FDA HEADQUARTERS

(Dollars in Thousands)	FY 2018 Enacted	FY 2018 Actual	FY 2019 Annualized CR	FY 2020 President's Budget	FY 2020 +/- FY 2019
FDA Headquarters Program	**290,638**	**315,684**	**299,587**	**320,164**	**20,577**
Budget Authority	***171,195***	***171,001***	***171,195***	***180,195***	***9,000***
User Fees	***119,443***	***144,683***	***128,392***	***139,969***	***11,577***
Prescription Drug (PDUFA)	*50,082*	*60,244*	*56,391*	*59,194*	*2,803*
Medical Device (MDUFA)	*7,811*	*7,297*	*8,463*	*9,209*	*746*
Generic Drug (GDUFA)	*34,489*	*27,947*	*35,243*	*35,784*	*541*
Biosimilars (BsUFA)	*706*	*1,393*	*632*	*1,022*	*390*
Animal Drug (ADUFA)	*446*	*828*	*1,004*	*734*	*-270*
Animal Generic Drug (AGDUFA)	*63*	*73*	*785*	*26*	*-759*
Tobacco Control Act	*24,491*	*46,921*	*24,491*	*30,867*	*6,376*
Mammography Quality Standards Act (MQSA)	*92*	*-20*	*92*	*102*	*10*
Food And Feed Recall	*75*	*---*	*75*	*78*	*3*
Food Reinspection	*480*	*---*	*480*	*499*	*19*
Voluntary Qualified Importer Program	*277*	*---*	*277*	*288*	*11*
Third Party Auditor Program	*39*	*---*	*39*	*41*	*2*
Outsourcing Facility	*392*	*---*	*420*	*225*	*-195*
Innovative Food Products	*---*	*---*	*---*	*1,900*	*1,900*
FTE	**943**	**943**	**1,001**	**1,018**	**17**

*FY 2017 and FY 2018 do not reflect the transfer of $1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2019, FDA proposes to discontinue the transfer.

Authorizing Legislation: The Federal Food Drug and Cosmetic Act (21 U.S.C. 321-399); Radiation Control for Health and Safety Act (21 U.S.C. 360hh-360ss); The Federal Import Milk Act (21 U.S.C. 142-149); Public Health Service Act (42 U.S.C. 201, et seq.); Foods Additives Amendments of 1958; Color Additives Amendments of 1960; Animal Drug Amendments (21 U.S.C. 360b); Controlled Substances Act (21 U.S.C. 801-830); The Fair Packaging and Labeling Act (15 U.S.C. 1451-1461); Safe Drinking Water Act (21 U.S.C. 349); Saccharin Study and Labeling Act; Federal Anti-Tampering Act (18 U.S.C. 1365); Medical Device Amendments of 1976; Infant Formula Act of 1980; Drug Enforcement, Education, and Control Act of 1986; Generic Animal Drug and Patent Term Restoration Act; Prescription Drug Marketing Act of 1987; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Prescription Drug Amendments of 1992; Safe Medical Device Amendments of 1992; Nutrition Labeling and Education Act of 1990; Dietary Supplement Health and Education Act of 1994; Animal Medicinal Drug Use Clarification Act of 1994; Animal Drug Availability Act of 1996; Food Quality Protection Act of 1996; Federal Tea Tasters Repeal Act (42 U.S.C. 41); Safe Drinking Water Act Amendments of 1996 (21 U.S.C. 349); Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Medical Device User Fee and Modernization Act of 2002; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Best Pharmaceuticals for Children Act of 2002 (21 USC 355a Sec. 505A); Animal Drug User Fee Act of 2003 (21 U.S.C. 379j-11 - 379j-12); Pediatric Research Equity Act of 2003 (21 USC 351 Sec. 505B); Project Bioshield Act of 2004 (21 U.S.C.360bbb-3); Minor Use and Minor Species Animal Health Act of 2004; Food Allergy Labeling and Consumer

Protection Act of 2004 Medical Device User Fee Stabilization Act of 2005; Sanitary Food Transportation Act of 2005 Dietary Supplement and Nonprescription Drug and Consumer Protection Act (21 U.S.C. 379aa-1); Pandemic and All-Hazards Preparedness Act, Food and Drug Administration Amendments Act of 2007; Protecting Patients and Affordable Care Act of 2010; The Family Smoking Prevention and Tobacco Control Act of 2009 (P.L. 111-31); The Federal Cigarette Labeling and Advertising Act (15 U.S.C. 1333); FDA Food Safety Modernization Act, Public Law 111-353 (January 4, 2011); The Food and Drug Administration Safety and Innovation Act (P.L. 112-144); Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, the Drug Quality and Security Act (2013), the 21st Century Cures Act (P.L. 114-255), Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

FDA Headquarters (HQ) provides strategic direction and a wide array of services, including cross-agency special medical, scientific, and regulatory programs, legal advice and counsel and litigation services across FDA's programs.

FDA reduces the burden of addiction crises that are threating American families by working to:

- reduce harms from opioid addiction and abuse
- implement a Comprehensive Nicotine Strategy and Youth Use/Enforcement Strategy.
- monitor post market safety of drugs.

HQ provides strategic leadership and coordination to enhance FDA's oversight of production, manufacturing, the global supply chain, and post market product use. FDA HQ provides policy direction and expertise to establish standards and guidance to protect patient and consumer safety. FDA HQ develops and standardizes policies and best practices across FDA consistent with statutes and regulations.

FDA's Oversight activities include:

- inspecting manufacturing and production facilities
- providing surveillance of adverse events
- preventing unsafe products from harming consumers.

The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.[110]

Foster Competition and Innovation

FDA HQ fosters competition and innovation by:

- continuing to implement FDARA and 21st Century Cures Act
- pricing/access with biosimilars
- supporting biotech innovation
- harnessing real-world evidence

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

- supporting international harmonization.

FDA HQ serves as the agency focal point for special programs and initiatives that are cross-cutting and clinical, scientific, and regulatory in nature. FDA HQ promotes high standards of scientific integrity to ensure ethical and responsible research practices such as human subject protection. FDA supports competition and innovation for medical products to improve greater access to safe and effective medical products for children, and rare disease populations.

FDA HQ plays a vital role in the coordination of:

- review of pediatric science to advance the development of pediatric therapeutics
- product development and an effective and efficient product review process
- data standardization and integrity
- consideration of health disparities and outcomes in regulatory decision making.

The following selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.

21st Century Cures Act and Food and Drug Administration Reauthorization Act (FDARA) of 2017

As part of the 21st Century Cures Act and the Food and Drug Administration Reauthorization Act (FDARA) of 2017, Congress is considering potential legislation that could impact medical product approval standards and regulatory pathways in an effort to expedite getting innovative products onto the market. FDA's work with respect to the initiatives has involved consolidating input from Centers and Offices across the Agency. Implementation of the 21st Century Cures Act and FDARA are priorities for FDA's authorizing committees, and the Agency has worked diligently to provide timely feedback to Congressional offices.

21st Century Cures Act and Human Subject Protection Harmonization

The 21st Century Cures Act (Cures Act) Section 3023 requires harmonization of the HHS and FDA human subject protection regulations. FDA is continuing to harmonize differences between its regulations and the Common Rule, that was revised January 19, 2017[111], to the extent applicable and permissible, given FDA's and HHS's different statutory mandates.

FDA HQ continues to coordinate with the Centers, ORA, and the National Institutes of Health (NIH) to further refine FDA's compliance program for the HHS regulations requiring clinical trial registration and results reporting on ClinicalTrials.gov (42 CFR part 11). FDA HQ continues to provide consultation to NIH to support reports required under the Cures Act related to ClinicalTrials.gov

[111] https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf The compliance date of the revised Common Rule has been delayed until January 21, 2019; see https://www.gpo.gov/fdsys/pkg/FR-2018-06-19/pdf/2018-13187.pdf

Regulatory Policy and Guidance

FDA HQ led the development of FDA's regulations on acceptance of clinical data for medical devices.[112] FDA developed a guidance to accompany the final rule; both were issued in February 2018.

