FDA HEADQUARTERS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
FDA Headquarters Program	**282,678**	**302,146**	**315,546**	**347,240**	**31,694**
Budget Authority	***182,237***	***187,063***	***180,980***	***198,565***	***17,585***
User Fees	***100,441***	***115,083***	***134,566***	***148,675***	***14,109***
Prescription Drug (PDUFA)	*46,202*	*53,970*	*56,236*	*59,272*	*3,036*
Medical Device (MDUFA)	*5,732*	*8,118*	*10,373*	*10,554*	*181*
Generic Drug (GDUFA)	*25,050*	*30,587*	*44,859*	*45,568*	*709*
Biosimilars (BsUFA)	*1,388*	*1,976*	*1,659*	*1,688*	*29*
Animal Drug (ADUFA)	*947*	*874*	*654*	*1,208*	*554*
Animal Generic Drug (AGDUFA)	*453*	*212*	*267*	*971*	*704*
Tobacco Control Act	*19,132*	*19,072*	*19,002*	*27,870*	*8,868*
Mammography Quality Standards Act (MQSA)	*253*	*274*	*253*	*253*	*---*
Food And Feed Recall	*75*	*---*	*75*	*75*	*---*
Food Reinspection	*480*	*---*	*480*	*480*	*---*
Voluntary Qualified Importer Program	*277*	*---*	*277*	*277*	*---*
Third Party Auditor Program	*73*	*---*	*39*	*39*	*---*
Outsourcing Facility	*379*	*---*	*392*	*420*	*28*
FTE	**1,168**	**1,195**	**1,268**	**1,298**	**30**

*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.

Enhance Oversight

FDA 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[98].

The FDA Food Safety Modernization Act (FSMA)

On January 4, 2011, the FDA Food Safety Modernization Act (FSMA) was signed into law, significantly reforming food safety laws. 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 faces unique food safety challenges in the 21st century. FSMA enables FDA to better protect the public health by:

- shifting the food safety paradigm from reactive to preventive

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

- strengthening FDA's technical expertise and capacity to support industry in implementing the new prevention standards
- furthering federal, state, local and territorial partnerships and investing in training and capacity to ensure efficient, high quality, and consistent oversight nationwide
- broadening interaction with foreign partners and increasing oversight of importers by placing more responsibility for the safety of imported foods on them.

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.[99] 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 recognizes that FDA had previously-established regulations that are specific to seafood, juice, and Low-Acid Canned Foods and, therefore, some exemptions were made in the FSMA rules for these products. However, there are still some requirements in the FSMA regulations that apply to processors of these products. In FY 2017, in order to help producers of low-acid canned foods, juice, and seafood products understand which parts of the FSMA rules apply to them and how the FSMA rules may affect their operations, FDA published three guidance documents: Low-Acid Canned Foods and FSMA, Juice HACCP and FSMA, and Seafood HACCP and FSMA.

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. State officials were instrumental in providing comments to help FDA create regulations that take into account the complexities of food production and are designed to be flexible and practical while meeting the agency's public health goals.

In September 2017, FDA awarded 43 states a total of $30.85 million in cooperative agreements to develop produce safety programs that will enable them to deliver education and technical assistance to farmers and create infrastructure to provide inspection, compliance and oversight.

2017 FSMA Rule Updates

In July 2017, FDA released a proposed rule to extend, for covered produce other than sprouts, the dates for compliance with the agricultural water provisions in the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption rule (FSMA Produce rule). Moreover, FDA is proposing to extend the compliance dates to address questions about the practical implementation of compliance with certain provisions and to consider how we might further reduce the regulatory burden or increase flexibility while continuing to achieve our regulatory objectives, in keeping with the Administration's policies. The FSMA Produce rule establishes, for the first time, science-based minimum standards for the safe growing, harvesting, packing, and holding of fruits and vegetables grown for human consumption.

In 2017, FDA released an online food safety training module for carriers engaged in the transportation of food by rail or motor vehicle in the United States. FDA is offering this training

[99] http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm

free of charge to help carriers meet the requirements of the FDA's Sanitary Transportation of Human and Animal Food Rule (Sanitary Transportation Rule). The Sanitary Transportation Rule requires rail and motor vehicle carriers covered by the rule to provide food safety training to their personnel engaged in transportation operations. The training must provide personnel with an awareness of 1) potential food safety problems, 2) basic sanitary practices, and 3) carrier responsibilities. The carrier training requirement applies when the shipper and carrier have agreed, in a written contract, that the carrier is responsible, in whole or part, for sanitary conditions during transportation operations. A carrier may wish to offer this FDA module to their operations personnel as a means of satisfying the training requirements of the Sanitary Transportation Rule or to complement other training offered by the carrier.

In August 2017, FDA announced the availability of a Small Entity Compliance Guide (SECG) to help small businesses comply with the Final Rule on Mitigation Strategies to Protect Food Against Intentional Adulteration (or Intentional Adulteration Rule), one of the seven foundational rules mandated by FSMA. It provides nonbinding recommendations on such topics as developing a food defense plan and records management. The compliance date for small businesses under the Intentional Adulteration Rule is July 27, 2020. Very small businesses are exempt from the rule, except for a documentation requirement described in the SECG, which has a compliance date of July 26, 2020.

21st Century Cures Act and Human Subject Protection Harmonization

The 21st Century Cures Act (Cures Act) Section 3023 requires harmonization of HHS' and FDA' human subject protection regulations. FDA is continuing its efforts to harmonize differences between its regulations and the Common Rule, 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 finalize FDA's compliance program for the HHS regulations requiring clinical trial registration and results reporting on ClinicalTrials.gov (42 CFR part 11). FDA HQ has also provided consultation to NIH in support of reports required under the Cures Act related to ClinicalTrials.gov

Regulatory Policy and Guidance

FDA HQ led the development of FDA's regulations on acceptance of clinical data for medical devices. FDA HQ has developed a guidance to accompany the final rule.

