have significant challenges related to the pandemic and resource constraints, so we don't expect to be back to pre-pandemic levels.

REGULAR SE REPORTS

The performance measure "review and act on" Regular SE Reports within 90 days of FDA receipt includes issuing a Deficiency letter (deficiency notification), Cancellation, Closure, Environmental Information Request letter, Substantial Equivalence (SE) Order, or Not Substantially Equivalent (NSE) Order and applies to cigarettes, cigarette tobacco, smokeless

tobacco, and roll-your-own tobacco products. Beginning in FY 2020, there was an exponential increase in the number of Premarket Tobacco Product Applications (PMTA), SE, and Exemption Request (EX) submissions. This influx of applications, which covered over eight million deemed products, was the result of a court ordered deadline 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 September 9, 2020. Due to the large increase in the volume of applications received, FDA did not meet the FY 2020 target for Regular SE Reports. At this time, FDA has decided to keep the FY 2022 and 2023 targets at 80%, despite the impact of the influx of applications in FY 2020. The 80% target is important to stay consistent with other areas where this goal is reported, and FDA believes the FY 2022 target of 80% is still a valid target and plans to meet this target when review times for Regular SE Reports return to normal.

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 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
Tobacco Retailer Inspections			
Number of Inspections	28,803	75,000	90,000
Tobacco Manufacture Inspections			
Number of Inspections [1,2]	257	750	850

[1] All estimates have been decreased due to interruptions in work related to COVID-19.

[2] Generally, 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 2021 actuals and outyear estimates include vape manufacturer inspections conducted by contractors.

Figure 55: CTP Workload and Outputs

FDA HEADQUARTERS

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
FDA Headquarters	**319,572**	**313,207**	**319,374**	**357,616**	**38,242**
Budget Authority 1/	***194,951***	***193,213***	***194,256***	***228,063***	***33,807***
User Fees	***124,621***	***119,994***	***125,118***	***129,553***	***4,435***
Prescription Drug (PDUFA)	*60,354*	*66,642*	*59,725*	*61,423*	*1,698*
Medical Device (MDUFA)	*10,459*	*9,146*	*10,652*	*10,912*	*260*
Generic Drug (GDUFA)	*34,575*	*32,821*	*35,561*	*36,841*	*1,280*
Biosimilars (BsUFA)	*1,417*	*1,617*	*1,009*	*1,032*	*23*
Animal Drug (ADUFA)	*1,172*	*962*	*937*	*957*	*20*
Animal Generic Drug (AGDUFA)	*740*	*668*	*788*	*963*	*175*
Family Smoking Prevention and Tobacco Control Act	*14,485*	*8,138*	*14,999*	*15,949*	*950*
Mammography Quality Standards Act (MQSA)	*76*	*---*	*77*	*79*	*2*
Food and Feed Recall	*78*	*---*	*80*	*81*	*1*
Food Reinspection	*499*	*---*	*509*	*519*	*10*
Voluntary Qualified Importer Program	*288*	*---*	*294*	*300*	*6*
Third Party Auditor Program	*41*	*---*	*41*	*42*	*1*
Outsourcing Facility	*437*	*---*	*446*	*455*	*9*
Innovative Food Products (Proposed)	*---*	*---*	*---*	*---*	*---*
FTE	**927**	**944**	**925**	**993**	**68**

1/ FDA Headquarters Budget Authority shown inclusive of the $1.5M OIG transfer amount

Figure 56: Narrative by Activity

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[175].

Office of Food Policy and Response

New Era of Smarter Food Safety

In July 2020, FDA released the New Era of Smarter Food Safety Blueprint[176]. 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 FDA 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,

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

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

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 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, modernization and values that are its building blocks. The Blueprint also outlines a partnership between governments (federal, state, local, tribal, and territorial), 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.

FDA published the New Era of Smarter Food Safety blueprint in July 2020. Since its release, FDA has made significant progress in working toward the goals outlined in the blueprint, even in the midst of the COVID-19 pandemic. The New Era of Smarter Food Safety initiative is also advancing the agency-wide commitment to modernize data and enhance inspections, priorities reinforced in the Data Modernization Action Plan (DMAP) and the Resiliency Roadmap for FDA Inspectional Oversight released in March and May 2021, respectively.

Outbreak Response Improvement Plan

In December 2021, FDA issues an improvement plan focused on modernizing foodborne illness outbreak response. This plan is designed to help the FDA and our partners enhance the speed, effectiveness, coordination and communication of foodborne outbreak investigations. The Foodborne Outbreak Response Improvement Plan focuses on four specific priority areas:

- Tech-enabled product traceback
- Root-cause investigations (RCIs)
- Strengthen analysis and dissemination of outbreak data
- Operational improvements

FDA collaborated with experts in both the public and private sectors for input on additional ways to strengthen the agency's outbreak response. The agency also contracted with the University of Minnesota's School of Public Health to assess the FDA's capacity to support, join, or lead multistate outbreak investigations and to provide recommendations in an independent report.

E-Commerce Summit

On October 19-21, 2021, FDA held the New Era of Smarter Food Safety Summit on E-Commerce: Ensuring the Safety of Foods Ordered Online and Delivered Directly to Consumers. The sale of human and animal foods sold through e-commerce models across the U.S. and globally has been steadily rising, but the pandemic has accelerated this change in consumer habits. The summit was an opportunity for FDA to further our collaboration on food safety with

our federal, state, local, and tribal, and international regulatory partners, and a broad array of stakeholders, including industry, consumers, consumer and public health organizations, and academia in order to ensure the safety of human and animal food sold through e-commerce. The interest in this summit was enormous, with more than 4,100 people registered from 44 countries and more than 13,000 views of the summit recording.

Webinar Series

FDA also began co-hosting a food safety culture webinar series in collaboration with Stop Foodborne Illness, a non-profit public health organization on November 4, 2021. The webinar series engages experts from the public and private sectors in a collaborative exchange of ideas and experiences related to the importance of a robust food safety culture in helping to ensure safe food production.

There is also substantial interest in FDA's new quarterly TechTalk podcast series, which focuses on the development and use of new technologies to strengthen the ability of FDA, regulated industry, and others to accelerate prevention, speed outbreak response, and more swiftly adapt to crises that could affect the human and animal food supply. The first episode on tech-enabled traceability aired on April 29, 2021, with an audience of more than 4,700 in the first month of its release. The second episode on whole genome sequencing aired on October 6, 2021, with an audience of about 1,600 after its release. Both podcasts were widely listened to, with interest still high.

Imported Seafood Artificial Intelligence/Machine Learning Pilot

As part of efforts to better leverage predictive analytics, FDA implemented a multiphase 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. ML allows for the rapid assessment of information for the automatic identification of connections and patterns in data that people or even our current rules-based screening system cannot see. The main goal of this pilot was to determine if AI/ML models and techniques could improve targeting of volatile products. In August 2020, the FDA announced the results of the proof-of-concept for imported seafood, which demonstrated that machine learning can 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. These results are promising and demonstrate that the AI/ML model may provide improvement in predicting violative lines when integrated with existing import systems. In February 2021, FDA launched the second phase of the AI imported seafood program, 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. The third phase is scheduled for implementation in CY 2022 and broadens the scope of the pilot to encompass all FDA-regulated human food products.

Tracking and Tracing of Food

In September 2020, FDA issued the Proposed Rule for Food Traceability as the first step to harmonize key data elements and critical tracking events needed for enhanced traceability. 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.

On June 1, 2021 FDA launched the New Era of Smarter Food Safety Low- or No-Cost Tech-enabled Traceability Challenge to encourage the development of traceability solutions that are cost effective for human and animal food operations of all sizes. Achieving end-to-end traceability – the ability to track a food's route from source to table – throughout the food supply system can help speed the response to foodborne illness outbreaks and deepen our understanding of what causes them and how to prevent them from happening again. The primary goal of this challenge was to encourage stakeholders, including technology providers, public health advocates, entrepreneurs, and innovators from all disciplines to develop traceability hardware. On September 13, 2021, FDA announced the 12 winners of the FDA New Era of Smarter Food Safety Low- or No-Cost Tech-Enabled Traceability Challenge. There were 90 submissions, with the winning teams representing the U.S., Canada, and New Zealand. Submitting teams also hailed from Australia, China, England, France, Germany, India, Ireland, Singapore, Spain, Switzerland, and Taiwan. Videos from the winning teams are available on the FDA website.

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 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. In July 2021, FDA released the Cyclospora Prevention, Response and Research Action Plan. Modeled after the Leafy Greens Shiga toxin-producing E. coli (STEC) Action Plan; the plan focuses on improving prevention, enhancing response activities, and filling knowledge gaps in order to help prevent Cyclospora contamination of foods and to help prepare for responding to future outbreaks.

In December 2021, FDA issued a proposed produce safety rule to enhance safety of agricultural water used on produce. It proposes to require farms to conduct comprehensive assessments that would help them identify and mitigate hazards in water used to grow produce. The proposed rule, if finalized, would change certain pre-harvest agricultural water requirements for produce and farms subject to the rule.

Key provisions of the proposed rule include:

- conduct an annual assessment of pre-harvest agricultural water to identify any conditions likely to introduce hazards into, or onto, covered produce or food contact surfaces
- manage agricultural water based on the results of a comprehensive water assessment
- implement expedited mitigation measures for hazards related to certain activities associated with adjacent and nearby lands, to protect the quality of the water used on produce
- replacing certain one-size-fits-all testing requirements for pre-harvest agricultural water and replacing them with the agricultural water assessments identified above.

The proposed revisions are intended to address stakeholder concerns about complexity and practical implementation challenges while protecting public health.

FDA-Mexico Food Safety Partnership

In October 2020, the United States and Mexico officially launched the FDA-Mexico Food Safety Partnership[177] (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 $25.0 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

[177] https://www.fda.gov/food/cfsan-constituent-updates/fda-and-mexico-sign-statement-intent-forging-food-safety-partnership

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.

To implement the FSP, four work groups have been established with membership from the FDA, SENASICA and COFEPRIS to increase cooperation in the areas of: strategic priorities, laboratory collaboration, outbreak response and prevention, and food safety training. Since the signing ceremony in October 2020, all work groups have been meeting jointly to advance their food safety objectives. In March 2021 the FDA, SENASICA, and COFEPRIS Steering Committee met to keep the momentum going and ensure alignment with our shared food safety priorities. As a result of this partnership there have been no further outbreaks of salmonella linked to papayas in 2020 and 2021.

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 FSMA supplier verification requirements.

In December 2021, FDA issued a final rule final rule establishing the Laboratory Accreditation for Analyses of Foods (LAAF) program. Under the LAAF program, the FDA will recognize accreditation bodies (ABs) that will accredit food testing laboratories to standards established in the final rule (referred to as LAAF-accredited laboratories).

The establishment of the LAAF program will improve the FDA's capacity to protect U.S. consumers from unsafe food by improving the accuracy and reliability of certain food testing through the uniformity of standards and enhanced oversight of participating laboratories.

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

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 food supply chain and the federal government organizations charged with maintaining its balance. 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.

Office of Security and Emergency Management

Emergency Preparedness and Response

Accomplishments during COVID-19 include playing key critical rolls in the COVID-19 FDA Incident Management Group (IMG). 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 and FY 2021 over seven 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.

From October 2020 through September 2021, FDA HQ coordinated emergency response to 131 significant incidents including:

- four serious adverse or injury event incidents
- 47 natural disasters

- 32 man-made disasters
- two National Special Security Events

Additionally, FDA HQ received and coordinated 444 emergency Investigational New Drug (eIND) calls and 68 non-eIND calls. FDA HQ also activated Incident Management Groups (IMGs) to provide headquarters coordination for COVID-19.

FDA HQ evaluated 4,735 consumer complaints (including 23 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.

Between October 2020 and September 2021, FDA HQ:

- Coordinated 40 agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products.
- Addressed nine draft notices of Public Health Emergency of International Concern (PHEIC) from the HHS International Health Regulations Program.
- Responded to and coordinated 236 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.
- Developed, conducted and evaluated a tabletop exercise for two Center Select Agent and Polio Containment Laboratory facilities.
- Developed, conducted and evaluated two multi-day food-related tabletop exercises for both headquarters and district personnel.
- Developing a tabletop exercise for the Center for Veterinary Medicine.
- Developing a mandated Radiation Laboratory Security tabletop exercise.
- Participated in an FDA Cybersecurity tabletop exercise.
- Participated in the DHS/Countering Weapons of Mass Destruction (CWMD) Office series of Mission Validation Exercises.
- Assisted with the planning efforts for the initial component of Eagle Horizon 2021, the federal government's annual continuity of operations exercise.
- Updated the FDA Joint Information Center (JIC) Handbook.
- Developing a multi-phase after-action report for the FDA response to COVID-19.
- Assisting in the re-development of the HHS All-Hazards Emergency Operations Plan.
- Participating in the National Biodefense Strategy Response Working Group.

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 2021 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 2021 COVID-19 Response. FDA HQ completed maps for 90 GIS project requests involving FDA-regulated industry.

Office of External Affairs

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 April 1, 2020 through September 30, 2021, FDA's Office of External Affairs issued or held:

- 310 MedWatch Safety Alerts (FDA's second largest e-list) to over 363,000 subscribers and approximately 54,000 MedWatch Twitter followers;
- Approximately 460 news releases and other press announcements in English and/or Spanish to more than 100,000 subscribers, with approximately 63% of those being COVID-related actions;
- Roughly 70 individual Consumer Updates (both new and updated content) offered in English and Spanish, with all COVID-19 articles also available in four Asian languages, sent to more than 148,000 subscribers in English and 39,000 in Spanish; 90 Consumer and Stakeholder Videos with 1.5 million views and 102,000 subscribers; 78 newsletters, which reach approximately 71,000 health care professionals, consumers and patients, and targeted emails to specific organizations;
- Approximately 142 Stakeholder Calls with the FDA Commissioner; issued over 210 targeted stakeholder outreach emails; 250 tweets and 125 Facebook posts per month with an estimated 18 million views. Of note, FDA has 1.8 million followers on Office of External Affairs accounts, and 3.25 million followers on all social media accounts across FDA.

Communication with Stakeholders - Improvements to FDA.gov and Social Media Channels

Throughout 2021, FDA continued to make data-driven, iterative improvements to its public-facing website, FDA.gov. This included regular updates to FDA's landing page for COVID-19. Through the first eighteen months of the pandemic this page grew considerably. It serves as the agency's hub to provide visitors with vital information on vaccines, testing, personal protective equipment, and Emergency Use Authorizations (EUAs). By regularly reviewing the analytics of the COVID-19 content, FDA is able to better understand the information being requested by our stakeholders and ensure that COVID-19 related information is easy to find. In addition, FDA conducted usability testing of FDA.gov during December 2021 to improve the usability of the website by having actual users of the site perform specific tasks. This round of usability testing focused on the consumer audience's use of mobile devices and was required as part of the 21st Century Integrated Digital Experience Act.

In July 2021 FDA launched an Instagram account to expand stakeholder reach and enhance message dissemination on critical public health issues with new audiences and younger populations. To date the account has over 53,000 followers and over 120 images have been shared.

In 2021, FDA implemented a new, web content archiving system which will help the Centers across FDA keep the web site current with the most up-to-date information, while older information is archived. FDA HQ continues to manage an FDA-wide enterprise contract for email marketing through GovDelivery. This state-of-the-art email platform enables stakeholders

to quickly sign up to receive critical public health information from FDA. In addition, this mobile-friendly and easy-to-use product simplifies the process of sending emails for FDA administrators who manage the email lists. Currently, FDA has over 185 content topics available and over 1 million stakeholders who have opted-in to receive information.

Stakeholder Outreach Activities

FDA works closely with Centers and Offices to enhance stakeholder relations to ensure the public's health is advanced and protected. FDA aims to build stronger relationships with health professional organizations, consumer groups, trade associations, patient advocacy organizations, think tanks, academia, and other stakeholders, in order to better inform FDA's policy making process, to identify policy hurdles or stakeholder misconceptions, and to create strategic collaborations.

Throughout 2021, FDA coordinated calls and conducted outreach with groups on a variety of COVID-19 topics, including agency announcements related to vaccines, therapeutics, and testing. In addition, FDA held engagements and conducted outreach with stakeholders concerning other agency priorities, such as the Closer to Zero Action Plan for baby food, sunscreen quality and efficacy, and tobacco regulation.

FDA HQ coordinated over 75 listening sessions since April 2020 to gather stakeholder concerns, feedback, and useful information regarding interest about testing, clinical trials, and therapeutic development in response to the COVID-19 pandemic. Listening sessions were also conducted on non-COVID topics such as regenerative medicine therapies, including certain human cells, tissues, or cellular or tissue-based products (HCT/Ps). FDA HQ coordinated a workshop with the Duke Margolis Center for Health Policy to discuss basic research, clinical trial infrastructure and community engagement to support drug development for amyotrophic lateral sclerosis (ALS) with agency leadership, stakeholders, industry, academia, and government partners.

In an effort to increase transparency, FDA posted video recordings of 10 stakeholder calls on FDA's YouTube page, which has over 85,000 subscribers. From March 2021 to the present, these videos have been viewed over 118,489 times. Following all stakeholder calls, FDA disseminates recordings on agency social media platforms. FDA HQ used social media to engage with 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.

Finally, FDA HQ managed 1,198 speaker requests received from over 195 trade associations and industry-based groups for issues that cut across agency organizational and product lines, as well as major meetings that involved various FDA Centers and Offices subject matter experts' participation in external meetings, conferences, and workshops.

Office of Enterprise Management Services

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.

Office of Clinical Policy and Programs

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

FDA HQ continues to implement the Orphan Drug Act through designation programs that provide financial incentives to sponsors for developing drugs and biologics for rare diseases and conditions. In FY 2021, FDA HQ received 641 first-time requests for orphan drug designation and designated 397 promising drugs and biological products for rare diseases

FDA HQ continues to implement provisions of the Safe Medical Devices Act for Humanitarian Use Device designations, encouraging the development of devices for rare disease. In FY 2021 FDA HQ received 21 first-time requests for Humanitarian Use Device designations and designated 5 promising devices for rare diseases and conditions.

FDA HQ continues to implement Section 529 of FDASIA encouraging development of new drugs and biologics for the prevention and treatment of qualifying rare pediatric diseases. This legislation created the Rare Pediatric Disease Priority Review Voucher (PRV) program where 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 and also "rare pediatric disease" designation, which may expedite a sponsor's future request for a priority review voucher. In FY 2021, FDA HQ received 82 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 58 drugs and biologics for rare pediatric diseases.

Orphan Products Grants programs

The Orphan Drug Act created the Orphan Product Clinical Trial Grants Program, to stimulate the development of promising products for rare diseases. HQ continues to administer approximately 70 clinical studies of promising therapies for rare diseases and has awarded 11 new clinical trial grants in FY 2021. In addition, in FY 2021, due to the challenges and increased costs for clinical trials from the COVID-19 pandemic, HQ provided existing grantees with additional funding to implement necessary steps to allow their research to continue, ensure subject safety, maintain compliance with good clinical practice, and minimize risks to trial integrity. However, FDA appropriated grant funds, which are significantly less than the $30 million congressionally authorized amounts, are covering less and less of total costs for conducting clinical trials due to the rising study costs.

Recognizing importance of information about the natural history of disease for prevention and intervention strategies, HQ is funding 8 natural history grants to inform medical product development by better understanding how specific rare diseases progress over time. Examples include studies to follow patients with medullary thyroid cancer and cardiac disease in Duchenne muscular dystrophy.

FDA HQ continues to implement Section 305 of the Pediatric Medical Device Safety and Improvement Act of 2007 (part of the 2007 FDAAA legislation) which mandates demonstration grants for improving pediatric device availability through pediatric device consortia. In FY 2021 FDA HQ provided funding for 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.

Rare Disease Outreach

In FY 2021, HQ participated in 15 individual industry outreach and 6 patient-oriented meetings for orphan diseases. In addition, HQ accepted 18 of the 22 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss the legislative incentives for rare disease issues. At these meetings, the missions of the FDA orphan products programs were explained, and questions and concerns from stakeholders were addressed. In addition, in FY 2021 HQ hosted an all-day virtual rare disease public meeting with approximately 1000 views by researchers, sponsors, patients and caregivers, national organizations and rare disease patient groups. HQ will continue the mission critical outreach efforts to enhance all stages of the development and approval process for products to treat rare disease patients.

Jurisdictional Determinations and Support for Combination Products Regulation

In FY 2021 (October 1, 2020 - September 31, 2021), with respect to combination products, FDA HQ managed the inter-center consult process for approximately 1200 inter-center consults. FDA HQ received and processed 66 Request for Designation (RFD) submissions and issued 2 decisions (1 combination product and 1 non-combination product), with 100% of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also received and processed 118 Pre-RFDs submissions and issued classification and jurisdictional feedback for 32 Pre-RFDs. FDA HQ consulted on 92 classification and assignment questions from the Centers, responded to 91 requests for product-specific assistance from sponsors, and attended over 200 meetings for investigational and marketing application review. All these efforts contributed to ensuring the timely and effective review of combination products.

FDA HQ continues to enhance the Pre-RFD/RFD Salesforce system to harmonize workflow and data collection, the Activity Tracker to track workload activities, and the post-market safety reporting dashboard to enable efficient assessment of safety activities.

In FY 2021, continues to develop guidance documents mandated by statute or requested by stakeholders. For example, FDA HQ published a significant final guidance in December 2020 entitled Requesting FDA Feedback on Combination Products which discusses ways in which sponsors can obtain feedback from FDA on scientific and regulatory questions, including the new combination product agreement meeting (CPAM) mandated under section 3038 of the Cures Act. Regarding staff development and support, FDA HQ continued to provide agency staff training on combination product regulation and inter-center coordination for premarket review and post-market activities.