FDA HQ led the development of a notice of proposed rulemaking (NPRM) to allow an exception from the requirements to obtain informed consent when a clinical investigation poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of human subjects.[113] This proposed rule, if finalized, would implement a provision of the 21st Century Cures Act and harmonizes with the revised Common Rule. FDA issued the NPRM in November 2018.

Guidance Documents – Human Subject Protection and Good Clinical Practice

Below are selected guidance documents on human subject protection issued by FDA HQ in 2018. This list does not represent any degree of importance or priority ranking among those items.

Publication Date	Formal Title	Description
October 2018	Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations[114]	This level 2 guidance clarifies the impact of certain provisions of the HHS revisions to the Common Rule regarding informed consent, expedited review, and continuing review, on FDA-regulated clinical investigations.
May 2018	IRB Written Procedures[115]	This joint final guidance with HHS describes regulatory requirements for IRB written procedures and provides recommendations on operational details to comply with the requirements.
February 2018	Acceptance of Data from Clinical Investigations for Medical Devices – Frequently Asked Questions[116]	This guidance provides recommendations for submission of information when clinical data from device investigations conducted within or outside the US are submitted to support research or marketing applications or other submission.

[112] 83 FR 7366; https://www.gpo.gov/fdsys/pkg/FR-2018-02-21/pdf/2018-03244.pdf

[113] 83 FR 57378; https://www.gpo.gov/fdsys/pkg/FR-2018-11-15/pdf/2018-24822.pdf%20

[114] https://www.fda.gov/RegulatoryInformation/Guidances/ucm623197.htm

[115] https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM512761.pdf

[116] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm597273.pdf

Publication Date	Formal Title	Description
January 2018	Payment and Reimbursement to Research Subjects – Information Sheet Guidance[117]	This information sheet guidance clarifies that reimbursement for human subjects' travel expenses to and from the clinical trial site and associated costs (e.g., parking, lodging) would not raise issues regarding undue influence.

Annually, FDA HQ responds to approximately 1,500 inquiries on human subject protection, informed consent, and best practices for the conduct of clinical trials. Archives of these questions and answers are available on https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm.

Geographic Information System Mapping

In FY 2018 the FDA HQ Geographic Information System (GIS) team conducted risk modelling and incident preparedness and recovery support for incidents including real-time support for the 2018 Hurricane Season. FDA HQ completed maps for 100 GIS project requests involving FDA regulated firms.

Global Health Security and Counterterrorism

FDA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security, counterterrorism efforts, and address emerging threats. FDA HQ:

- serves as point of entry on policy and planning matters
- serves as a focal point for the FDA's involvement in the HHS-led Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and the Department of Defense (DoD) medical countermeasure (MCM) programs
- coordinates the Medical Countermeasures Initiative (MCMi) to facilitate the development and availability of safe and effective MCMs against chemical, biological, radiological, and nuclear (CBRN) agents and emerging threats, such as pandemic influenza, Ebola virus, and Zika virus.

As part of the MCMi, FDA HQ funds a robust regulatory science research program to improve FDA's ability to perform science-based review of MCMs designed to lessen the effects of CBRN and emerging infectious disease threats. Accomplishments in FY 2017 and FY 2018 include:

- developing gastrointestinal, bone marrow, and lung models based on 'organs-on-a-chip' technology to use to develop drugs to treat acute radiation syndrome
- mapping immune responses to biothreats and MCMs in humans and developing animal models to support MCM development
- sponsoring nonclinical research studies to help inform FDA recommendations regarding potential transmission of Zika virus via organs and tissues

[117] https://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm

- developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during public health emergencies.
- expanding a database of regulatory-grade nucleic acid sequences to include antimicrobial-resistant organisms as well as Ebola- and Zika-related sequences
- developing Zika virus RNA reference materials that were distributed to manufacturers to validate nucleic acid based diagnostic tests and blood screening testing methods
- making available a Zika serological reference panel to aid in the regulatory evaluation of serological tests for the specific detection of recent Zika virus infection
- continuing the development of improved small animal models for Ebola and Zika
- developing a toolkit to assess efficacy of Ebola vaccines and therapeutics
- conducting survivor studies to better understand Ebola's after-effects, to help find new treatments
- addressing potential production bottlenecks for seasonal and pandemic influenza vaccines by developing novel alternative methods to measure influenza vaccine potency and generate reagents needed for vaccine standardization.

FDA HQ develops and coordinates the implementation policies and procedures to facilitate the availability of MCMs, including safeguarding MCMs from adulteration or disruption of supplies during public health emergencies and enabling access to MCMs through an appropriate mechanism such as an Emergency Use Authorization (EUA).

Accomplishments in FY 2017 and FY 2018 that support MCMs include:

- issuing final guidance that explains FDA's general recommendations and procedures applicable to the authorization of the emergency use of certain medical products
- issuance of emergency dispensing orders for doxycycline and ciprofloxacin for anthrax preparedness
- issuing draft guidance for local, state, and federal government stakeholders on testing to extend the labeled expiry dating of doxycycline to support efforts to sustain adequate supplies for anthrax preparedness
- issuing draft guidance on implementation of the Material Threat Medical Countermeasure Priority Review Voucher program
- using the expiry dating extension authority to authorize use of MCMs beyond their labeled expiry date to prevent shortages of critical products
- advancing efforts to create a national capability to track, collect, analyze, and evaluate information related to MCMs used during public health emergencies to inform real-time decisions about the safety and effectiveness of these MCMs
- addressing issues related to use of expanded access mechanisms and EUAs to make available unapproved MCMs for CBRN and other emerging infectious disease threats
- clarifying regulatory issues around building frameworks for conducting clinical studies during public health emergencies

FDA HQ facilitated coordination of response activities to emerging public health threats including the Ebola outbreak in the Democratic Republic of Congo and the Zika virus outbreak in the Americas. FDA HQ facilitated the expedited development and availability of MCMs – including vaccines, drugs, protective equipment, and diagnostic tests – and authorized the use of 8 diagnostic tests for Zika virus under the EUA authority (in addition to 12 similar EUAs issued

for Zika virus diagnostic tests issued in FY2016) and a rapid, single-use diagnostic test for the detection of Ebola virus,which is the second Ebola rapid antigen fingerstick test available under EUA, but the first that uses a portable battery-operated reader, which can help provide clear diagnostic results outside of laboratories and in areas where patients are likely to be treated.

FDA HQ also developed policies for the development, use, and export of investigational MCMs as necessary and helped to design clinical trials to evaluate investigational MCMs for Ebola and Zika virus. FDA HQ:

- supported monitoring for products with unsubstantiated or fraudulent claims for the diagnosis, treatment, or prevention of Ebola and Zika
- led domestic and supported international policy development activities related to Ebola and Zika virus response
- provided technical support to the World Health Organization and international regulatory counterparts.

FDA HQ also continued to advance the FDA's efforts to improve domestic and military preparedness for potential public health emergencies with chemical threats. For example, FDA HQ helped lead the FDA's efforts to prevent shortages of critical auto-injector products stockpiled by DoD, the SNS, and first responders for the treatment of nerve agent and insecticide poisoning due to ongoing manufacturing quality issues of the USG's sole-source supplier by:

- determining that, if properly stored, certain lots of the manufacturer's auto-injector products held for emergency use could be used beyond the original labeled expiration date for a period specified by FDA
- providing updates about continued use of stockpiled product beyond its labeled expiry date to impacted stakeholders
- working closely with HHS, CDC, and DoD partners to enable the import, availability and use of a new auto-injector product for the treatment of nerve agent and insecticide poisoning under FDA's EUA authority (FDA has subsequently approved this product).

FDA HQ also continued to advance efforts to facilitate the development and availability of medical products to support American military personnel. For example, FDA issued an EUA to enable the emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma for the treatment of hemorrhage or coagulopathy of U.S. Military personnel during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. FDA HQ also established a Memorandum of Understanding with the DoD setting forth a framework for the ongoing partnership with DoD and the creation of a robust program that can better serve the health care needs of American military personnel.