Below are selected guidance documents on human subject protection issued by FDA HQ in 2016 and 2017. This list does not represent any degree of importance or priority ranking among those items.

Publication Date	Formal Title	Description
September 2017	Minutes of Institutional Review Board (IRB) Meetings - Guidance for Institutions and IRBs	This joint final guidance with HHS describes requirements for IRB meeting minutes and provides recommendations on the type and amount of information needed to comply with the FDA and HHS regulations.

Publication Date	Formal Title	Description
July 2017	IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects	This final guidance informs sponsors, investigators, and IRBs that FDA does not intend to object to an IRB waiving or altering informed consent requirements for certain minimal risk clinical investigations.

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 in order 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 Late Duty Officers coverage after-hours, weekends, and holidays through the Office of Emergency Operations (OEO). FDA HQ also provide surveillance and signal monitoring, including FDA's Emergency Operations Network Incident Management System, and Consumer Complaint reporting and monitoring functions.

In FY 2017 , FDA HQ coordinated the emergency response to 74 significant incidents including:

- 244 serious adverse or injury event incidents
- 34 natural disasters
- 13 man-made disasters
- 3 National special security events

FDA HQ evaluated 3,859 consumer complaints including 44 reports of suspected product tampering in FY 2017 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 responding to emergencies.

In FY 2017 FDA HQ coordinated nine Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products (flour, eggs, infant formula, tuna, etc.). FDA HQ also addressed five draft notices of Public Health Emergency of International Concern (PHEIC) in FY 2017, including novel influenza variants, a regulated commodity with potential health concerns, etc. Additionally, FDA HQ responded to/coordinated 120 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.

In FY 2017, FDA HQ conducted, evaluated and reported Table Top and Full Scale Exercises, for two separate Center Select Agent Laboratory facilities. These included a medically downed patient in a High Containment Laboratory, with associated minor contamination, and federal, state and local resource participation. A second Table Top exercised actions involved with a fire in the high containment area. The resulting after action reports emphasized the need for

additional training in basic patient assessment and patient transport to a "clean area" for further triage, as well as the need for additional Incident Command training. FDA HQ created and presented three training opportunities for laboratory researchers centering on patient assessment, monitoring, movement and turn over to medical authority.

FDA HQ provided training for key emergency response staff on how to better respond to complex incidents and make informed decisions during an event. FDA HQ supports ready access to classified information transmitted through secure government networks to ensure complete risk assessments during actual events.

FDA HQ completed a Table Top and Full Scale Exercise Series for cyber events. The cyber exercise is part of a series of exercises specifically designed to establish a learning environment for players to exercise emergency response notifications and procedures. The purpose of the exercise was to practice establishing an incident common operating picture and specifically focus on headquarters response efforts to a significant cyber incident.

In addition, FDA HQ supported HHS and FEMA plans with the following incident annex updates:

- Food Agriculture Incident Annex, including plant, animal and food agriculture inputs
- the Federal Evacuation Annex
- the Chemical Incident Annex
- the Biological Incident Annex

Geographic Information System Mapping

In FY 2017, FDA HQ expanded the use of the Geographic Information System (GIS) to support advanced work planning analysis related to changes in regulatory operations resulting from the Office of Regulatory Affairs realignment. FDA also used GIS to provide real-time support for the 2017 Hurricane Season. FDA HQ completed maps for 117 project requests involving FDA regulated firms.

Global Health Security and Counterterrorism

DA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security, counterterrorism efforts, and address emerging threats. The portfolios include serving as point of entry on policy and planning matters; serving 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; and coordinating 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 research to improve FDA's ability to perform science-based review of MCMs designed to lessen the effects of CBRN and emerging infectious disease threats. Notable accomplishments in FY 2016 and FY 2017:

- 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

- analyzing disease progression and effects of Zika Virus in non-human primate animal models as part of an FDA-established interagency collaboration to inform guidance regarding organ transplant safety and related tissue products
- developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during public health emergencies.

FDA scientists continued activities to support the development of MCMs for the Ebola virus, including:

- developing improved small animal models
- identifying potential markers of Ebola virus disease progression in animal models
- developing and validating analytical procedures for evaluating Ebola to use outside of specialized, high-containment laboratories
- establishing correlates of protection to support the development of Ebola vaccines
- analyzing Ebola survivors with and without chronic health problems to identify factors responsible for driving prolonged disease

FDA regulatory science initiatives to respond to the Zika virus outbreak included:

- understanding the effectiveness of technologies that reduce pathogens in blood
- evaluating the impact of red blood cell storage on Zika virus infection
- expanding the database of Zika virus-infected samples essential to the development of diagnostic devices
- developing mouse model to study the long-term effects of Zika virus infection and to support MCM development
- establishing correlates of protection to support the development of Zika vaccines.

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 2016 and FY 2017 that support MCMs include:

- issuance of 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
- using the expiry dating extension authority to authorize use of MCMs beyond their labeled expiry date to prevent shortages of critical products
- finalization of revised draft guidance Product Development Under the Animal Rule.

FDA HQ facilitated international coordination of response activities to emerging public health threats including the Ebola outbreak in West Africa 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 11 Ebola diagnostic tests and 20 Zika virus diagnostic tests under the EUA authority.

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 also accomplished the following:

- 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 (including West African and Brazilian counterparts)[100].
- provided public information and education on response activities via events, press releases and interviews, the FDA website and social media (see Communications with Stakeholders for more information).

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; and
- 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.

International Inspections

FDA HQ works with regulatory counterparts and stakeholders abroad to improve global product development and manufacturing standards, and ultimately ensure that products coming to the US market are safe, effective and of high quality. FDA HQ oversees four FDA country and regional offices (China, Europe, India, and Latin America) in seven locations abroad. Engagements involving other countries and regions are also covered by FDA HQ. These offices expand FDA's decision-making and actions by:

- expanding FDA inspectional capacity targeting firms of highest risk
- building relationships and partnering with foreign regulators and other stakeholders
- leveraging the authority of foreign regulatory counterparts
- sharing information and expertise to strengthen foreign regulatory systems for the benefit of the U.S. consumer.