Pediatric Coordination

FDA HQ continued collaborations and coordination 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), Japan's Pharmaceuticals and Medical Devices Agency (PMDA), and Australia's Therapeutic Goods Administration (TGA). In FY 2021, these efforts included discussion of 212 issues, for which harmonization was achieved for 73 percent. In FY 2021, the Pediatric Cluster was the forum for the timely discussion of 6 potential therapeutics for the treatment of COVID-19 in pediatric patients, which included 12 discussions.

FDA HQ promoted high standards of scientific integrity by providing expert ethical opinions to agency Centers and Offices on a variety of ethical issues, including pediatric rare disease, study design, and informed consent, with the completion of more than 82 consult reviews in FY 2021 and by the ongoing guidance development. Additionally, FDA HQ developed a multimedia web-based application to assist reviewers in the Centers with analyzing a protocol and assessing the ethical considerations for the inclusion of children in clinical investigations.

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 2021, these efforts included

presenting one product before the PAC and completing 28 web-posted pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews).

FDA HQ promoted therapeutic product development for neonates through internal and external collaborations. These efforts included initiating and participating in guidance development with the FDA Centers as well as contributing to consortium efforts of developing tools to streamline neonatal development programs. In FY 2021, the neonatal-perinatal medicine consultation service provided 77 consultations across the FDA Centers, and neonatal indications were included in 11 drug labels. Neonatology consultation was included in the discussion of all pediatric study plans (PSPs) and emergency use authorizations (EUAs) for several COVID-19 products.

FDA HQ promoted 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.

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 2017 revised Common Rule to the extent practicable given FDA's and HHS's different statutory mandates. For example, 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 anticipates publication of the final rule in early 2022. FDA HQ is currently developing two additional NPRM to further harmonize certain aspects of FDA's informed consent and institutional review board regulations with the revised Common Rule .

Clinical Trial Transparency and Disclosure

FDA HQ continues to coordinate with the Centers, ORA and the National Institutes of Health (NIH) in stakeholder engagement and on compliance activities related to submission of clinical trial registration and results information to the ClinicalTrials.gov databank under42 CFR part 11. Since January 1, 2020, FDA HQ has issued over 45 Preliminary Notices of Noncompliance with the ClinicalTrials.gov requirements, and 3 Notices of Noncompliance to responsible parties for applicable clinical trials. 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, three Reports to Congress have been submitted since 2018, the most recent on April 16, 2021.

Human Subject Protection and Good Clinical Practice Consults

Each year, FDA HQ responds to approximately 650 inquiries related to FDA's requirements for the conduct, oversight, and reporting of clinical trials. Archives of these questions and answers are available on FDA's website. Additionally, in FY 2021 FDA HQ coordinated with the Centers to respond to approximately 250 inquiries from the healthcare community and patients related to the COVID-19 public health emergency.

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. In FY 2021, FDA HQ advised on complex ethics issues arising during the conduct of research related to or impacted by the COVID-19 pandemic.

Additionally, in FY 2021, FDA HQ participated in a wide variety of clinical research-related activities, such as serving as ex-officio on the Secretary's Advisory Committee on Human Research Protections (SACHRP), participating in FDA Advisory Committees, supporting and/or leading over 35 internal policy working groups, driving modernization efforts through FDA's public-private partnerships, and conducting 10 virtual outreach sessions for internal staff and external stakeholders on the principles of human subject protection and good clinical practice.

Patient Engagement and Listening Sessions

The HQ Patient Affairs' Patient Listening Sessions are discussions between patient communities and agency staff on a range of topics related to experiences with a disease or condition or healthcare considerations for specific populations. These sessions educated support patient-related mandates included in the Prescription Drug User Fee Act and the 21st Century Cures Act by educating review staff about patient experiences and their priorities in managing their symptoms to inform regulatory decision-making and providing a starting point to guide or accelerate early-stage research and development. The sessions also educated patients, caregivers, their advocates, and others in better understanding the FDA's mission and work around FDA's role in the regulatory medical product development process and review.

Major accomplishments include:

- Hosted 19 Patient Listening Sessions during 2021 (Jan 1 – Dec 31, 2021), the most Patient Listening Sessions conducted in a year since the inception of the program.
- Organized the first-ever opportunity for FDA to hear directly from the transgender community about their needs and concerns related to medical product regulation.
- Organized the first-ever Listening Session featuring only minor (below 18 years of age) participants during the transgender adolescent Listening Session. Previously, the agency has included pediatric participants alongside their parent/caregiver.
- Expanded Patient Listening Session program to include topics and diseases outside the rare disease space, as well as to underrepresented communities, (e.g. three sessions on clinical trial perspectives with the lupus patient community & two sessions related to healthcare challenges and needs with the transgender community)

Published an article in American Academy of Pediatrics (AAP) News about the agency's adolescent transgender listening session in Dec 2021 (*link not available til publishing date).* The article follows upon a Nov 2020 publication on the agency's Patient Listening Session program https://www.fda.gov/science-research/pediatrics/aap-news-fda-updates.

Office of the Chief Scientist

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 University with Mayo Clinic, University of Maryland, and the University of California San Francisco with Stanford University. Twenty-five newly established collaborative research projects include addressing the COVID-19 pandemic, the opioid epidemic, underrepresented populations, real-world evidence, product safety, and digital health.

Chief Scientist Challenge Grants

FDA HQ established, and now manages and coordinates the review and granting of an intramural research awards for five competitive programs, including the Chief Scientist Challenge Grants; research areas include Medical Countermeasures, Nanotechnology, Minority Health and Health Equity, and Women's Health. The Chief Scientist Grants funded twelve projects that reflect the overarching scientific priority areas for FDA and were recognized as highly innovative and high-risk. All projects involve cross-agency collaborations that display rigorous thought, focus, and excellent scientific merit. The scientific areas of the recent projects include biomarkers for oncology, detection of radiation in the Nation's food supply, bioprinted human skin, postmarket product safety and surveillance, and COVID-19 pandemic.

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 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.

Using federal technology transfer authorities implemented through FDATT programs, the following FY 2021 accomplishments highlight instances where FDATT enabled FDA to successfully engage with external partners to advance regulatory science initiatives, to participate in the federal technology transfer mandate through reporting inventions, and to update its knowledge of methods to increase the utilization of inventions through collaboration and transfer:

- Provided intellectual property and partnership guidance to FDA, completing over 500 actions including technology and partnership consultations; invention evaluations; patent application drafting and filing; patent prosecution activities; negotiation and establishment of research collaborations for staff across the FDA.
- Evaluated 17 new inventions for commercial viability and impact of the potential product on improving public health, with inventions ranging from bacterial fluorescent control strains for food pathogen detection to a thermoacoustic sensor to measure acoustic power of ultrasound transducers to cancer therapy based on novel chimeric immunotoxins. These FY 2021 inventions added to FDA's invention portfolio of over 150 technologies protected by over 450 patents and patent applications arising from research activities throughout the agency.
- Established 6 new technology license agreements, resulting in 82 total active licenses in FY 2021 that made FDA inventions available for use through the commercial sector to support the public health mission. The technology license agreements generate a range of outcomes, from making unique reagents available for research to development of commercially available tests that detect foodborne pathogens. One of these technology licensing agreements concerns the development of an FDA invention entitled "Direct Impact Corona Ionization (DII) Mass Spectrometry," made by inventors at OCS/NCTR and protected under U.S. Patent Number 8,704,169. One of the licensed uses of the FDA invention is for the partner to incorporate it into its mass spectrometry platform for development of a SARS-CoV-2 rapid test. If successful, this licensed FDA invention could play a key part of a new SARS-CoV-2 detection method that doesn't rely on PCR or immune-based detection and contribute to a new approach in COVID-19 testing.
- Established 9 new Cooperative Research and Development Agreement (CRADA) projects, through new CRADAs or amendments to existing CRADAs, making 36 active partnerships using CRADAs to address research topics such as 1) using intestine on a chip model to study the effects of drug residues on the human intestinal microbiome and antimicrobial resistance development, 2) evaluating capabilities of next-generation sequencing for adventitious virus detection as an alternative method for in vivo animal assays, in vitro cell culture and PCR assays, 3) and exploring applications of lung-on-a-chip systems to obtain physiologically relevant parameters that may predict in vivo effects of locally acting inhalation drug products.
- Ensured technology transfer policies and processes were up to date and compliant with relevant laws and regulations, so that FDA has clarity in its use of technology transfer authorities to protect, develop, and maintain access to its intellectual property; promote the use of its inventions; and engage with partners to advance the agency's regulatory science priorities.

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 leading the FDA COVID-19 Incident Management Group and COVID-19 Joint Information Center, supporting the development of MCMs, the issuance of over 420 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 continually communicating FDA's agency-wide response efforts (including the issuance of 350+ press releases, 220+ new web pages, thousands of tweets, providing consumer-friendly information—including issuing COVID-19 response recap emails twice weekly, hundreds of topic- and center-specific emails, and stakeholder calls to answer questions about FDA actions—and making consumer-focused information available in multiple languages).178 FDA HQ also worked to improve EUA processed and promote supply chain resilience based on recommendations from the FDA PREPP Initiative.

Additionally, FDA HQ continued to facilitate coordination of FDA response activities to Ebola outbreak in the Democratic Republic of Congo and Guinea. 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 continued to support a robust regulatory science research program to further the development of the tools (including innovative analytical approaches and alternative models) that support regulatory decision-making and help facilitate the development of advances in science and technology—including platform technologies and manufacturing processes—into safe and effective MCMs to respond to CBRN and emerging infectious disease threats, such as pandemic influenza, SARS-CoV-2, and Ebola.. FDA HQ also continued to support regulatory science to advance innovation in advanced manufacturing to increase

[178] More information about FDA's COVID response efforts is available on the FDA website at: www.fda.gov/coronavirus

manufacturing and supply chain resilience, increase domestic manufacturing, and support public health emergency preparedness and response.

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 EUA.

Accomplishments that support MCM availability and access include:

- ensuring consistent implementation and 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-19 and for certain DoD-related threat agents 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)
- supporting an adequate supply of MCMs through efforts to extend shelf life of certain MCMs, including through extensions under 564A of the Federal Food, Drug and Cosmetic Act
- identifying and developing new legislative proposals, including efforts to make more transparent those products eligible for material threat MCM priority review vouchers (PRVs), to amend the EUA authority to clarify FDA's ability to disclose the information upon which EUA decisions are based, to provide categorical exclusion for certain EUA activities under the National Environmental Policy Act (NEPA), and to clarify authority for use of in vitro clinical diagnostics needed for immediate emergency responses, as well as providing technical assistance on others' legislative proposals
- 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 PRV program
- clarifying regulatory issues around the conduct of clinical studies during public health emergencies, including continued efforts to advance 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

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.[179]

Office of Scientific Integrity

Preserving and Promoting Scientific Integrity

The Office of Scientific Integrity (OSI) continues to coordinate agency-wide efforts to preserve and promote integrity in FDA's scientific decision-making and research, as well as consistency on such issues. OSI identifies the need for additional policies and procedures through its frequent work with agency components to resolve both formal and informal disputes. OSI also continues to work with the Office of Science and Technology Policy at the White House to implement at the agency government-wide requirements and initiatives designed to ensure scientific integrity.

Resolving Agency Disputes

The Office of Scientific Integrity (OSI) continues to coordinate the resolution all disputes elevated to the Office of the Commissioner and most hearing requests on proposed regulatory actions. The disputes may originate with requests from either internal or external stakeholders and typically involve issues related to the underlying science or the agency's regulatory authority for specific agency actions, including product approvals and emergency use authorizations. The hearing requests come in response to proposed regulatory actions by other components of the agency and involve similar issues. OSI also continues to receive and assess any incoming allegations related to the conduct of scientific research to determine whether they constitute research misconduct under the regulations (i.e., falsification, fabrication, or plagiarism), and refers the allegations to a board of inquiry and/or an investigatory panel, as necessary.

Office of Women's Health

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 448 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

[179] More information about these efforts is available on the FDA website at: https://www.fda.gov/medicalcountermeasures

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. Throughout FY 2021 and continuing into FY 22, OWH continues to provide subject matter expertise on a variety of FDA policy initiatives.

Over the past year, Office of Women's Health has continued to support women's health research, and in FY 2021, committed funds for 12 research projects. Nine were funded through the OWH intramural program on a wide variety of topics relevant to women, including research aimed at predicting the response to therapy for advanced breast cancer, research evaluating intravaginal rings for menopausal women, and research studying the effect of sex differences on the drug absorption, biological responses, and adverse events of paclitaxel containing medical devices. In FY 2021 and continuing into FY 2022-2023, OWH plans to support women's health research by providing funding for research initiated by FDA investigators and their collaborators. OWH represents the agency on interagency working groups, participates on committees and scientific panels. Delivers numerous scientific lectures each year to a diverse array of stakeholders nationally and international to advance FDA's mission to protect, promote and advance the health of women.

Office of Women's Health is 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 addition, one project studying differential effects of smoking on male and female gene expression in the lung and other tissues was completed, and a manuscript is under development.

In FY 2021, the COVID-19 pandemic created substantial barriers to research. Due to social distancing restrictions and building closures, many researchers were unable to access their labs and faced considerable supply chain delays. OWH took a proactive approach to this difficult situation by allowing researchers to defer funds to FY 2022. OWH was then able to pivot available resources to fund three new CERSI projects examining the effects of COVID-19 in women. One study will examine the sex differences in immune profiles of post-acute sequelae of COVID-19 (i.e., long haulers) before and after vaccination, and another will investigate real-world sex-specific clinical factors influencing the susceptibility to infection, immune response, treatment utilization and outcomes among individuals infected with SARS-CoV-2. A third study will define SARS-CoV-2 vaccine-induced immunity in pregnant and lactating people.

OWH continues to advance the science of pregnancy and lactation. In addition to the study of COVID in pregnant and lactating people, in FY 21, OWH continued funding for three ongoing studies; one to assess real-world use of pharmaceuticals among pregnant women, one to evaluate a system to help determine drug passage into breast milk, and a third, the CURE Pregnancy Treatment Repository. In FY 2021 OWH also committed funding to several new studies involving pregnancy and lactation, including one to define a biomarker to predict recurrent pregnancy loss.

In addition, in FY 2021 and continuing into FY 22, OWH is funding a project to enable FDA's Data Analysis Search Host (DASH) to collect demographic data (referred to as DASH-D). This database will allow the agency to monitor women's participation across clinical trials and therapeutic areas. This database is accessible to anyone in the agency who wishes to query the available data.

In 2021, OWH staff and funded investigators published a variety of 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.

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 FY 2021-2022, 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 assess sex differences in efficacy and selected safety events from 2011-2020. The study compares weight gain in people who take certain antiretroviral therapies for HIV, with presentations planned at several upcoming national meetings. Manuscripts detailing the work are also under development.

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. FDA Office of Women's Health (OWH) conducts educational initiatives and outreach to connect women with FDA health and safety information.

Some key FY 2021 OWH program accomplishments include:

- Advancing the health of pregnant and lactating individuals, including serving as the FDA Commissioner's representative to the Task Force on Research.
- Hosting Scientific Speaker Series webinars to provide scientific evidence and consideration regarding sex and gender differences to support regulatory decision making across FDA.
- Utilizing a multi-pronged communication approach that includes monthly OWH newsletter, social media and digital outreach, outreach collaborations and partnerships with stakeholders, stakeholder conference presentations and exhibitions, and dissemination of women's health publications.
- 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 11,000 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).

- In November 2021, OWH launched new diabetes video under the KNOWH campaign, *Be Empowered: Understanding Diabetes*. This video highlights some of the ways diabetes can impact women differently and shares the unique experiences of women affected by diabetes.
- In May 2021, 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.

From January 2021 to date, OWH has implemented 10 blog posts on the topics such as insights on how recent updates to the Nutrition Facts label can help individuals living with diabetes, HPV resources in recognition of National Young Adult Cancer Awareness Week, which aims to highlight issues surrounding cancer for young people under the age of 40, and how women to take an active role in your health and learn what it takes to keep your heart healthy to help prevent cardiovascular disease. To date, the blog posts have garnered nearly 20,000 page views.

Featured COVID-19 specific updates from FDA and agency partners (e.g. CDC) in monthly electronic newsletters 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[180]. In observance of 2021 National Women's Health Week (NWHW) set out to raise awareness among women about the importance of prioritizing their health by sharing FDA OWH resources including a dedicated newsletter/e-update.

Office of Minority Health and Health Equity

The FDA Office of Minority Health and Health Equity (OMHHE) was established in 2010 to protect and promote the health of racial and ethnic minority, underrepresented, and underserved populations through research and communication that addresses health disparities. The OMHHE Outreach and Communication Program develops culturally and linguistically tailored health education materials for racial and ethnic minority, Tribal populations, and other diverse groups, written at low literacy levels and translated into multiple languages including Native languages (e.g., Cherokee and Navajo). These communications are designed to strengthen consumer's decision-making regarding FDA-regulated products and include items like brochures, fact sheets, post cards, infographics, and digital content such as videos and social media messages.

[180] http://www.fda.gov/pregnancy

Over the past 18 months, OMHHE has reached over 168 million consumers through digital outreach such as social media messages, four Twitter chats, one blog, weekly communications with FDA COVID-19 updates, and over 147 e-alerts focused on health topics disproportionately impacting minority groups. In February 2021, OMHHE collaborated with the Center for Biologics Evaluation and Research (CBER) and conducted a virtual question and answer session 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 confidence among racial and ethnic minority and Tribal groups. The office also joined the U.S. Department of Health and Human Services' "Vaccine Ready" campaign and released two public service announcement videos (PSAs) to address vaccine confidence among diverse populations. The videos were translated into multiple languages including Native languages (Cherokee and Navajo) and American Sign Language. Additionally, 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, Portuguese, Hmong, Somali, 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.

In FY 2020 and 2021, FDA OMHHE also continued to lead the Language Access Program (LAP) (FDASIA Section 1138) by: managing the Language Access Services contract that provides flexible means for OMHHE and other FDA centers and offices to acquire language services; leading the LAP cross-agency steering committee aimed at strengthening culturally appropriate communications for English learners populations; providing support to FDA centers and offices on the implementation of language access services across the agency; and leading the LAP Volunteers' Group with cross agency native speakers that help proofread translated materials for accuracy and cultural sensitivity. OMHHE added multi-media health education resources in multiple languages to our ongoing Diversity in Clinical Trials Initiative to help address barriers preventing diverse populations from participating in clinical trials. In FY 2020, OMHHE also 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 2,666 views on YouTube.

To further advance culturally and linguistically appropriate communication, FDA OMHHE educated and trained 206+ staff through the "Communicating with Confidence" training series. The "Communicating with Confidence: Strategies to Create Effective Communications for Diverse Audiences" workshop educated staff on strategies to create culturally tailored health education materials. The "Communicating with Confidence: The Impact of Bias on Health Education and Communications" training provided 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.

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 stakeholders, including, academia, government agencies, and non-profit organizations to advance health equity-focused research, education, and scientific exchange. OMHHE has led significant investments with internal and external stakeholders to advance minority health and heath equity efforts, including COVID-19 response efforts. 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.

In FY 21, OMHHE led the development and announcement of a new Notice of Funding Opportunity: "COVID-19 and Health Equity," for up to five (5) awards not to exceed $5M. OMHHE will select innovative research advancing (1) racial and ethnic minority participation in COVID-19/COVID-19 variant clinical trials, (2) the evaluation of the safety and efficacy of FDA approved products (therapeutics, diagnostics, and vaccines) for the treatment, prevention, or diagnosis of COVID-19, and (3) understanding diverse patient perspectives, preferences, and unmet needs.

In addition, OMHHE launched the Enhance Equity Initiative which highlights research projects and communication resources to enhance EQUITY in clinical trials by supporting efforts to advance diversity in clinical trials, EQUITABLE data efforts by increasing data available on diverse groups including, but not limited to, ethnicity, race, age, disability and geography, and EQUITY of voices by amplifying FDA's communication with diverse groups and to ensure stakeholders, including consumers, are informed about FDA's efforts and to understand diverse patient perspectives, preferences and unmet needs. Under this initiative, OMHHE executed 9 awards totaling over $5 million for health equity focused regulatory science research projects including (1) Using Big Data, Machine Learning, and Infoveillance Approaches to Detect and Characterize Adoptions and Adherence to PrEP Therapy Among Minority Populations; (2) Improving clinical trial diversity and participation among people living with Chronic Hepatitis B; (3) Integrating patient and consumer-generated discursive data to inform and enhance FDA One Health Initiative communication strategies; (4) Reagan Udall Foundation - Skin Lightening Products: Understanding Consumer Perspectives and Effective Educational Messages; (5) Howard University: Bridging Gaps - Recruiting Black and Asian American Participants in Clinical Trials and Creating Culturally Competent Messages; (6) Yale University and the Cultural Ambassadors Program: Leveraging Community Engagement and Electronic Health Record Strategies to Promote Diverse Participation in COVID-19 Clinical Trials; (7) Using Big data, machine learning, and infoveillance approaches to increase understanding of COVID-19 among racial and ethnic minority populations; (8) Stanford University (co-funded with OCET): Medical Countermeasures for All; and (9) U.S. Department of Veterans Affairs: Exploring the use of Real-World Data to Generate Real-World Evidence to support COVID-19 treatment outcomes among racial and ethnic minority groups.