FDA HQ also continued to provide public information and education on FDA preparedness and response activities via events, press releases and interviews, the FDA website and social media.

International Inspections, Information Sharing, and Strategic Engagement

FDA HQ works with its regulatory counterparts and stakeholders abroad to ensure that products coming to the US market are safe, effective and of high quality. FDA HQ through its Office of Global Policy and Strategy, oversees four FDA country and regional offices, China, Europe, India, and Latin America, in seven locations abroad, with additional countries and regions

covered by HQ. Interactions with foreign regulators and stakeholders that benefit American public health include: expanding FDA inspectional capacity and making improvements to inspections; partnering to share information and expertise to strengthen foreign regulatory systems; strategic engagement and outreach to our foreign counterparts; and continued implementation of the China Safety Initiative.

During FY 2018, according to data as of November 1, 2018, investigators based in-country or on short-term assignments to China, India and Latin America from ORA conducted 536, 443, and 389 inspections respectively, slightly increasing its capacity from the previous year. FDA country and regional office staff, as well as investigators based in country or on short-term assignment to those offices, conduct foreign inspections that provide invaluable in-country insight and lead to improved future inspections. An example of improvements to inspections occurred this past fiscal year when the India Office developed a Foreign Export Inspection Guidance for CSOs. After its FY 2018 analysis of inspectional trends, and India export data and seasonality harvesting information, the Office added Guar Gum inspections to its inspection workplan for FY 2019. Guar gum is the second highest (by value) food commodity exported by India to the US, but there was minimal inspection data on these firms in the past. This action by the India Office will provide more targeted inspections on an important commodity.

The Office of Global Policy and Strategy's foreign offices often collaborate with regulatory authorities to create solutions to issues found in inspections. For example, in FY 2018, the India Office participated in a Canada/EU/India/FDA Workshop entitled "Indian Food Exports: Understanding Regulatory & Safety Requirements." The India Office provided information on FDA food facility inspections, food safety issues, and FSMA. Relevant to the region, over 350 participants gained information on seafood HACCP. The workshops were held in Delhi, Chennai, and Mumbai and provided opportunities for strategic partnership-building with counterparts from the Canada, the EU and India.

An example of FDA's foreign offices partnering to share information and expertise occurred in in FY 2018 in the FDA's China and Europe Offices. The China Office planned and conducted an inspection workshop between the China Food and Drug Administration and FDA. It shared FDA important inspection practices with attendees in Beijing. The Europe Office organized a bilateral conference with the European Medicines Agency to promote regulatory cooperation and alignment. The conference included sessions on generic drugs and tobacco regulation and included attendance and participation from international leads and FDA Center leadership. The conference sessions led to better understanding of FDA's regulatory requirements and positions on key issues by EU counterparts and the identification of strategic areas for future cooperation.

During FY 18, FDA established 3 new 21 CFR 20.89 Confidentiality Commitments with:

- The Health Canada Regulatory Operations and Regions Branch (RORB) regarding Drugs, Biologics, Medical Devices, Radiation-Emitting Products, Tobacco, Foods, Animal & Veterinary regulated products as part of cooperative law enforcement or cooperative regulatory activities.
- Chile National Director of Fisheries and Aquaculture Service (SERNAPESCA) regarding seafood regulated products as part of cooperative law enforcement or cooperative regulatory activities.
- South African Health Products Regulatory Authority (SAHPRA) regarding Drugs, Biologics, Medical Devices (including in vitro diagnostics and radiological health

products), Cosmetics and Dietary Supplements as part of cooperative law enforcement or cooperative regulatory activities.

FDA also established 23 new trade secret information confidentiality commitments pursuant to section 708c of the Food, Drug, and Cosmetic Act, to help advance the goals of the Mutual Reliance Agreement (MRA). Eighteen of these were signed with EU member states to facilitate the exchange of non-public information related to FDA regulated human drugs, while five of them were signed to facilitate the exchange of non-public information related to FDA regulated veterinary drugs. In addition, FDA signed one Cooperative Arrangement in October 2017 to facilitate regulatory activities. This research MOU with the Canadian Food Inspection Agency promotes sharing information and data. Specifically, it facilitates collaborative research projects related to the research, development, and validation of microbiological and chemical detection methodologies, and the evaluation of novel and innovative technologies.

In-country relationships with foreign regulatory counterparts enable FDA to leverage their respective regulatory capabilities, ensuring safer regulatory programs throughout the world, and ultimately protecting public health in the US. A demonstration of the FDA engaging its foreign counterparts and therefore leveraging that authority can be seen from late 2017 through early 2018 in Mexico during an investigation of a U.S. Salmonella outbreak. After learning from its regulatory counterparts in Mexico of suspected salmonella stemming from Mexican papaya, the FDA's Latin America Office's in Mexico City provided feedback to FDA's CORE network. This intel was used by CORE to change their list of possibly-suspect firms. FDA's Mexico City post then shared CORE's modified list with Mexican regulatory counterparts, who agreed to deploy their own investigators to the identified sites. The Mexican regulatory authorities subsequently shared the results of their investigations with FDA. This was important for assisting FDA in its outbreak traceback activities and regulatory decision-making with respect to whether FDA should conduct its own investigations of identified firms and to identify the appropriate type of such investigation for a specified firm.

In other engagement activities, FDA Europe and China Offices, working with CFSAN and Office of Food Policy and Response (OFPR) supports, have continued the trilateral scientific and technical engagement initiated in 2016 with the Directorate General of Health and Food Safety of the European Commission, and China's General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) to enhance cooperation and exchange about food safety. In late 2017, the parties met to discuss import and export controls, e-Commerce, and risk communication, all important topics to implementing existing legislative authorities.

In addition, in 2017 and 2018 the Europe Office has taken a more prominent role in advancing the Mutual Recognition Agreement (MRA) for pharmaceutical good manufacturing practice inspections that was finalized on March 1, 2017. Once fully implemented, FDA anticipates significant efficiencies regarding GMP inspections to be realized by FDA and our European counterparts in one another's territory, enabling those resources to be shifted to higher priority/higher risk areas.

FDA's India Office engaged in a series of in-person Seafood HACCP and U.S. Food Labeling workshops in Mumbai and Nellore in late 2017. These workshops improved participants' understanding of sanitation and prevent seafood safety hazards, and in turn, protect American public health. Almost 100 individuals were trained, providing the India government and industry participants with this important information.

In another engagement example, the Latin America Office collaborated with the Chilean Agriculture Commission (SAG) and ANASAC Chile (pesticide manufacturer) to identify potentially adulterated table grapes, wine grapes, and tomatoes from Chile. The testing results were shared with FDA through their International Arrangement and demonstrated SAG's commitment to providing safe food products, which is then passed on to the American consumer. In this case, the Latin American Office was able to act in coordination with the SAG when a Chilean pesticide manufacture notified it that one of its products was incorrectly formulated.

Engagement and outreach also includes interaction with international organizations. For example, at HQ the Office of Regional and Country Affairs (ORCA) established a new Cooperative Agreements (CoAg) with WHO to strengthen regulatory systems and ensure the safety and quality of food and medical products in FY 2018. The CoAg supports well-established collaborations between WHO and FDA in support of data-driven and science-based public health, research strategies, and approaches that align with FDA domestic and global goals. This agreement contributes to the knowledge base of the current regulatory efforts in support of global efforts to ensure quality of food and medical product quality and safety.

Continued Implementation of the China Safety Initiative International Partnerships

The China Safety Initiative (CSI) continues to allow FDA to expand its efforts to regulate the quality, safety and efficacy of FDA-regulated products exported to the United States from China. The primary focus of CSI was the expansion of the number of in-country FDA investigators, which was accomplished through a negotiated agreement with the Chinese government. In FY 2018, the China office completed 226 inspections focused on foods, animal feed, and animal drugs. The China Office conducted all assigned FDA food facility inspections in China.