During FY 2017, according to data as of October 31, 2017, investigators based in country or on short-term assignments to China, India and Latin America from ORA conducted 196, 80 and 5 inspections, respectively. In addition, Latin America Office's CSO conducted an onsite investigation/inspection at papaya fields and a packing house involved in a Salmonella outbreak

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

as part of FDA's outbreak investigation, alongside with the Mexican Regulatory Authority SENASICA.

In late 2016, the China Office conducted an inspection at a dietary supplement manufacturer and discovered that Ephedra was used as an ingredient in one of their products although not declared on the finished product label. The inspection also found significant deviations from dietary supplement cGMPs, as well as multiple product labels with disease claims and undeclared ingredients. The firm voluntarily recalled the product, and the firm and its products were placed on four different Import Alerts. The China Office then worked with the New York District Office to follow-up with the recall at the distributor in the U.S.

In another case, FDA cancelled an inspection of an Indian manufacturer after the firm informed ORA, and provided documentation, that an inspection was impossible because its employees were striking and had blocked the company's entrance. Working through in-country contacts, OIP's India Office confirmed that the company had neither experienced a workers' strike nor suspended operations. FDA then gained access to the facility for an inspection. In early 2017, because the company used false and misleading statements to delay and deny the FDA's inspection of its facility, FDA deemed all drugs manufactured at that facility to be adulterated. FDA placed the establishment on two Import Alerts and in April 2017, issued a Warning Letter under which FDA may withhold approval of any new applications or supplements listing the company as a drug manufacturer.

During an inspection of a food manufacturer in India, the inspector recognized that two of the ingredients observed contained soy, although there was no declaration of soy on the finished retail product. People with food allergies to soy can experience severe, life-threatening allergic reactions. As a result, a Recommendation for Recall Classification was submitted for 7 shipments of the product to remove the product from the market.

The Foreign Offices also share risk information with FDA HQ that informs FDA regulatory actions. For example, the Latin America Office provided information to ORA regarding a recall of tilapia in Costa Rica. This intelligence was used by FDA to place the firm and product on an import bulletin, which increased the surveillance of products from that firm coming into the United States to ensure that products entering the United States did not experience the same safety issues observed in Costa Rica. The Latin America Office also worked with their regulatory counterparts in Mexico to provide strategic information and support the Agency during multiple outbreaks over the last year. The Agency gained valuable intelligence on outbreak investigations from multiple-States associated to diverse Salmonella serotypes from the Latin America Office facilitating risk assessment.

Additionally, the Latin America Office routinely shares locally-acquired risk information with FDA's Coordinated Outbreak Response and Evaluation (CORE) Network to assist in investigations of U.S. food-borne illness outbreaks. For example, during an investigation of a U.S. Salmonella outbreak suspected of stemming from Mexican papaya, the Latin America Office's post in Mexico City provided feedback to CORE based on information they obtained from their regulatory counterparts in Mexico which was used by CORE to modify their list of possibly-suspect firms. The 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 in 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 this helped FDA to identify the appropriate type of such investigation for a specified firm.

Another example of communicated risk information includes India's work on tracking down information related to firms with potentially contaminated products exported to the United States. When India's Consumer Education and Research Centre published a report identifying findings of pesticides and toxic elements in specific brands of rice, the India Office was able to determine that three firms identified in the report were actively exporting rice to the United States. At the request of the India Office, ORA implemented screening criteria so that ORA would collect border samples for pesticides and toxic elements in products from the three firms.

At HQ, the Office of International Program's Office of Regional Country Affairs Office worked with ORA in 2017 and provided guidance on the protocol for obtaining contact information for competent authorities needed to be informed of upcoming inspections. The Office of Regional Country Affairs reached out to FDA counterparts in Canada, Japan, Vietnam, Egypt, Ghana and Nigeria to obtain their updated contact information. This allowed ORA to effectively notify FDA counterpart authorities of planned inspections.

International Partnerships

In FY 2017, FDA implemented 16 new Confidentiality Commitments with:

- Public Health England, to facilitate information sharing about tobacco products
- the European Commission's Directorate General for Internal Market, Industry, Entrepreneurship and SMEs, to facilitate information sharing related to cosmetics and medical devices
- the Netherlands' National Institute for Public Health and the Environment, to facilitate information sharing about tobacco and biologics, among other FDA-regulated products
- the National Agro-Alimentary Health, Safety and Quality Service of the United Mexican States to facilitate information sharing about food related issues, among other FDA-regulated products, assuring that FDA will protect the information provided
- the World Health Organization through its Department of Essential Medicines and Health Products to disclose information regarding the identification of pharmaceutical substances and active pharmaceutical ingredients
- the European Medicines Agency to facilitate the exchange of non-public information related to FDA regulated drugs, including pre- and post-market activities, as appropriate, as part of cooperative law enforcement or cooperative regulatory activities
- several European Union member states to facilitate the exchange of non-public information related to FDA regulated drugs, including pre- and post-market activities, as appropriate, as part of cooperative law enforcement or cooperative regulatory activities. Specifically, FDA signed confidentiality commitments with:
    - the Bulgaria Drug Agency
    - the Croatia Agency for Medicines Products and Medical Devices
    - the Denmark Medicines Agency
    - the Estonia State Agency of Medicines
    - the Finland Medicines Agency
    - the France National Agency for Medicine and Health Products Safety
    - the Latvia State Agency of Medicines

- the Romania National Agency for Medicines and Medical Devices
- the Slovakia State Institute for Drug Control
- the Spain Agency for Medicines and Health Products.