The OMHHE Challenge Grants also support innovative, intramural minority health focused research through collaborations across FDA product centers. During FY 2020 and FY 2021, OMHHE awarded funding for two (2) projects totaling $300,000 with CDER investigators, "Define and Overcome Gaps Between Clinical Trial Evidence (CTE) And Real-World Evidence (RDE) for Sickle Cell Disease (SCD) Therapy And Outcomes," and "Racial and Ethnic

Differences in Severe and Critical Hospitalizations and Mortality Among COVID-19 Patients Under Age 65."

During the last 18 months, OMHHE also sponsored a health equity "Special Collections Issue: FDA's Strategies to Close the Health Equity Gap Among Diverse Populations" in the Journal of Primary Care and Community Health. This issue was published in March 2021 and 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. In addition, OMHHE published over 8 manuscripts in peer reviewed journals during this time period on health equity and health disparity focused research.

In addition, OMHHE has a robust Student and Fellows Program to expand expertise in regulatory science and diversify of the workforce. In FY 2020-2021, OMHHE launched the Postdoctoral Fellowship in Genomic Science and Health Equity, co-sponsored by the National Human Genome Research Institute (NHGRI) at NIH, to prepare fellows to use genetic, genomic and pharmacogenomic approaches to advance minority health and health equity. The office also precepted seven pharmacy students through the FDA Pharmacy Student Experiential Program and funded six teachers serving students in underserved areas to attend the CFSAN Professional Development Program in Food Science to learn the accredited "Science and Our Food Supply" curricula.

Office of Policy, Legislation and International Affairs

Support for FDA's Priority Rulemakings and Guidance Documents

FDA's Office of Policy (OP) advances the agency's public health mission by coordinating clearance and issuance of Federal Register documents; providing strategic leadership of high priority or cross-cutting FDA policy initiatives; and playing a pivotal role in supporting FDA's response to the COVID-19 public health emergency. Specifically, OP's core mission includes supporting all agency components in the development and issuance of regulations, guidance documents, and other Federal Register documents, the volume of which has increased significantly in recent years and now routinely exceeds 700 or more actions per year. In addition, on behalf of the Commissioner's office, OP provides leadership for priority FDA initiatives related to fostering competition and increased access to medical products; reauthorization of medical product user fees; reducing the death and disease caused by tobacco products; and enhancing food safety. OP also leads cross-cutting initiatives to develop strategic agency priorities, as well as advance regulatory policy through maintenance of FDA's Quality System for Regulations and good guidance practices. To support FDA's COVID-19 pandemic response, OP works closely with FDA program offices to coordinate review and clearance of FDA's COVID-19 guidance documents, including the more than 100 initial and updated guidance documents that have been issued. These guidance documents support the rapid development and review of critical products needed in the fight against the pandemic. In addition, OP provides substantive and logistical support for FDA's review of COVID-19 documents that are routed to FDA for clearance from HHS and other federal agencies, and which have included 173 clearances since the start of the public health emergency.

Congressional Engagement

Office of Legislation (OL)

The Office of Legislation (OL) advances FDA and Administration priorities with Congress and provides information requested by Congress in order to inform policymaking on new issues. Through OL, the agency works diligently to provide timely feedback to authorizing committees and other Congressional offices on public health, COVID-19, and many other issues of concern to them. From January 1, 2020 to July 31, 2021, OL responded to over 1,000 requests pertaining to members' policy interests, including issues surrounding the use of public health data and real-world evidence, by providing 346 briefings, staffing 57 Commissioner and Acting Commissioner calls, developing 125 requests for Technical Assistance, preparing for over 16 hearings, and responding to 537 letters. OL works proactively to anticipate members' interests by outreaching agency actions, monitoring the media accounts for each member of Congress and the agency's authorizing committees, and tracking legislative activity. In the same time period, OL managed close to 1,000 congressional outreaches and calls on wide-ranging issues, such as the agency's "New Era of Smarter Food Safety" initiative, FDA's Real-World Evidence program established under the 21st Century Cures Act, and efforts to advance health equity ranging from efforts to improve diversity in clinical trials, promoting better nutrition in the food supply to reduce disparate chronic nutrition related morbidity and mortality, and addressing unsafe chemicals in FDA-regulated products. In addition to the activities stated above, OL has responded to more than 1,000 inquiries regarding the COVID-19 pandemic and FDA's response efforts.

Office of Congressional Appropriations (OCA)

The Office of Congressional Appropriations (OCA) dual mission is to serve as a liaison to congressional appropriators and their staff in support of FDA's resource needs and its public health mission, as well as advise the FDA Commissioner and other senior leadership on appropriations and budget matters. Over the past year, in addition to managing the agency's outreach to Congress related to the fiscal years 2021 and 2022 budgets, OCA has managed hundreds of Congressional inquiries and staff briefing requests, and shared hundreds of FDA announcements, policy updates, and other press and stakeholder materials with Congressional Appropriators, as well as represented FDA's resource needs related to a number of critical agency initiatives. Regarding the COVID-19 pandemic and FDA's response efforts, over the past year, OCA has worked closely with FDA senior leadership to develop, refine, and effectively communicate the agency's current, short-term, and long-term resource needs to respond to the COVID-19 outbreak, as well as future pandemics. Since the COVID-19 pandemic began, Congress has worked on six separate supplemental and stimulus bills and the OCA team has provided critical technical assistance to the Appropriations Committee throughout that process as well as worked with FDA's Centers to advance the agency's Advanced Manufacturing priorities with Congress. And since passage of the appropriations supplemental bills, OCA has worked with the Budget team and the Centers to meet all budgetary reporting requirements.

Engagement with State, Local, Territorial and Tribal Officials

The Intergovernmental Affairs (IGA) Staff within the Office of Policy, Legislation, and International Affairs is the lead staff dedicated with working with state, local, territorial, and tribal (SLTT) governments within the Office of the Commissioner, coordinating across FDA components to proactively engage with and respond to inquiries from SLTT policymaking

stakeholders, including officials such as governors, attorneys general, mayors, state/local/territorial legislators, tribal officials/organizations, and the national associations representing those officials. IGA serves as the lead agency tribal liaison and guides FDA components on the tribal consultation process, coordinates data calls regarding the agency's interactions with tribal governments, and serves as the agency liaison on tribal issues for USG partners, including the Indian Health Service As an example of this work, IGA has managed the agency's involvement in several HHS-led tribal consultations, including six HHS-led tribal consultations in the fall of 2020 on COVID-19 response, six consultations led by HHS with tribal leaders to act on the President's memorandum in the spring of 2021, and nine regional consultations led by HHS in the Summer of 2021. The IGA team has been an active participant in the agency's response to the COVID-19 pandemic by responding to hundreds of COVID-19 inquiries from SLTT stakeholders and proactively engaging on issues related to testing, therapeutics, vaccines, hand sanitizers, PPE, and others, providing support for senior FDA officials in their engagement with SLTT officials during the pandemic. IGA is leading the agency's engagements with SLTT stakeholders on cannabis issues, and the agency has received formal inquiries from dozens of federal, state, local, territorial and tribal officials regarding cannabis, including cannabidiol (CBD), and hemp-related inquiries. In the compounding space, IGA facilitates FDA's annual intergovernmental meeting on drug compounding, which brings together regulators from across the country, as well as representatives from key state associations, to discuss pressing issues in the compounding space, a crucial partnership that has helped to guard against a repeat of the 2012 multistate outbreak of fungal meningitis. The 10th such meeting was held in FY 2022 (October 26-27, 2021). IGA works in close coordination with other FDA's offices on all food, cosmetic, and dietary supplement safety matters, interfacing with SLTT policymaking stakeholders to ensure that important updates regarding food recalls, outbreaks of foodborne illnesses, and other important safety issues are shared in a timely manner. IGA has also engaged with SLTT stakeholders on a variety of issues related to tobacco products, including Tobacco 21, Cigarette Health Warnings, final rules for premarket tobacco product applications and substantial equivalence reports, and several ENDS-related topics. IGA also strives to monitor state, local and territorial legislation and other activity that may have an impact on FDA regulations and programs. Finally, IGA also engages with federal intergovernmental partners, including the White House, HHS, and other federal entities.

Critical Public Health and Economics Analyses

FDA's Office of Economics and Analysis (OEA) builds the foundational data and knowledge base that informs and improves FDA's evidence-based policymaking. OEA is vital to work across a range of FDA initiatives and priorities, including but not limited to public health emergencies, supply chain and shortages, health equity, economic impact analysis of key FDA food, tobacco, and medical products regulations, and GAO/OIG oversight management. OEA staff responded to the critical analysis and oversight needs of FDA during the ongoing COVID-19 pandemic. In 2020-21, 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. OEA's support informed policy decisions throughout the rulemaking process. OEA's Economics Staff also provided critical analytic support for FDA's Medical Device User Fee Amendments negotiations. In support of the Administration's initiative to examine prescription drug pricing and drug importation, OEA conducted analyses characterizing the international market dynamics of drugs and biosimilars as

well as drug importation and drug prices. Aligned with the President's Executive Order on enhancing competition, and particularly competition in generic drugs and biosimilars markets, OEA is engaged in a robust research agenda to better understand the extent and causes of bottlenecks in the generics drug market, market dynamics of these products, and the extent of competition in biosimilars markets, to facilitate identifying appropriate policy levers to address these problems. OEA's Public Health Strategy and Analysis 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). OEA's GAO/OIG Liaison team leads agency responses to GAO and OIG studies which have increased in number over time requiring extensive staff engagement. 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.

Office of Global Policy and Strategy

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) was formed after the OC reorganization in 2019 and 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) including 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 (OGO). Bilateral engagements for countries where there is not an FDA Office are managed by OGO. 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 inspections in China, India, and Latin America conducted in a manner consistent with FDA guidelines on ensuring the safety of FDA and regulated facility personnel during the COVID-19 pandemic; strategic engagements (trainings, seminars, etc.), and observed inspections with regulatory counterparts to enhance global inspectional capacity in China, 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 World Trade Organization; 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.

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.

FDA played a key role in the drafting of the USG report focusing on the supply chain for drugs, particularly small-molecule drugs and therapeutic biological products, including active pharmaceutical ingredients (APIs). The report highlights that the pharmaceutical supply chain is complex, global, and vulnerable to disruptions; and it includes extensive recommendations to address the reliability of the pharmaceutical and API supply chain. OGPS represents FDA in interagency discussions to (a) identify unfair foreign trade practices that have eroded U.S. critical supply chains and to bring trade actions to address such practices, and (b) examine how existing U.S. trade agreements and future trade agreements and measures can help strengthen the United States and collective supply chain resilience.

Inspections

FDA foreign office staff as well as ORA investigators on short-term assignment to China, India, and Latin America offices conduct inspections in their respective country or region. In FY 2021 OGPS has completed 125 foreign inspections in China (93), India (14), and Mexico (18). In addition to in-person inspections during the pandemic OGPS investigators have performed 46 (25 FY 2020, 21 FY 2021 year-to-date) remote regulatory assessments of critical drug facilities and sites conducting clinical trials of drugs and biologics to continue FDA oversight in accordance with local lockdowns or travel restrictions.

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 which facilitate regulatory cooperation, including the sharing of certain types of non-public information.

During FY 2020 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 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 2021, FDA established two new confidentiality commitments with Australia (human and animal foods and medical products) and Canada (medical products) to support FDA's regulatory collaboration with foreign counterparts. FDA developed instructional e-learning modules for FDA staff on topics related to international disclosure pursuant to FDA's confidentiality commitment with foreign counterparts.

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 and FY 2021, 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 Asia Pacific Economic Cooperation (APEC), the Global Fund, the Gavi vaccine alliance, the Joint Institute for Food Safety and Applied Nutrition (JIFSAN), and the Inter-American Institute for Cooperation on Agriculture (IICA).

Building on the momentum of the first international global food safety conferences co-convened by WHO, WTO and FAO in FY 2019, 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, and the creation in 2021 of a United Nations Food Safety Summit where FDA and USDA represent U.S. Government interests.

Leveraging the Authority of Foreign Regulators

OGPS is FDA's lead for the negotiation of Mutual Recognition Agreement negotiation. 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 2020 and FY 2021, OGPS furthered implementation of the Revised Pharmaceuticals Annex to the United States – European MRA by completing 22 capability assessments of Member States for their ability to perform GMP inspections of veterinary drug facilities (8 for FY 2020, and 14 for FY 2022 year-to-date). OGPS also negotiated and facilitated the implementation of the U.S.-U.K. mutual recognition agreement which continues FDA's ability to leverage U.K. GMP inspection reports post-Brexit.

Office of Laboratory Safety

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 lives, 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.

Oncology Center of Excellence

Enacted through 21 Century Cures, the Oncology Center of Excellence (OCE) is the first "intercenter institute" focused on the review of products across CDER, CBER and CDRH that diagnose or treat patient with cancer. The OCE's mission is to achieve patient-centered regulatory decision-making through innovation and collaboration. Many OCE programs are facilitating product development for rare cancers including pediatric oncology, rare biomarker defined populations (precision medicine), support for pragmatic and decentralized trials as well as expanding our source of evidence through patient-generated data and real-world evidence. OCE's review and scientific collaboration has resulted in 49 manuscripts on oncology review products or regulatory science issues in FY 2021, 9 draft or final guidances, and substantive stakeholder engagement through execution of 51 mini-symposia and workshops. International regulatory collaboration has been strengthened with Project Orbis and other outreach. In FY 21, clinical review of cancer products was supported by OCE Medical Oncology Review and Evaluation (MORE) teams for 52 CBER and CDRH collaborative reviews of drugs, biologics, and devices by providing a unified clinical review supported by subspecialist oncologists.

Under the Global and Regulatory Outreach Program, Project Orbis provides a framework for concurrent submission and review of oncology products among international partners. Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions, regardless of whether the product has received FDA approval. Pivotal clinical trials in oncology are commonly conducted internationally and these global trials are increasingly important for investigating the safety and effectiveness of cancer drugs for approval in the United States. Project Orbis expanded international regulatory participation with the inclusion of both United Kingdom MHRA and Israel Ministry of Health. The number of submissions from FY 2020 to FY 2021 increased by 70% and regulatory actions by 110%) for applications submitted across Project Orbis countries. FY 2020 summary on FDA approvals were published in the Clinical Cancer Research Journal, regulatory authorities of Australia, Brazil, Canada, Switzerland, and Singapore were co-authors. In addition to Project Orbis, OCE leads monthly teleconferences to discuss on-going regulatory reviews and drug development topics with EMA, Swiss Medic, TGA (Australia), Health Canada, and PMDA (Japan) and bilateral meetings twice a year between FDA oncology and regulatory authorities of Australia, Brazil, Canada, Switzerland, Singapore, Israel, and the UK.

The OCE Oncology Regulatory Affairs and Policy Program provides regulatory support across OCE cross-cutting review programs, executes innovative regulatory review tools focused on expedited product review, and runs a novel expanded access program "project facilitate" within the agency and across external partners. One cross-cutting review program is the OCE Patient-Focused Drug Development (PFDD) program which provides consultative scientific advice across Centers regarding use of patient-reported outcomes (PRO) and other clinical outcome assessments. PFDD completed 115 product specific consultations. Additionally, the program developed and published a draft guidance entitled "Core Patient-Reported Outcomes in Cancer

Clinical Trials" and executed the 6th annual COA-CCT public workshop with over 600 registrants. PFDD continued to broaden collaborations in the field of patient-reported outcomes within the agency, across governmental organizations, and including international working groups. (e.g., FDA Digital Health Center of Excellence, National Cancer Institute Cancer Moonshot Consortia, Center for Medicare, Medicaid Innovation and SISAQOL). Innovative review tools like Real-Time Oncology Review (RTOR) and Assessment Aid, aim to explore efficient review processes to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality. RTOR allows the FDA to review much of the data earlier before the applicant formally submits the complete application. By the time the applicant submits the complete application to the FDA, the agency's review team has completed the analysis and is in a better position to conduct a more efficient review. In 2021, OCE working collaboratively across FDA Centers facilitated 25 NDAs or BLAs where RTOR was used and presented RTOR and the consolidated review document, Assessment Aid, at a DIA conference. To facilitate expanded access to investigational therapies, the OCE Project Facilitate call center was launched in 2019 to assist oncology healthcare providers or regulatory professionals in requesting access to investigational therapies for patients with cancer. Project Facilitate is a single point of contact where FDA oncology staff will help physicians and their healthcare team through the process to submit an Expanded Access request for an individual patient with cancer. In FY 2021, Project Facilitate coordinated cross Center meetings to discuss 632 (369 pediatric) Single patient INDs, for both emergency and non-emergency applications.

Another cross-cutting OCE review program is the Pediatric Oncology Program that provides focused expertise in cancer drug development for childhood cancer. Facilitating early pediatric studies of appropriate new, targeted cancer therapeutics and eliminating the 6 1/2-year time lag between first in human and first in children studies of approved cancer drugs is the first step in achieving 2025 goals to accelerate pediatric cancer drug development. The Pediatric Oncology Program published final FDARA Sec 504 Implementation Guidance; facilitated 19 meetings with sponsors for Early Advice (Type F) and increased international engagement to facilitate regulatory alignment of global pediatric development programs, including negotiation of EMA/PDCO observers at these advice meetings and joint development and publication with the EMA of a Common Commentary Template and paper recommending simultaneous submission of PIPs and iPSP to facilitate regulatory alignment of global pediatric development. Another important OCE program is the OCE Real World Evidence Program, which engages in evidence development modernization through scientific collaboration and policy development to advance the appropriate fit-for-purpose application of RWD to generate RWE to support oncology product development. The OCE RWE program focuses on rigorous methodological use of RWD to advance the development of oncology products in the pre- and post-approval settings. OCE launched the Oncology RWE Program in 2020 and includes partnerships with stakeholders throughout FDA Centers to ensure communication and consistency across cancer-specific submissions. RWE program engagement efforts included external presentations to include International Conference on Pharmacoepidemiology and Therapeutic Risk All Access 2021, American Association for Cancer Research, Duke Margolis Center for Health Policy Workshop, and the National Academies of Medicine Oncology. RWE program supported oncology regulatory review, policy, and research with 61 consults and publications to include; Rapid real-world data analysis of patients with cancer, with and without COVID-19, across distinct health systems https://pubmed.ncbi.nlm.nih.gov/34014037/, The Friends of Cancer Research Real

World Data (RWD) Collaboration Pilot 2.0: Methodological Recommendations from Oncology Case Studies https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.2453.

OCE Diversity in Oncology Program expanded external engagements. Project Community is an OCE national initiative introducing the work of FDA oncologists and hematologists to people in the community, especially under- represented and underserved communities. The primary audience includes patients, advocates, survivors, families, and others interested in increasing minority participation in clinical trials (CT) and increasing knowledge and minority participation in genetic databases. In FY 21, Project Community and National Black Family Cancer Awareness Week initiative held 4 external stakeholder meetings; a June 2021 Conversation on Cancer public panel discussion with 850 registrants, 469 attendees, 600+YouTube views; produced exclusive webpage/social media toolkit and video with 1000+ YouTube views and increased FDA social media traffic (Twitter, FB, Instagram) by direct SM engagement of 50+ external stakeholder organizations. Project Community also conducted 4 meetings with 25 NCI-designated Cancer Center Outreach Leads (totaling 46 attendees); and participated in or organized 5 listening sessions or public-facing meetings with external stakeholders resulting in registration of 633 and noted attendance of approx. 272. Project Equity works to improve access to clinical trials of oncology medical products for populations that have historically been underrepresented in clinical research such as racial and ethnic minorities, individuals who live in rural areas, sexual and gender minorities, and individuals with economic, linguistic, or cultural barriers to healthcare services." Project Equity enhanced collaboration with external stakeholders to advance evidence generation for subgroups that are historically under-represented in CTs and addressed barriers to clinical trial participation with the following engagement: Sponsored a two-part FDA/OCE Symposium: "Understanding Barriers to Oncology Clinical Trial Participation for Sexual and Gender Minorities" and collaborated with the American Society of Clinical Oncology (ASCO), Association of Community Cancer Centers (ACCC), American Association for Cancer Research (AACR) and American Society of Hematology (ASH).

Other Accomplishments

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

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[181]

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

User Fees

FY 2021 also marked the start of FDA's user fee reauthorization cycle for FDA's four main user fees statutes. These are: 1) Prescription Drug User Fee Act (PDUFA); 2) Biosimilars User Fee Act (BsUFA); 3) Generic Drug User Fee Act (GDUFA); and 4) Medical Device User Fee Act (MDUFA). OP coordinates Administration review and clearance of all user fee packages, and advises FDA and HHS leadership on policy and process issues that arise in connection with user fee reauthorization.

FDA fosters 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 crosscutting 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.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$307,092,000	$187,776,000	$119,316,000
FY 2020 Actuals	$308,089,000	$186,919,000	$121,170,000
FY 2021 Actuals	$313,207,000	$193,213,000	$119,994,000
FY 2022 Annualized CR	$319,374,000	$194,256,000	$125,118,000
FY 2023 President's Budget	$357,616,000	$228,063,000	$129,553,000

Figure 57: Funding History

BUDGET REQUEST

The FY 2023 President's Budget for FDA Headquarters is $357,616,000, of which $228,063,000 is budget authority and $129,553,000 is user fees. The budget authority increases by $33,807,000 compared to the FY 2022 Annualized CR and User Fees increase by $4,435,000.