To protect US consumers and enhance public health, inspections conducted by foreign office consumer safety officers (CSOs) the China Office conducts High Risk, For Cause, Follow-up priority inspections, collects regulatory information, and conducts regulatory trend analysis in conjunction with its CSOs and International Relations Specialists. It also ensures timely reporting via existing regulatory systems, as appropriate. This includes eNSPECT, FACTS, and/or Global Watch. This reporting allows the Agency to make informed decisions based on significant risk and provide critical regulatory intelligence to Centers and ORA that will assist in better risk-based regulatory decision making and work planning. This effort maximizes regulatory compliance and minimizes risk associated with those products from China exported to the US.

China also provides its Chinese regulatory counterparts with training to ensure the safety of its products being exported. In FY 2018, FDA's China Office also conducted a regulator-to-regulator workshop with the China National Drug Administration (CNDA)'s Center for Food and Drug Inspection (CFDI) in Beijing, China, focused on promoting and enhancing mutual understanding of how inspections are conducted by each regulatory authority. In collaboration with the India Office, FDA headquarters, and high-level representatives from U.S. FDA's Office of Regulatory Affairs (ORA), the China Office planned and conducted the workshop ensuring participants had opportunities to share their inspection experiences with others.

Leveraging the Regulatory Capabilities of Foreign Counterparts, Leading FDA's Engagements with the Government Accountability Office (GAO) and the Office of the Inspector General (OIG)

FDA HQ staff coordinates the Agency response to all requests from GAO and OIG. For each of the several dozen ongoing engagements, FDA HQ staff complete the following:

- identify appropriate subject matter experts
- coordinate and develop of FDA responses
- collect and submit data in response to requests
- assemble and edit Agency responses to draft reports
- ensure consistency with Agency legal and policy positions.

The staff also coordinates the annual updates to recommendations contained in the final reports and the Agency's responses to GAO's High-Risk List. In recent years, a greater number of these recommendations have been closed, and a greater proportion have been closed as implemented.

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

In FY 2018, FDA HQ:

- received 410 first-time requests for orphan drug designation and designated 289 promising drugs and biological products for rare diseases
- received 14 first-time requests for Humanitarian Use Device designations and designated 16 promising devices for rare diseases and conditions
- received 45 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 39 drugs and biologics for rare pediatric diseases
- funded 11 new clinical trial grant awards and 75 ongoing grants funding clinical studies of promising therapies for rare diseases
- funded 6 natural history grant awards to inform medical product development by better understanding how specific rare diseases progress over time
- funded 5 new pediatric device consortia with 3 real world evidence projects to provide multidisciplinary advice and funding to assist pediatric device innovators.

Premarket and Postmarket Support

In FY 2017, with respect to combination products, FDA HQ provided clarification and support for approximately 560 premarket applications, 1,419 inter-center consults and 74 post market activities. FDA HQ issued 8 formal requests for designation decisions (5 for combination products and 3 for non-combination products) with 100 percent of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also provided timely informal jurisdictional assistance for 78 separate Pre-RFD submissions (informal inquiries) and 48 FDA center-requested classification and assignment consultations. In FY 2017, FDA HQ also responded to 525 requests for product-specific assistance, the responses to which contributed to ensuring the timely and effective review of combination products.

In FY 2018, FDA HQ issued guidance on How to Prepare a Pre-Request for Designation (Pre-RFD) and on Postmarketing Safety Reporting for Combination Products Draft. As required by the 21st Century Cures Act (Cures Act), the FDA proposed a list of alternative or streamlined mechanisms for complying with the current good manufacturing practice (CGMP) requirements

for combination products. The FDA also proposed to amend 21 CFR Part 3 concerning the classification and assignment of medical products. The proposed rule clarifies the scope of the regulations, streamlines and clarifies the appeals process, and aligns the regulations with more recent legislative and regulatory measures. The Agency also issued Staff Manual Guide (SMG) 4101 entitled Combination Products Inter-center Consult Request Process and SMG 4103 entitled Expectations and Procedures for Engagement Among Medical Product Centers and Office of Combination Products on Regulations and Guidance Pertaining To Combination Products. Both SMGs are intended to promote inter-center collaboration and enhance efficiency and consistency in combination products regulation.

In late 2017, FDA HQ hosted an EMA fellow's visit to FDA to learn more about how FDA regulates combination products and also to share experience between EMA and FDA on regulatory, development and assessment challenges of different kinds of combination products. FDA also shared how the medical product Centers and the Oncology Center of Excellence collaborate in regulating oncology products including combination products. Subject matter experts from CBER, CDER, CDRH, and OCE participated in this effort.

In FY 2017, FDA HQ provided clarification and support for approximately 560 premarket applications, 1,419 intercenter consults and 74 combination product post market activities. FDA HQ issued 8 formal requests for designation decisions (5 for combination products and 3 for non-combination products) with 100 percent of these decisions meeting the 60-day statutory decision time requirement. FDA HQ also provided timely informal jurisdictional assistance for 78 separate Pre-RFD submissions (informal inquiries) and 48 FDA center-requested classification and assignment consolations.

Pediatric Coordination

FDA HQ, working in conjunction with Center subject matter experts through the Pediatric Cluster, met to discuss pediatric scientific issues with European Medicines Agency (EMA) on 170 issues in FY 2018. Of the 170 issues discussed with the EMA, harmonization was achieved for 70 percent. Examples of the most frequent issues discussed included scope of pediatric development, dosing, regulatory issues/actions, safety and study design.

FDA HQ promoted high standards of scientific integrity by providing expert ethical opinions to agency Centers and Offices on a variety of ethical issues, with the completion of more than 50 consult reviews in FY 2018. These ethical issues included:

- study design considerations in pediatric rare disease populations
- gathering Pediatric Advisory Committee and patient and caregiver input on ethical and scientific issues related to the development of appropriate study endpoints
- review of research involving the exceptions from informed consent requirements for emergency research.

FDA HQ promoted the support of therapeutic product development for neonates through internal and external collaborative efforts. These collaborative efforts included:

- enhancing communication between FDA scientists and external neonatal groups on specific scientific issues, primarily through the International Neonatal Consortium (a consortium facilitated by the Critical Path Institute)

- initiating research studies with colleagues across the FDA Centers as well as with external scientific researchers
- providing neonatal-perinatal medicine consultations across the FDA Centers with 31 consults completed in FY 2018
- co-organizing an expert workshop with the Duke-Margolis Center for Health Policy on "Advancing Endpoint Development for Preterm Neonates with Pulmonary Morbidities"
- co-developing a draft Guidance document on Neonatal Clinical Pharmacology studies.

FDA HQ enhanced the efficiency of its pediatric safety review process which examines and provides the post-market pediatric adverse events and safety reporting issues to the Pediatric Advisory Committee (PAC).

In FY 2018, these efforts included:

- completed 67 pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews) that were reviewed by FDA's PAC in comparison to 34 in FY2017.

This is a direct result of the risk-based assessment process in which the low safety risk products now have their mandated pediatric-focused safety reviews posted on FDA's website. The new pediatric safety review process has resulted in a profound reduction in the backlog of mandated safety reviews. FDA HQ, enhanced international pediatric collaborations by working in conjunction with Center subject matter experts through the Pediatric Cluster to discuss pediatric scientific issues with European Medicines Agency (EMA), Health Canada, PMDA, and TGA.

In FY 2018, these efforts included discussion of 188 issues, where a number of issues could be discussed with respect to an individual product. Out of the 188 issues discussed, harmonization was achieved for 70 percent. Examples of the most frequent issues discussed included scope of pediatric development, dosing, regulatory issues/actions, safety and study designs.

Empower Consumers and Patients

FDA is committed to empowering consumers and patients to make better and more informed decisions about their diet and health and to expand opportunities to use nutrition to reduce illness and death from disease.

FDA HQ leads the effort to enhance FDA's communications to better serve the public. FDA HQ manages the communications to key stakeholders including the media, Congress, health professionals, patient advocates, and the general public. FDA HQ ensures important information about the benefits and risks of products is readily available in plain language using different communication methods, such as social media and the FDA website. FDA HQ also educates the public and encourages healthy choices by providing more general information about nutrition and tobacco prevention.