FDA signed two Cooperative Arrangements during 2017 to facilitate regulatory activities:

- a food safety systems recognition arrangement with Australia's Department of Agriculture and Water Resources
- a Memorandum of Understanding with China's Certification and Accreditation Administration related to the export of U.S. dairy, seafood, and infant formula products to China.

In other partnership activities, FDA Europe and China Offices, working with CFSAN and OFVM, 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 FY 2017, the parties met to discuss import and export controls, e-Commerce, and risk communication, all important topics to implementing existing legislative authorities. Planning has begun for the next meeting to focus on risk assessment, expected to take place in Q3 of FY 2018.

In 2017, 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. The Europe Office directly contributed to multiple member State capability determinations through inspectorate audit observation and reporting, conflict of interest analysis, and capability assessment. All 28 Member States will be assessed by July 2019, and the Europe Office is expected to continue to play a central role in contributing to these assessments. Furthermore, the Europe Office and the Office of Regions and Country Affairs have been working together to finalize expanded confidentiality commitments with the European Union and all 28 individual Member States (expected to be completed through FY 2017 and FY 2018) that will allow all parties to more fully benefit from the MRA. Europe Office is also a key participant in implementation and coordination planning for operationalizing the MRA with FDA Centers and the European Medicines Agency (EMA). The Europe Office also participates on the Joint Sectoral Committee (i.e., governance committee). 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.

The India Office engaged in a series of in-person Seafood HACCP and U.S. Food Labeling workshops in Mumbai and Nellore in 2017. Almost 100 individuals were trained, providing India government and industry participants with information about FDA seafood HACCP regulatory requirements provided at 21 CFR Sec. 123 – specifically information concerning the key areas of sanitation, developing a HACCP plan, and preventing seafood safety hazards. In addition, participants were provided information on procedures for importing seafood products into the United States, including Customs and Border Protection and FDA regulatory oversight and information about responding to FDA product detentions. Moreover, FDA provided information about FDA labeling requirements for food products sold in the United States, including labeling requirements for the nutrition fact label and food allergens and updates to U.S. food labeling regulations. The workshops also strengthened relationships between FDA officials and the Export

Inspection Council of India. In addition, the India Office worked with the Pharmacovigilance Programme of India to determine ways to strengthen the pharmacovigilance program in India through U.S.-Indian collaboration.

Leveraging the Regulatory Capabilities of Foreign Counterparts

On-site relationships with foreign regulatory counterparts enable FDA to leverage their respective regulatory capabilities. The following items are examples of these relationships.

The Latin America Office regularly shares information with Mexico about products that do not conform to FDA standards and may pose a risk to human health if they enter the United States. In response, Mexico has implemented a process to follow up on this information and prevent the distribution of such products in Mexico. Additionally, in response to several Cyclospora outbreaks in 2013-2015, the Latin America Office worked closely with Mexican Authorities to develop a process by which selected Mexican packing houses and supplier farms can be added to the Import Alert #24-23 Green List that allows cilantro imports to the United States when such firms comply with the Mexican voluntary verification and certification programs. Since the implementation of Import Alert #24-23 and its Green Listing process, 30 supplier farms and 12 packaging houses/firms, 22 supplier farms and 9 packaging houses/firms have been added to the Green List without concomitant outbreaks linked to Cyclospora.

The Latin America Office shared information on six specific drug products with the Brazilian regulatory authority under the terms of our Confidentiality Commitment, resulting in Brazilian regulatory actions. For example, in one case, the Brazilian regulatory authority initiated closer monitoring of GMP compliance. In other cases, the information was taken under consideration for Brazilian regulatory decisions related to marketing and clinical trial authorizations as well as in the evaluation and authorization of post-approval changes to marketing authorizations.

Chinese regulators conducted a year-long investigation after FDA's China Office notified them of a firm that FDA alleged was manufacturing and distributing counterfeit drugs to multiple countries via internet sales. In October 2016, the Chinese government reported that several suspects were arrested, many processing sites were shut down and fake labels found on site were seized. The estimated income generated from these illegal activities was $1.8 billion.

In 2017, the Europe Office facilitated work between European Food Safety Authority and CFSAN experts on issues such as open data, specific requests for FDA scientific reports/findings, and risk communication. This collaboration is extremely important as the health policy landscape in Europe is often politicized around issues such as endocrine disruptors and biotechnology derived products intended for human and animal consumption and EFSA often represents the most completely science-based voice in the region on relative risk and safety.

Responding to an ORA and CDER request, the Europe Office facilitated dialogue with their United Kingdom regulatory partner and ORA's Office of Enforcement and Import Operations, resulting in development of a strategy and work between joint enforcement and compliance teams. The collaboration resulted in the halt of a longstanding path of shipment of violative drugs from several United Kingdom-based companies intended for the U.S. market. The India Office shared information of FDA refusals of Indian seafood through the Confidentiality Commitment with the Export Inspection Council of India. The Export Inspection Council of India used this refusal data to follow-up at processing facilities determined to be the root cause of the deviation and were able to elicit corrective actions from the facilities.

International Exchange of Information and Sharing of Expertise

In addition to information sharing that leverages the authority of foreign regulators, FDA Foreign Offices work closely with FDA product centers and the ORA to exchange regulatory knowledge and expertise with foreign stakeholders to improve understanding of FDA regulatory requirements. For example, during FY 2017, the China Office conducted outreach to Chinese regulatory authorities on topics such as Good Clinical and Manufacturing Practices, Generic Drug Review, Medical Device Review, Good Inspection Practices, Regulation of Dietary Supplements, Combination Products, User Fee Program Updates, Postmarket Medical Device Reporting and Surveillance, the Medical Device Sing Audit Program and FSMA. The Europe Office trained foreign regulatory authorities on FSMA rules, the amended MRA, key provisions of the 21st Century Cures Act, newly issued guidance on biosimilars/interchangeability, and the potential use of big data in regulatory decision making. The India Office provided Indian regulators with training on Good Clinical Practices, FSMA, Good Aquaculture Practices and Food Safety Preventive Controls for Aquaculture Farms, and the Federal Food, Drug, and Cosmetic Act.