The FY 2023 President's Budget Request will ensure FDA HQ continues providing critical support to FDA's overall mission, including support in the following areas:

- continuing work 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. evaluate and improve the effectiveness of preventive control standards, and advance the development of predictive safety models
- evaluating and improving the effectiveness of preventive control standards, and advance the development of predictive safety models
- coordinating 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
- providing 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 ($3.0 million / 6 FTE)

Smarter Food Safety (+$500,000 / 1 FTE)

In support of on-going implementation efforts for the New Era of Smarter Food Safety, the FY 2023 budget provides a targeted increase of $3.0 million / 6 FTE for FDA HQ (OFPR) to strengthen data sharing and predictive analytics capabilities as well as ensure effective strategic and project management across the four core elements of the New Era of Smarter Food Safety Blueprint.[182]

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.

The FY 2023 Budget will enhance FDA's ability to organize and share data across the Foods Program and with external partners. FDA will develop standards for identifying and assimilating external sources of data and information, including evaluation of best practices for cloud-based data-sharing. FDA will explore and capitalize on the new data streams generated by modern food safety approaches and new tools for rapidly analyzing big data. This investment will also increase the amount and quality of data that FDA has through mechanisms that include expanded use of information-sharing agreements with regulatory and public health partners, academic

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

institutions, industry, and others, building on lessons learned from COVID-19 response efforts. This funding will thereby enable FDA to implement data-driven approaches to protecting consumers, allocating regulatory oversight resources based on risk, and improving the agency's capacity to quickly respond to dynamic public health challenges and better monitor the food supply chain.

With new resources in FY 2023, FDA will also 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 $52 million total request for the New Era of Smarter Food Safety in FY 2023, 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.

Data Modernization and Enhanced Technologies and Smarter Food Safety (+$2.5 million / 5 FTE)

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $2.5 million for FDA Headquarters for Data Modernization and Enhanced Technologies and Smarter Food Safety efforts. The Budget will enable FDA to leverage the latest science on foodborne outbreaks for human and animal food and apply new technologies and data analytics to strengthen prevention of human and animal foodborne illnesses, enable food contamination to be rapidly traced to its source, improve the efficiency and effectiveness of FDA's oversight activities, and better understand food safety challenges. With strengthened traceback capabilities, FDA will incorporate root cause data to develop commodity-specific prevention plans for human food – expanding on our experience with targeted, action-oriented initiatives (i.e. leafy greens) – and improve prevention-oriented food safety practices to better avoid identified risks, including the development of training materials for FDA inspectors and state partners. Using standardized criteria and reports for post-action activities, 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.

Medical Product Safety ($20.0 million / 5 FTE)

Cancer Moonshot, Oncology Center of Excellence ($20.0 million / 5 FTE)

This new funding will enable the FDA/Oncology Center of Excellence (OCE) to strengthen current initiatives and launch new programs to support Moonshot goals. Funding will advance research, external collaborations, expand and launch educational outreach programs, and support programs that expedite the development of oncology and malignant hematology products using an integrated approach to the clinical evaluation of drugs, biologics, and devices for the treatment of patients with cancer. Resources will enable FDA/OCE to expand efforts that facilitate approval of important cancer treatments by international regulatory authorities at the time of FDA approval and will foster harmonization of cancer treatments in other countries with the U.S. standard of care. This will also enable FDA/OCE to advance efforts in streamlining design, conduct, and inspection of multinational clinical trials, aid in standardization and harmonization of trial data and safety collection in global regulatory policy and advance international collaboration on pediatric drug development. Funds will advance efforts to foster development of novel therapeutics for patients with ultra-rare cancers through scientific innovation, education, guidance, and regulatory engagement and collaboration with a focus on academic life science incubators and accelerators as well as small pharmaceutical companies.

FDA/OCE will increase intra- and extramural research and expand the Precision Oncology efforts to address unmet needs for rare cancers, diagnostics, and translational research to support drug development and regulatory advice and allow for guidance development on topics such as liquid biopsy and diagnostics for cancer that could have significant impact throughout a patient's diagnosis and treatment. Funding will also be applied to FDA/OCE outreach to diverse communities and support of decentralized trials to assure that screening tests and other in vitro diagnostic tests are developed with a representative population of patients with cancer. Funding will enable FDA to advance Oncology Center of Excellence Diversity in Oncology Program with additional resources to support outreach to the cancer community, including familiarizing patients with clinical trial participation in underserved areas, hold workshops regarding issues faced by patients with cancer for under-represented groups to determine the cause of issues, implement a social media strategy to reach more patients and caregivers, expand education and encouragement of decentralized trials to help bring trials to where patients live thereby reducing some barriers to clinical trial participation that may particularly impact underrepresented populations and implement pending guidance document on Diversity Plan with companies developing drugs whereby companies proactively design clinical trials and tools to improve diverse enrollment.

New funds will enable FDA/OCE to expand and increase programs supporting research, review and policy in the areas of real-world data in oncology as well as patient generated data informing tolerability. Funding for the Oncology Real World Evidence program will be used to evaluate real-world oncology endpoints sourced from electronic health records and other data from routine healthcare. Support will also be applied to enhance cancer-specific regulatory review support to provide rapid and efficient advice to commercial sponsors related to oncology-specific RWE study design advice, and support review Divisions with consistent and efficient oncology-specific RWE consultation for regulatory submissions. Funding will be applied to the Oncology patient-focused drug development program to expand an FDA/OCE-National Cancer Institute collaboration to advance patient-generated data and digital endpoints and deploy measures in early clinical development to assist in dose evaluation and characterization of tolerability. In

addition, education, outreach and analytic support will be applied to expand OCE's novel pilot program Project Patient Voice; a public-facing FDA website that provides graphic visualization of patient-reported symptomatic side effects assessed during pivotal cancer trials leading to FDA approval. Funds will enable expanded educational activities surrounding availability of FDA/OCE Facilitate Call Center, which is the single point of contact where FDA oncology staff will help physicians and their healthcare team with requesting single patient INDs, emergency INDs, and expanded access to patients with cancer, often without any alternative options. Additionally, it will provide resources to conduct research on drugs being used via expanded access to identify novel molecular targets and support rare tumor drug development, and collect, collate, and make publicly available information learned from expanded access.

Crosscutting (+$30.8 million / 60 FTE)

Capacity Building (+$16.4 million / 48 FTE)

The FY 2023 President's Budget includes $59.4 million for Capacity Building, including $16.4 million for FDA Headquarters. This funding will support essential services and business functions including efforts to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Capacity Building request also will support legal services within the Office of the Chief Counsel and improve safety efforts within the Office of Laboratory Safety.

Office of the Chief Counsel (OCC) ($9.1 million / 34 FTE)

The FY 2023 Budget includes an increase of $9.1 million above the FY 2022 Annualized CR for the Office of Chief Counsel (OCC). FDA continues to have a critical need for legal services, including such as medical product reviews, food safety assessments, enforcement cases, defense of agency decisions, and other high-profile matters involving multiple motivated stakeholders. FDA has identified the lack of adequate legal resources as a risk to agency activities. The FY 2023 Budget increase will support critical OCC recruitment and retention incentives, including student loan repayment for OCC attorneys.

Essential Services ($658,000 / 3 FTE)

The FY 2023 Budget includes $43.7 million for investments in the Essential Services, including $658,000 for FDA Headquarters. This new funding will allow FDA to bolster recruitment and retention efforts, continue documentation of the agency's COVID-19 response, increase capacity for responding to eDiscovery and FOIA requests, and increase support staff for critical business functions that support all of FDA's work. The Budget will improve FDA's recruitment efforts to hire additional staff such as investigators, microbiologists, chemists, and reviewers.

The increased capacity will strengthen critical human capital efforts, including training, conflict prevention and resolution, anti-harassment initiatives, and employee and labor relations. These central investments will increase FDA's capacity to support Centers and Offices across the human capital portfolio. The Budget will provide expanded support for FDA's eDiscovery program, in order to support litigation, freedom of information requests, Congressional requests, and investigations inquiries. The Budget supports other vital functions, including technical engineering services to manage and oversee FDA's presence at over 360 buildings across the nation. The increase also bolsters FDA's capacity to conduct critical compliance, oversight, and

quality control over the $6 billion in annual funding and $940.5 million in COVID-19 supplemental appropriations.

Office of Laboratory Safety (+$6.6 million / 11 FTE)

The FY 2023 Budget includes an increase of $6.6 million above the FY 2022 Annualized CR 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 Minority Health and Health Equity (+$4.7 million / 3 FTE)

The FY 2023 Budget includes an increase of $4.7 million above the FY 2022 Annualized CR, 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.

Public Health Employee Pay Costs (+$2.9 million)

The FY 2023 Budget includes an increase of $51.9 million, including $2.9 million for FDA Headquarters, to partially fund salary and benefits increases which include a 4.6% Cost of Living Adjustment (COLA) for civilian and military, anticipated awards, and a 1.1% increase related to the agency's contribution to the Federal Employees Retirement System (FERS). This funding will support FDA public health employee costs.

Reducing Animal Testing Through Alternative Methods (+$629,000 / 2 FTE)

The FY 2023 President's Budget includes $5.0 million in new funding, including $629,000 for FDA Headquarters, to implement a cross-agency New Alternative Methods Program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them. The New Alternative Methods Program will be centrally coordinated and managed through the Office of

the Commissioner/Office of the Chief Scientist, with FDA Centers responsible for specific programmatic objectives, including expansion of capacity to qualify alternative methods and fill information gaps with applied research that will support advancement of new policy and guidance development.

The FY 2023 Budget request will allow FDA to establish a cohesive and comprehensive program that advances the development, qualification, and implementation of new alternative methods for product testing. While animal studies are critical to evaluating safety and, at times, effectiveness, premarket animal-based assessments are time and resource intensive and do not always fully predict/detect potential toxicities of FDA-regulated products for proposed uses in humans and animals. New alternative methods have the potential to provide both more timely and more predictive information to accelerate product development and enhance emergency preparedness for the benefit of US patients, consumers, and animals. Additionally, reducing the need for animal testing is a priority for FDA, and implementing the New Alternative Methods Program will demonstrate a clear and strong commitment from FDA to the 3Rs.

There is significant public support for these goals and while recent advances in new alternative methods including complex in vitro models (e.g. microphysiological systems or "organs-on-a-chip") and advanced in silico computer models hold promise, there are multiple steps required to translate this new science into regulatory use and maintain the same standard of safety, efficacy and quality of FDA-regulated products. FDA has already had success in this area through individual Center's regulatory research programs and implementation of general qualification processes in some Centers, but continued progress is resource limited and to date no targeted program has existed across the agency.

An agency-wide program will promote the adoption of alternative methods as a normal part of the premarket regulatory review process and support the 3Rs. FDA cannot develop and implement alternative methods alone, so through this initiative FDA will expand qualification processes, provide clear guidelines to external stakeholders developing alternative methods, and fill information gaps with applied research to advance new policy and guidance development. Collaborations with industry and other government agencies are vital and the resulting qualified methodologies will streamline both the development and regulatory processes.

Data Modernization and Enhanced Technologies: Enterprise Wide Technology and Data (+$6.2 million / 7 FTE)

The FY 2023 Budget includes an increase of $75.9 million for Data Modernization and Enhanced Technologies, including $6.2 million for FDA Headquarters for Data Modernization and Enhanced Technologies Enterprise Wide efforts 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.

User Fees

Current Law User Fees (+$4.4 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 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products.(Output)	FY 2021: Developed 85 mapping products in support of FDA's emergency preparedness, response, and recovery activities. 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 2021: 64 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards (Target Met)	70 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards	76 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards	+6 CORES projects
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship programs. (Outcome)	FY 2021: 66% Target: 20% (Target Exceeded)	20%	20%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2022 Target	FY 2023 Target	FY 2023 +/- FY 2022
293205: Percentage of requests for combination product designations processed within the 60-day statutory requirement. (Output)	FY 2021: 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 2021: 212 Target: 100 (Target Exceeded)	125	125	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 2021: 29 Target: 30 (Target Not Met)	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 2021: 90 Target: 40 (Target Exceeded)	45	50	+5
291406: Percentage of invoices issued on time within predefined dates in the month. (Output)	FY 2021: 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 has added a new target 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 quality, 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 this strategic objective. FDA reset the retention target to 20% in FY 2021 to reflect the new expanded program's expected baseline. Although the Traineeship program has not yet been fully implemented, and additional programs will come online over the next few years, FDA has met the initial target of 20% in FY 2021. FDA will continue to monitor and adjust the target for retention moving forward as necessary. For now, the target will remain at 20% in FY 2022 and 2023.

Pediatric Labeling

Pediatric studies on medical products that result in labeling changes and safety reviews are important to improve the safety of children using these products. Although FDA has always met this goal in the past, this year staffing shortages and priorities focused on COVID related work resulted in narrowly missing the FY 2021 target. The FY 2022 and 2023 targets will remain at 30, and FDA believes that is still a realistic level.

INFRASTRUCTURE - GSA RENT, OTHER RENT, AND WHITE OAK

(Dollars in Thousands)	FY 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
FDA White Oak Campus	**52,944**	**53,053**	**53,082**	**56,011**	**2,929**
Budget Authority	***45,914***	***45,914***	***45,914***	***48,414***	***2,500***
User Fees	***7,030***	***7,139***	***7,168***	***7,597***	***429***
Prescription Drug (PDUFA)	*3,886*	*3,886*	*3,925*	*4,004*	*79*
Medical Device (MDUFA)	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	*3,144*	*3,253*	*3,243*	*3,593*	*350*
Other Rent and Rent Related	**150,557**	**146,293**	**136,862**	**161,106**	**24,244**
Budget Authority	***98,262***	***98,262***	***84,262***	***107,095***	***22,833***
User Fees	***52,295***	***48,031***	***52,600***	***54,011***	***1,411***
Prescription Drug (PDUFA)	*26,652*	*24,308*	*26,919*	*27,457*	*538*
Medical Device (MDUFA)	*5,344*	*5,344*	*5,398*	*5,506*	*108*
Generic Drug (GDUFA)	*13,338*	*12,428*	*13,472*	*13,741*	*269*
Biosimilars (BsUFA)	*1,092*	*522*	*1,102*	*1,125*	*23*
Animal Drug (ADUFA)	*805*	*781*	*806*	*822*	*16*
Animal Generic Drug (AGDUFA)	*269*	*200*	*272*	*274*	*2*
Family Smoking Prevention and Tobacco Control Act	*4,301*	*4,406*	*4,128*	*4,572*	*444*
Food and Feed Recall	*45*	---	*46*	*47*	*1*
Food Reinspection	*212*	---	*216*	*220*	*4*
Voluntary Qualified Importer Program	*177*	---	*180*	*184*	*4*
Third Party Auditor Program	*25*	*7*	*25*	*26*	*1*
Outsourcing Facility	*35*	*35*	*36*	*37*	*1*
GSA Rental Payments	**221,661**	**212,103**	**237,390**	**238,801**	**1,411**
Budget Authority	***153,119***	***153,119***	***167,119***	***166,286***	***-833***
User Fees	***68,542***	***58,984***	***70,271***	***72,515***	***2,244***
Prescription Drug (PDUFA)	*36,052*	*31,147*	*36,412*	*37,141*	*729*
Medical Device (MDUFA)	*8,479*	*7,424*	*8,564*	*8,735*	*171*
Generic Drug (GDUFA)	*12,975*	*10,609*	*13,105*	*13,367*	*262*
Biosimilars (BsUFA)	*460*	*345*	*465*	*474*	*9*
Animal Drug (ADUFA)	*856*	*680*	*857*	*873*	*16*
Animal Generic Drug (AGDUFA)	*314*	*225*	*316*	*320*	*4*
Family Smoking Prevention and Tobacco Control Act	*8,557*	*8,542*	*9,686*	*10,721*	*1,035*
Food and Feed Recall	*76*	---	*77*	*79*	*2*
Food Reinspection	*362*	---	*369*	*377*	*8*
Voluntary Qualified Importer Program	*302*	---	*308*	*314*	*6*
Third Party Auditor Program	*49*	*12*	*50*	*51*	*1*
Outsourcing Facility	*60*	---	*62*	*63*	*1*

Figure 58: Narrative by Activity

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).

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 priorities. 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 Capital 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.

FDA is also collaborating with GSA to update the master plan for the FDA-owned Muirkirk Road Complex (MRC) in Laurel, Maryland, as a good management practice and to ensure current information is available to consider all options related to headquarters consolidation.

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 regulated products and manufacturers annually
- Collecting and analyzing thousands of samples of regulated products annually
- Recalling unsafe products
- Reviewing millions of 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 outbreaks caused by E. coli, listeria monocytogenes, Cyclospora, and salmonella
- Interdicting opioids at International Mail Facilities (IMFs) to combat the addiction crisis, which is a dominant public health problem in the U.S., killing more than 93,000 individuals in the U.S. in 2020
- Conducting criminal investigations, which result in arrests, convictions, billions of dollars of assets forfeited and seized, and billions of dollars in fines and restitution annually.

FDA occupies almost 6.8 million rentable square feet of GSA-owned and GSA-leased office, laboratory, warehouse, and border/inspection-station space.

Approximately 67 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 266 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 2021, FDA:

- completed the construction of and relocated operations to the new Office of Regulatory Affairs (ORA) laboratory near Kansas City, Kansas

- 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 Laboratory and the Southeast Tobacco Laboratory
- began coordinating design activities required to replace an aging facility and improve operations of ORA's human and animal foods laboratory near Denver, Colorado
- continued 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 to protect public health
- continued 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
- continued to coordinate design and construction activities to expand the Center for Drug Evaluation and Research's (CDER) laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis
- continued to coordinate design and construction of a new CDER laboratory near the White Oak Campus to house a pilot plant for simulating the processing of drug substances and products manufacturing
- 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 2022, FDA plans to:

- continue coordinating design activities and initiate construction activities required to replace an aging facility and improve the operations of the ORA laboratory near Atlanta, Georgia, that houses the Southeast Food and Feed Laboratory and the Southeast Tobacco Laboratory
- continue coordinating 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 construction activities required to renovate and expand operations at ORA's Forensic Chemistry Center located in Cincinnati, Ohio
- 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 construction activities to expand CDER's laboratory in St. Louis, Missouri, that houses the Division of Pharmaceutical Analysis
- continue coordinating construction 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
- complete 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 began to provide benefits to the Campus, including utilities to FDA-occupied buildings, FDA was 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 initiated a feasibility study in FY 2020 to address additional facility improvements at the Muirkirk Road Complex. 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-joint 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) 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.

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 and contractors currently assigned to the White Oak Campus is approximately 11,300 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 59 - State-of-the-Art Laboratories at White Oak

Figure 60 - State-of-the-Art Laboratories at White Oak

Figure 61 - Anechoic Chambers Laboratory

Figure 62 - Nuclear Magnetic Resonance Laboratory Supporting CBER and CDER

Figure 63 - State-of-the-Art White Oak Infrastructure: Advanced Air Terminal Units Supporting Laboratories

Figure 64 - 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:

- infrastructure modifications and improvements 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 2019 Actuals	$218,907,000	$170,208,000	$48,699,000
FY 2020 Actuals	$219,334,000	$171,208,000	$48,126,000
FY 2021 Actuals	$212,103,000	$153,119,000	$58,984,000
FY 2022 Annualized CR	$237,390,000	$167,119,000	$70,271,000
FY 2023 President's Budget	$238,801,000	$166,286,000	$72,515,000

Figure 65: Funding History - GSA Rental Payments

FUNDING HISTORY - OTHER RENT AND RENT-RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$120,201,000	$71,943,000	$48,258,000
FY 2020 Actuals	$119,877,000	$80,172,000	$39,705,000
FY 2021 Actuals	$146,293,000	$98,262,000	$48,031,000
FY 2022 Annualized CR	$136,862,000	$84,262,000	$52,600,000
FY 2023 President's Budget	$161,106,000	$107,095,000	$54,011,000

Figure 66: Funding History - Other Rent and Rent-Related Activities

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$49,255,000	$43,044,000	$6,211,000
FY 2020 Actuals	$59,744,000	$45,913,000	$13,831,000
FY 2021 Actuals	$53,053,000	$45,914,000	$7,139,000
FY 2022 Annualized CR	$53,082,000	$45,914,000	$7,168,000
FY 2023 President's Budget	$56,011,000	$48,414,000	$7,597,000

Figure 67: Funding History - White Oak

BUDGET REQUEST

The FY 2023 President's Budget Request for the Infrastructure Program is $455,918,000, of which $321,795,000 is budget authority and $134,123,000 is user fees. At this level, the budget authority increases by $24,500,000 compared to the FY 2022 Annualized CR, and user fees increase by $4,084,000.

The increase in budget authority and user fees reflected in the President's Budget 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 2023 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 priorities.

GSA Rental Payments

The FY 2023 President's Budget Request for GSA Rental Payments is $238,801,000, of which $166,286,000 is budget authority and $72,515,000 is user fees. The budget authority decreases by $833,000 compared to the FY 2022 Annualized CR and user fees increase by $2,244,000.

The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2023 Budget for GSA Rental Payments covers the cost of rental payments to GSA for FDA's approximately 6.8 million square feet of GSA-managed space. FDA's real property footprint, which includes relocated laboratories as part of FDA's laboratory

modernization effort, 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 considers new leases coming online for which rent will begin, 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 2023 Budget Request for Other Rent and Rent-Related is $161,106,000, of which $107,095,000 is budget authority and $54,011,000 is user fees. The budget authority increases by $22,833,000 compared to the FY 2022 Annualized CR, and user fees increase by $1,411,000.

The FY 2023 Budget will allow FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support the FDA mission. It will also provide additional funding to address increased utility and maintenance costs associated with FDA's aging owned buildings.

White Oak

The FY 2023 Budget Request for White Oak is $56,011,000, of which $48,414,000 is budget authority and $7,597,000 is user fees. The budget authority increases by $2,500,000 compared to the FY 2022 Annualized CR and user fees increase by $429,000.