The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities[118]

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

Communication with Stakeholders - Improvements to FDA.gov

FDA is working to improve the usability of FDA.gov, our public-facing web site, by transitioning to Drupal, a new state-of-the-art content management system (CMS), in February 2019. The Drupal platform will offer visitors better navigation tools to more easily find and share FDA content through web sites, mobile applications, and social media channels. In addition, the new platform will make it easier for the agency to highlight priority content and most requested content on our home page and topic landing pages, which reflects feedback from visitors to FDA.gov. To prepare for this transition, the FDA has archived over 65,000 old and outdated content items. In addition, the FDA is working to improve the information architecture across the web site to better organize our content in more intuitive ways for our visitors. This new organization of content will be based on our most requested information to ensure this content is easy for our visitors to find.

FDA is also working to specifically enhance the For Patients webpages to best meet informational needs of patients, family members, and advocates that will assist them in locating medical product information and opportunities to engage with FDA. For example, HQ has developed a table summarizing several of the agency's patient engagement initiatives. In addition, HQ has initiated the development of a centralized point of entry into FDA for inquiries and meeting requests from patients, family members, and patient advocates. The central entry point will streamline routing processes to ensure inquiries are received and responded to in an effective and efficient manner. Finally, an education video series about the agency's mission, patient engagement initiatives and how to begin navigating the agency is also part of these web enhancements and improvements.

Communicating with Stakeholders -Eloqua Email Delivery Service

FDA HQ has implemented the Eloqua email delivery system to send priority agency announcements/content to stakeholders who opt-in to receive these notifications. The FDA uses Eloqua to send device-friendly emails on important topics to keep stakeholders informed and drive traffic to FDA.gov. Currently, the FDA has 140 content topics available and over 1.5 million stakeholders who have subscribed to receive information. The topic of Recalls currently has more than 405,000 subscribers.

Meetings with Stakeholders (non-media)

Since May 2017, FDA HQ has conducted nearly 685 meetings or interactions with a wide range of stakeholders representing trade associations, consumer groups, healthcare professional organizations, research and policy institutions, and patient/disease-specific groups.

FDA HQ has also used social media to engage with our stakeholders, via Facebook, multiple Twitter accounts, Instagram, YouTube, and other channels. The agency conducted two Twitter chats, including one targeting a bilingual (English- and Spanish-speaking) audience.

The agency has also recruited and trained over 40 new patient representatives, selected for their experience and advocacy with specific medical conditions and diseases. The new representatives, who serve as special government employees to the FDA's Advisory Committees, bring the total number of patient representatives to approximately 200. In July 2017, the FDA conducted a workshop for patient representatives, providing them with an opportunity to learn about the FDA regulatory process and understand their responsibilities in this valuable collaboration.

Additionally, the FDA HQ co-chairs the Patient Engagement Cluster with the European Medicines Agency (EMA). The cluster allows FDA and EMA to meet on a regular basis to exchange information on how the organizations engage with and involve patients in regulatory decisions and on ways to enhance future engagement with patients.

Annually, FDA HQ responds to approximately 1,500 inquiries on human subject protection, informed consent, and best practices for the conduct of clinical trials. Archives of these questions and answers are available on fda.gov.

In collaboration with the Clinical Trials Transformation Initiative, FDA HQ established the Patient Engagement Collaborative, comprised of external patient community stakeholders, who will offer their experiences and perspectives on patient engagement in FDA's regulatory processes. Following an official call for nominations, a selection committee chose 16 individuals to serve as the first slate of members. An emphasis was placed on ensuring involvement of representatives with a variety of perspectives and inclusion of patients, caregivers, and representatives from a diversity of patient communities. The first slate begins their 2-3 year terms in August 2018.

Stakeholder Outreach Activities

MedWatch Product Safety Communications: FDA HQ issued over 221 MedWatch Safety Alerts since May 2017 to inform health care professionals, consumers and patients about current and urgent product safety information. Two videos were developed, produced and disseminated to consumers and healthcare providers on reporting medical product problems to FDA, including one in Spanish. These videos were accepted by the American Public Health Association and showcased at their annual meeting (November 2017) attended by over 12,000 international public health professionals. Articles on the topic of boxed warning highlights on the drug label were published in four health care professional journals/publications: the American Journal of Health-System Pharmacy, the Hospital Pharmacy Journal, Federal Practitioner, and Medscape since May 2017.

Healthcare Practitioners: FDA HQ has six stakeholder engagement related MOUs currently in place to facilitate interaction with health care provider groups, which allows the agency to leverage relationships to extend communication and learning opportunities for providers across the county, designed to ultimately benefit patients and improve outcomes. For example, as part of a Memorandum of Understanding (MOU) with the American Nurses Association, HQ conducted a joint webinar on November 16, 2017, "An Opioid Primer: Legislative, Policy, & Practice Implications." The webinar described early and later opioid effects on the brain and illustrated how the brain changes over time with opioid use, IOM's four level barriers to effective pain management, the Prescription Drug Management Program and its role in state and national drug monitoring efforts, and current drug treatment options and list three barriers to medication assisted treatment programs were also discussed. ANA is the only full-service professional organization representing the interests of the nation's 3.1 million registered nurses through its constituent and state nurse's associations and its organizational affiliates.

Rural Health Symposium: FDA HQ held its inaugural Rural Health Symposium on October 26, 2017. The Symposium provided a forum for key stakeholders in rural and tribal communities to discuss opportunities to address the critical and unique health challenges relative to the opioids crisis; tobacco use among youth; and telemedicine. The symposium was a cross-center effort and involved other federal agencies (VAMC, HIS, FCC, HRSA).

Rare Disease Listening Sessions Pilot: FDA HQ also established a Memorandum of Understanding (MOU) with the National Organization for Rare Disorders to help conduct outreach (e.g., pilot listening sessions) on ways to expand the inclusion of patient-related experience into FDA regulatory decisions on rare diseases and conditions. HQ has identified therapeutic areas to help foster early and iterative engagement on key clinical and regulatory issues. The first therapeutic area is genetic disorders.

Providing Historical Content about FDA's Activities

FDA HQ collects, processes and preserves materials that capture the history of FDA's work and the breadth of the agency's responsibilities, conducts oral histories/interviews of selected staff, educates the public, and provides counsel on precedents to regulations, statutes, policies and legal cases.

In FY 2017, the FDA acquired 300 artifacts, saw to the preservation through digital conversion of 33,000 pages of textual documents, and just over 2,900 pages of graphic rich materials from the 1940s to the 1980s, and arranged for the preservation through digital conversion of over 6,450 historical images and 200 historical videotapes in an antiquated format. The FDA also promoted on social media 5 history video blogs and 19 written stories about historically significant FDA artifacts.

Thus far in FY 2019, the FDA produced three important exhibits on different aspects of the agency's history to inform staff and the public about critical turning points in the agency's evolving regulatory powers, and is currently finalizing a contract on a fourth but more prominent Smithsonian quality exhibit. The FDA arranged for the preservation through digital conversion of approximately 100 historical film reels in various states of deterioration, and promoted on social media 2 history video blogs and 13 written stories about historically significant FDA artifacts. The FDA also coordinated efforts to accept a gift of approximately 4,500 historically significant pharmaceutical artifacts.

Communication Products for Consumers, Health Care Professionals and Others

FDA HQ regularly develops communication products about FDA-regulated products, key issues, and other news for consumers, health care professionals, patients, news media, policymakers, regulated industry and others.

From May 1, 2017 through November 2018 FDA HQ issued:

- 221 MedWatch Safety Alerts (FDA's second largest e-list) to more than 425,000 subscribers;
- More than 400 News Releases and other press announcements in English and/or Spanish with a total reach of more than 89,000 subscribers;
- 161 FDA Voice Blogs with more than 53,000 subscribers;
- 449 Consumer Updates (both new and updated content) in English and Spanish to more than 117,000 subscribers; and
- more than 100 newsletters, which reach approximately 700,000 patients and health care professionals.