An objective of the foreign offices is to improve regulatory decision making and prevent divergence of regulatory standards and approaches, when appropriate, through facilitation of technical exchange with trusted international regulatory counterparts. This is done through workshops, meetings, fellowships (technical exchanges) that are intensive and topic specific. For example, the Europe Office and EMA International Affairs held a formal meeting in November 2017 to discuss collaboration in the multilateral space, MRA implementation progress, collaboration with expedited review programs and scientific advice, and technical exchange platforms. In addition, the Europe Office oversees the management and maintenance of over a dozen technical working groups - "Clusters" - with EMA and in some cases the national competent authorities of Canada, Australia, Switzerland, and Japan. In depth exchanges and efforts to align thinking on regulatory science and strategies to promote public health are themes of these exchanges. In the second half of FY 2016 and FY 2017, the Europe Office facilitated in-depth technical exchanges on topics including food fraud, Unique Medical Device Identifier database, data transparency, drug quality inspections, pediatric drugs, orphan products, real-world evidence/big data, antimicrobial resistance, combination products, MRA Implementation, statistical extrapolation, master data management, and application review management.

The Europe Office held a one-day technical experts meeting of some key European Member State regulators. The meeting focused primarily on genome editing applications in the area of plant-derived foods for humans or animals. Sharing information on regulatory challenges associated with new technologies will encourage a science-based rather than political debate. Joining FDA experts were representatives from Belgium, Germany, Ireland, Sweden, and the Netherlands.

In 2017, the European Union adopted the most sweeping medical device regulation reform in a generation. This regulation includes a number of provisions designed to move the European Union toward FDA-standards, while maintaining Europe as the regulator of first resort for new medical devices. Through regular reporting on progress, as well as challenges from stakeholders including U.S. firms operating in Europe, the Europe Office has collaborated with CDRH to provide real time reporting on progress toward the implementation.

The India Office coordinated with the Government of India's Central Drugs Standard Control Organization to develop a strategic action plan to advance drug safety in the U.S. and India. The two conducted a joint workshop to share feedback from FDA inspections observed by Government of India inspectors. The India Office will utilize this knowledge and work with the Office of Regulatory Affairs to establish best practices.

During the 2017 bilateral meeting coordinated by the China Office, the China Food and Drug Administration shared their inspection report from 2015 and 2016 with the FDA. Among other topics, these reports addressed observed inspections with multiple regulatory agencies conducting inspections in China and shared the differences observed in approaches to drug inspections. During multiple interactions with China Office staff in September and October, central and provincial investigators from the China Food and Drug Administration also shared their experiences with observed inspections of foreign regulatory agencies. The information gathered from these meetings is being utilized to develop an Inspectional Cooperation Work plan utilizing best practices to establish with the China Food and Drug Administration, expected in 2018. Additionally, after repeated diplomatic engagements on the importance of international harmonization, in FY 2017 CFDA announced joining the International Council for Harmonization.

The Latin America Office participated in meetings with Mexico's regulatory authority regarding the NIH Zika vaccine trial. FDA and COFEPRIS worked closely together to clarify questions for COFEPRIS in their regulatory protocol review, allowing COFEPRIS' review to be completed within 30 days – a time period which is significantly shorter than their typical review time. As a result, the trial is already recruiting patients, which is essential to coincide with the rainy mosquito season in Mexico. Additionally, the regulatory authorities in Mexico expressed interest in learning about FDA's expedited review process for vaccines and in developing a process aligned with FDA's that allows for an improved response to cases of public health relevance. The Latin America Office coordinated input from CBER to collaborate on the development of an alternative pathway for vaccine product approval.

In addition, the Latin America Office held two virtual meetings with Brazil's regulatory authority, along with CDER subject matter experts, during which the parties exchanged information about best practices and regulations, and discussed specific procedures and the scientific and technical basis for regulation development. These meetings resulted in Brazil's actions on program streamlining and regulatory alignment with FDA on pharmacovigilance IT systems and over-the-counter drugs.

When the FDA Drug Shortage Team identified a shortage of domestically-produced antimicrobial drugs, the Europe Office rapidly engaged with the European Medicines Agency to obtain information on the production capacities of firms in Europe that produce such drugs. Since production by those firms could help mitigate the impact of the shortage in the United States, FDA's Drug Shortage Team included that information in FDA's strategy to address the drug shortage. Additionally, to address potential drug shortages, the China Office had regular communication with FDA's Drug Shortage staff during a government controlled industry shutdown of drug substance manufacturing during over the winter, as well as when an explosion occurred at a Chinese facility that supplied certain antibiotics to the US that had to cease production until remediation efforts were completed.

The China Office interacted with the World Health Organization's local Beijing Office in 2017 on the China Food and Drug Administration's Market Authorization Pilot. The World Health Organization is providing an assessment from all the provinces involved in the pilot, and the China Office contributed to the discussion topics for further consideration. The pilot is intended to spur innovation and is expected to be an integral part of the reform taking place relating to regulatory oversight under revisions to China's Drug Administration Law.

At HQ, the Office of International Program's Office of Regional and County Affairs sent information and requested input from international counterparts in Canada, Israel, Japan, Philippines, South Africa, South Korea and Thailand on the FY 2017 microbiological surveillance sampling model for selected food products. The Office provided this information to CFSAN, and consequently, CFSAN could work more efficiently and decrease the impact on trade.

In addition, the FDA HQ Office of Women's Health has established a network of international institutes academicians and scientists within the field of sex and gender-specific women's health. In FY 2016 and FY 2017, this network has resulted in multiple international speaking opportunities enabling FDA to communicate updates in policies, guidances, and research discoveries related to women's health. These international activities included educating The Matera Group, which consists of scientific experts from across the world, about FDA policies and regulations regarding analysis and reporting of sex differences in safety and efficacy. While FDA HQ is not a formal member of the Matera Group we are often contacted to provide clarifying information on FDA regulations related to women's health. Engagement such as this assists in ensuring accurate understanding of applicable women's health policies and regulations in the United States.