The FY 2023 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 approximately 11,300 employees and contractors, as well as 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 2021 Final	FY 2021 Actuals	FY 2022 Annualized CR	FY 2023 President's Budget	FY 2023 PB +/- FY 2022 CR
Buildings and Facilities (Budget Authority).....	12,788	11,091	12,788	30,788	18,000

Figure 68 - Narrative by Activity

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 critical mission.

Supporting the FDA Mission

The B&F Program is a critical element of FDA's real property Asset Management Program (AMP) 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 69 - Newly Renovated Lab Building at the Jefferson Labs Complex

HHS developed a real property 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
- safety
- 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 lives. The BMAR also identifies and prioritizes short- and long-term projects using B&F funding. The most recent facility condition assessments were completed in FY 2021.

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 and Analytical Center, Winchester, Massachusetts

Activities in FY 2021 and Planned for FY 2022

Gulf Coast Seafood Laboratory – Dauphin Island, Alabama

The Gulf Coast Seafood Laboratory (GCSL) is FDA's sole marine laboratory and represents 80 percent of FDA research capacity for addressing seafood safety.

In FY 2021, FDA:

- continued coordinating the strategy for improving the laboratory and office building operations
- completed construction of the seawall.

In FY 2022, FDA plans further develop plans to improve the laboratory and office building operations.

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 2021, FDA:

- completed repair and improvements to the site water-treatment plant
- completed the design of exterior lighting upgrades between the campus entrance and the main mall area
- completed construction of Well #2
- continued to coordinate the design for the renovation for a critical Pathology lab
- initiated a project to design and replace the campus Motor Control Center
- initiated a project to replace an air-handling unit (AHU) in a lab building

- initiated a project to replace the capacitor bank in the main electrical substation
- initiated a project to upgrade exterior lighting to address a safety deficiency
- initiated a project to design roof renovations for several buildings
- initiated a project to make additional repairs to site infrastructure (roadways, drainage, sidewalks)
- initiated a project to design the replacement of the main sewer line from JLC to the Pine Bluff Arsenal's wastewater-treatment plant.

In FY 2022, FDA plans to initiate projects to:

- construct the Motor Control Center and capacitor renovations campus wide
- construct a new main sewer line from JLC to the Pine Bluff Arsenal's wastewater treatment plant
- renovate roofs on several buildings
- design roof renovations for Buildings 26 and 60
- design and construct the renovation of Building 62
- complete the design for a critical Pathology lab
- complete the design for Building 53E
- complete the design for Building 43
- complete the design and installation of a renovated campus fire-alarm system
- construct exterior lighting upgrades
- design Building 26 exterior upgrades
- design and construct Water Tower upgrades
- design and construct Guard Station upgrades
- perform a campus façade improvement study.

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 2021, FDA:

- completed coordinating the design for the replacement of the substation housing, switchgear, and electrical feeders on campus
- provided supplemental funding for the NEF projects for facility improvement measures to replace generators and correct the main laboratory's AHUs

- initiated installation of eyewash stations in select MOD2 research buildings to correct safety deficiencies
- initiated a project to evaluate the hot-water system at MOD2 out-buildings to correct flow and temperature issues
- continued design activities for the upgrade and renovation of Building H
- completed the campus draft master plan that began in FY 2020
- Initiated a project for preparation of program of requirements and building assessments for MOD1 and MOD2 laboratory buildings to address several scientific needs in support of the CVM and CFSAN missions.

In FY 2022, FDA plans to:

- complete coordinating the design for replacement of the substation housing, switchgear, and electrical feeders on campus and begin construction
- continue construction of the projects for replacement of generators and correcting the main laboratory AHUs and provide supplemental funding if needed
- complete construction of eyewash stations in select MOD2 research buildings to correct safety deficiencies
- initiate a project for design of hot-water system to resolve issues with MOD2 animal-research buildings
- complete the project to prepare a program of requirements and building assessment for MOD1 and MOD2 laboratory buildings and initiate a project for the design of MOD2 laboratory renovations to meet CVM requirements
- initiate a project to add exhaust fans to Building E and an AC unit to Building F
- complete design and begin construction for upgrade and renovation of Building H
- initiate a project to address campus backflow-preventer deficiencies
- complete the campus master plan.

Pacific Southwest Laboratory – Irvine, California

The Pacific Southwest Laboratory provides analytical laboratory support to FDA's regulatory mission in the Pacific Region.

In FY 2021, FDA:

- completed installation of security gates at building exits
- continued construction of HVAC system and controls improvements
- initiated a project to design and upgrade the HVAC systems in LAN closets to support additional IT equipment
- initiated a project to test exterior building shear walls for withstanding seismic activity
- initiated a construction project to address interior building cracks
- continued coordinating the design for the upgrade of the building nitrogen system
- continued coordinating the design for the replacement of the building cooling-tower system.

In FY 2022, FDA plans to:

- complete construction of HVAC system and controls improvements
- complete the project to design and upgrade the HVAC systems in the LAN closets to support additional IT equipment

- continue to study exterior wall cracks and begin a construction project to address identified issues
- complete construction project addressing interior cracks in the building
- initiate construction of nitrogen-system upgrade
- initiate construction of cooling-tower system replacement
- initiate a project for design of fire-alarm-system upgrades to meet current fire- and life-safety codes
- initiate a project for design and construction of the laboratory vacuum-system replacement and upgrade to increase its capacity.

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 $33.0 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 2021, FDA initiated design activities and provided supplemental funding for a new office building addition for the District Office.

In FY 2022, FDA plans to:

- initiate construction activities for the new office building addition for the District Office
- initiate a project to replace the north perimeter fence
- initiate a project to add exterior lighting for improved security
- initiate a project to replace five roof-top HVAC units in Building 1
- initiate a project to replace compressed-air lines in Building 1.

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 2021, FDA continued construction of the new laboratory building.

In FY 2022, FDA plans to complete construction of the new laboratory.

FDA Owned Facilities Condition and Sustainability Assessment

In FY 2021, FDA completed a project to assess the condition of owned facilities at JLC, MRC, Irvine, and San Juan. A report was produced for each site that included the updated FCI and

BMAR projects for site infrastructure and buildings by site. The GCSL and WEAC sites were not assessed since projects to improve operations at the aged, existing GCSL building and replace the existing aged WEAC building with a new building are in progress and will essentially eliminate the BMAR at these two locations. The identified BMAR projects will improve reliability and efficiency of failing infrastructure systems and allow CFSAN, CVM, NCTR, and ORA to continue their research, testing and oversight programs without disruption.

- CFSAN is responsible for promoting and protecting public health by ensuring that the nation's food supply is safe, sanitary, and wholesome, and honestly labeled.
- CVM is responsible for protecting human and animal health by ensuring that animal food and drugs are safe and effective.
- NCTR conducts FDA mission critical, peer reviewed, critical path (translational) research targeted to develop a scientifically sound basis for regulatory decisions and reduce risk associated with FDA-regulated products.
- ORA is the lead office for all agency field activities. ORA inspects regulated products and manufacturers, conducts sample analysis of regulated products, and reviews imported products offered for entry into the United States.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2019 Actuals	$11,477,000	$11,477,000	---
FY 2020 Actuals	$43,289,000	$43,289,000	---
FY 2021 Actuals	$11,091,000	$11,091,000	---
FY 2022 Annualized CR	$12,788,000	$12,788,000	---
FY 2023 President's Budget	$30,788,000	$30,788,000	---

Figure 70: Funding History

BUDGET REQUEST

The FY 2023 Budget Request is $30,788,000, an increase of $18,000,000 compared to the FY 2022 Annualized CR, 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 infrastructure and facilities.

At the Gulf Coast Seafood Laboratory facility, no projects are being planned in FY 2023 as we continue our project to improve operations in the existing office and laboratory space.

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 and campus generators
- correct exterior waterproofing issues throughout the campus
- upgrade domestic-water-system towers, including code-compliance issues
- replace roofs for two mission-critical lab and animal-research buildings

- repair or replace a freight elevator in the main administration building.

At the Muirkirk Road Complex, FDA will:

- correct loading-dock deficiencies and correct AAALAC-compliance items
- renovate laboratory space.

At the Pacific Southwest Laboratory, FDA will:

- replace and upsize emergency generators
- replace aged and undersized chillers in the main laboratory building
- remediate shear-wall cracking and provide additional structural support.

At the San Juan District Office and Laboratory, FDA will:

- provide communication protocol (BACnet) and integration of all HVAC units into campus-wide main monitoring system
- tie fire-alarm-communications system among buildings and modify sprinklers in Building 1
- address Building 1 settlement.

At the Winchester Engineering and Analytical Center, FDA will initiate a project to abate asbestos and lead paint in the existing main laboratory building in preparation for demolition.

The following table provides an allocation plan by site for use of the FY 2023 funds.

FY 2023 Buildings and Facilities Allocation Plan

BUILDINGS AND FACILITIES ALLOCATION PLAN **FY 2023** **Congressional Justification**	
Site	**President's Budget**
CFSAN Gulf Coast Seafood Laboratory – Dauphin Island, AL	$0
Jefferson Laboratories Complex (NCTR & ORA Arkansas Lab) – Jefferson, AR	$9,900,000
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	$10,930,000
ORA Pacific Laboratory SW – Irvine, CA	$8,000,000
San Juan District Office and Laboratory – San Juan, PR	$738,000
Winchester Engineering and Analytical Center – Winchester, MA	$1,220,000
B&F Project Total	**$30,788,000**

In FY 2023, 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 2023 will help reduce Scope 1, 2, and 3 greenhouse gas emissions by replacing or repairing aged, inefficient roofs and building equipment.

PROGRAM ACTIVITY DATA

Facility	Average FCI Score		
	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
CFSAN Gulf Coast Seafood Laboratory	81	81	81
Jefferson Laboratories Complex	65	68	70
Muirkirk Road Complex	51	62	64
ORA Pacific Southwest Laboratory	94	94	94
San Juan District Office and Laboratory	62	62	62
Winchester Engineering And Analytical Center	62	99	99

Figure 71 - Program Activity Data for Buildings and Facilities

NONRECURRING EXPENSES FUND

BUDGET SUMMARY

(Dollars in Thousands)

	FY 2021[2]	FY 2022[3]	FY 2023[4]
Notification[1]	$8,000	$81,200	$42,570

Authorizing Legislation: Section 223 of Division G of the Consolidated Appropriations Act, 2008

Allocation Method: Direct Federal, Competitive Contract

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Nonrecurring Expenses Fund (NEF) permits HHS to transfer unobligated balances of expired discretionary funds from FY 2008 and subsequent years into the NEF account. Congress authorized use of the funds for capital acquisitions necessary for the operation of the Department, specifically information technology (IT) and facilities infrastructure acquisitions.

Historically, FDA's Buildings & Facilities (B&F) and Infrastructure budgets have been unable to correct deficiencies in its backlog of maintenance and repairs, and in turn, the condition of FDA's owned assets have worsened. Additionally, the annual B&F funding levels have not provided adequate funding for owned-laboratory repairs, improvements, and replacements. With the exception of the White Oak provision that provides funds for laboratory repairs only on the White Oak Campus, FDA's Infrastructure budget does not provide funding for the relocation, repair, or improvement of FDA's General Services Administration (GSA)-owned and GSA-leased laboratories, forcing FDA to use program funds for these purposes.

Budget Allocation FY 2023 - $42.57 million

Jefferson Labs Complex (JLC), Data Recovery Center, $22.00 million – FDA will construct a Disaster Recovery Center on its FDA-owned Complex in Arkansas that will accommodate FDA-wide Information Technology disaster-recovery equipment and operations that are necessary to protect FDA operations. The project is part of FDA's data center consolidation plan and will also allow the relocation of the National Center for Toxicological Research (NCTR)

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[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 October 22, 2020.

[3] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on June 17, 2021.

[4] The NEF CJ indicates the amounts HHS intends to notify for in 2023; these amounts are planned estimates and subject to final approval.

Data Center to address critical reliability concerns, replace equipment and systems that are past their useful lives, and ensure the constructability of the JLC Master Plan.

Jefferson Labs Complex, Pathology Lab Fit Out, $20.57 million – FDA will relocate, consolidate, and modernize pathology operations on its FDA-owned Complex in keeping with the JLC Master Plan. Relocating the pathology suite will consolidate operations for efficiency and provide cutting-edge labs and storage for the program**.**

Budget Allocation FY 2022 - $81.2 million

Jefferson Labs Complex, $38.7 million – With FY 2022 NEF funding, FDA will construct a new central chiller plant to replace two separate, functionally obsolete chiller plants in accordance with the JLC Master Plan.

Denver Laboratory, $42.5 million – FDA will use NEF funding to address changing market conditions for replacing the existing laboratory in an aged and functionally obsolete GSA-owned building with a new, flexible, modern GSA-owned laboratory building.

Budget Allocation FY 2021 - $8.0 million

Muirkirk Road Complex, $8.0 million – This funding will correct laboratory building infrastructure deficiencies at the Muirkirk Road Complex by replacing two cooling towers; three air-handling units; control systems; and miscellaneous boiler components, pumps, piping, valves.

Budget Allocation FY 2020 and Prior

FDA received $59.3 million in FY 2020 NEF resources to advance the ongoing laboratory relocation project at the Office of Regulatory Affairs (ORA) Southeast Laboratory in Atlanta. Additionally, this funding supports infrastructure and laboratory renovation projects at FDA's owned Muirkirk Road Complex in Laurel, Maryland, and FDA's owned Pacific Southwest Laboratory in Irvine, California.

Starting in FY 2015 and 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 GSA-leased and GSA-owned laboratories. These NEF resources allowed FDA to fund replacement of the ORA's functionally obsolete owned laboratory at FDA's Winchester Engineering and Analytical Center in Winchester, Massachusetts, with an efficient, modern laboratory and to renovate laboratory buildings and an animal research processing area at FDA's owned JLC. Funds were also used for building and site infrastructure improvements, such as renovations, building system upgrades, roadway and drainage repairs, and building equipment replacement, at FDA-owned locations.

These resources have also allowed FDA to initiate the process of relocating ORA's aged, GSA-leased laboratories in Kansas City, Kansas, and Atlanta, Georgia, and ORA's GSA-owned laboratory in Denver, Colorado, into new, modern, and efficient laboratories designed to meet ORA's mission. Without the NEF resources received for these GSA-managed laboratory relocations, ORA would have had to cut critical items from its foods programs, including delaying hiring of personnel that could conduct critical inspections and/or delaying laboratory equipment purchases required to keep up with changing technology.

SUPPLEMENTARY TABLES

OBJECT CLASS TABLES

Budget Authority by Object Class

(Dollars in Thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget	FY 2023 President's Budget +/- FY 2022 CR
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	972,413	992,104	1,072,888	80,784
Other than full-time permanent (11.3)	81,065	82,707	89,441	6,735
Other personnel compensation (11.5)	50,500	51,522	55,718	4,195
Military Personnel - Basic Allowance for Housing (11.6)	150	153	157	4
Military personnel (11.7)	87,213	88,979	91,381	2,402
Special personnel services payments (11.8)	1,440	1,469	1,589	120
Subtotal, Personnel Compensation	**1,192,780**	**1,216,934**	**1,311,174**	**94,240**
Benefits:				
Civilian benefits (12.1)	401,726	409,860	443,234	33,374
Military benefits (12.2)	9,127	9,311	9,563	251
Benefits to former personnel (13.0)				
Subtotal, Benefits	**410,852**	**419,172**	**452,797**	**33,625**
Total Personnel Compensation and Benefits	**1,603,632**	**1,636,106**	**1,763,970**	**127,864**
Contractual Services and Supplies				---
Contractual Services:				---
Travel and transportation of persons (21.0)	12,861	12,293	15,083	2,790
Transportation of things (22.0)	4,097	3,916	4,805	889
Rental payments to GSA (23.1)	153,119	167,119	166,286	-833
Rent payments to others (23.2)	59	57	70	13
Communication, utilities, and misc. charges (23.3)	16,317	15,596	19,136	3,540
Printing and reproduction (24.0)	467	446	547	101
Subtotal, Contractual Services	**186,920**	**199,427**	**205,927**	**6,500**
Other Contractual Services:				
Consulting services (25.1)	62,522	59,761	73,324	13,564
Other services (25.2)	428,342	409,421	502,345	92,925
Purchase of goods and svcs from Govt Acts. (25.3)	480,739	459,503	563,795	104,292
Operation and maintenance of facilities (25.4)	76,679	73,292	89,926	16,635
Research and Development Contracts (25.5)	50,240	48,021	58,920	10,899
Operation and maintenance of equipment (25.7)	52,116	49,814	61,120	11,306
Subsistence and support of persons (25.8)				
Subtotal, Other Contractual Services	**1,150,639**	**1,099,811**	**1,349,431**	**249,620**
Supplies and Materials:				
Supplies and materials (26.0)	50,572	48,338	59,309	10,971
Equipment (31.0)	32,871	31,419	38,550	7,131
Land and Structures (32.0)	43,560	41,635	51,085	9,450
Grants, subsidies, and contributions (41.0)	215,251	205,742	252,439	46,697
Insurance claims and indemnities (42.0)	772	737	905	167
Interest and dividends , Refunds (43.0, 44.0)				---
Subtotal, Supplies and Materials	**343,025**	**327,872**	**402,288**	**74,416**
Total Contractual Services and Supplies	**1,680,584**	**1,627,110**	**1,957,646**	**330,536**
Total Budget Authority by Object Class	**3,284,216**	**3,263,216**	**3,721,616**	**458,400**

User Fees by Object Class

(Dollars in Thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget	FY 2023 President's Budget +/- FY 2022 CR
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	817,273	832,409	858,010	25,602
Other than full-time permanent (11.3)	94,328	96,075	99,030	2,955
Other personnel compensation (11.5)	83,425	84,970	87,584	2,613
Military Personnel - Basic Allowance for Housing (11.6)	12	12	12	
Military personnel (11.7)	78,032	79,612	81,762	2,150
Special personnel services payments (11.8)	216	220	227	7
Subtotal, Personnel Compensation	**1,073,286**	**1,093,298**	**1,126,625**	**33,326**
Benefits:				
Civilian benefits (12.1)	351,214	357,719	368,721	11,002
Military benefits (12.2)	11,381	11,612	11,925	314
Benefits to former personnel (13.0)				
Subtotal, Benefits	**362,595**	**369,331**	**380,646**	**11,316**
Total Personnel Compensation and Benefits	**1,435,881**	**1,462,629**	**1,507,271**	**44,642**
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0)	29,980	32,052	34,662	2,610
Transportation of things (22.0)	244	261	282	21
Rental payments to GSA (23.1)	68,542	70,271	72,515	2,244
Rent payments to others (23.2)	5	5	5	
Communication, utilities, and misc. charges (23.3)	4,280	4,575	4,948	373
Printing and reproduction (24.0)	997	1,066	1,153	87
Subtotal, Contractual Services	**104,047**	**108,230**	**113,565**	**5,335**
Other Contractual Services:				
Consulting services (25.1)	30,592	32,707	35,370	2,663
Other services (25.2)	452,329	483,591	522,970	39,379
Purchase of goods and svcs from Govt Acts. (25.3)	432,274	462,151	499,784	37,633
Operation and maintenance of facilities (25.4)	19,534	20,884	22,585	1,701
Research and Development Contracts (25.5)	63,846	68,259	73,817	5,558
Operation and maintenance of equipment (25.7)	46,149	49,339	53,357	4,018
Subsistence and support of persons (25.8)				
Subtotal, Other Contractual Services	**1,044,725**	**1,116,931**	**1,207,883**	**90,952**
Supplies and Materials:				
Supplies and materials (26.0)	18,030	19,276	20,846	1,570
Equipment (31.0)	4,212	4,503	4,870	367
Land and Structures (32.0)	26,980	28,844	31,193	2,349
Grants, subsidies, and contributions (41.0)	101,321	108,324	117,145	8,821
Insurance claims and indemnities (42.0)	299	319	345	26
Interest and dividends , Refunds (43.0, 44.0)	30,087	32,166	34,786	2,619
Receivables-collected (61.7)				
Subtotal, Supplies and Materials	**180,929**	**193,433**	**209,185**	**15,751**
Total Contractual Services and Supplies	**1,329,701**	**1,418,594**	**1,530,632**	**112,038**
Total User Fees by Object Class	**2,765,582**	**2,881,223**	**3,037,903**	**156,680**