FDA Office of Women's Health (OWH) responds to key agency priorities regarding women's health by delivering credible, accurate, and easy-to-understand health information on a variety of health topics related to FDA regulated products and safety and health alerts.

These materials help women and their families make informed health decisions. The materials include fact sheets, brochures, purse cards, and medication discussion guides. Select materials are available in multiple languages and all are free and written at a 4th through 6th grade reading comprehension level. To date, in partnership with other national organizations, more than 100 million publications have been distributed nationwide. Notable

FY 2017 and 2018 accomplishments include:

- Reaching more than 14 million people via special promotions and stakeholder engagement initiatives using print and digital outreach
- Distributing approximately 1.7 million print and electronic patient education materials in 19 languages
- Disseminating FDA safety alerts and health information via the OWH twitter account to approximately 70,000 followers, of which 58% are health professionals and researchers, and approximately 2,500 are Pinterest followers
- Conducting webinars, conference presentations, and consumer outreach to over 20 national health professional and women's advocacy organizations.

Support for FDA's Priority Rulemakings

In 2018, FDA HQ continued to support the agency's public health mission by issuing a final regulation to classify Blood Establishment Computer Software into Class II subject to special controls with premarket review. This ensures that the special controls established and imposed by this final rule, together with general controls, will provide a reasonable assurance of safety and effectiveness of these medical devices.

FDA also finalized the extension of the compliance date for Nutrition Food Labeling and Serving Sizes requirements. This action provides manufacturers with additional time to reconfigure their food labels to reflect amounts of food customarily consumed at one eating occasion, furthering the Administration's deregulatory initiative and providing industry with additional time to comply with this nutrition requirement.

Women's Health Research

FDA HQ provides leadership and policy direction for the Agency on issues of women's health and coordinates efforts to establish and advance a women's health agenda through research funding that:

- identifies potential differences between males and females on the safety and efficacy of FDA regulated medical products
- promotes a better understanding of medical conditions that disproportionately or solely affect women.

Women's Health research provides evidence for the biological and physiological differences between males and females, and advocates for the adequate representation of women in clinical studies. In the areas of human drug, biologic and medical device development, the design and analysis of clinical trials can answer fundamental questions related to sex-based differences in the safety and efficacy of these products.

Since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 378 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 398 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

FDA HQ developed a "Women's Health Research Roadmap," an agency-wide strategic research plan that identifies regulatory and scientific knowledge gaps in women's health and defined seven priority research areas. The results include:

- A Research Impact and Outcomes (RIO) Framework, which is a first of its kind, to measure the impact of the Women's Health research program.
- Published a historic study in JAMA examining "Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs" which included 224,000 patients, supporting 36 drug approvals, over a ten-year period (2005-2015).

FDA HQ implemented the Research Impact and Outcomes (RIO) Framework to measure the impact of the Women's Health research program. This first of its kind framework is currently in use by FDA HQ and two FDA product Centers. FDA HQ is hosting three virtual workshops for national and international scientists and their organizations to facilitate the adaptation and application of the FDA RIO Framework.

In addition, since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 378 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 398 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

In May 2018, the Office of Women's Health published a decadal review titled "Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs, 2005-2015" in the Journal of the American College of Cardiology. This manuscript is the largest study to date. Given the large gaps in information about participation, FDA wished to add updated data on cardiovascular clinical trials participation, based on data collected over a large time-period and highlighted the data analyses that FDA performs on participation by gender for new drug applications to ensure safety and efficacy of products that are approved for use in both men and women. This study also evaluated the detail inclusion exclusion of individual screens across 5 clinical trials and found that inclusion exclusion criteria minimally impacted enrollment by gender.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ established a new Women's Health Medical Initiatives and Scientific Engagement program to promote women's health through medical and scientific education and collaborations with health professional organizations. FY 2018 program accomplishments are described below.FDA hosted a quarterly Scientific Speaker Series to provide education for staff across HHS to help ensure sex and gender are incorporated into research, professional education and consumer information. Pre- and post- polls of attendees exhibited a 30 to 60 percent knowledge gain by attendees across topics such as insilico research, opioid use disorder, and sex differences in cardiovascular disease.

In collaboration with NIH's Office of Research on Women's Health, FDA HQ provided the expert educational development model in the creation of a national six hour continuing education series focused on sex as a biological variable in disease and medical research. This series of six courses is designed to educate scientists, clinicians, and health professional students. The series will result in an increase in the incorporation of sex differences into research programs and therefore application of research to both men and women.

In honor of Women's Health Week 2018, FDA HQ led a scientific session focusing on the science and statistics of including women in cardiovascular clinical trials. In addition to a robust discussion and debate, this session served to expand FDA transparency and communications to an audience of clinicians, scientists, women's health advocacy and patient representatives. Over 1200+ attendees participated in-person or via remote viewing.

Along with CDER and CTP, OWH is sponsoring a public meeting entitled "Opioid and Nicotine Use, Dependence, and Recovery: Influences of Sex and Gender" on September 27-28, 2018. This public meeting will feature researchers, clinicians, and policy experts discussing sex and gender influences on substance use, misuse, and recovery

OpenFDA

OpenFDA is an FDA initiative to provide software developers and researchers Application Programming Interfaces (APIs) to several high-value structured datasets, including adverse events, product labeling, and recall enforcement reports.

Since its launch, on June 2, 2014, OpenFDA has received more than 120 million data calls. Many of the calls came from outside the US. There are more than 6,600 registered users, tens of thousands connected systems worldwide, and dozens of new software applications that the community has built. Within a year's time, FDA plans to conduct an app-a-thon to encourage more users to develop healthcare information apps which utilize openFDA as a data source.

OpenFDA provides access to:

- Drug Adverse events – over 9.1 million records
- Device classifications – over 6,400 records
- Structured Product Labeling for FDA-regulated human drugs – prescription or over the counter– and biologics with over 132,000 records
- Medical device adverse event reports – 7.7 million records
- Food adverse event reports – over 76,000
- Food enforcement reports over 16.9 records
- Unique Device Identifiers – over 1.9 million records
- 510Ks – over 151,000 records
- Device pre-market approvals – over 39,000 records
- Drug enforcement reports – over 9,000 records
- Device registration and listing – over 256,000 records
- Device recalls – over 58,000 records
- Device enforcements – over 18,000 records
- medical device adverse event reports – over 6.1 million records
- unique device identifiers – over 1.3 million records

Strengthen Science and Efficient Risk-Based Decision Making

FDA is committed to strengthening its scientific workforce and tools for efficient risk management. This includes:

- advancing new tools and policies to improve FDA's ability to combat diversion and counterfeiting of drug products.
- expanding the use of high performance computing to make product review more efficient and advanced
- strengthening food safety
- strengthening the scientific workforce.

FDA HQ ensures the timely and effective implementation of operations and the high quality delivery of services across FDA. FDA HQ plans and manages all resources including:

- budget and financial management
- human resources
- information technology and cybersecurity
- facilities, security and safety
- ethics and equal employment opportunity
- acquisitions activities.

FDA HQ is committed to developing its workforce, recruiting, retaining, and strategically managing diversity. FDA HQ invests in infrastructure, evolving management systems and practices to ensure accountability for accomplishing meaningful results to enhance productivity and workforce capabilities. The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.[119]

The FDA Food Safety Modernization Act (FSMA)

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

FDA finalized seven foundational FSMA rules in 2015 and 2016, and is conducting extensive outreach to industry to ensure that stakeholders understand the new requirements. These seven foundational FSMA rules provide a framework for the food industry to implement effective measures to prevent contamination. In 2017, FDA launched a new web page on fda.gov which compiles compliance dates for all of the foundational FSMA rules into a single graphic.

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. To date, FDA has awarded 46 states and 1 territory a total of $85 million in cooperative agreements to develop produce safety programs that will enable them

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

to deliver education and technical assistance to farmers and create infrastructure to provide inspection, compliance and oversight. FDA also issued a cooperative agreement with the National Association of State Departments of Agriculture (NASDA) to develop a national consortium of state and federal regulators to further states' implementation of their produce safety programs.