China Safety Initiative

FDA expanded its efforts to regulate the quality, safety and efficacy of FDA-regulated products exported to the United States from China through the China Safety Initiative (CSI), with the primary focus being the expansion of the number of in-country FDA investigators, which was accomplished through a negotiated agreement with the Chinese government.

The increase in in-country full-time investigators and those on temporary detail (TDY) to the China Office, allowed for the completion of 69 inspections in FY2017 focused on medical products. Furthermore, the China office also completed 128 inspections focused on foods, animal feed, and animal drugs. The China Office conducted all assigned FDA food facility inspections in China. The China Office, in collaboration with the Europe office and CFSAN, led a trilateral meeting between FDA, EU and Chinese regulators on food safety issues of mutual interest with the EU, and China agreed to a set an agenda as well as participate at a two-day event in March 2017.

In September 2017, the China Office spearheaded a workshop with international regulators and industry on GMP issues that focused on Out of Specification (OOS) Investigations and Corrective and Preventive Actions (CAPAs). The FDA China Office utilized internal expertise and assembled an international panel of experts from FDA's Center for Drug Evaluation and Research (CDER) Office of Compliance and Office of Regulatory Affairs (ORA), Medicines and Healthcare Products Regulatory Agency, European Medicines Agency (EMA), Health Canada, World Health Organization (WHO), and China Food and Drug Administration (CFDA) to take part in the event. The content built upon previous efforts that focused on data integrity and

expanded to the laboratory and manufacturing operations by covering global regulatory best practices in identifying, investigating and properly resolving issues.

In addition, the China Office works closely with FDA product Centers and ORA by providing monitoring and reporting on conditions, trends and events that could affect the safety, quality, and effectiveness of FDA-regulated products exported to the United States from China.

Improve and Safeguard Access

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 accelerated research and development 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.[101]

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

In FY 2017, FDA HQ:

- received 541 first-time requests for orphan drug designation and designated 449 promising drugs and biological products for rare diseases
- received 20 first-time requests for Humanitarian Use Device designations and designated 8 promising devices for rare diseases and conditions
- received 61 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 39 drugs and biologics for rare pediatric diseases[102]
- funded 15 new clinical trial grant awards and 70 ongoing grants funding clinical studies of promising therapies for rare diseases
- reviewed 89 natural history grant applications and funded 6 new natural history grant awards to inform medical product development by better understanding how specific rare diseases progress over time
- funded 7 pediatric device consortia to provide multidisciplinary advice and funding to assist pediatric device innovators.

Premarket and Postmarket Support

In FY 2017, FDA HQ responded to approximately 700 requests for combination product premarket review assistance from FDA staff and regulated industry (including products that are on the shortage list). FDA HQ issued four formal combination product requests for designation decisions with 100 percent of these decisions meeting the 60-day statutory decision time

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

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

requirement. FDA HQ provided timely informal jurisdictional assistance for approximately 157 separate Pre-RFD (informal inquiries). FDA HQ provided clarification and support for approximately 350 premarket applications, 1,130 intercenter consults and 50 combination product post market activities.

Pediatric Coordination

FDA HQ promoted high standards of scientific integrity by providing expert ethical opinions to agency Centers and Offices for more than 100 pediatric ethics issues, more than 600 pediatric development programs and more than 50 adult ethics issues. These ethical consultations include complex issues related to the development of FDA policies for emergencies and crises such as the Zika outbreak and the opioid crises, study design considerations in pediatric rare disease populations and research involving the exceptions from informed consent requirements for emergency research. Each of these efforts have continued at similar levels in 2017.

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). Additional research studies have been initiated with colleagues across the FDA Centers as well as with external scientific researchers. Consultations were provided across the FDA Centers with 33 consults completed in 2017.

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). Over 390 products have been reviewed by the PAC. In FY 2017, 34 pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews) were reviewed by FDA's PAC. All CDER products with mandated pediatric safety reviews undergo the same FDA review process. Through the risk-based assessment, low safety risk products will have their mandated pediatric-focused safety reviews posted on FDA's website. Over the last five years the PAC's workload has increased as a result of the legislatively mandated safety assessments on Humanitarian Device Exemptions that have asked for an exclusion from the limitation on profit-making and this will become an increasing part of the workload required to be performed by this committee.

FDA HQ, working in conjunction with Center subject matter experts through the Pediatric Cluster, met to resolve pediatric scientific differences between European Medicines Agency (EMA) and FDA on 156 issues in FY 2017. Of the 156 issues discussed with the EMA, harmonization was achieved for 74 percent. Examples of the most frequent issues discussed included study population, primary endpoint, study design, extrapolation and safety concerns.

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 regarding 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.

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 where knowledge gaps exist in order to maximally leverage research funding impact. Implementation of the Women's Health Research Steering Committee has created a direct connection regarding cross agency priorities and issues of importance to women's health.

To measure the impact of the Women's Health research program, the Research Impact and Outcomes Framework was developed. This first of its kind framework is currently in use by FDA HQ, two FDA product Centers, and upon request shared with three offices within the National Institutes of Health. It is an available resource to academic, federal, and non-government organizations and allows tangible measurement and reporting of the impact of research, education, and outreach programs.

In addition, since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 371 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 375 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ established a 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 2017 program accomplishments include:

- Collaborations with two national clinical trials professional organizations. Activities included providing training to hundreds of national scientists and clinical trials staff on methods to increase enrollment and retention of women in clinical trials.
- A quarterly Scientific Speaker Series provides 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% knowledge gain by attendees.

In FY 2017, FDA HQ also co-led development of a half day Workshop for the Women's Health Congress, which highlighted initiatives including women in clinical trials, precision medicine, and expanding FDA transparency and communications to an audience of clinicians, scientists, women's health advocacy and patient representatives. The workshop increased stakeholder engagement and understanding related to FDA's policies and procedures to ensure the health of women.