Program Level by Object Class

(Dollars in Thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget	FY 2023 President's Budget +/- FY 2022 CR
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	1,789,685	1,824,513	1,930,898	106,385
Other than full-time permanent (11.3)	175,393	178,781	188,471	9,689
Military Personnel - Basic Allowance for Housing (11.6)	133,925	136,493	143,301	6,809
Other personnel compensation (11.5)	162	165	170	4
Military personnel (11.7)	165,245	168,591	173,143	4,552
Special personnel services payments (11.8)	1,656	1,689	1,815	126
Subtotal, Personnel Compensation	**2,266,066**	**2,310,232**	**2,437,798**	**127,566**
Benefits:				
Civilian benefits (12.1)	752,940	767,579	811,955	44,376
Military benefits (12.2)	20,508	20,923	21,488	565
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**773,447**	**788,502**	**833,443**	**44,940**
Total Personnel Compensation and Benefits	**3,039,513**	**3,098,735**	**3,271,241**	**172,506**
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0)	42,840	44,344	49,744	5,400
Transportation of things (22.0)	4,342	4,177	5,088	910
Rental payments to GSA (23.1)	221,661	237,390	238,801	1,411
Rent payments to others (23.2)	64	62	75	13
Communication, utilities, and misc. charges (23.3)	20,596	20,171	24,084	3,912
Printing and reproduction (24.0)	1,464	1,512	1,700	188
Subtotal, Contractual Services	**290,967**	**307,657**	**319,492**	**11,835**
Other Contractual Services:				
Consulting services (25.1)	93,115	92,467	108,694	16,227
Other services (25.2)	880,671	893,012	1,025,316	132,304
Purchase of goods and svcs from Govt Acts. (25.3)	913,013	921,654	1,063,578	141,925
Operation and maintenance of facilities (25.4)	96,213	94,176	112,511	18,335
Research and Development Contracts (25.5)	114,087	116,280	132,738	16,457
Operation and maintenance of equipment (25.7)	98,265	99,153	114,477	15,324
Subsistence and support of persons (25.8)	---	---	---	---
Subtotal, Other Contractual Services	**2,195,364**	**2,216,742**	**2,557,313**	**340,572**
Supplies and Materials:				
Supplies and materials (26.0)	68,602	67,614	80,155	12,541
Equipment (31.0)	37,083	35,922	43,420	7,498
Land and Structures (32.0)	70,539	70,480	82,278	11,799
Grants, subsidies, and contributions (41.0)	316,572	314,066	369,583	55,517
Insurance claims and indemnities (42.0)	1,070	1,057	1,250	193
Interest and dividends , Refunds (43.0, 44.0)	30,087	32,166	34,786	2,619
Receivables-collected (61.7)	---	---	---	---
Subtotal, Supplies and Materials	**523,953**	**521,306**	**611,473**	**90,167**
Total Contractual Services and Supplies	**3,010,285**	**3,045,704**	**3,488,278**	**442,574**
Total Program Level by Object Class	**6,049,798**	**6,144,439**	**6,759,519**	**615,080**

SALARIES AND EXPENSES TABLE

(Dollars in Thousands)	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget	FY 2023 President's Budget +/- FY 2022 CR
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1)	972,413	992,104	1,072,888	80,784
Other than full-time permanent (11.3)	81,065	82,707	89,441	6,734
Other personnel compensation (11.5)	50,500	51,522	55,718	4,196
Military Personnel - Basic Allowance for Housing (11.6)	150	153	157	4
Military personnel (11.7)	87,213	88,979	91,381	2,402
Special personnel services payments (11.8)	1,440	1,469	1,589	120
Subtotal, Personnel Compensation	**1,192,781**	**1,216,934**	**1,311,174**	**94,240**
Benefits:				
Civilian benefits (12.1)	401,726	409,860	443,234	33,374
Military benefits (12.2)	9,127	9,311	9,563	252
Benefits to former personnel (13.0)	---	---	---	---
Subtotal, Benefits	**410,853**	**419,171**	**452,797**	**33,626**
Total Pay Costs	**1,603,634**	**1,636,105**	**1,763,971**	**127,866**
Travel and transportation of persons (21.0)	12,861	12,293	15,083	2,790
Transportation of things (22.0)	4,097	3,916	4,805	889
Rental payments to GSA (23.1)	153,119	167,119	166,286	-833
Rent payments to others (23.2)	59	57	70	13
Communication, utilities, and misc. charges (23.3)	16,317	15,596	19,136	3,540
Printing and reproduction (24.0)	467	446	547	101
Subtotal, Contractual Services	**186,920**	**199,427**	**205,927**	**6,500**
Other Contractual Services:				
Advisory and assistance services (25.1)	62,522	59,761	73,324	13,563
Other services (25.2)	428,342	409,421	502,345	92,924
Purchase of goods and svcs from Govt Acts. (25.3)	480,739	459,503	563,795	104,292
Operation and maintenance of facilities (25.4)	76,679	73,292	89,926	16,634
Research and Development Contracts (25.5)	50,240	48,021	58,920	10,899
Operation and maintenance of equipment (25.7)	52,116	49,814	61,120	11,306
Subtotal, Other Contractual Services	**1,150,638**	**1,099,812**	**1,349,430**	**249,618**
Supplies and materials (26.0)	50,572	48,338	59,309	10,971
Total Non-Pay Costs	**1,388,130**	**1,347,577**	**1,614,666**	**267,089**
Total Salary and Expense	**2,991,764**	**2,983,682**	**3,378,637**	**394,955**
Direct FTE	**10,042**	**10,042**	**10,545**	**503**

DETAIL OF FULL-TIME EQUIVALENTS

	FY 2021 Actuals			FY 2022 Annualized CR			FY 2023 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Food Safety and Applied Nutrition	1,121	45	1,166	1,112	45	1,157	1,232	45	1,277
Center for Drug Evaluation and Research	5,102	483	5,585	5,226	483	5,709	5,289	483	5,772
Center for Biologics Evaluation and Research	1,207	51	1,258	1,166	51	1,217	1,174	51	1,225
Center for Veterinary Medicine	716	11	727	680	11	691	751	11	762
Center for Devices and Radiological Health	1,820	77	1,897	1,762	77	1,839	1,794	77	1,871
National Center for Toxicological Research	308	---	308	276	---	276	280	---	280
Office of Regulatory Affairs	4,819	351	5,170	4,546	351	4,897	4,690	351	5,041
Headquarters and Office of the Commissioner	885	59	944	866	59	925	934	59	993
Export Certification	26	---	26	26	---	26	26	---	26
Color Certification	37	---	37	37	---	37	37	---	37
Family Smoking Prevention and Tobacco Control Act	1,141	44	1,185	1,158	44	1,202	1,174	44	1,218
Priority Review Vouchers (PRV) Pediatric Disease	11	---	11	11	---	11	11	---	11
21st Century Cures (BA Only)	187	---	187	187	---	187	187	---	187
Cancer Moonshot (BA Only)	---	---	---	---	---	---	5	---	5
Total	**17,380**	**1,121**	**18,501**	**17,053**	**1,121**	**18,174**	**17,584**	**1,121**	**18,705**

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 77 reimbursable, 1 FOIA, 32 PEPFAR, 4 IDDA, and 42 COVID Supplemental.

DETAIL OF POSITIONS

	FY 2021 Final	FY 2022 Enacted	FY 2023 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	47	47	48
Total Executive Service	**47**	**47**	**48**
Total - ES Salary	**$9,070,718**	**$9,131,787**	**$9,606,811**
General Schedule (GS)			
GS-15	1,535	1,534	1,582
GS-14	4,024	4,020	4,146
GS-13	4,840	4,836	4,987
GS-12	2,001	1,999	2,062
GS-11	767	766	790
GS-10	6	6	6
GS-9	523	522	538
GS-8	39	39	40
GS-7	264	264	272
GS-6	64	64	66
GS-5	24	24	25
GS-4	17	17	18
GS-3	12	12	12
GS-2	3	3	3
GS-1	4	4	4
Total General Schedule	**14,121**	**14,110**	**14,550**
Total - GS Salary	**$1,681,867,584**	**$1,693,190,822**	**$1,781,268,518**
Administrative Law Judges (AL)	---	---	---
Scientific/Senior Level (ST/SL)	4	4	4
Senior Biomedical Research Service (RS)	45	45	46
Scientific Staff Fellows (RG) (Title 42)	963	962	992
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	127	127	131
Former Performance Mgmt Recognition System Employees (GM)	---	---	---
Physicians and Dentists - (GP) (Title 38)	700	699	721
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06	280	280	280
Commissioned Corps - Other	841	841	841
Total Commissioned Corps	**1,121**	**1,121**	**1,121**
Administratively Determined (AD) (includes Title 42)[2]	1,026	1,025	1,057
Wage Grade	10	10	10
Consultants[2]	22	22	23
Total FTE (End of Year)[1]	**18,187**	**18,174**	**18,705**
Average ES Level	1	1	1
Average ES Salary	$192,994	$194,441	$198,379
Average GS grade	13	13	13
Average GS Salary	$119,104	$119,997	$122,427
Average GM Salary	$0	$0	$0
Average GP Salary	$220,060	$221,710	$226,200

[1] Does not include FTE estimates for 77 reimbursable, 1 FOIA, 32 PEPFAR, 4 IDDA and 42 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

APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

House Committee Report (117-82)

1. Access to Compounded Hormones

Access to Compounded Hormones.—As the FDA reviews recommendations from the National Academies of Sciences, Engineering, and Medicine's report on the Clinical Utility of Compounded Hormones, the committee urges FDA to engage with compounders and other stakeholders to help ensure access to compounded drugs for patients who need them.

FDA Response:

Compounded drugs can address an important medical need for certain patients; however, they also present risks to patients because they do not receive premarket review for safety, effectiveness and quality. FDA's compounding program aims to help protect patients from poor-quality compounded drugs, while preserving access to lawfully marketed compounded drugs for those patients whose medical needs cannot be met by an FDA-approved drug. Compounded "bioidentical hormone replacement therapy" products are used at times instead of FDA-approved drug products for hormone replacement therapy. Some compounders market these products as superior to FDA-approved drugs by making assertions that they are more natural or safer or better for patients than FDA-approved drug products. However, like other compounded drugs, compounded "bioidentical hormone replacement therapy" products are not FDA-approved, which means these products have not undergone an FDA assessment of quality, safety, or effectiveness prior to marketing.

To help inform the public and FDA's policies regarding compounded "bioidentical hormone replacement therapy" products, the agency entered into an agreement with the National Academies of Sciences, Engineering, and Medicine (NASEM) to convene an ad hoc committee to conduct a study on the clinical utility of these products. The committee also reviewed which populations may benefit from the use of these preparations and considered whether the available evidence support their use to treat patients. The committee issued its report, "The Clinical Utility of Compounded Bioidentical Hormone Therapy," on July 1, 2020.[183] The NASEM report explores the uncertainties of the benefits and potential safety risks with the use of these compounded products.

FDA believes the results of NASEM's research provide important information that will increase public understanding regarding compounded hormone products. FDA intends to consider the information in the report when developing agency policies, while also taking into account various concerns, including patient access concerns. FDA will continue to engage with compounders, regulators, healthcare professionals, and patients as we develop policies that ensure continued access to compounded drugs for patients who need them, while also protecting patients from the risks of receiving a compounded drug when an FDA-approved product is appropriate for their medical care.

[183] https://www.nationalacademies.org/our-work/clinical-utility-of-treating-patients-with-compounded-bioidentical-hormone-replacement-therapy

2. Hand Sanitizer Safety

Hand Sanitizer Safety.—The Committee is concerned that FDA has not issued communication on the risks of refillable hand sanitizer dispensers. The Committee directs FDA to consider guidance or other communication to stakeholders on the risks and requirements of using open refillable dispensers for hand sanitizers, which may result in adulterated and mislabeled products.

FDA Response:

FDA is aware that issues have been raised regarding refillable hand sanitizer dispensers, including possible quality concerns with products and potential eye splashing. FDA is evaluating the potential risks and will take appropriate action, as needed. We note that FDA generally issues guidance documents for industry and not the general public.

3. Listeria

House Committee Report (117-82)

Listeria.—The Committee emphasizes reducing incidence of foodborne illness as an important public health goal and believes that coordinated and targeted resources are required to appropriately assess and combat the public health risks of foodborne pathogens. The Committee is aware that FDA is in the process of finalizing industry guidance regarding Listeria monocytogenes (Lm) in foods under their jurisdiction. Reducing incidence of listeriosis is indeed an important public health goal and the Committee supports efforts to accomplish this objective. Accordingly, the Committee urges FDA to apply a risk-based approach and direct its regulatory efforts toward high risk ready-to-eat (RTE) foods, those which support the growth of Lm. Additionally, the Committee urges FDA to utilize current scientific knowledge regarding the public health impact of foods that do not support growth of Lm to inform compliance policies. Recently published scientific research from food safety and public health experts recommends a regulatory action level of Lm for these low-risk foods to encourage industry to adopt quantitative Lm testing schemes and facilitate robust environmental monitoring programs, and ultimately result in significant reductions in disease incidence. Policies reflecting these developments align with other national regulatory standards and restore a level playing field for U.S. food processors in the global marketplace. Further, the Committee calls on FDA to define not-ready-to-eat foods in its guidance in a manner that aligns with the approach of FSIS and to ensure that this guidance is protective of public health, science-based and practical.

FDA Response:

FDA agrees that reducing incidence of listeriosis is an important public health goal. We are considering the latest science in developing three guidance documents to help achieve illness reductions. First, FDA is developing a revised draft compliance policy guide (CPG) to provide guidance to FDA staff on the agency's enforcement policy for Listeria monocytogenes (Lm) in foods. The revised draft CPG will update a 2008 draft CPG to reflect our current thinking based on updated scientific information, including current thinking regarding the enforcement policy for foods based on whether they are ready-to-eat (RTE) foods or not ready-to-eat (NRTE) foods and whether RTE foods support the growth of Lm. Second, FDA is developing a draft guidance to assist in classifying food as RTE or NRTE, since whether a food is RTE or NRTE has implications for which requirements of the preventive controls for human food regulation apply, including environmental monitoring for Lm. Third, FDA is preparing a final guidance, "Control

of Listeria monocytogenes in Ready-to-Eat Foods," based on comments received on a 2017 draft guidance on this subject. Our goal is to issue Listeria policies that are grounded in the best available science, protective of public health, and practical to implement.[184]

4. Lupus

House Committee Report (117-82)

Lupus.—The Committee is aware of barriers that have long affected the development of therapeutics for lupus, a disease that primarily targets women and disproportionately impacts African Americans, Latinas, Native Americans, and Asian Americans. The Committee is pleased that FDA participated in an externally-led, patient-focused drug development meeting with the lupus community and identified some of these barriers and that potential treatments are now in clinical trials. The Committee urges FDA to expedite its ongoing work with the lupus community to develop solutions to identified barriers that will accelerate development of new therapies.

FDA Response:

Systemic lupus erythematosus (SLE) is a serious disease, affecting a variety of organ systems, that can result in significant morbidity and mortality. FDA has recognized the challenges with studying SLE and its manifestations and has been collaborating with all stakeholders to facilitate expedited drug development in this space. This includes participation in and speaking at events including, the Lupus Foundation of America meetings in 2015 and 2018, the externally-led Patient Focused Drug Development meeting, Lupus Policy Summit in 2017, the Lupus 21st Century Conference in 2020, and the ongoing Lupus Federal Working Group. FDA has also collaborated with the U.S. Department of Health and Human Services' Office of Minority Health and launched the "Let's Take Charge!" campaign[185], an initiative that aims to make lupus research more inclusive and diverse. As a result of FDA engaging with stakeholders, several successful drug development programs resulted in recent approvals of products for lupus nephritis (belimumab and voclosporin) and pediatric SLE (belimumab), and most recently anifrolumab for general SLE in adults. FDA continues its active work with the scientific community, patients, and sponsors to encourage drug development and diverse participation in this space to address the remining unmet medical needs.[186]

5. Non-human Primates

Non-Human Primates.—The Committee continues to encourage the FDA to reduce primate testing, prioritize alternative research methods to relocate primates to sanctuaries and requests that a progress report be included in the FDA's fiscal year 2023 budget justification.

FDA Response:

FDA takes seriously the responsibility to ensure the welfare of research animals in our care and is deeply committed to ensuring the responsible and humane care of animals, including adhering

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[184] This response addresses similar FY22 Senate Report (117-34) language item "Ready-to-Eat [RTE] Foods".

[185] https://minorityhealth.hhs.gov/letstakecharge

[186] This response addresses similar FY22 Senate Report (117-34) language item "Lupus".

to the important principles of replacing, reducing, and refining animal studies (the 3Rs). FDA shares the nation's interest in reducing the need for non-human primates (NHPs) in FDA intramural research. In recent years, the agency has successfully supported industry in eliminating some animal-based tests and replacing some others with in vitro methods. An important example of FDA's leadership in development of alternatives is the replacement of the use of NHPs for poliovirus vaccine neurovirulence testing. However, 10 years of intense work was necessary for this alternative to be adopted. FDA continues to engage in developing, evaluating, and validating the feasibility of alternatives to using NHPs. In 2021, FDA continued its active participation and sponsorship with the National Academies of Sciences, Engineering, and Medicine, Institute for Laboratory Animal Research working groups and advisory board, including efforts related to nonhuman primate research and alternatives in alignment with the 3Rs. We look forward to continuing to work with the Committee and our partners on this important issue.

6. Orphan Products Grants Program

Orphan Products Grants Program (OPGP).—The Committee includes an additional $5,000,000 for the Orphan Products Grants Program at FDA. The Committee notes that this program can fund ALS clinical trials and invest in regulatory science to speed the approval of ALS treatments. The Committee encourages FDA to increase the number of ALS clinical trials to help expedite treatment developments, foster innovative trial designs that complement and speed the FDA regulatory processes, and enable natural history studies to more quickly understand ALS progression and pathology. In addition, the Committee directs FDA to increase engagement between government agencies, such as FDA and NIH, and other entities such as academic institutions and industry with respect to ALS and other neurodegenerative diseases.

FDA Response:

FDA is committed to supporting the development and evaluation of new treatments for rare diseases and understands the particular need for advancing understanding of, and investing in clinical trials studying products for ALS and other rare neurodegenerative diseases. The Orphan Product Grants Program at FDA has a track record of successfully funding clinical trials and natural history studies that have helped bring over 75 products (drugs, biological products, devices, and medical foods) to market 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 products through human clinical trials in extremely vulnerable populations often with life-threatening conditions. Currently, the program supports studies in rare diseases, including ALS and other rare neurodegenerative diseases, and provides flexibility for funding clinical trials and natural history studies at any stage of product development. The additional appropriations proposed here would allow the program to consider more grants focused on ALS and other rare neurodegenerative diseases.

FDA works with stakeholders, including other government agencies such as NIH, patients, patient advocates, sponsors, and researchers to support development and evaluation of safe and effective drugs, biological products, and devices for rare diseases, including ALS and other neurodegenerative diseases.

With respect to ALS specifically, FDA staff have engaged, and continue to engage, with various stakeholders, including patient groups, sponsors, and researchers regarding the needs of the patient community and industry's continued efforts to develop treatments for ALS. FDA has also engaged the Robert J. Margolis, MD, Center for Health Policy at Duke University to convene a series of workshops and meetings between FDA, patient advocates, academic researchers, and industry sponsors to identify promising approaches to support development of ALS therapies. FDA will continue to use all appropriate regulatory tools to facilitate rapid development and approval of products for ALS. FDA also looks forward to implementation of the Act for ALS legislation, recently enacted in December 2021, with the goal of improving access to, and research of, treatments for ALS. FDA appreciates the Committee's intention to fund this initiative and would be happy to provide an update, if relevant, at a later date.

7. Pancreatitis Guidance Document

House Committee Report (117-82)

Pancreatitis Guidance Document.—The Committee notes the important ongoing work to ensure safe and effective therapies become available for patients impacted by pancreatitis. The Committee urges FDA to build on recent community engagement efforts, including the externally-led Patient-Focused Drug Development meeting on this topic by continuing engagement with stakeholders in this area with the aim of developing and releasing Guidance for Industry in this area to stimulate additional activity and further guide ongoing efforts.

FDA Response:

Pancreatitis occurs when digestive enzymes and inflammation cause cellular damage or tissue death. The agency recognizes there is an unmet need for those affected by the disease, and we continue to play our part to further progress.

As part of the Patient-Focused Drug Development (PFDD) program, FDA welcomes patient organizations to identify and organize patient-focused collaborations to generate public input on disease areas, using the process established by FDA-led PFDD meetings as a model. These externally-led PFDD meetings give FDA and other key stakeholders, including medical product developers, health care providers, and federal partners, an important opportunity to hear directly from patients, their families, caregivers, and patient advocates about the symptoms that matter most to them, the impact the disease has on patients' daily lives, and patients' experiences with currently available treatments. FDA continues this and other stakeholder engagement, in the form of holding mini-symposia and planning public workshops with the aim of developing and releasing Guidance for Industry in this area to stimulate additional activities and further guide ongoing efforts.[187]

8. Sesame

Sesame.—The committee is concerned that the recent FDA Draft Guidance for Industry on Voluntary Disclosure of Sesame is insufficient to protect Americans with sesame allergy, and directs FDA to consider further action to require sesame to be labeled the same as other major allergens.

[187] This response addresses similar FY22 Senate Report (117-34) language item "Pancreatitis Guidance Document".

FDA Response:

With passage of the Food Allergen Safety, Treatment, Education, and Research Act (FASTER Act) in April 2021, Congress amended Section 201(qq) of the Federal Food, Drug, and Cosmetic Act to add sesame to the list of major food allergens, making it the ninth major food allergen when the FASTER Act takes effect January 1, 2023. Although there is no need for FDA to promulgate any regulations to implement its provisions, FDA is in the process of updating any relevant guidance documents and other materials to include sesame in the list of major food allergens. Additionally, FDA is developing various stakeholder educational materials to provide information on the provisions of the FASTER Act. The Draft Guidance for Industry on Voluntary Disclosure of Sesame will remain in place until January 1, 2023, to encourage industry to clearly identify sesame on product labeling.

9. Traceback

Traceback.—The Committee recognizes that the ability to trace back contaminated products is critical to containing food safety outbreaks but that challenges associated with tracing these products from the end-consumer through the supply chain continue to persist. The Committee directs FDA to emphasize in its final rulemaking the importance of capturing at the point of sale details such as the lot number and product identifier instead of prescribing the mechanism by which the information is shared through the supply chain. The Committee also directs FDA to ensure these details are maintained from the point of origination, creation, and/or transformation through to the retail food or food service establishment. To avoid duplication, the Committee urges FDA to clearly define traceability requirements that, where possible, align with existing consensus standards for traceability utilized by industry and allow for records to be maintained in electronic and paper form.