In 2018, FDA worked with NASDA to finalize resource materials and to train states to implement the On-Farm Readiness Review (OFRR) program, which allows farms to request a review by regulators of the readiness of their operations for produce safety rule (PSR) implementation.

Emergency Preparedness and Response

FDA HQ coordinates Agency emergency response to adverse events with FDA-regulated products, foodborne illnesses, product tampering issues, man-made and natural disasters, and emergencies affecting FDA staff, systems, and facilities. FDA HQ will continue to enhance agency preparedness and response capabilities through intra- and inter-agency exercises, plan development and execution, standard operating procedures, and enhanced incident management systems to improve the overall operation and effectiveness of FDA's emergency response.

FDA HQ provides nationwide, 24-hour, seven-day-a-week emergency response system, including rotating Late Duty Officer coverage by Emergency Coordinators for issues arising after-hours, weekends, and holidays. FDA HQ also provides surveillance and signal monitoring, including FDA's Emergency Operations Network Incident Management System, and Consumer Complaint reporting and monitoring functions.

In FY 2018, FDA HQ coordinated the emergency response to 94 significant incidents including:

- 20 serious adverse or injury event incidents
- 52 natural disasters
- 21 man-made disasters
- 1 National Special Security Event.

In FY 2018, FDA HQ also established four Incident Management Groups (IMG) to provide headquarters coordination for:

- three separate hurricane responses for Hurricanes Maria, Lane, and Florence
- IMG for the 2018 Cyclospora Outbreak.

FDA HQ evaluated 3,799 consumer complaints (including 34 reports of suspected product tampering), to ensure FDA's timely identification of and response to emergency safety concerns related to FDA-regulated products. FDA HQ worked diligently to develop, maintain, and coordinate an effective emergency response capability for public health emergencies by developing guidance detailing FDA's operational approach for emergency response.

In FY 2018, FDA HQ:

- coordinated 18 Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products.
- addressed three draft notices of Public Health Emergency of International Concern (PHEIC) from the HHS International Health Regulations Program.

- responded to and coordinated 200 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.
- conducted, evaluated and reported Table Top and Full Scale Exercises, for two Center Select Agent Laboratory facilities, included a medically downed patient in a High Containment Laboratory.
- A second Table Top exercised actions involved with a fire in the high containment area, with the resulting after action reports emphasized the need for additional training.
- created and presented three trainings for laboratory researchers on patient assessment, monitoring, movement and turn over to medical authority.
- trained key emergency response staff on how to better respond to complex incidents and make informed decisions during an event.
- supported The Gotham Shield Functional Exercise (a mandated Federal Emergency Management Agency-led exercise that examined tribal, local, state and federal capabilities multiple mission areas through a series of linked exercises involving numerous federal and state partner agencies).

Economic Analysis and Support for Medical Product Regulations Published

In 2018, along with the publication of the proposed or final rules themselves, FDA published the economic analyses for rules related to medical device products (Acceptance of Data from Clinical Investigations for Medical Devices; Classification of Blood Establishment Computer Software and Accessories; Medical Device Submissions: Amending Premarket Regulations that Require Multiple Copies and Specify Paper Copies to be Allowed in Electronic Format) and human drug products (Repeal of Regulation Requiring an Approved New Drug Application for Drugs Sterilized by Irradiation; Removal of Certain Time of Inspection and Duties of Inspector Regulations for Biological Products). The support provided via economic analysis spanned more than five years and informed policy decisions throughout the rulemaking process. The results of data analysis and economic modeling were vital inputs into, and key to the publication of, the proposed and final rules that will clarify regulatory uncertainty among the regulated industry.

FDA Laboratory Modernization

Modernizing FDA's aged, inflexible, and unreliable laboratories is critical to FDA's ability to effectively carry out its mission and respond to food safety and medical product emergencies. A large majority of FDA's owned labs were transferred to FDA from other federal agencies, and these buildings, as well as the associated site infrastructure, were constructed between 30 to 60 years ago.

Similarly, many of FDA's leased lab facilities were constructed over 20 years ago. All of these labs are aged and the building systems, finishes, and layouts are past their useful life, creating unsafe and unhealthy work environments, which in turn compromises FDA's ability to meet scientific needs. The facilities and budget organizations within FDA's Office of Operations (OO) have developed and implemented a strategy to modernize FDA's laboratories. The strategy consists of:

- assessing facility conditions
- collaborating with the program utilizing the laboratories to fully understand mission impact

- prioritizing laboratories as needing replacement, relocation within the same geographic area, or repairs and improvements
- requesting resources needed to carry out high priority projects.

In FY 2015 through FY 2017, FDA received a total of $155.2 million from the HHS Non-Recurring Expenses Fund (NEF) to replace one owned laboratory, significantly renovate two owned laboratories, address other urgent owned facilities and infrastructure needs, and relocate two aged and deteriorated leased labs. These NEF resources have allowed FDA to replace the Office of Regulatory Affairs' (ORA) functionally obsolete owned laboratory at FDA's Winchester Engineering and Analytical Center in Winchester, Massachusetts, with an efficient, modern laboratory and to renovate laboratory Buildings 14 and 53A as well as an animal research processing area in Building 53B for the National Center for Toxicological Research (NCTR) located at FDA's owned Jefferson Laboratories Complex (JLC), in Jefferson, Arkansas. These resources have also allowed FDA to relocate ORA's aged, leased laboratories in Kansas City, Kansas, and Atlanta, Georgia, into new, modern, and efficient laboratories designed to meet ORA's mission. Without the NEF resources received for these leased lab relocations, ORA would have had to cut critical items in its foods programs, such as delaying hiring, which would possibly reduce ORA's ability to train staff and conduct inspections, and/or delaying lab-equipment purchases required to keep up with changing technology.

The $89 million FY 2019 NEF resources that were received will advance the ongoing laboratory relocation project at the Southeast Regional Laboratory in Atlanta. Funding will also support construction and facilities needs at ORA's Denver Laboratory, FDA's owned San Juan Complex, and infrastructure projects at FDA's owned Pacific Southwest Laboratory in Irvine, California. Funds will also be used for building and site infrastructure improvements, such as renovations, building system upgrades, roadway/drainage repairs, and building equipment replacement at FDA owned locations.

FDA HQ continues to work to:

- identify ongoing laboratory replacement, relocation, repair, and improvement projects;
- prioritize these projects
- develop resource requests to implement the highest priority projects.

FUNDING HISTORY[120]

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2016 Actual	$301,574,000	$191,374,000	$110,200,000
FY 2017 Actual	$302,146,000	$187,063,000	$115,083,000
FY 2018 Actual	$315,684,000	$171,001,000	$144,683,000
FY 2019 Annualized CR	$299,587,000	$171,195,000	$128,392,000
FY 2020 President's Budget	$320,164,000	$180,195,000	$139,969,000

BUDGET REQUEST

The FY 2020 Budget Request is $320,164,000 of which $180,195,000 is budget authority and $139,969,000 is user fees. This level provides a net increase of $20,577,000 compared to the FY 2019 Annualized Continuing Resolution level. Budget authority increases by $9,000,000 and user fees increase by $11,577,000.

FDA HQ will continue to provide policy direction and oversight, advance scientific development, and provide oversight of the global supply chain. FDA HQ will continue working to increase transparency and accountability in the supply chain, developing better enforcement and regulatory tools, encouraging greater responsibility by industry, and enhancing collaboration with international regulatory counterparts and other third parties. FDA HQ along with the Centers and Offices, will evaluate and improve the effectiveness of preventive control standards, and advance the development of predictive safety models. FDA HQ will coordinate across FDA to develop improved methods for rapidly detecting, investigating, and stopping foodborne contaminants, as well as develop comprehensive regulatory approaches for integrating pre- and post-approval and compliance functions. In addition, FDA HQ will continue to provide program direction and administrative services, ensuring FDA's public health mission is managed effectively and efficiently. FDA HQ is committed to delivering cutting-edge technology, innovation, and support to all stakeholders.