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.

Promote Informed Decisions

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[103].

Leading FDA's Engagements with the Government Accountability Office (GAO) and the Office of the Inspector General (OIG)

In this role, FDA HQ staff coordinates the Agency response to all these requests from GAO and OIG. For each of the several dozen engagements that are ongoing at any moment in time, this requires the identification of appropriate subject matter experts, coordination of FDA responses at a series of meetings and in writing, submission of data in response to requests, and assembly and editing of Agency responses to draft reports. In addition, all responses must be consistent with Agency legal and policy initiatives. 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, FDA HQ staff has assured that a greater number of these recommendations have been closed, and that a greater proportion of those have been closed as implemented.

Support for FDA's Priority Rulemakings

FDA HQ provided crucial support, which included developing and drafting rules and regulatory impact analyses, to ensure the publication of several key proposed and final rules in 2017. A key final rule that issued in 2017 included Refuse to Accept Procedures for Premarket Tobacco Submissions. This rule clarified FDA's process for tobacco premarket submissions. In addition to these key final rules, FDA issued 7 other final rules that are related to product approvals or technical amendments to existing FDA regulations.

One of the key proposed rules FDA issued in 2017 included Nutrition Food Labeling and Serving Sizes which proposes to extend the compliance date for requirements that update the food labeling to reflect amounts of food customarily consumed at one eating occasion and provides manufacturers with additional time to reconfigure their labels. FDA also proposed to extend the compliance date for parts of the FSMA produce rule. The extension applies to provisions related to agriculture water and produce other than sprouts. This will reduce the burden on farms that require additional resources to comply with the original rule. In addition to these two proposed rules, FDA issued four additional proposed rules that related to product approvals and responded to litigation.

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

Economic Analysis and Support for Medical Product Regulations Published

In 2016, along with the publication of the final rules themselves, FDA published the economic analyses for rules related to medical device products (Use of Symbols in Labeling) and human drug products (Abbreviated New Drug Applications and 505(b)(2) Applications). 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 final rules that will clarify regulatory uncertainty among the regulated industry.

Communication with Stakeholders – Improvements to FDA.gov

FDA is working to improve the usability of FDA.gov, our public-facing web site, by implementing a new, state of the art content management system (CMS), in May 2018, named Drupal. Drupal will help visitors more easily find our content and share it through web sites, mobile applications, and social media channels. In addition, Drupal will allow FDA to more easily highlight priority content and most requested content on our home page and topic landing pages. This greater flexibility displaying top task information is what visitors to FDA.gov are looking for. To prepare for this implementation, FDA has implemented a new archiving capability and 60,000 old and outdated content items have been removed from FDA.gov and are now available through archive. In addition, FDA is working on a project to identify a new and improved information architecture for 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.

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, medical professionals, patients, journalists and others.

From January 1, 2017 through November 2017 FDA HQ issued:

- 132 MedWatch Safety Alerts (FDA's second most popular e-list) to more than 450,000 subscribers.
- 203 News Releases and other press announcements in English and/or Spanish with a total reach of more than 89,000 subscribers
- 78 FDA Voice Blogs with more than 44,000 subscribers
- 260 Consumer Updates (some new material, some revisions) in English and Spanish with more than 117,000 subscribers
- more than 100 newsletters that reach approximately 700,000 patients and health care professionals.

FDA HQ responds to key agency priorities regarding women's health by delivering credible, accurate, and easy-to-understand health messages on topics related to FDA regulated products. These materials help women and their families make informed health decisions. These materials include fact sheets, brochures, purse cards, and medication discussion guides. All materials are free and written at a fourth through sixth grade reading comprehension level. To date, in partnership with other national organizations, more than 100 million publications have been distributed nationwide. Notable FY 2017 accomplishments include:

- Reaching more than 14 million people via special campaigns and stakeholder engagement initiatives using print and digital outreach
- Distributing 2.1 million patient education materials in 19 languages
- Disseminating FDA safety alerts and health information via the Office of Women's Health (OWH) twitter account to approximately 70,000 followers, of which 58% were health professionals and researchers
- Providing grants to FDA field staff to conduct women's health outreach in 15 cities in the U.S. and Puerto Rico
- Conducting webinars, conference presentations, and consumer outreach with over 25 public and private partners through the Diverse Women in Clinical Trials Initiative.

Meetings with Stakeholders

Since January 2017, FDA HQ has conducted nearly 630 meetings or interactions with a wide range of stakeholders. Noteworthy among these has been meetings or interactions with:

- The American Congress of Obstetricians and Gynecologists (ACOG)
- American Medical Association (AMA)
- Health Professional Student Engagement
- Consumers Union (CU)
- Atrial Fibrillation (AFib) Patient Organization
- American Academy of Dermatology
- Leukemia and Lymphoma Society.

FDA HQ has also used social media to engage with our stakeholders including two Twitter chats, with one including a bilingual audience. In additional, FDA recruited and trained 30 new patient representatives, selected for their experience and advocacy with medical conditions and diseases. The added representatives, who serve as a special government employee to FDA's Advisory Committees, brought the total number of patient representatives in the program to approximately 200. In July 2017, FDA conducted a workshop for patient representatives, providing them with an opportunity to learn about the FDA regulatory process and understanding their responsibilities.

FDA HQ fully participated in 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.

Stakeholder Outreach Activities

MedWatch Product Safety Communications: FDA HQ issued over 135 MedWatch Safety Alerts since January 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. 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. A MedWatch video was developed and distributed to consumers and health care professionals in Spanish that provides instructions for completing a MedWatch form as a way the U.S. public can

inform FDA about possible adverse effects attributable to an FDA-regulated product or a product of poor quality. Multiple 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 January 2017.