FDA Response:

FDA is committed to promulgating a final rule under section 204(d) of the FDA Food Safety Modernization Act (FSMA) regarding requirements for additional traceability records for certain foods that is both protective of public health and workable for industry.

In accordance with FSMA 204(d)(1), FDA is required to make the recordkeeping requirements scale-appropriate, and the agency is prohibited from requiring the creation and maintenance of duplicate records, prescribing specific technologies for the maintenance of records, and, to the extent practicable, requiring a facility to change business systems. Accordingly, the final rule will describe the specific traceability information a covered entity must establish, maintain, send to subsequent recipients, and make available to FDA upon request, but will not specify the form, mechanism, or type of system in which those records must be established, maintained, or shared.

10. Valley Fever

Valley Fever.—The Committee notes that FDA decided in July 2020 not to add coccidioidomycosis, also known as Valley Fever, to the list of tropical diseases under section 524 of the Federal Food, Drug, and Cosmetic Act for purposes of PRV eligibility. The Committee directs the FDA to consider any additional data and information provided by subject matter experts and other stakeholders to its public docket, and make a new determination based on this additional information if appropriate.

FDA Response:

FDA recognizes the challenges of developing new therapies for the treatment of Valley Fever, or coccidioidomycosis, a fungal disease that poses a growing public health threat within the endemic region of the United States. On August 5, 2020, FDA brought together subject matter experts from academia, industry, and other government agencies to discuss the disease landscape and strategies to facilitate product development for treatment of coccidioidomycosis. Furthermore, a summary of this workshop was recently published in Clinical Infectious Diseases.[188] FDA continues to encourage collaboration among stakeholders to further these important efforts.

Consistent with its established processes for review of candidates for addition to the list of tropical diseases for the purpose of tropical disease PRV eligibility, FDA will consider additional information provided to its docket regarding coccidioidomycosis and make a new determination based on this information if appropriate.

Senate Committee Report (117-34)

1. Added Sugar Labeling

Added Sugar Labeling.—The Committee remains concerned about potential consumer confusion over FDA nutritional labeling requirements and guidelines for added sugar for single ingredient products like maple syrup and honey, where sugar is naturally occurring in the product rather than added to the product. The Committee notes that the FDA issued guidance to the industry on June 18, 2019, to verify that the phrase ''added sugar'' is not required in the regulated portion of the nutrition facts label for these products. This guidance instructed producers that the percent daily value would be required to appear on the label and allowed for the voluntary use of a footnote to explain that this refers to a percent daily value of ''added sugar.'' The Committee is concerned, and industry- conducted consumer studies suggest, that continued use of the term ''added sugar'' in relation to percent daily value will mislead consumers to think that sugar has been added to a pure single-ingredient maple or honey product, and directs the FDA to continue working with impacted industries to ensure clear and appropriate labeling.

FDA Response:

FDA has met and corresponded with the maple syrup and honey industries, including the International Maple Syrup Institute and the National Honey Board (NHB), about the optional Added Sugars percent Daily Value (DV) explanatory statement in the Nutrition Facts label (NFL) for single-ingredient sugars and syrup products, and how to address their concerns. In February 2020, NHB submitted a summary of findings from consumer research NHB conducted regarding the optional Added Sugars percent DV explanatory statement in the NFL for single-ingredient sugars and syrup products. We reviewed NHB's summary of findings from their consumer research, but NHB has not provided the agency with the full study.

It is important to provide information about added sugars on the NFL to allow consumers to maintain healthy dietary practices, as was reiterated in the *Dietary Guidelines for Americans, 2020-2025*. Additional time and education is still needed to allow consumers to adjust to and better understand the updated NFL and the declaration of added sugars in the NFL. FDA launched our NFL consumer education campaign in March 2020 and conducted a second media

[188] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab904/6397685

push in March 2021, and we are continuing our outreach efforts. The campaign aims to raise awareness about the changes to the NFL to help consumers make more informed food choices that contribute to lifelong healthy eating patterns. The campaign includes information about added sugars generally, as well as added sugars on single-ingredient sugar and syrup products, plus information on determining how much a nutrient in a serving of food contributes to a daily diet. FDA is sensitive to the honey and maple syrup industries' concern regarding consumers' potential perception of the term "Added Sugars" on the labeling of such products, and we welcome a continued dialogue with these industries.

2. Inspections

Inspections. —The Committee is concerned that the ongoing pandemic has forced the FDA to postpone hundreds of facility inspections, creating a backlog that may delay new drug approvals and lead to possible shortages of existing medicines. When practicable, the Committee urges the FDA use the authorities provided to them under Sec. 704 of the Food, Drug, and Cosmetic Act [FDCA] to conduct remote inspections and evaluations to help ensure drug application approvals assessments are not delayed by limitations on in person inspections. As previously noted, the Committee provides a $15,000,000 increase for inspection activities.

FDA Response:

At the beginning of the COVID-19 pandemic, to mitigate the spread of the virus, FDA made the decision to pause most foreign and domestic inspections, with the exception of mission-critical work.

FDA prioritized inspections by identifying those that were mission-critical, on a case-by-case basis. This means that conducting the inspection was key to our public health mission and that the activity could not be accomplished in any other way. FDA's assessment of whether an inspection was mission-critical carefully considered many factors related to the public health benefit of the product subject to inspection, including whether the product:

- received breakthrough therapy or regenerative medicine advanced therapy designation;
- is used to diagnose, treat, or prevent a serious disease or medical condition for which there is no other appropriate substitute;
- requires follow-up due to recall, or there is evidence of serious adverse events or outbreaks of a foodborne illness; or
- is related to our nation's COVID-19 response (e.g., drug shortages).

Throughout the pandemic, FDA has continued to conduct foreign and domestic mission-critical inspections and has successfully conducted inspections in nearly 30 countries.

In July 2020, following the pause on all non-mission-critical inspections that began in March 2020, FDA resumed prioritized domestic inspections. In July 2021, FDA transitioned to the Base-Case Scenario described in the Resiliency Roadmap (Roadmap) for FDA Inspectional Oversight, a transition to "standard operational levels" for domestic inspections, where in addition to continuing with mission-critical work, FDA was conducting domestic surveillance inspections, investigations and sample collections based on consideration of risk and identified FDA priorities. FDA exceeded the base-case scenario projections for FY 2021, and as detailed

in the Update to the Resiliency Roadmap for FDA Inspectional Oversight[189], had transitioned to standard operational levels for domestic inspections in October 2021. Although some travel restrictions and other pandemic-related uncertainties remained, FDA continued to work through mission-critical, other higher priority and surveillance inspections using risk-based approaches for evaluating public health impact.

The emergence of the highly contagious Omicron variant required FDA to update its operational status once again, to ensure the safety of FDA staff as well as industry personnel. On December 29, 2021, FDA announced that it would limit domestic inspections to those considered to be mission-critical and would also postpone the planning of prioritized surveillance inspections, which were set to begin in February 2022[190]. This announcement was in effect through January 19, 2022, at which time FDA would evaluate whether these limitations should continue.

On January 18, 2022 FDA extended the previously announced changes to inspectional activities to ensure the safety of its employees and those of the firms it regulates as the agency further adapts to the evolving COVID-19 pandemic and the spread of the omicron variant. FDA is extending the pause on domestic surveillance inspections through February 4, 2022 with the goal of restarting these activities as soon as safely possible. The agency will proceed with previously planned foreign surveillance inspections that have received country clearance and are within the CDC's Level 1 or Level 2 COVID-19 travel recommendation; otherwise, the inspection will be rescheduled. FDA's goal is to return to a regular cadence for foreign surveillance inspections in April 2022.

The agency also continues to provide robust oversight to as many facilities as possible through its development of new approaches and expanded use of a variety of alternative tools for oversight of FDA-regulated products, including remote inspections. These alternative tools also helped FDA gather information that informed other oversight and critical public health needs.

For example:

- As noted in the Roadmap, during the COVID-19 pandemic the agency has leveraged alternative oversight tools, including requests for records or other information from drug establishments under section 704(a)(4) of the FDCA. Although the agency does not currently have authority to mandate participation in remote interactive evaluations, we have used them on a voluntary basis, and in April 2021, FDA issued a final guidance entitled *Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency Guidance for Industry*, which describes how the agency will request and conduct voluntary remote interactive evaluations at facilities. The use of these tools has supported application approval decisions and helped FDA identify areas of focus for future inspections.
- The agency has established the FDA Inspectional Advisory Council (FIAC) to enhance the agency's coordinated approach to inspections, information sharing, and other processes to accelerate evaluation and potential integration of new oversight methods and tools. One of the top priorities of the FIAC is to develop an enterprise-wide policy and procedure for the use of Remote Regulatory Assessments, which include record requests

[189] https://www.fda.gov/media/154293/download

[190] https://www.fda.gov/news-events/press-announcements/fda-roundup-january-4-2022

made under section 704(a)(4) of the FDCA and requests for voluntary submission of records and remote interactive evaluations. These tools have been used throughout the pandemic to fortify our oversight efforts where in-person inspections were not possible. The FIAC initiative increases efficiency and consistency, and improves transparency and business processes.

As the ongoing public health crisis evolves, FDA will continue to evaluate the situation and consider how best to exercise its authorities, capabilities, and resources in order to most effectively conduct inspections. Note: FDA appreciates the Committee's intention to fund this initiative and would be happy to provide an update, if relevant, at a later date.

3. Pathogen Reduction and Deferral Policies for Blood Donation

Pathogen Reduction and Deferral Policies for Blood Donation.—The Committee is pleased that FDA plans to continue to expand its use of real-world evidence, including the Transfusion Transmissible Infections Monitoring System [TTIMS], and encourages greater investment in real-world evidence to inform its policies concerning blood donor deferral policies and the safety of the U.S. blood supply. The Committee also encourages FDA to prioritize risk of transfusion-transmitted infections and safeguard the blood supply. The Committee directs the FDA to swiftly collect, analyze, and act on the necessary scientific data to update its blood product donor deferral policies to ensure that its recommendations are based on current science and on individualized risk assessment rather than community-wide prevalence while maintaining the safety of the blood supply and not impeding HIV prevention efforts including uptake of HIV pre-exposure prophylaxis (PrEP], and to work with the Secretary and appropriate agency and stakeholder partners to ensure that any revisions to its policies are appropriately communicated to stakeholders and potential donors.

FDA Response:

FDA is committed to making science-based decisions in all areas, including with regard to blood donor deferral policies. FDA uses real-world evidence (RWE) to help inform its policies on subjects such as blood donor eligibility by actively monitoring over 60 percent of the U.S. blood supply for incidence and prevalence of HIV, hepatitis B virus, and hepatitis C virus.

The Transfusion Transmissible Infections Monitoring System (TTIMS) gathers and uses RWE 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 has made investments to support TTIMS over the last several years and continues to evaluate deferral policies based on available scientific evidence.

In 2021, FDA recompeted and awarded a contract for the TTIMS Laboratory and Risk Coordinating Center (LRCC), which serves as the biostatistical and analytical center for all analyses relevant to the evaluation and monitoring of HIV (incident and prevalent), HCV (incident), and HBV (incident) positive blood donors. The TTIMS LRCC will monitor antiretroviral drugs (ARV) and PrEP/ post-exposure prophylaxis (PEP) use in the U.S. allogeneic blood donor population based on testing of both HIV-positive and infection negative donations for the presence of ARV drugs and explore the characteristics of blood donors who use ARV/PrEP/PEP to better understand their risks, knowledge, and motivations for donating while using these therapies.

FDA remains actively engaged in efforts to advance science-based blood donor deferral policies that will maintain the safety of the blood supply. In response to the current coronavirus disease (COVID-19) pandemic, and the resulting urgent need for life-saving blood and blood components, the agency accelerated its review of the existing data and determined that a revision to the blood donor policy for certain groups was warranted. The agency issued guidance for immediate implementation on April 1, 2020, reducing the deferral period for men who have sex with men from twelve months to three months from the most recent sexual contact.

FDA is currently funding the ADVANCE (Assessing Donor Variability and New Concepts in Eligibility (HIV Risk Questionnaire)) study, a pilot study intended to provide data to help determine if a donor history questionnaire based on individual risk assessment would be as effective as time-based deferrals in identifying individuals at risk of transmitting HIV by blood and blood components. The study has launched in eight cities and is currently ongoing. FDA intends to share results of the study and welcomes collaboration with stakeholders as we continue to study science-based deferral policies. This is an issue the agency takes seriously, and we will continue to communicate and share information with stakeholders.

4. Shellfish Safety

Shellfish Safety.—The Committee urges the FDA to complete the single laboratory validation of the liquid chromatography mass spectrometry [LC–MS]-based method for detecting brevetoxins association with neurotoxic shellfish poisoning in molluscan shellfish. The Committee further urges the Interstate Shellfish Sanitation Conference to adopt the FDA's proposal for the LC–MS method for brevetoxin testing of shellfish as an Approved Method under the National Shellfish Sanitation Program.

FDA Response:

FDA has completed the single laboratory validation of the liquid chromatography mass spectrometry (LC-MS) method to detect brevetoxins analytes, and its proposal package for the Interstate Shellfish Sanitation Conference (ISSC) on this method is in development, pending work to resolve some outstanding issues regarding measurements. FDA expects to submit the proposal soon, at which point it will be reviewed by the ISSC.

5. Sunscreen Labeling Regulations

Sunscreen Labeling Regulations.—The Committee is encouraged that the FDA has proposed regulations dealing with the sunscreen monograph and urges the FDA to issue a revised sunscreen order in accordance with the procedures described in section 505G(b)(2) of the Federal Food, Drug, and Cosmetic Act (Public Law 75–717) as required by section 3854(c) of the CARES Act The Committee is pleased that the proposed sunscreen monograph aims to make sunscreens more effective and safer, and that the proposal addresses issues related to maximum Sun Protection Factor [SPF] and sunscreen sprays. The Committee encourages FDA to educate stakeholders about its administrative order process and ensure that any final order related to sunscreen ingredients balances the value of currently marketed sunscreens as a proven skin cancer prevention tool. The Committee also encourages FDA to coordinate with the National Academy of Sciences, Engineering, and Math [NASEM] in coordination with EPA as directed by House Report 116–446 to help inform its upcoming study on sunscreen's effects on the environment and the public health as authorized under the Further Consolidated Appropriations

Act, 2020, and to communicate its jurisdiction over the regulatory status of over-the-counter drug products.

FDA Response:

On September 24, 2021, FDA posted the deemed final order[191] for sunscreens[192] and also issued a proposed revised sunscreen order consistent with the procedures set forth in section 505G(b)(2) of the Federal Food, Drug & Cosmetic (FD&C) Act.[193] This proposed order proposes changes to the requirements set forth in the deemed final order to bring them up to date with the current science. When finalized, the proposed order will fully replace the deemed final order with new requirements for sunscreens.

The CARES Act did not change the applicable scientific standards; accordingly, the proposals in the proposed order[194] are substantively the same as those described in FDA's 2019 proposed rule on sunscreens. FDA is using the proposed order as a vehicle to transition its ongoing consideration of the appropriate requirements for OTC sunscreen products from the previous rulemaking process to the new administrative order process. The proposed requirements described in the proposed order are aimed at bringing sunscreens marketed without approved applications up to date with the latest science to better ensure consumers have access to safe and effective sunscreen products. As the 2019 proposed rule did, the proposed order addressed several important areas including provisions related to dosage forms (including sunscreen sprays), maximum SPF values, and broad-spectrum requirements.

FDA is also committed to educating the public about the new administrative order process and has developed and is implementing a robust communication plan to do so, including a webinar series and a new website about the administrative order process with information and frequently asked questions.[195] FDA also launched a revised sunscreen website[196] that provides detailed information about both the deemed final order and proposed order for sunscreens. The agency

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[191] https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm?event=NewMonograph&ID=D1-D673977F06B1486C355A8162942E5B9CC2734AE65E4585CB6C013EDD5B03F3&OMUFID=OTC000006

[192] The deemed final order for sunscreens (the contents of which were established by operation of the CARES Act) reflects requirements in the 1999 final monograph regulation for sunscreens (which never took effect) and a 2011 final labeling and effectiveness testing rule. The deemed final order essentially preserves the pre-CARES status quo marketing conditions for OTC sunscreens marketed without approved applications. Before CARES was passed, these sunscreens were marketed according to nearly identical terms that were described in an FDA enforcement discretion policy. The deemed final order will remain in effect until the FDA issues another final order revising it. It is available at https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm?event=NewMonograph&ID=D1D-673977F06B1486C355A8162942E5B9CC2734AE65E4585CB6C013EDD5B03F3&OMUFID=OTC000006.

[193] The proposed revised sunscreen order is available at https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm-?event=NewMonograph&ID=E3DB1802A561C0EDEB894098532BC3BBAF94258EC18309569469E770134A3003&OMUFID=OTC000008

[194] https://www.federalregister.gov/documents/2021/09/27/2021-20780/amending-over-the-counter-monograph-m020-sunscreen-drug-products-for-over-the-counter-human-use-over

[195] https://www.fda.gov/drugs/over-counter-otc-nonprescription-drugs/over-counter-otc-drug-review-otc-monograph-reform-cares-act

[196] https://www.fda.gov/drugs/understanding-over-counter-medicines/sunscreen-how-help-protect-your-skin-sun

held a stakeholder call on September 27,2021 to provide additional education about the new sunscreen administrative orders and hosted a webinar for stakeholders and the public on the sunscreen orders on December 15, 2021. In addition, to help inform the National Academy of Sciences, Engineering, and Math's (NASEM) upcoming study "Environmental Impact of Currently Marketed Sunscreens and Potential Human Impacts of Changes in Sunscreen Usage," FDA presented to the NASEM committee on FDA regulation of sunscreens.[197]

[197] https://www.nationalacademies.org/event/06-17-2021/sunscreen-study-perspective-from-the-food-and-drug-administration

FDA DRUG CONTROL PROGRAM AGENCY

Budget Authority (in millions)	FY 2021 Final	FY 2022 Annualized CR	FY 2023 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)	$3.286	$3.265	$3.723
Drug Resources percentage	1.96%	1.98%	2.70%

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.

The agency recognizes that the nation continues to face a drug overdose crisis. While the number of prescription opioids dispensed has steadily declined since 2012, opioid overdose deaths continue to rise. Between October 2020 and September 2021, there were an estimated 78,000 overdose deaths involving legal and illicit opioids. In recent years illicit opioids, largely driven by fentanyl and its analogues, have become key contributors to the overdose crisis. We are additionally aware of other controlled substances – including benzodiazepines and stimulants, particularly methamphetamine – being used in combination with opioids. The complexity of addressing polysubstance use makes our efforts even more important.

FDA also recognizes the risk of opioids and other controlled substances as well as the benefits of these drugs for patients who need them, including those with debilitating chronic conditions. It

will take carefully developed, coordinated, and sustained action by multiple stakeholders to reduce the incidence of drug misuse, abuse, addiction, overdose, and death, while preserving appropriate access to these drugs for patients who need them. Doing our part to ensure the safe use of opioids and other controlled substances and ameliorate the overdose crisis is among FDA's highest priorities. FDA is engaging in many ongoing activities aimed at furthering these goals.

In alignment with HHS' new Overdose Prevention Strategy, FDA is focusing our efforts on opioids and other controlled substances in the following four areas:

- Support primary prevention by reducing unnecessary initial prescription drug exposure and inappropriate prolonged prescribing
- Encourage harm reduction through innovation and education
- Advance development of substance use disorder treatments
- Protect the public from unapproved, diverted, and counterfeit drugs presenting serious overdose risk

Methodology

FDA identified the drug control budget by using the dedicated budget authority for activities involving opioids and other controlled substances. 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 2023 request of $100.5 million for drug control activities is +$36.0 million above the FY 2022 Annualized CR.

Center for Drug Evaluation and Research

FY 2023 Request: $46.0 million, +$26.0 million above the FY 2022 Annualized CR

The FY 2023 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 overdose crisis. In particular, the FY 2019 appropriation provided CDER with base funding for regulatory science, enforcement, and innovation activities, to combat the opioid epidemic. CDER continues to utilize the $20.0 million in opioids base funding to further develop and implement evidence-based actions to address FDA's 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)
- Researching chronic pain therapies to inform the ongoing discussion about the appropriate use of opioid analgesics in chronic pain care

- Studying 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
- Enhancing 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)
- 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
- Exploring the impact of different packaging components of packaged opioids on opioid use as experienced by patients, prescribers, and pharmacists
- Assessing trends in opioid analgesic use in patients with and without cancer to understand the impact of opioid-reduction efforts on cancer patients
- Supporting development and regulatory assessment of new and generic intranasal naloxone sprays by generating new testing and evaluation models

FDA-supported research initiatives that have enhanced our understanding of appropriate opioids use for pain treatment, as well as risks and mitigating factors to address opioid misuse, abuse, overdose, and death. However, as fatal overdoses continue to increase in the U.S., further work is needed to address the overdose crisis, including the impact of other addictive substances as well as the impact of the COVID-19 pandemic.

Office of Regulatory Affairs – Field Activities

FY 2023 Request: $54.5 million, +$10.0 million above the FY 2022 Annualized CR

The FY 2023 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 International Mail Facilities (IMFs) to prevent unsafe, counterfeit, and unapproved drugs from entering the United States. FDA's IMF staff works diligently to examine parcels referred by U.S. Customs and Border Protection (CBP) that appear to contain drug product; however, FDA investigators are only able to inspect a fraction of the incoming international mail packages. Monitoring drug products in the IMFs helps FDA intercept any opioids that may have been missed by CBP. This in turn assists in the effort to prevent these opioids from reaching the consumer. 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.

Around 2018, Omnibus Spending Bill provided FDA with additional resources to support work within the IMFs. FDA increased the number of investigators it has in the IMFs from 8 to a total of 70 full-time equivalent (FTE) employees. Thus far, over 95 percent of these FTE have been hired and it is anticipated the IMFs will be fully staffed by the end of the 2022 calendar year. In FY 2021, FDA reviewed over 95,000 products at the IMFs. This is almost double the number of products processed in FY 2020. As the IMFs continue to increase staff with additional space and IT improvements at the IMFs, in cooperation with the United States Postal Service (USPS) and the General Services Administration (GSA), the number of products reviewed by FDA should continue to increase.

A record volume of FDA regulated commodities are being introduced for import inspection at the southern border. With additional funding provided in the FY 2022 budget request, ORA will bolster coverage at critical ports of entry, including enhancing IT infrastructure and tools as well as enhancing staff presence.

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, In August 2021, 57 analogues of 801(u) drugs identified in ORA testing and 6 APIs were added to the list bringing the total number of APIs on the list to 24. 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 85% 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 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 U.S. 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, partner in an expanded scientific presence and collaborate at selected IMFs and reduce duplication of efforts and facilitate mission responsibilities. FDA's Forensic Chemistry Center (FCC) is currently working with CBP's Laboratories and Scientific Services SS (LSS) to assist in the development of approaches to develop chemical fingerprints or signatures of illicit materials to aid in these investigations.

FDA, CBP, and Homeland Security Investigations (HSI) 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, continued expansion of the presence of scientific personnel at selected IMF locations, and facility improvements at the IMFs.

FDA's efforts to combat the opioid crisis includes criminal investigations by ORAs Office of Criminal Investigations (OCI). OCI strategically targets rogue medical professionals that tamper with and divert opioids intended for patients misusing their positions of public trust, breaches in the FDA-regulated pharmaceutical supply chain, bad actors who sell counterfeit and other illicit opioid products through the surface and dark nets and multi-national pharmaceutical companies that unlawfully contribute to the opioid crisis.

OCI continues to bring to justice health care professionals who take advantage of their unique position and compromise their patients' health and comfort by tampering with opioids intended for patients. For example, a recent OCI investigation resulted in the conviction of a nurse in July 2021 for fraudulently obtaining and tampering with opioids used to treat patients with pain. The nurse, who worked in a surgical and trauma ward of the healthcare facility, diverted the pain killing narcotic hydromorphone from pre-loaded syringes for his personal use, replaced the pain medication with saline solution, and then returned the syringes containing greatly reduced amounts of the pain killer for medical use by other hospital staff.

Furthermore, OCI's Cybercrime Investigation Unit (CCIU) continues to target online marketplaces and vendors selling counterfeit opioids through arrests and the seizure of assets. Thus far, CCIU's Operation CyberPharma has led to the arrest of 47 darknet vendors the takedown of a major darknet marketplace, and the seizure of more than $6.9 million in virtual currencies, drug counterfeiting tools and other assets. In addition, OCI also conducts investigations into corporate misconduct to ensure the proper parties are held responsible for their unlawful actions. OCI recently concluded a multi-year investigation involving pharmaceutical company Indivior (formerly known as Reckitt Benckiser Pharmaceuticals) and its executives for the illegal promotion of the opioid addiction treatment drug Suboxone. The investigation resulted in approximately $2.0 billion in settlement and the conviction of Indivior's CEO and Medical Director.

OCI's International Operations Program (IOP) conducts investigations into the shipment of violative FDA-regulated products, including illicit opioids, into the United States through domestic ports and facilities. IOP works to identify the source and destination of these drugs and collaborates with other federal agencies, such as CBP, HSI, Drug Enforcement Administration (DEA), and the Postal Inspection Service. OCI also works closely with our global law enforcement partners to help protect American consumers from illicit opioids. This

includes joint enforcement operations with our foreign law enforcement partners—for example, operations conducted with the United Kingdom and India to disrupt the flow of illegal drugs shipped to the United States through or from both countries. In addition, OCI also conducts international training programs to build and strengthen our relationship with foreign partners to protect the supply chain from counterfeit drugs, share techniques to identify counterfeit products, and identify trends and patterns of transnational criminal organizations exploiting trade routes.

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 proposing to debar an individual for a felony conviction involving two counts of illegal importation of a drug under this new authority. Since that time, FDA has issued an additional twenty (20) notices of debarment for drug importers based on felony convictions and has finalized 13 final orders of debarment. Furthermore, one of the twenty-one notices of debarment includes 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 on November 30, 2020. This individual attempted to import numerous 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 unapproved and counterfeit pharmaceuticals, including opioids, and adulterated supplements. In 2019, ten ORA chemists were trained at the FCC on the use of these instruments, a satellite laboratory unit, shared by both FDA and CBP scientists, was purchased from the US Army, 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 sample s were found to contain either DEA 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. FDA continues to partner with CBP/LSS in the Chicago IMF satellite lab and resumed operations there in June 2021. Two scientists have been hired and trained to permanently staff the CHI IMF satellite lab with plans to establish full operations at the Miami IMF satellite lab by the end of FY 2022.

HEALTH EQUITY

FDA's mission to facilitate the development and availability of therapeutics, vaccines, diagnostics, and other medical products, as well as advance efforts to ensure food safety and promote healthy eating, has a clear impact on underserved and vulnerable communities. FDA is dedicated to advancing the health of our nation's most vulnerable and underrepresented populations to achieve health equity for all and is working to support the Administration's Executive Orders, including Executive Order 13950, "On Advancing Racial Equity and Support for Underserved Communities Through the Federal Government."

FDA continues to work to address gaps, including efforts to advance clinical trial diversity. Moreover, health disparities that existed long before COVID-19 have been amplified during the pandemic, especially for racial and ethnic minority and other underserved populations. FDA's responsibilities to protect those most at risk and advance health equity, including across racial, ethnic, and rural/urban lines, have exponentially grown and become increasingly complex. FDA expects health equity focused efforts to significantly increase, including the amount and urgency of work, not only to address current priorities and COVID-19, but also efforts to address the gaps and needs of racial and ethnic minority, and other diverse populations disproportionately impacted by certain diseases and conditions (e.g., lupus, cardiovascular disease, Sickle Cell Disease, HIV/AIDS etc.).

FDA is working to advance equity through our present work utilizing multiple strategies and approaches. For example:

- FDA's active and passive vaccine surveillance systems can be leveraged to assess safety in specific subpopulations, including underserved communities.
- FDA's advancements can support communities with a high prevalence of medical comorbidities, as well as those individuals with rare diseases by allowing for monitoring of the safety and effectiveness of therapies in specific populations, and by addressing supply chain challenges and mitigating drug shortages to improve overall availability of critical drugs and devices.
- Finally, FDA utilizes acquisition strategies to ensure that our funding announcements provide opportunities for minority-owned, women-owned, veteran-owned and HUBZone small businesses, as well as minority institutions of higher learning. FDA coordinates with the Small Business Administration (SBA) for contract actions prior to their announcement. Any contract not designated for a small business will include a requirement for subcontracting with small businesses, if applicable.

FDA SPECIFIC ITEMS

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES

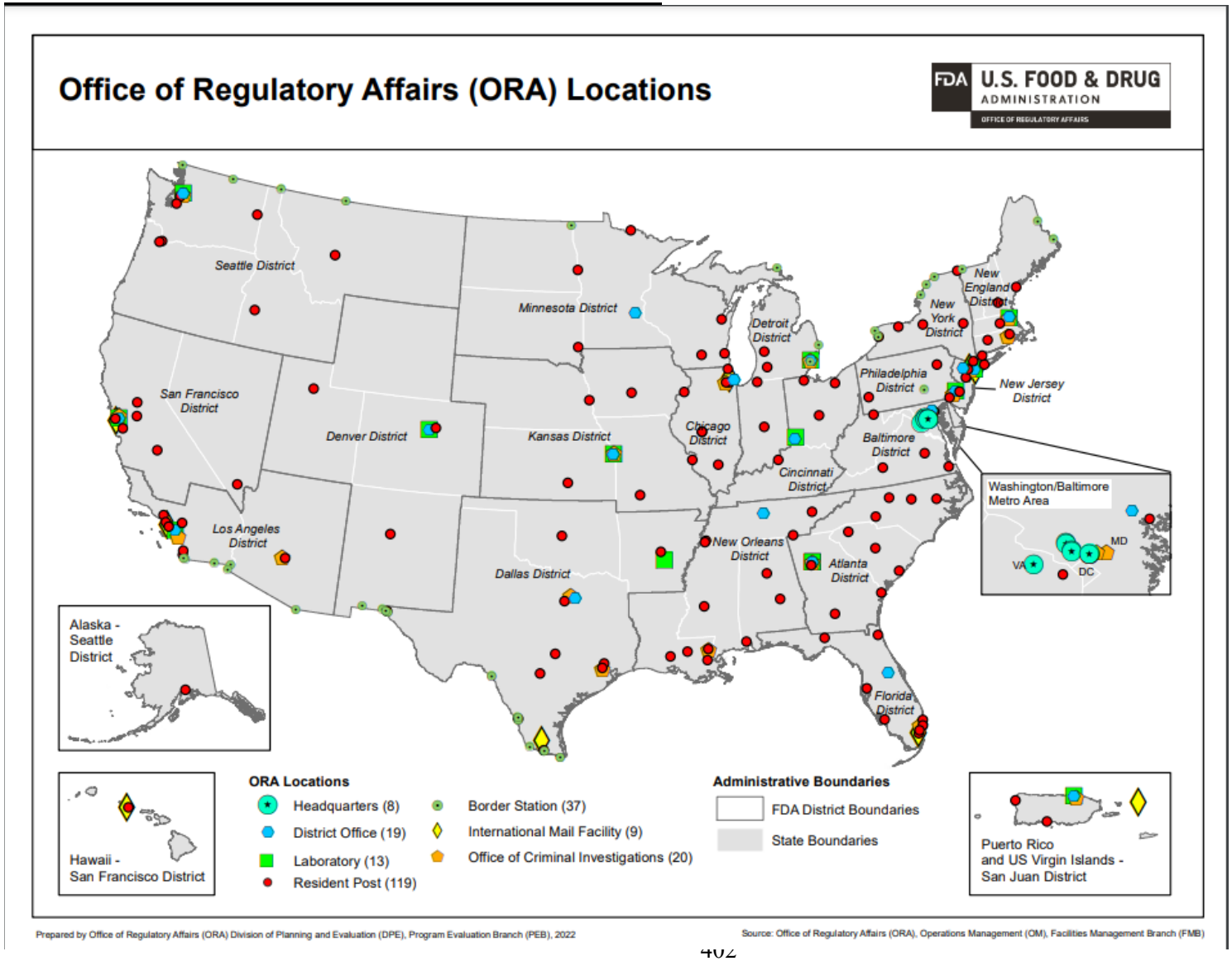

Figure 72 - Geographical Distribution of FDA Facilities

HIV/AIDS FUNCTIONAL TABLE

Food and Drug Administration
HIV/AIDS Resource Funding
(Dollars in Thousands)

Program	FY 2021 Estimate	FY 2022 Estimate	FY 2023 Estimate
Human Drugs	$29,869	$29,869	$29,869
Biologics	$12,054	$12,112	$12,558
Medical Devices	$343	$347	$352
Field Activity	$37,620	$38,240	$38,940
Other Activities	$3,395	$3,395	$3,395
Total HIV/AIDS	**$83,281**	**$83,963**	**$85,114**

Figure 74 - HIV/AIDS Resource Funding

CROSSCUTS

Food and Drug Administration
FY 2021-FY 2023 Crosscutting Information
(Program Level in Thousands)

(dollars in thousands)	FY 2021 Estimate	FY 2022 Estimate	FY 2023 Estimate
Alzheimer's Disease	13,126	13,408	13,374
HIV/AIDS	83,281	83,963	85,114
Antimicrobial Resistance	50,803	51,960	51,680
Bioterrorism-Medical Countermeasures	188,995	191,152	196,851
Cosmetics	13,829	14,002	16,471
Diabetes	25,850	26,362	26,636
Drug Abuse	14,749	15,062	15,062
Global Health	39,386	38,516	38,913
Immunization	161,858	163,720	170,203
Mental Health	16,554	16,553	16,567
Minority Health	5,344	9,831	10,056
Opioids 1/	75,011	75,011	113,011
Pandemic Influenza	28,279	28,617	29,304
Patient Safety	582,605	582,134	624,407
Pediatric Drugs	17,464	18,174	18,292
Tobacco 2/	712,000	712,000	812,000
Women's Health	67,601	69,144	71,481

*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

***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
2/ Reflects proposed increase of $100M in FY 2023 for the Family Smoking Prevention and Tobacco Control Act

Figure 75 - FY 2021-FY 2023 Crosscutting Information

CENTRAL ACCOUNTS

Program (dollars in thousands)	FY 2021 Actuals		FY 2022 Estimates		FY 2023 Estimates	
	BA	UF	BA	UF	BA	UF
Foods	**19,356**	-	**20,159**	-	**20,159**	-
Center	4,366	-	4,876	-	4,876	-
Field	14,990	-	15,283	-	15,283	-
Human Drugs	**19,816**	**29,872**	**15,702**	**30,015**	**15,702**	**30,015**
Center	14,035	28,394	11,112	28,319	11,112	28,319
Field	5,780	1,478	4,590	1,696	4,590	1,696
Biologics	**5,586**	**4,527**	**5,347**	**4,362**	**5,347**	**4,362**
Center	4,312	4,468	4,004	4,299	4,004	4,299
Field	1,273	60	1,344	62	1,344	62
Animal Drugs and Feeds	**3,893**	**1,123**	**3,984**	**1,117**	**3,984**	**1,117**
Center	2,145	1,123	2,177	1,117	2,177	1,117
Field	1,748	-	1,807	-	1,807	-
Devices and Radiological Health	**9,873**	**4,498**	**9,803**	**5,080**	**9,803**	**5,080**
Center	7,097	4,317	6,992	4,901	6,992	4,901
Field	2,776	181	2,812	178	2,812	178
National Center for Toxicological Research	**639**	**-**	**935**	**-**	**935**	**-**
Family Smoking Prevention and Tobacco Control Act	-	**9,601**	-	**10,191**	**-**	**10,191**
Center	-	9,296	-	9,752	-	9,752
Field	-	304	-	438	-	438
FDA Headquarters	**8,320**	**4,148**	**7,549**	**3,591**	**7,549**	**3,591**
Total	**67,483**	**53,769**	**63,479**	**54,354**	**63,479**	**54,354**

Figure 76 - Central Accounts

HHS CHARGES AND ASSESSMENTS

Fiscal Year 2021 Actuals	
Assessments:	**284,582**
NIH eRA Grants Management System Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	280,000
Federal Audit Clearinghouse	4,582
Fee For Service:	**75,663,706**
Program Support Center/ Office of the Secretary Provides various services to the FDA, including some Information and Systems Management Services	**20,921,354**
Financial Management Portfolio (FMP)	540,103
Real Estate and Logistics Portfolio Includes building operations, shredding, storage, property disposal	10,903,011
Equal Employment Opportunity Compliance and Operations Includes Complaint Investigations, FAD/Counseling, Mediation	1,231,650
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	8,246,590
Occupational Health Portfolio FDA agency health units and services	**2,253,542**
Information & System Management Services	**40,185,755**
Freedom of Information (FOIA)	
Unified Financial Management Systems (UFMS) Includes services for Consolidated Financial Reporting System (CFRS), Financial Business Intelligence System (FBIS), Governance and UFMS O&M support	13,983,756
HCAS Operations and Maintenance HCAS O&M services provide support for daily operations of the HCAS application.	2,864,000
Office of Operations Telecommunications team offers expertise on Application Support / Capacity Management / Intranet	2,223,192
Office of Enterprise Services	2,296,118
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	4,328,750
Office of Information Security (OIS) Includes computer security incident reponse center. Trusted Internet Connections and IT Security.	5,837,488
Digital Communications	8,652,451
Office of Human Resource Services Includes HR Center services teir I, payroll liaison, systems planning and implemenation	**12,303,055**

Figure 77 - HHS Charges and Assessments 1/2

Jointly Funded Projects:	**3,870,045**
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	1,550,000
CFO Audit of Financial Statements Audit services to be performed at the FDA in support of the fiscal year 2010 financial statement audit of the Department of Health and Human Services (DHHS) contracted and monitored by Office of the Inspector General (OIG) and its components, and related services.	541,707
Advisory Committee for Blood and Tissue Safety and Availability Agreement to provide funding for the advisory committee on Blood Safety	300,000
Regional Health Administrators IAG with OS/Office of Public Health & Science to support ten Regional Health Administrators. Their core mission is to promote understanding of and control functions within their respective regions improvements in public health and to conduct specific management.	308,010
Intra-department Council on Native American Affairs IAG with DHHS, Administration on Children and Families, for staff and administrative support for the Interdepartmental Council for Native American Affairs Committee meetings and assignments.(ICNAA), to conduct semi-annual Council meetings, Executive	17,000
National Science Advisory Board for Biosecurity Agreement with NIH to develop improved biosecurity measures for classes of legitimate biological research that could be misused to threaten public health or national security	225,000
NIH Negotiation of Indirect Cost Rates Agreement with NIH/OD to support costs associated with the negotiation of indirect cost rates with commercial organizations	36,937
OPM USAJOBS Fees charged by OPM to Federal Agencies to cover the cost of providing Federal Employment Information and services. OPM assesses an annual per-capita-fee based on each OPDIV percentage of the Departments total FTE on all paid employees with access to USAJOBs. The cost is distributed within HHS based on each OPDIV percentage of the Departments total FTE.	132,530
President's Advisory Committee on Combating Antibiotic-Resistant Bacteria Combating Antibiotic Resistant Bacteria, directs that "the Federal Government will work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections by implementing measures that reduce the emergence and spread of antibiotic-resistant bacteria and help ensure the continued availability of effective therapeutics for the treatment of bacterial infections"	175,000
Biosafety and Biosecurity Coordinating Council This will support the administrative management of the Council in efforts to coordinate and collaborate on biosafety and biosecurity issues within HHS.	84,351
Implementation of the DATA Act (PMO)	61,931
Tick-Borne Disease Working Group The work group will provide expertise and review all efforts within the Department of HHS related to all tick-borne diseases, to help ensure interagency coordination and minimize overlap and to examine research priorities.	150,000
National Clinical Care Commission The Commission is required to establish a committee to evaluate and make recommendations regarding improvements to the coordination and leveraging of progams within the Department and other Federal agencies related to awareness and clinical care for at least one, but not more than two, complex metabolic or autoimmune diseases resulting from issues related to insulin that represent a significant disease burden in the US.	90,000
Secretary's Tribal Advisory Committee Outreach with Tribal Governments and Organizations; communication and coordination of HHS activities and initiatives, which enhance the government-to-government relationship that HHS has with Indian Tribes. In addition IEA will find ways to educate HHS and guide the Department in developing future programs, initiatives, and other interactions with tribal governments and tribal organizations.	8,000
Grants Quality Service Mgmt. Office Grants QSMO PMO work on behalf of HHS awarding agencies and shared service providers. The PMO provides support by working with the HHS Offices of Grants, Finance and the Chief Operating Officer to support the goals of OMB memoranda M-19-16; the President's Management Agenda Cross Agency Priority Goals 5 and 8. Benefits of this work include in depth review of shared service cost models across the current 'As-Is' marketplace; right sizing cost models to determine equitable pricing for non-HHS customer support; and outreach to potential customers for existing and new HHS shared services.	6,910
Secretary Policy System SPS is the official records repository of the Immediate Office of the Secretary (IOS) for documents relevant to the Secretary, Deputy Secretary, Chief of Staff, and Executive Secretary. It is used to manage regulations, reports to Congress, correspondence, memoranda, invitations, and other documents.	48,433
Center for Health Innovation To coordinate and collaborate across the HHS enterprise and lead cross-functional health innovation efforts to accelerate the innovation journey from discovery to health. The mission is to identify critical health innovation gaps/challenges that are currently not being addressed and develop a coordinated plan to address these critical health gaps through public-private partnerships that span government, non-profit, and private sectors.	134,236

Figure 78 - HHS Charges and Assessments 2/2

DHHS Charges and Assessments Summary

Activity	FY 2021 Actuals	FY 2022 Estimate	FY 2023 Estimate
Assessments	**$ 284,582**	**$ 293,801**	**$ 303,335**
Fee for Service	**$ 75,663,706**	**$ 75,234,254**	**$ 81,237,861**
Program Support Center/OS	$ 20,921,354	$ 21,810,206	$ 24,232,000
Occupational Health Portfolio	$ 2,253,542	$ 2,435,187	$ 2,166,000
Information System Management Service	$ 40,185,755	$ 38,522,000	$ 42,373,000
Office of Human Resource Services	$ 12,303,055	$ 12,466,861	$ 12,466,861
Jointly Funded Services	**$ 3,870,045**	**$ 4,433,684**	**$ 4,647,355**
Total	**$ 79,818,333**	**$ 79,961,740**	**$ 86,188,551**

Figure 79 - HHS Charges and Assessments Summary

HHS DIGITAL MODERNIZATION

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 December 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 developed a Digital Communications Strategy that aligns with the requirements of IDEA. In FY 2020, 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.

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 and FDA Super Offices. 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

The WCF also supports Information Technology (IT) services provided by FDA Super Office the Office of Digital Transformation (ODT). 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.