Budget Authority

Medical Product Safety (+$10.5 million)

New Platform for Drug Development - Oncology Center of Excellence: +$5 million / 25 FTE

The FY 2020 Request includes $5 million for the Oncology Center of Excellence (OCE) to stand up a new model for team-based product review that fosters collaboration across FDA's medical product centers, improves review efficiency, and expedites the development of novel science that can improve the lives of patients with cancer. Section 3073 of the 21st Century Cures Act required FDA to establish one or more intercenter institute(s) to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and

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

device centers. FDA has established the OCE to create a unified policy approach and clinical review for all drugs, biologics, and devices used in medical oncology.

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

Promote Domestic Manufacturing: +$1.5 million / 4 FTE

As part of FDA's initiative to promote domestic manufacturing, FDA will help reduce the cost and uncertainty of adopting new manufacturing technologies by developing a science-based framework that includes the regulatory tools and guidance for how products will be evaluated, and by funding research, development and testing of these technologies. In support of these research efforts, the FY 2020 Request includes $1.5 million for the Office of Laboratory Safety (OLS), which will serve as the Agency's coordinator and lead for implementation of policies and procedures, centralized training, and oversight for all laboratory operations related to laboratory science, safety, and security related activities. These funds will be used to support the development and implementation of a new electronic standardized laboratory safety audit/inspection program and an FDA laboratory quality management program across the Agency.

Medical Countermeasures Initiatives

OCS/OCET: +$3.0 million

Supporting the development and availability of medical countermeasures (MCMs) to counter chemical, biological, radiological and nuclear threats as well as emerging infectious diseases, such as pandemic influenza and Zika virus, remains a high priority for FDA. MCM development often presents unique and complex challenges with respect to generating the data necessary to support regulatory decision-making, such as a lack of animal models to support MCM development or insufficient biomarkers to enable the extrapolation of data generated in animal models to humans. Without such tools, it is difficult to generate the data necessary to support regulatory decision making. FDA supports cutting-edge regulatory science research under the Medical Countermeasures Initiative (MCMi) Regulatory Science Program to help develop these tools and promote innovation in the development of MCMs. The requested increase of $3.0 million for the MCMi Regulatory Science Program would allow FDA HQ to support intra- and extramural collaborative research to create the tools that support regulatory decision-making and help facilitate the development of advances in science and technology, including platform technologies and manufacturing processes, into safe and effective medical countermeasures (MCMs).

Office of Laboratory Safety

OLSS: +1.0 million

The $1.0 million request increase will enable OLSS to continually improve IT solutions for efficient Occupational Safety and Health program management (via contractual services), improve FDA-wide training programs, enhance communication efforts, laboratory safety programs, biological safety programs, establish a safety and engineering contract, and enhance the industrial hygiene program. The funding will support improvements to the enterprise Safety, Inventory, and Protocol System (SIPS) and establish, improve, and sustain FDA-wide training programs. In addition, the funding will support communication services, laboratory safety management, oversight and resources for biological safety, and the FDA-wide industrial hygiene (IH) program.

Food Safety (+1.9 million UF)

Promoting Innovation and Emerging Technology While Maintaining Product Safety

OFPR: +$1.9 million

FDA supports industry as it develops and implements new technologies in food, cosmetics, and veterinary products, including biotechnology products. This initiative will ensure that FDA keeps pace with how changes in the marketplace affect the human and animal food supply. This includes modernizing the regulatory system for biotechnology products (consistent with the administration's Agriculture and Rural Prosperity Task Force Report) to improve transparency, coordination, and predictability of the system. It also includes:

- supporting public confidence by assessing products in a risk-based manner;
- providing predictable pathways for commercialization; and
- increasing capacity for the scientific review of human and animal food ingredients to foster innovative products getting to market and improve nutrition.

FDA's goal is to promote and support industry innovation in the growing biotechnology space while also assuring consumers of the safety of these products.

FDA HQ will provide oversight and coordination of these crosscutting innovation and emerging technology activities. For example, FDA HQ develop a platform to track performance measures and evaluate metrics to understand program effectiveness. FDA HQ will also support and ensure policy alignment for new data analytic and risk prioritization activities.

USER FEES

Current Law User Fees (+$9.8 million / -12 FTE)

FDA HQ will utilize the requested increase in current law user fees to provide support to the FDA Centers and Offices. FDA HQ will provide strategic coordination, direction, and oversight across FDA UF programs.

PERFORMANCE

The FDA Headquarters' performance measures focus on emergency response, women's health, science, global cooperation, premarket application review of orphan, pediatric and combination products, outreach, and organization efficiency, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2019 Target	FY 2020 Target	FY 2020 +/- FY 2019
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products.*(Output)*	FY 2018: Develop 50 mapping products to support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinated 20 incidents involving FDA regulated products during the year. Participated in four exercises during the year. (All Targets Met or Exceeded)	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in five exercises during the year.	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in seven exercises during the year.	+2 exercises
293206: Promote innovation and predictability in the development of safe and effective nanotechnology-based products by establishing scientific standards and evaluation frameworks to guide nanotechnology-related regulatory decisions. *(Outcome)*	FY 2018: FDA completed annual milestones for 7 additional projects, for a total of 45 intramural research projects under the Nanotechnology CORES program to promote cross-center and external collaborative regulatory science research opportunities, focusing on studies evaluating nano-materials. (Target Met)	52 CORES projects with completed annual milestones	58 CORES projects with completed annual milestones Complete review of 80% of Medical Product nanotechnology standards	+6 projects
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship	FY 2018: 53% Target: 50% (Target Exceeded)	50%	50%	Maintain

programs. (Outcome)				
293205: Percentage of requests for combination product designations processed within the 60 day statutory requirement. *(Output)*	FY 2018: 100% Target: 95% (Target Exceeded)	95%	95%	Maintain
293203: Number of pediatric scientific, ethical, product, and product class issues identified through collaboration with the 27 European Union countries coordinated with the EMA, Japan, and Canada, with Australia as observers. *(Output)*	FY 2018: 188 Target: 45 (Target Exceeded)	90	90	Maintain
293204: Number of medical products studied in children with labeling changes and safety reviews completed and presented to FDA's Pediatric Advisory Committee. *(Output)*	FY 2018: 67 Target: 30 (Target Exceeded)	30	30	Maintain
291306: The number of targeted engagements, which are strategic interactions between FDA and stakeholders that produce a tangible	FY 2018: 49 Target: 25 (Target Met)	25	27	+2

result in support of FDA's global mission. *(Outcome)*				
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2018: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain

Nanotechnology

The Office of the Chief Scientist is adding a new target in FY 2020 to reflect the additional work this office does in reviewing Medical Product nanotechnology standards like ISO TC 229 and ASTM E56. Standards are an invaluable resource for industry and FDA staff. Effective and meaningful participation in standards development organizations (SDOs) for the products FDA regulates are critically important in the emerging area of nano technology. The use of standards can increase predictability, streamline premarket review, and facilitate market entry and use for safe and effective regulated products. For example, standards can help address certain aspects of the evaluation of nano medical products safety and effectiveness, such as material specifications, testing methods, pass/fail performance criteria, and processes to address areas, such as risk management and usability.

Fellowship Program

To support the Department's mission and FDA's scientific expertise, FDA is expanding its fellowship efforts by launching a new FDA Traineeship Program while continuing other Fellowship programs. This performance goal focuses on FDA's efforts to retain a targeted percentage of the scientists who complete these programs. The size and focus of the new agency-wide Traineeship program will be greater in number and scope than the current Fellowship, and FDA will be resetting the retention target in FY 20 and beyond when the new FDA Traineeship Program is launched. Additionally, whether "graduates" from these programs continue to work for FDA or choose to work in positions in related industry and academic fields, they are trained in using an FDA-presented understanding of the complex scientific issues in emerging technologies and innovation, which furthers the purpose of HHS Strategic Objective 4.2: Expand the capacity of the scientific workforce and infrastructure to support innovative research.