Healthcare Practitioners: As part of an MOU with the American Nurses Association, FDA HQ planned/conducted a joint webinar on November 16, 2017, "An Opioid Primer: Legislative, Policy, & Practice Implications." The joint 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 nurses associations and its organizational affiliates.

Rural Health Symposium: FDA HQ held its inaugural Rural Health Symposium on October 26, 2017, providing 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).

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, FDA acquired 300 artifacts, saw to the preservation through digital conversion of several thousand documents from the 1940s to the 1980s, and arranged for the preservation through digital conversion of over 200 historical videotapes in an antiquated format. FDA also promoted on social media 5 history video blogs and 19 written stories about FDA artifacts of historical significance.

Strengthen Organizational Excellence

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[104].

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.

These efforts have resulted in FDA receiving a total of $140 million in Non-recurring Expense Fund (NEF) resources to complete a major laboratory project that is a critical first step at implementing the Master Plan at FDA's owned Jefferson Labs Complex (JLC), replace FDA's Winchester Engineering and Analytical Center (WEAC) lab, relocate the Kansas City and SE Regional labs to new, modern and flexible leased lab space, and improve an additional lab at JLC. In addition, FDA continued efforts to relocate the leased San Francisco lab in FY 2017. FDA initiated the development or review of a Program of Requirements for three lab expansion projects (ORA's Forensic Chemistry Center and Detroit Lab, and CDER's Division of Pharmaceutical Analysis Lab in St. Louis) and for two lab relocation projects (ORA's Philadelphia Pharmaceutical Lab and CFSAN's Moffett Center Lab). A project was also initiated to make improvements for certification of a specialized lab at ORA's Northeast Human and Animal Food Lab.

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.

OpenFDA

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

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

Since the launch, on June 2, 2014 OpenFDA has received more than 45 million data calls. Half of the calls came from outside the US. There are more than 6,000 registered users, 21,000 connected systems worldwide, and dozens of new software applications that the community has built. 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 7.1 million records
- Device classifications – over 6,000 records
- Structured Product Labeling for FDA-regulated human drugs – prescription or over the counter– and biologics with over 105,000 records
- Medical device adverse event reports – 6.1 million records
- Food adverse event reports over 55,000
- Food enforcement reports12,811 records
- Unique Device Identifiers – over 1.3 million records
- 510Ks – over 145,000 records
- Device pre-market approvals – over 34,000 records
- Drug enforcement reports – over 7,000 records
- Device registration and listing – over 230,000 records
- Device recalls – over 99,000 records
- Device enforcements – over 13,916 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 of FDA-regulated products – over 100,000 recalls records

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$261,099,000	$173,292,000	$87,807,000
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 Annualized CR	$315,546,000	$180,980,000	$134,566,000
FY 2019 President's Budget	$347,240,000	$198,565,000	$148,675,000

BUDGET REQUEST

The FY 2019 Budget Request is $347,240,000 of which $198,565,000 is budget authority and $148,675,000 is user fees. This level provides a net increase of $31,694,000 compared to the FY 2018 Annualized CR. Budget authority increases by $17,585,000 and user fees increase by $14,109,000.

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 (+$26.0 million / 17 FTE)

New Platform for Drug Development - Oncology Center of Excellence (+$20 million / 13 FTE)

As part of this initiative to support new drug development, the FY 2019 Budget includes $20 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 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 (+$6.0 million / 4 FTE)

As part of FDA's FY 2019 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 2019 Budget includes $6.0 million for the Office of Laboratory Science and Safety (OLSS), 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. OLSS will work closely with the Office of the Chief Scientist, the Office of Operations, the Office of Regulatory Affairs, and the other product centers and directorates across the Agency.

Food Safety (+$0.5 million)

The FY 2019 funding level restores the FY 2018 Annualized CR rescissions to the food safety program. In FY 2019, FDA will continue its statutory mission of promoting and protecting public health by ensuring that the food supply is safe, sanitary, wholesome, and properly labeled. The FY 2019 level will also allow FDA to continue its critical FSMA implementation activities.

Other Reductions (-$8.9 million)

As part of the FY 2019 budget, FDA HQ will reduce investments in lower priority areas in order to support higher priorities for food and medical product safety. In FY 2016 and 2017, FDA HQ received funding to bolster the important ongoing development and utilization of a targeted, risk-based, and efficient inspection model for foreign high-risk facilities. However, these funds ($7.4 million at the FY 2018 Annualized CR level) are no longer required in FY 2019. In addition, FDA is proposing to discontinue the transfer of $1.5 million from FDA HQ to the HHS Office of Inspector General.

USER FEES

Medical Product Safety (+$14.1 million / 13 FTE)

The FDA HQ Program request includes an increase of $14.1 million for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring the safety and efficacy of medical products and accelerating innovation in the industry.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products.*(Output)*	FY 2017: Maintained 99.62% efficiency on response to calls to the FDA After Hours Call Center. Successfully coordinated 49 incidents involving FDA regulated products during the year. Participated in nine exercises during the year. (All Targets Met or Exceeded)	Develop 50 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinate 20 incidents involving FDA regulated products during the year. Participate in four exercises during the year	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in five exercises during the year.	+ 10 mapping products +1 exercise

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 2017: FDA completed annual milestones on 7 more 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)	40 CORES projects with completed annual milestones	47 CORES projects with completed annual milestones	+7
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship programs. (Outcome)	FY 2017: 72% Target: 40% (Target Exceeded)	50%	50%	Maintain
293205: Percentage of requests for combination product designations processed within the 60 day statutory requirement. *(Output)*	FY 2017: 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 2017: 156 Target: 45 (Target Exceeded)	45	45	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 2017: 38 Target: 30 (Target Exceeded)	30	30	Maintain
292301: The number of new multi-faceted educational programs for patient advocates and health professionals on major FDA public health issues. *(Output)*	FY 2017: 4 Target: 4 (Target Met)	4	4	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 2017: 27 Target: 25 (Target Met)	25	25	Maintain
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2017: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain