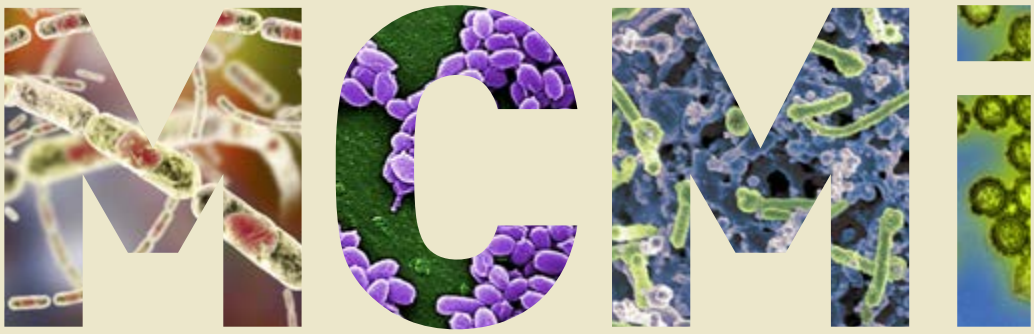


PROGRAM UPDATE

FY 2019

FDA MEDICAL COUNTERMEASURES INITIATIVE (MCMi)

FDA U.S. FOOD & DRUG ADMINISTRATION

Contents

Background 4
FY 2019 Resources for MCM Activities 5
Objectives, Activities & Achievements 6
Medical Countermeasure Approvals 7
Supporting an Adequate Supply of Medical Countermeasures 9
Enabling Access to Medical Countermeasures Under FDA's Emergency Use Authorization Authority 10
Responding to Emerging Infectious Disease Public Health Threats 11
Action Teams 14
Regulatory Advice and Guidance 16
Collaboration and Communication 19
Enhanced FDA/DoD Collaborations 21
Medical Countermeasure Regulatory Science 23
Advanced Manufacturing 28
Medical Countermeasure Regulatory Policy 30
Professional Development 32
Appendix 1: FY 2019 Medical Countermeasure Approvals 34
Appendix 2: Current Emergency Use Authorizations 39
Appendix 3: MCM-Related Guidance Issued in FY 2019 41
Appendix 4: Key MCM-Related Meetings Held in FY 2019 47
Appendix 5: Acronyms 50

List of Tables

Table 1: FY 2019 resources obligated to MCM activities 5
Table 2: FY 2019 formal meetings between CBER/CDER and MCM sponsors or applicants 17
Table 3: FY 2019 formal meetings between CDRH and MCM sponsors or applicants 17
Table 4: MCMi Regulatory Science Program activities in FY 2019 25

List of Boxes

Box 1: Key FDA activities to facilitate development of and access to MCMs 6
Box 2: Key FDA emerging threat response activities 13
Box 3: Priority research areas supported under the MCMi Regulatory Science Program 24

BACKGROUND

The United States (U.S.) Food and Drug Administration (FDA) plays a critical role in protecting the U.S. from chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats such as pandemic influenza and Zika virus. FDA is responsible for reviewing the safety and effectiveness of **medical countermeasures** (MCMs)—including drugs, therapeutic biologics, vaccines, and devices, such as diagnostic tests—to counter these threats.[1]

In addition to its regulatory responsibilities, FDA works closely with interagency partners through the U.S. Department of Health and Human Services (HHS) **Public Health Emergency Medical Countermeasures Enterprise** (PHEMCE) to build and sustain the MCM programs necessary to effectively respond to public health emergencies.[2] FDA also works closely with the U.S. Department of Defense (DoD) to facilitate the development and availability of MCMs to support the unique needs of American military personnel, including under a framework established in FY 2018 under Public Law 115-92 for enhanced FDA/DoD collaborations. FDA supports the PHEMCE and DoD by providing subject-matter expertise in MCM development and by providing scientific and regulatory input to inform MCM development, procurement and stockpiling decisions. In addition, FDA facilitates access to available MCMs to respond to public health and military emergencies, even when products are still investigational or not yet approved for that particular use, provided certain criteria are met.[3, 4]

In 2010, FDA launched its Medical Countermeasures Initiative (**MCMi**) Program, building on the substantive MCM work ongoing at FDA and focusing increased resources on promoting the development of MCMs by establishing clear regulatory pathways for MCMs, instituting effective regulatory policies and mechanisms to facilitate timely access to available MCMs, and advancing MCM regulatory science to create the tools that support timely regulatory decision-making.

Many of FDA's activities under the MCMi Program foster the development and availability of MCMs and authorities to enable FDA to more effectively support preparedness and response efforts have been codified.[5] The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (**PAHPRA**)[6] requires FDA to issue an annual report detailing its MCM activities. This report responds to that requirement for fiscal year (FY) 2019 (October 1, 2018 – September 30, 2019).[7]

---

[1] MCMs include qualified countermeasures as defined in section 319F–1(a)(2)(A) of the Public Health Service Act (PHS Act) (42 USC. § 247d–6a(a))(2)(A); qualified pandemic or epidemic products as defined in section 319F–3(i)(7) of the PHS Act (42 USC. § 247d–6d(i)(7)); and security countermeasures as defined in section 319F-2(c)(1)(B) of the PHS Act (42 USC § 247d–6b(c)(1)(B)). Some items included in this report, such as traumatic brain injury (TBI) diagnostics and some activities discussed, such as combatting antimicrobial resistance, may not meet the statutory definition of MCMs or relate directly to products defined as MCMs, but were included in this report as examples of additional work supported by MCMi Program staff because of its connection to public health preparedness. Inclusion of such examples is not intended as comprehensive reporting on Agency activities related to these topics.

[2] Section 2811-1 of the PHS Act [42 U.S.C. 300hh-10a], available at: **https://legcounsel.house.gov/Comps/PHSA-merged.pdf**

[3] See e.g., sections 561 and 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

[4] For purposes of this document, "approved" refers to "FDA-approved, licensed, or cleared" under sections 505, 510(k), 512, 515, or 571 of the FD&C Act or section 351 of the PHS Act.

[5] For a listing of MCM-related legislation, see: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-counterterrorism-legislation**

[6] Public Law 113-5, 127 Stat. 161.

[7] Detailed information on FDA's MCM development and review activities covering FY 2011-2018 can be found at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/publications-and-reports**

FY 2019 RESOURCES FOR MCM ACTIVITIES

FDA obligated an estimated $107.2 million in FY 2019 to support CBRN and pandemic influenza-related MCM activities (***Table 1***). These resources comprised a combination of base funding and no-year funding. This funding supported 416.2 full-time equivalents (FTEs).

Table 1: FY 2019 resources obligated to MCM activities (dollars in millions)

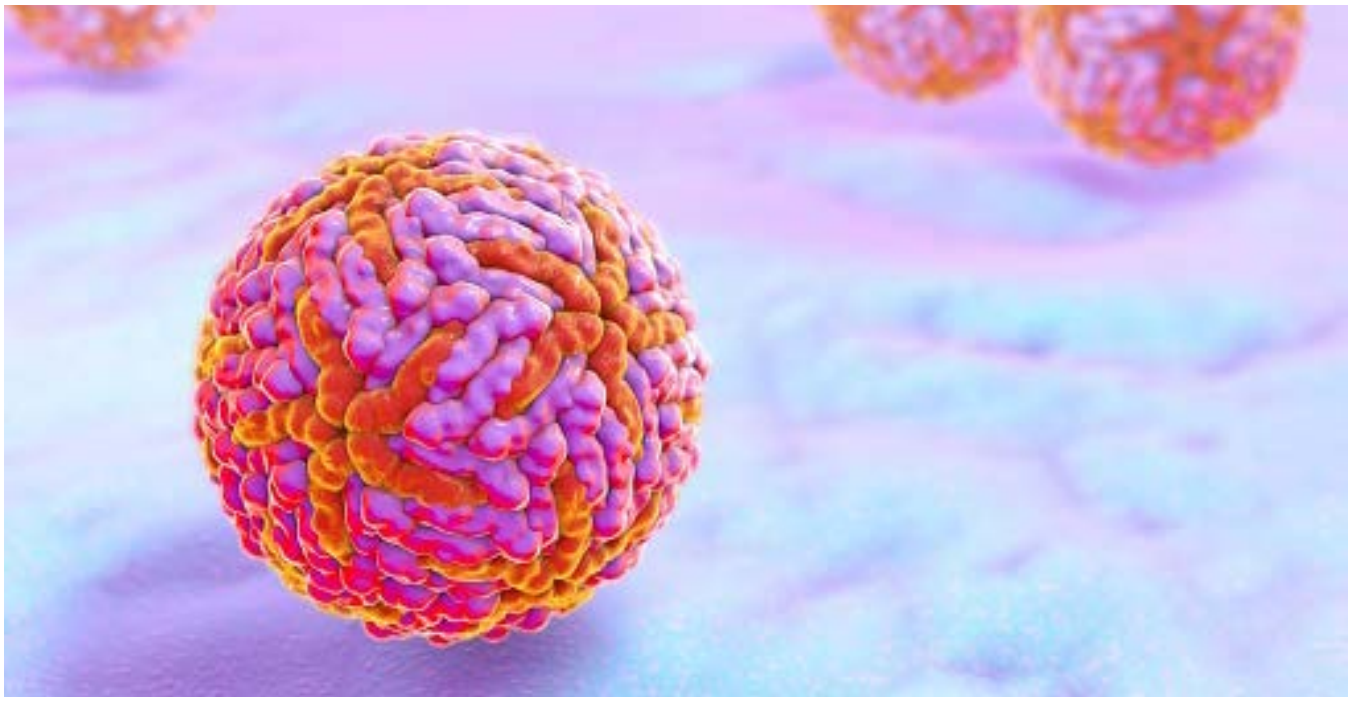
	FY 19 Estimate	FY 19 FTE Estimate
CBRN Base Funding	$34.1	150.5
Pandemic Influenza Base Funding	$43.9	179
MCMi Base Funding	$24.6	80.5
Subtotal	**$102.6**	**410**
Emerging Health Threats Funding (No-Year)	$4.6	6.2
Total	**$107.2**	**416.2**

Base Funding

FDA obligated $102.6 million from its FY 2019 base resources to support CBRN and pandemic influenza-related MCM activities. This funding included $34.1 million for CBRN preparedness activities, $43.9 million for pandemic influenza preparedness activities, and $24.6 million for the MCMi Program.

No-Year Funding

In FY 2017, FDA received $10 million in supplemental, no-year funding to prevent, prepare for, and respond to emerging health threats (EHTs). In FY 2019, FDA obligated the remaining $4.6 million of the original $10 million, supporting 6.2 FTEs and obligated $2.9 million in regulatory science research with EHT funds.



Zika Virus, illustration

OBJECTIVES, ACTIVITIES & ACHIEVEMENTS

FDA's overarching objective with respect to MCMs—which cuts across all FDA centers and offices engaged in the MCM mission space—is to facilitate the timely development of and access to safe and effective MCMs to counter CBRN and emerging infectious disease threats for civilian populations, as well as MCMs to support American military personnel.[8]

The following sections provide detail on achievements in FY 2019 with respect to these activities.

Box 1: Key FDA activities to facilitate development of and access to MCMs
Providing **regulatory advice, guidance, and technical assistance** to sponsors developing investigational MCMs for CBRN or emerging infectious disease threat indications
Discussing questions with potential product sponsors to help **clarify requirements** for approval
Reviewing MCM marketing applications and **approving** those that meet standards for approval
Supporting the establishment and sustainment of an adequate **supply** of MCMs
Enabling **access** to available MCMs that are not yet approved for use—when necessary—through an appropriate regulatory mechanism
Responding to **emerging and re-emerging public health threats**
Establishing and sustaining Public Health and Security **Action Teams** to identify and catalyze the resolution of regulatory and scientific challenges associated with MCMs to address high-priority threats
Developing capabilities to **monitor and assess MCMs** used during public health emergencies
Collaborating with U.S. government partners developing MCMs
Sustaining the **MCMi Regulatory Science Program** to create tools, standards, and approaches to develop and assess MCM safety, efficacy, quality, and performance
Ensuring that the FDA **regulatory and policy framework** adequately supports MCM development and enables preparedness and response activities
Sustaining the **MCMi Professional Development Program** to ensure that FDA personnel maintain the requisite skills and abilities to support the MCM mission

[8] High-priority threats identified by the Enterprise for which MCMs are needed include biological threats: *Bacillus anthracis* (anthrax); *Clostridium botulinum* toxin (botulism); emerging infectious diseases (including pandemic influenza); gram-negative organisms (*Francisella tularensis* (tularemia), *Yersinia pestis* (plague), *Burkholderia mallei* (glanders), *Burkholderia pseudomallei* (melioidosis), *Rickettsia prowazekii* (typhus)); multi-drug resistant *Bacillus anthracis* (MDR anthrax); variola virus (smallpox); and viral hemorrhagic fevers (Marburg and Ebola); chemical threats including: nerve agents and cyanide; radiological agents (e.g., radiological dispersal devices); and nuclear agents. See the *2017-2018 PHEMCE Strategy and Implementation Plan* for more information at: **https://www.phe.gov/Preparedness/mcm/phemce/Documents/2017-phemce-sip.pdf** (see Box 1, page 8).

MEDICAL COUNTERMEASURE APPROVALS

During FY 2019, FDA continued to review marketing applications for MCMs against CBRN and emerging infectious disease threats and approve safe and effective MCMs. FDA approved the majority of MCM marketing applications under review[9] in FY 2019 (see ***Appendix 1: FY 2019 Medical Countermeasure Approvals***).[10]

MCMs to treat or prevent diseases or conditions caused by CBRN threats

To support smallpox preparedness, FDA approved Jynneos Smallpox and Monkeypox Vaccine, Live, Non-Replicating, for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection.[11] This is the only FDA-approved vaccine for the prevention of monkeypox disease. FDA issued a material threat MCM priority review voucher (PRV) with this approval.

For chemical nerve agent and burn care preparedness, FDA expanded the indication for Silverlon, a first-of-its-kind wound contact dressing to include management of certain injuries caused by exposure to sulfur mustard vapor, commonly known as mustard gas. The Biomedical Advanced Research and Development Authority (BARDA) provided technical expertise and funding to support the studies necessary to show that the product, Silverlon, is appropriate for use on first- and second-degree skin burns caused by exposure to sulfur mustard.[12]

Diagnostics and screening tests for CBRN threats and emerging diseases

FDA cleared for marketing two diagnostic tests to detect Zika virus immunoglobulin (IgM) antibodies in human blood. The ZIKV Detect 2.0 IgM Capture ELISA was the first Zika diagnostic test FDA allowed to be marketed in the U.S., in May 2019; in July 2019, FDA cleared the ADVIA Centaur Zika test. Previously, tests for detecting Zika virus IgM antibodies had been authorized only for emergency use under the FDA's Emergency Use Authorization (EUA) authority.[13, 14]

Pandemic influenza preparedness

FDA approved Xofluza (baloxavir marboxil) for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours. Xofluza is one of several FDA-approved antiviral drugs to treat acute uncomplicated influenza, and is the first in nearly 20 years with a novel mechanism of action.[15]

In addition, FDA approved a Biologics License Application (BLA) supplement for Afluria and Afluria Quadrivalent Influenza Vaccines, to extend the indi-

---

9 For purposes of this document, "under review" indicates that a marketing application has been submitted to FDA for approval by the product's sponsor.

10 More information is available at: *Drugs@FDA*: **https://www.accessdata.fda.gov/scripts/cder/daf/**, *Biologics Products & Establishments*: **https://www.fda.gov/vaccines-blood-biologics/biologics-products-establishments**, and *Medical Device Databases*: **https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases**

11 For more information, see the FDA news release, *FDA approves first live, non-replicating vaccine to prevent smallpox and monkeypox*, available at: **https://www.fda.gov/news-events/press-announcements/fda-approves-first-live-non-replicating-vaccine-prevent-smallpox-and-monkeypox**, and *JYNNEOS*, at: **https://www.fda.gov/vaccines-blood-biologics/jynneos**

12 For more information, see the HHS news release, *First medical product cleared in U.S. for use on certain injuries caused by sulfur mustard*, available at: **https://www.phe.gov/Preparedness/news/Pages/FDA-blister-injuries.aspx**

13 For more information, see *Zika Virus Response Updates from FDA, Medical Products (Vaccines, Therapeutics, Diagnostics)* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/zika-virus-response-updates-fda#medical**

14 BARDA supported development of the ZIKV Detect 2.0 IgM Capture ELISA. See *BARDA-supported Zika Virus Test Receives FDA Clearance; Ready for Clinical Laboratory Use* at: **https://www.phe.gov/ASPRBlog/pages/BlogArticlePage.aspx?PostID=345**

15 For more information, see *FDA approves new drug to treat influenza*, available at: **https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treat-influenza**

> FDA approved the first new antiviral with a novel mechanism for treatment of influenza in nearly 20 years.

cation for use in persons 6 through 59 months of age. Afluria Quadrivalent was first approved in the U.S. in August 2016, for adults 18+ and helps protect against two influenza A strain viruses and two B strain viruses. FDA also approved an expanded age indication for use of the 0.5 milliliter (mL) dose of Fluzone Quadrivalent Influenza Vaccine for children ages 6 to <36 months.

FDA also approved 4 new influenza tests and approved modifications to 11 previously approved influenza detection *in vitro* diagnostic (IVD) devices to, for example, include additional specimen types, additional instrument options, and software modifications, and requested a Clinical Laboratory Improvement Amendments of 1988 (CLIA) waiver for a previously CLIA-categorized test and update package inserts. These steps forward in influenza prevention and diagnostics facilitate preparedness for both seasonal and pandemic influenza, as new tests and technologies may be applied more rapidly to emerging pandemic influenza strains once approved for seasonal influenza use.

All-hazards preparedness

FDA cleared the Trilogy Evo Universal Ventilator with new features such as intrinsic positive end-expiratory pressure (PEEP), or auto-PEEP and carbon dioxide monitoring. This ventilator was **supported by BARDA** as an advanced all-hazard stockpile ventilator.

To address traumatic brain injury (TBI), FDA approved Oculogica's EyeBox which is intended to measure and analyze eye movements as an aid in the diagnosis of concussion, also known as mild traumatic brain injury (mTBI), within one week of head injury in patients 5 through 67 years of age in conjunction with a standard neurological assessment of concussion. FDA also cleared a Modified BrainScope One multi-modal, multi-parameter assessment indicated for use as an adjunct to standard clinical practice to aid in the evaluation of patients who have sustained a closed head injury within the past 72 hours (including patients with concussion/mTBI), and ImPACT, a computer-based neurocognitive test battery to aid in the assessment and management of concussion.

To support trauma care, including military medical needs, FDA cleared the Sense System With IBT Electrodes, for external prosthetic fittings of upper limbs; the Phoenix, intended to enable individuals with spinal cord injury at levels T4 to L5 to perform ambulatory functions in rehabilitation institutions; and the Dome Electrode, for non-invasive use with recording and monitoring equipment of electromyography (EMG). FDA also cleared the Quantum Blood and IV Fluid Infusion Warmer for warming blood, blood products, and intravenous solutions prior to administration in adult patients; it is intended for use by healthcare professionals in hospital, clinical, field, and transport environments to help prevent hypothermia.

Additional marketing applications in progress

Ten additional marketing applications for new MCMs or new MCM indications were under review in FY 2019; these reviews were still ongoing at the end of the reporting period for this report. While FDA anticipates meeting the goal date for a decision for each of these submissions, FDA is generally prohibited from disclosing any determinations regarding the filing or approvability of any marketing application for a medical product under applicable statutory and regulatory provisions unless the application is approved or other grounds for disclosure apply.[16]

[16] For updated information about MCM approvals after the FY 2019 reporting period, see *MCMi News and Events* at: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/mcmi-news-and-events**

SUPPORTING AN ADEQUATE SUPPLY OF MEDICAL COUNTERMEASURES

FDA continued efforts to support the establishment and sustainment of an adequate supply of MCMs during FY 2019. One way FDA does this is by supporting the **Shelf-Life Extension Program** (SLEP). SLEP is a federal fee-for-service program for extending the useful shelf life of military-significant and contingency use medical products, including MCMs that are owned by components of DoD or other federal program participants such as the **Strategic National Stockpile** (SNS). SLEP is designed to defer drug replacement costs for date-sensitive stockpiles of drugs by extending their useful shelf life beyond the manufacturer's original labeled expiration date. FDA laboratory personnel test and evaluate drugs submitted for shelf-life extension to assure stability and quality before an expiry dating extension is granted. In FY 2019, as a result of SLEP testing that assured drug stability and quality, FDA granted shelf-life extensions for approximately 2,000 lots (batches) of MCM drugs.

To help ensure an adequate supply of MCMs for potential emergencies, FDA may also extend the expiration dating of MCMs outside of SLEP based on FDA's review of scientific data.[17] For example, FDA issued final guidance to support government public health and emergency response stakeholder testing to support FDA extensions of the expiration date of specific lots of doxycycline hyclate 100 mg capsules held in strategic stockpiles for anthrax emergency preparedness and response purposes.[18] Previously issued FDA-authorized extensions under the recommendations of the draft guidance remain in effect through June 2020. Based on government stakeholder needs, FDA continues to review scientific data to determine whether additional extensions of other MCMs may be supported outside of SLEP.

Working to resolve MCM shortages as quickly as possible when they occur is another way FDA helps ensure an adequate supply of MCMs. In FY 2019, FDA continued to collaborate with U.S. government partners and the manufacturer of auto-injector products used for the treatment of nerve agent and insecticide poisoning to help prevent shortages of these products when production stopped after quality issues were identified in the manufacturing process. FDA reviewed applicable scientific data, including through SLEP, to assess whether, if properly stored, certain lots of this manufacturer's auto-injector products held for emergency use can continue to be used beyond the original labeled expiration date for a period specified by FDA, to help ensure ready access to these products. FDA also reviewed scientific data to assess whether certain lots are no longer useable and, therefore, should be properly disposed of.[19]

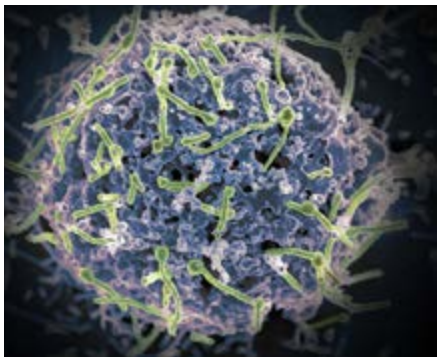
FDA also responded to numerous stakeholder inquiries on nerve agent auto-injector **expiry dating extensions** to assist in determinations about whether stockpiled auto-injector products made by the same manufacturer should be retained. Meanwhile, FDA continued to work with the applicant on manufacturing issues.

---

[17] FDA. *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Guidance for Government Public Health and Emergency Response Stakeholders*. April 2019. **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/extending-expiration-dates-doxycycline-tablets-and-capsules-strategic-stockpiles**

[18] For more information, see *Expiration date extensions of certain lots of doxycycline hyclate capsules* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-date-extensions-certain-lots-doxycycline-hyclate-capsules**

[19] For the latest updates on expiry dating extensions for chemical nerve agent auto-injectors, see *FDA alerts health care providers and emergency responders of expiration date extensions of certain auto-injectors manufactured by Meridian Medical Technologies* at: **https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-providers-and-emergency-responders-expiration-date-extensions-certain-auto**



Ebola virus from Mali.

Another way FDA works to ensure an adequate supply of MCMs is by conducting post-marketing current good manufacturing practices (cGMP) inspections for facilities that produce MCMs to ensure that these products were produced under cGMP and to help identify and resolve any issues that could potentially lead to a shortage due to manufacturing issues.[20] In 2018, FDA **established a framework** to help assure product quality and transparency at foreign drug manufacturing facilities. This framework will help ensure that drug products all meet the same high-quality standards—regardless of where these are manufactured—whether they are brand name or generic products, or prescription or over-the-counter drugs. Under the **Mutual Recognition Agreement** (MRA), in FY 2018 FDA notified 15 countries that they are recognized, based on quality, of being able to conduct inspections of manufacturing facilities that meet FDA requirements; in FY 2019 FDA accepted 13 additional countries to perform quality inspections under the MRA.[21]

ENABLING ACCESS TO MEDICAL COUNTERMEASURES UNDER FDA'S EMERGENCY USE AUTHORIZATION AUTHORITY[22]

During FY 2019, FDA continued to work with PHEMCE partners, including DoD, and product sponsors to enable access to unapproved MCMs when necessary.[23] One way FDA does this is by issuing **Emergency Use Authorizations** (EUAs). The EUA authority allows FDA to authorize the use of an unapproved MCM, or the unapproved use of an approved MCM, in anticipation of a potential emergency or during an actual emergency involving CBRN agents, or, for DoD purposes, other agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces, if certain statutory criteria are met (see ***Appendix 2: Current Emergency Use Authorizations for a list of current EUAs***).[24]

In November 2018, FDA **issued an EUA** for a rapid, single-use test for the detection of Ebola virus (*Zaire ebolavirus*). This was the second Ebola rapid antigen fingerstick test available under EUA, but the first that uses a portable battery-operated reader, which can help provide clear diagnostic results outside

---

[20] cGMPs provide for systems that ensure proper design, monitoring, and control of manufacturing processes and facilities. Adherence to the cGMP regulations ensures the identity, strength, quality, and purity of medical products by requiring that manufacturers adequately control manufacturing operations.

[21] The MRA between FDA and the European Union allows drug inspectors to rely upon information from drug inspections conducted within each other's borders. Under the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in 2012, FDA has the authority to enter into agreements to recognize drug inspections conducted by foreign regulatory authorities if the FDA determines those authorities are capable of conducting inspections that met U.S. requirements. For more information, including the list of countries, see: **https://www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra**

[22] Section 564 of the FD&C Act (21 USCS § 360bbb-3)

[23] This support includes numerous activities including availability of pre-IND [Investigational New Drug] consultations for drug development proposals and pre-market consultations for device development proposals, advice, and feedback on clinical trial preparation, discussions related to expanded access protocols and pre-EUA discussions.

[24] The Project BioShield Act of 2004 [PL 108-276] established section 564 of the FD&C Act, granting the Secretary of HHS the authority to authorize the "emergency use" of MCMs under certain terms and conditions. The authority to issue EUAs was delegated to the FDA Commissioner. Section 564 of the FD&C Act was amended by PAHPRA in 2013, the 21st Century Cures Act in 2016 [PL 114-255], and PL 115-92 in 2017.

> FDA issued an EUA for a rapid, single-use test to detect Ebola virus—the first that uses a portable battery-operated reader.

of laboratories in areas where patients are likely to be treated. In January and February 2019, FDA amended the EUAs previously issued for Ebola rapid antigen tests: one whole-blood fingerstick test (originally issued in 2015) and the other for cadaveric oral fluid (originally issued in 2016). In FY 2019 FDA received a total of 22 amendment requests for EUA diagnostic devices and granted or acknowledged 18.

In addition to issuing EUAs when necessary, FDA engages in ongoing pre-EUA submission processes by which FDA works with product sponsors or government agencies, such as the Centers for Disease Control and Prevention (CDC) and DoD, to facilitate the development of pre-EUA packages that will form the basis of an EUA request and issuance when circumstances justify. During FY 2019, FDA continued to work with government partners and industry on pre-EUA activities for MCMs against a diverse array of threats.[25, 26]

Finally, FDA engaged its Internal Message Testing Network to assess the understandability of a representative IVD EUA fact sheet. Responses from a series of individual interviews with FDA physician volunteers were analyzed for recurring ideas and themes and used to develop improved EUA fact sheet templates for diagnostic devices.[27]

RESPONDING TO EMERGING INFECTIOUS DISEASE PUBLIC HEALTH THREATS

During infectious disease outbreak and epidemic responses, FDA works proactively with U.S. government partners, medical product developers, and international partners (including the World Health Organization (WHO) and international regulatory counterparts) to provide scientific and regulatory advice to help facilitate the development and availability of MCMs.

In addition to responding to specific threats, including Ebola and Zika, FDA also engages in numerous activities to support public health emergency preparedness for a variety of threats. Emerging infectious disease-specific response activities in FY 2019 included:

Ebola

FDA continued to support the international response to outbreaks of Ebola virus disease, including follow-up activities related to the 2014-2016 West Africa outbreak and ongoing response to the most recent Democratic Republic of the Congo (DRC) outbreak continuing into 2019. In FY 2019, FDA:

- Continued to work closely with interagency partners, medical product developers, the WHO, and international regulatory counterparts to help move candidate medical products for Ebola

---

[25] A pre-EUA package contains data and information about the safety, quality, and efficacy of the product, its intended use under an EUA, and information about the potential emergency situation that might unfold. The pre-EUA process allows FDA scientific and technical subject matter experts to begin a review of information and assist with the development of conditions of authorization, fact sheets, and other documentation needed for an EUA in advance of an emergency. For more information about EUAs, see *Emergency Use Authorization of Medical Products and Related Authorities* at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities**

[26] For more information applicable to *in vitro* diagnostic pre-EUAs, see *How to Submit a Pre-EUA for In vitro Diagnostics to FDA* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/how-submit-pre-eua-vitro-diagnostics-fda**

[27] An EUA issued on November 9, 2018, uses the new templates. See the DPP Ebola Antigen System fact sheet for health care providers at: **https://www.fda.gov/media/117736/download**

forward in development as quickly as possible. For example, FDA participated in discussions of potential clinical trial approaches including a trial comparing several investigational therapeutics against a control arm that began in 2018 and issued preliminary results in 2019.[28] Based on preliminary findings in this National Institutes of Health (NIH) trial, FDA continues to provide regulatory guidance to product developers.[29] FDA also provided to WHO study recommendations for the evaluation of rapid Ebola antigen-based diagnostic tests to facilitate data collection for future marketing submissions.

- Continued work to facilitate access to available medical products through appropriate regulatory mechanisms when necessary and to protect consumers from fraudulent products and false product claims related to Ebola.
- Continued to work with manufacturers of authorized Ebola diagnostics to make rapid tests available, as well as advance these products toward market approval. As noted above, in November 2018, FDA issued an EUA for a rapid, single-use test for the detection of Ebola virus—the first with a portable, battery-operated reader. FDA also continued to work with Ebola diagnostic manufacturers on EUA amendments to address technical issues.
- Funded new extramural research to conduct the largest Ebola virus and host gene expression study to date. This **research** will help fill significant gaps in the scientific community's understanding of how Ebola virus disease progresses at the molecular level. FDA also continued Ebola-related research begun in previous fiscal years under the MCM Regulatory Science Program. (*Also see* ***Medical Countermeasure Regulatory Science***)

Zika

FDA also continued to actively support the national and international **response to Zika virus.** In FY 2019, FDA:

- Cleared for marketing two diagnostic tests to detect Zika virus IgM antibodies in human blood. *(Also see* ***Diagnostics and screening tests for CBRN threats and emerging diseases****)*
- Held a Blood Products Advisory Committee meeting in March 2019 to discuss and make recommendations on strategies to reduce the risk of Zika virus transmission by blood and blood components.[30]
- Continued to work with Zika diagnostic manufacturers to amend EUAs, and help advance Zika diagnostics toward market approval.

> FDA cleared two Zika diagnostic tests in FY 2019—the first allowed to be marketed in the U.S.

MERS-CoV

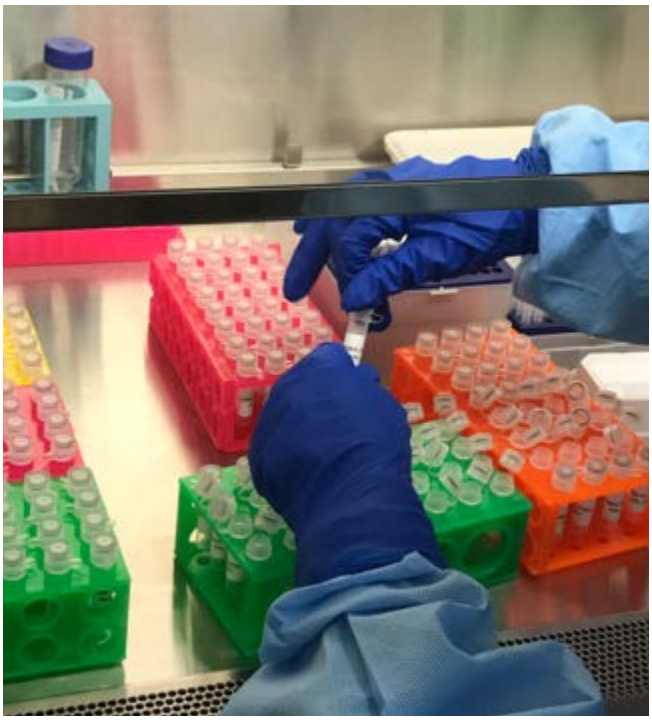
FDA continued activities to respond to the Middle East Respiratory Syndrome coronavirus (MERS-CoV) outbreak, which was first observed in the Middle East in 2012, with subsequent importations by international travel into a number of other countries. FDA continues to work with manufacturers toward making more MERS-CoV IVD tests available. In FY 2019, FDA

---

[28] For more information, see *NIH Clinical trial of investigational Ebola treatments begins in the Democratic Republic of the Congo* at: **https://www.nih.gov/news-events/news-releases/clinical-trial-investigational-ebola-treatments-begins-democratic-republic-congo**

[29] For more information, see *Independent Monitoring Board Recommends Early Termination of Ebola Therapeutics Trial in DRC Because of Favorable Results with Two of Four Candidates* at: **https://www.niaid.nih.gov/news-events/independent-monitoring-board-recommends-early-termination-ebola-therapeutics-trial-drc**

[30] Meeting materials are available at: **https://www.fda.gov/advisory-committees/advisory-committee-calendar/blood-products-advisory-committee-march-20-21-2019-meeting-announcement-03202019-03212019**



Zika refence panel

cleared two devices involving MERS-CoV. The first was a multiplex panel IVD test that detects bacteria, viruses (including MERS-CoV), and select antimicrobial resistance (AMR) genes to include a new specimen type, and the second was an external assayed quality control material.

Box 2: Key FDA emerging threat response activities
Collaborating closely with HHS, other federal agencies, and international partners in preparedness and response decisions regarding MCM development and use
Providing **review and feedback** on development proposals including clinical trial design and data assessment
Maintaining contact with drug, vaccine, and device (including diagnostic test) developers, and **expediting the regulatory review** of data for products that are currently in the pipeline and products that are still very early in development
Advising on design and set-up of **clinical trials** for establishing the safety and efficacy of investigational products for the treatment and/or prevention of emerging infectious diseases, including Ebola and Zika
Supporting FDA's ongoing efforts to **protect the safety of the nation's blood supply** and human cells, tissues, and cellular and tissue-based products (HCT/Ps) for transplantation
Enabling **access to investigational MCMs**—when necessary—through an appropriate mechanism such as under an expanded access protocol or under an EUA, including review of expanded access protocols that may be used in Ebola outbreaks when a suitable clinical trial is not available, and updating of EUA information for Zika and Ebola diagnostics that have not yet met requirements for full marketing clearance
Issuing EUAs as needed, including authorizing use of a freeze dried plasma product and a rapid Ebola diagnostic test with a battery-operated portable reader
Addressing issues related to the **import and export** of investigational MCMs
Preparing to implement **safety surveillance** programs for adverse events associated with MCM use and take appropriate action if safety issues are identified
Monitoring the **MCM supply chain** to identify product shortages and distribution of misbranded/counterfeit products
Monitoring **false product claims**, and taking appropriate action when necessary to protect consumers

ACTION TEAMS

Under the MCMi Program, FDA established multi-disciplinary Public Health and Security Action Teams (Action Teams) as necessary to advance MCMs for priority threats by working with internal and external entities—as appropriate—to identify and catalyze the resolution of regulatory and scientific challenges to MCM development. The following information summarizes activities of the Action Teams that were active in FY 2019.

Microbial Sequencing and Multiplex *In Vitro* Diagnostics Action Team

This Action Team continued its work to support sequence-based diagnostic device development. Such diagnostics may include multiplex diagnostic devices, which test for multiple pathogens simultaneously from a single clinical specimen, providing valuable information when responding to a public health emergency. Key activities during FY 2019 included:

- Continuing collaboration with the National Center for Biotechnology Information (NCBI), the Lawrence Livermore National Laboratory (LLNL), and the Institute for Genome Sciences at the University of Maryland to establish quality criteria for microbial reference databases that will be critical to developers seeking to validate their candidate next-generation sequencing (NGS)-based IVD tests.
- Continuing to facilitate the population of a publicly available **database** for reference-grade microbial genomic sequences (FDA dAtabase for Regulatory Grade micrObial Sequences, or **FDA-ARGOS**).[31] In FY 2019, through additional new collaborations with Stanford University, the FDA Center for Biologics Evaluation and Research (CBER), the National Institute of Allergy and Infectious Diseases – Integrated Research Facility (NIAID-IRF), the Antibiotic Resistance Monitoring, Analysis and Diagnostics Alliance (**ARMADA**), ARUP Laboratories, and the Paul Ehrlich Institute, FDA has initiated reference genome sequencing for 1,587 microbial constituents, of which 861 are currently publicly available. The FDA-ARGOS database generates and publishes regulatory-grade microbial genomes, which enable ID-NGS developers to perform *in silico* validation of their workflows, and was the subject of a recent publication in **Nature Communications**. To enable independent evaluation of bioinformatics workflows, in FY 2018, FDA and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) partnered to co-sponsor a **crowdsourcing challenge**. The FDA Center for Devices and Radiological Health **(CDRH) ID NGS Diagnostics Biothreat Challenge Team** asked participants to benchmark their detection algorithms on a task to identify and quantify biothreat organisms in clinically relevant metagenomics NGS samples.[32] Work on this crowdsourcing challenge continued in FY 2019. This novel crowdsourced challenge will encourage development of innovative detection algorithms for identifying and quantifying emerging pathogens, such as the Ebola virus, from their genomic fingerprints.

---

[31] FDA-ARGOS was established in FY 2014, through NCBI, to sequence approximately 2,000 isolates. This database is being expanded to generate 150 high-quality, nearly complete draft genome sequences of mosquito-borne viral pathogens, including Zika virus sequences. As part of this project, FDA set up collaborations to acquire the following prospective samples: 1) clinical isolates from Children's Hospital and George Washington University in Washington, D.C., to enhance diversity of GenBank, 2) biothreat and near-neighbor isolates/gDNA from USAMRIID/Critical Reagents Program (CRP), 3) Ebola isolates/gDNA from Public Health Canada/National Institute of Allergy and Infectious Diseases (NIAID) collaboration and USAMRIID/CRP, 4) antimicrobial resistance (AMR) isolates from Children's Hospital, and 5) difficult-to-acquire isolates from the American Type Culture Collection (ATCC). The FDA-ARGOS database is available at **https://www.ncbi.nlm.nih.gov/bioproject/231221**

[32] The reference database is fixed in this challenge, eliminating potential variation from different databases that are typically connected to bioinformatics detection algorithms.

- Continuing collaboration with the National Institute of Standards and Technology (NIST) to develop mixed microbial **reference materials** that will be critical to developers seeking to validate their candidate NGS-based IVD tests, and produce both microbial and human reference genome samples and materials to support the development and validation of NGS instrumentation/software platforms for sequencing microorganism and human nucleic acids.
- Sustaining an interactive collaboration with DoD on the development of its Next-Generation Diagnostic System (NGDS Increment II).

FDA/DoD Enhanced Engagement Action Team

This Action Team[33] continued its efforts to facilitate the development and regulatory assessment of MCMs and related technologies primarily to support U.S. military personnel and trauma victims. Key FY 2019 activities included:

- Continuing a joint program to prioritize the efficient development of safe and effective medical products intended for deployed American military personnel. (See ***Enhanced FDA/DoD Collaborations*** for details.)
- Meeting with DoD offices, commands, and programs to discuss regulatory and scientific issues related to developing and providing access to medical products for the warfighter. Focus areas include traumatic injury (including TBI), hemorrhage, nerve agents, and research that involves minimal risk to human subjects.[34]
- Continuing a formal fellowship program between FDA and DoD to support the training of DoD scientific and medical personnel in medical product development and FDA's regulatory processes. Two DoD laboratory experts are currently being cross-trained in regulatory review at FDA.

Acute Radiation Syndrome (ARS) Action Team

This Action Team continued its efforts to clarify the regulatory requirements for development of MCMs for ARS indications, to improve survival and mitigate and treat injuries from radiological/nuclear (rad/nuc) events. Key activities during FY 2019 included:

- Facilitating cross-agency interaction and supporting FDA rad/nuc MCM activities. In FY 2019, FDA co-sponsored two meetings with NIAID and BARDA on the pathophysiology of radiation-induced lung injury and cutaneous radiation injuries.
- Continuing interaction with BARDA to address issues and challenges related to development of radiation biodosimetry medical devices.
- Assisting NIAID with development of cellular therapy products and discussing scientific and regulatory challenges.
- Providing regulatory input on the HHS Assistant Secretary of Preparedness and Response (ASPR) radiation emergency medical management guidance document for myeloid cytokine treatment of acute exposure to myelosuppressive doses of radiation (H-ARS).
- Providing FDA reviewers with training and information on the latest scientific research related to radiation-induced lung injury and cutaneous radiation injury to enable appropriate regulatory decisions.

---

[33] In previous reports, accomplishments of this team were listed under Warfighter Action Team. The name was updated in FY 2019 to better reflect FDA/DoD collaborations under PL 115-92, enacted in December 2017, and the subsequent FDA/DoD Memorandum of Understanding, signed in November 2018, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001**

[34] Minimal risk research is research in which the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. See 45 Code of Federal Regulations (CFR) 46.303(d).

REGULATORY ADVICE AND GUIDANCE

During FY 2019, FDA continued to provide regulatory advice and guidance to sponsors and applicants of MCMs and our federal partners funding MCM development, to help foster the development and availability of various MCMs. FDA provides regulatory advice and guidance through a variety of mechanisms including direct engagement with sponsors and applicants, issuing **guidance documents**, and holding **Advisory Committee** meetings and public workshops.

FDA medical product review centers engage with MCM sponsors and applicants throughout the product life cycle. For example, FDA reviews Investigational New Drug (IND) applications and Investigational Device Exemptions (IDEs) and responds to questions from sponsors, applicants, and federal agencies supporting product development. FDA medical product review centers have extensive interactions to discuss testing, data requirements, and nonclinical development plans to move candidate MCMs into clinical development and assess progress as these specialized product candidates move through clinical development toward a marketing application. FDA also continues to engage with sponsors and applicants to address any issues that arise during regulatory review as well as during the post-marketing phase for these MCMs.

FDA has established policies and procedures for conducting formal meetings with product sponsors or applicants. For detailed information on meetings about product development with the Center for Drug Evaluation and Research (CDER) and CBER, see the revised draft guidance ***Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products.*** The revised draft guidance updates the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* (Revision 1) and the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* published March 11, 2015, and, when finalized, will represent the Agency's current thinking on the topic.[35] Formal meetings are held—as needed—at the request of a product sponsor or applicant, and requests for meetings are granted unless there is a substantive reason for denying the request (e.g., the product for which the meeting is requested is not sufficiently developed to warrant the type of meeting sought).[36] When FDA denies a request for a meeting, the sponsor or applicant is provided feedback on steps required to warrant a meeting.

CBER and CDER categorize formal meetings with product sponsors and applicants as Type A, B, and C. Type A meetings are meetings to help an otherwise stalled product development program proceed (such as a dispute resolution meeting, a meeting to discuss a clinical hold,[37] and a Special Protocol Assessment (SPA) meeting[38]).

Type B meetings are meetings held at pivotal points during product development to help products move into and through clinical development to marketing application (i.e., pre-IND application meetings, certain end-of-phase 1 meetings, end-of-phase 2/pre-phase 3 meetings, and pre-New Drug Application (NDA)/BLA). Type B meetings also include pre-EUA meetings,

---

[35] See for example, *Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA (Prescription Drug User Fee Act) Products* (December 2017) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-meetings-between-fda-and-sponsors-or-applicants-pdufa-products-guidance-industry** and *Requests for Feedback on Medical Device Submissions: The Q-Submission Program* (May 2019) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program**

[36] Formal meetings may also be rescheduled or canceled based on criteria described in FDA guidance.

[37] A clinical hold is an order issued by FDA to a product sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. See 21 CFR 312.42 for more information on clinical holds.

[38] For more information on Special Protocol Assessments see *Guidance for Industry – Special Protocol Assessment* (April 2018) available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-protocol-assessment-guidance-industry**

Table 2: FY 2019 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	0	4
Type B	26	6
Type C	13	12
Total	**39**	**22**

Risk Evaluation and Mitigation Strategies (REMS) meetings, and certain meetings for breakthrough therapy-designated products, as explained in the revised draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

Type C meetings are any meetings other than a Type A or Type B meeting, and can address a range of issues related to product development (e.g., discussions related to data requirements, scientific issues related to product development and manufacturing, post-marketing commitments or requirements, etc.). Meetings that are not categorized as Type A, B, or C are non-PDUFA meetings such as meetings on a sponsor's compliance status or follow-up on post-marketing commitments.

In FY 2019, CBER held 39 formal meetings with MCM sponsors or applicants and 47 other (non-PDUFA) meetings, and CDER held 22 formal meetings (***Table 2***) and 53 other (non-PDUFA) meetings.

The Center for Devices and Radiological Health (CDRH) categorizes its formal meetings with product sponsors as Pre-Submission (Pre-sub) and 510(k)/Premarket Approval (PMA) Submission meetings. Pre-sub meetings are designed for FDA staff to provide feedback in response to specific questions related to product development, including planned nonclinical evaluations, proposed clinical study protocols, regulatory pathways, or data analysis recommendations prior to making a submission.

CDRH reviewed 81 Pre-subs and 38 Submissions (marketing applications) for MCM medical devices in FY 2019. FDA provided extensive written feedback on the Pre-subs, and many of these sponsors elected to cancel additional formal follow-up meetings after receiving this information, as they did not see the need for the originally requested formal meeting. If the sponsor wanted to further discuss the written Pre-sub feedback, a formal Pre-sub meeting was held. Submission issue meetings are sometimes held to discuss deficiencies identified during premarket review of device marketing applications and to provide clarification of FDA's questions or to discuss an approach to address any complex issues identified. In FY 2019, CDRH provided written feedback for 51 MCM Pre-sub or Submission applications and held 55 formal Pre-sub and 5 formal Submission meetings with MCM sponsors or applicants (***Table 3***).

Table 3: FY 2019 formal meetings between CDRH and MCM sponsors or applicants

Meeting Type	CDRH
Pre-Submission	55
Submission	5
Total	**60**

In addition to the marketing applications discussed in the previous paragraph, CDRH had significant interactions with MCM sponsors during the pre-EUA and EUA Interactive Review process. The **Interactive Review** process was developed to facilitate the efficient and timely review and evaluation of pre-EUA and EUA submissions through increased interaction between FDA and sponsors, including the exchange of scientific and regulatory information.[39] In FY 2019, CDRH reviewed and provided written feedback on 7 pre-EUAs and 9 EUA submissions, with many submissions involving multiple rounds of written feedback provided during interactive review, and held 7 pre-EUA and EUA meetings. FDA also published new diagnostic EUA web pages in FY 2019: **How to Submit a**

[39] For more information on the Interactive Review Process see *Types of Communication During the Review of Medical Device Submissions - Guidance for Industry and FDA Staff* available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/types-communication-during-review-medical-device-submissions**

Pre-EUA for In vitro Diagnostics to FDA[40], and **Information for Laboratories Implementing IVD Tests Under EUA.**[41]

In addition, eligible MCM sponsors or applicants can request a Regulatory Management Plan (RMP), setting forth a process whereby the terms for interactions between FDA and the product sponsor or applicant can be delineated.[42] FDA did not receive any written MCM-related RMP requests in FY 2019.

FDA also conducted enhanced inspection and compliance activities to support early identification of any problems that might impede MCM product development. FDA provided technical advice to minimize risk during MCM product manufacturing, including pre-approval inspections or site visits to ensure that manufacturing establishments are capable of adequately manufacturing MCM products, and that submitted application data are accurate.

> In FY 2019, FDA finalized requirements to foster access to safe, effective tests to detect anthrax

In addition to its direct work with MCM sponsors and applicants, FDA also issues guidance documents that help foster MCM development and availability.[43] Guidance documents issued during FY 2019 directly related or applicable to MCMs policies or regulatory issues are listed in ***Appendix 3: MCM-Related Guidance Issued in FY 2019***.

FDA also holds Advisory Committee meetings and public workshops to obtain independent input and expert advice on scientific, technical, and policy matters to facilitate MCM development. Key meetings and public workshops held during FY 2019 are listed in ***Appendix 4: Key MCM-Related Meetings Held in FY 2019***. In addition to these FDA-hosted meetings, FDA experts continued to participate in and present at a wide variety of other meetings, workshops, and conferences.[44, 45]

Anthrax bacteria, 3D illustration

---

[40] Available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/how-submit-pre-eua-vitro-diagnostics-fda**

[41] Available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua**

[42] Under PAHPRA, MCMs eligible for RMPs are security countermeasures with respect to which the Secretary of HHS has entered into a procurement contract under section 319F-2(c) of the PHS Act (42 USCS § 247d-6b(c)); or MCMs with respect to which BARDA has provided funding under section 319L of the PHS Act (42 USCS § 247d-7e) for advanced research and development. (FD&C Act Sec. 565(f); 21 U.S.C. § 360bbb-4(f)). The Director of BARDA, in consultation with the FDA Commissioner, prioritizes which eligible MCMs may receive RMPs if resources are not available to establish RMPs for all eligible MCMs for which requests are submitted.

[43] Guidance documents are documents prepared for FDA staff, applicants/sponsors, industry, and the public that describe FDA's interpretation of or policy on a regulatory issue. Guidance documents include, but are not limited to, documents that relate to: the design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies. (21 C.F.R. § 10.115(b))

[44] A list of MCM-related events by year is available in the *MCMi Events Archive*: **https://www.fda.gov/emergency-preparedness-and-response/about-mcmi/mcmi-events-archive**

[45] Where available, MCM-related legal and policy presentations given by FDA staff can be found at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-legal-and-policy-presentations-publications-and-qas** and MCMi regulatory science presentations can be found at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/mcmi-regulatory-science-presentations**

COLLABORATION AND COMMUNICATION

During FY 2019, FDA continued to **collaborate** extensively with PHEMCE and DoD (more on page 21) partners to foster the development and availability of MCMs. FDA provided subject matter expertise and technical assistance to 63 standing interagency and PHEMCE- and DoD-specific committees and working groups that develop MCM requirements, plans, priorities, and policies and conduct program oversight and integration. These standing committees and working groups met on a weekly, monthly, bimonthly, quarterly, semi-annually, or as-needed basis depending on the requirements of the issues at hand. These committees and working groups addressed a range of topics across the full spectrum of activities associated with MCMs including threat assessment, requirements setting, product development, procurement, stockpiling, utilization, and **monitoring and assessment** of MCMs after they have been dispensed or administered. In addition, FDA supported PHEMCE partners by providing subject matter expertise for various MCM-related proposal reviews. FDA also continues to support implementation of the 2018 **National Biodefense Strategy** (PDF, 919 KB).

FDA continued to work with state, local, tribal, and territorial (**SLTT**) public health authorities and responders and public health non-governmental organizations (NGOs) to support MCM preparedness and response capabilities at the state and local levels, including responding to numerous legal and regulatory inquiries concerning EUA and other emergency use authorities, and MCM stockpiling, expiry dating, distribution, and dispensing. FDA continues to participate in multiple national-level workshops and meetings on public health and legal preparedness. For example, FDA continues to sustain support for and participate in:

- The annual Public Health **Preparedness Summit** convened by the National Association of County and City Health Officials (NACCHO).
- The National Academies of Sciences, Engineering, and Medicine Health and Medicine Division (NASEM-HMD) **Forum on Medical and Public Health Preparedness for Disasters and Emergencies**, to provide national leadership in coordinating ongoing efforts among members from federal, state, and local government; business; and professional associations to develop sustainable partnerships between the public and private sector so that communities are adequately prepared for natural or human-made catastrophic events.
- The Tri-Agency Task Force for Emergency Diagnostics, launched in February 2019, to help leverage the expertise of each agency to better coordinate implementation of diagnostic tests in clinical and public health laboratories during public health emergencies.[46]

Other key collaborations in FY 2019 include:

DoD

On November 2, 2018, FDA and DoD signed a Memorandum of Understanding (MOU) to establish the framework under which DoD and FDA will implement Public Law 115-92 (enacted December 2017) for enhanced engagements to facilitate the development and availability of safe and effective medical products that serve the military's needs.[47] *(See **Enhanced FDA/DoD Collaborations** for details.)*

HHS ASPR

In April 2019, FDA and ASPR signed an MOU renewal to provide a framework for coordination and collabo-

[46] For more information, see *Information for Laboratories Implementing IVD Tests Under EUA* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua**

[47] MOU 225-19-001, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001**

rative efforts related to the development and availability of MCMs in public health medical emergencies.[48] The original MOU was signed in 2012.

International collaborations

In addition to working with federal and SLTT governments and NGOs, FDA continued to work with international partners such as WHO to foster the development and availability of MCMs.

Agreements between FDA and its international counterparts established in previous fiscal years have continued to support information-sharing and collaboration, and have better prepared the international regulatory community to respond to future public health emergencies.

Examples of FDA's key international MCM collaborations include:

- Working with HHS to help establish an international framework for sharing MCMs during an international public health emergency.
- Supporting and participating in the U.S. government's Global Health Security Agenda (GHSA) and strategy,[49] as well as other HHS-led efforts related to global MCM policies, including through Joint External Evaluation (JEE) efforts.[50]
- Implementing CBER-WHO Cooperative Agreements[51] to advance global access to safe and effective vaccines and build capacities for the import, registration, and emergency use of prequalified MCM vaccines.
- Supporting HHS/ASPR's Global Health Security Initiative (GHSI) efforts to strengthen WHO processes for evaluating and making recommendations related to use of MCMs during public health emergencies. The GHSI includes efforts to finalize the WHO operational framework for deployment of smallpox vaccine, and based on this work, establish a generic international framework for sharing MCMs during public health emergencies.
- Participating in international consultations to advance efforts to conduct research, pharmacovigilance, and product development during public health emergencies. For example, FDA is an active participant in:
  - **WHO's R&D Blueprint** - The R&D Blueprint is a global strategy and preparedness plan intended to allow the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large-scale crisis.
  - **Coalition for Epidemic Preparedness Innovations (CEPI)** - CEPI is an innovative partnership between public, private, philanthropic, and civil organizations that aims to stop future epidemics by developing new vaccines.
  - **Global Research Collaboration for Infectious Diseases Preparedness (GloPID-R)** - GloPID-R is the only network of major research funding organizations

---

[48] MOU 225-19-013, available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-013**

[49] "Through a growing multisectoral partnership of international organizations, non-governmental stakeholders, and more than 50 countries, GHSA is accelerating efforts to build countries' capacity to prevent, detect, and respond to infectious diseases and achieve the core capacities required by the International Health Regulations (IHR)." HHS. *Global Health Security Agenda*. **https://www.hhs.gov/about/agencies/oga/global-health-security/agenda/index.html**

[50] For more about JEE efforts, see from HHS, *U.S. Health Security National Action Plan: Strengthening Implementation of the International Health Regulations*, at: **https://www.phe.gov/Preparedness/international/Pages/JEE.aspx**

[51] For example, *CBER-WHO Cooperative Agreement: Supporting Influenza Vaccine Introduction to Low-Middle Income Countries* (**https://www.fda.gov/vaccines-blood-biologics/international-activities/cber-who-cooperative-agreement-supporting-influenza-vaccine-introduction-low-middle-income-countries**); for more about CBER's WHO Cooperative Agreements, see: **https://www.fda.gov/vaccines-blood-biologics/who-engagements/who-cooperative-agreements**

working on a global scale. Together, these organizations strive to facilitate an effective research response within 48 hours of an infectious disease outbreak.

- **International Coalition of Medicines Regulatory Authorities (ICMRA)** - The ICMRA is comprised of medicines regulators worldwide who have committed to enhanced cooperation with the WHO and among regulatory agencies to encourage submission of regulatory dossiers and evaluation of the submitted information on potential new medicines to address emerging public health threats.
- **Foundation for Innovative New Diagnostics (FIND)** - A WHO Collaborating Centre for Laboratory Strengthening and Diagnostic Technology Evaluation, FIND is a global nonprofit organization driving innovation in the development and delivery of diagnostics to combat major diseases affecting the world's poorest populations.

Enhancing communication

In FY 2019, FDA worked to enhance communication related to MCM preparedness and response by continuing ongoing outreach activities (e.g., MCMi **email newsletter**, social media,[52] and various presentations). FDA also continued to publish new web pages to centralize information on topics including **advanced manufacturing** activities at FDA, and EUA information for manufacturers developing and labs using IVD devices.

ENHANCED FDA/DOD COLLABORATIONS

In FY 2018, FDA established a framework for enhanced collaboration with DoD as established under **Public Law 115-92** (PDF, 201 KB), which authorized DoD to request, and FDA to provide, assistance to expedite development and FDA's review of products to diagnose, treat, or prevent serious or life-threatening diseases or conditions facing American military personnel.

Utilizing these expanded authorities, FDA is working closely with DoD's **Office of Health Affairs** to better understand the military's medical needs for deployed personnel; to give the highest level of attention to and to expedite review of priority DoD medical products in a manner similar to products under the **breakthrough therapy designation program**; to provide ongoing technical advice to DoD to aid in the rapid development and manufacturing of medical products for use by the military; and to take a closer look at products currently under development to determine opportunities to expedite their availability.[53]

Related to FDA-DoD ongoing and frequent collaborations, in FY 2019, FDA:

- Issued a draft guidance, ***Considerations for the Development of Dried Plasma Products Intended for Transfusion***. Currently approved plasma products intended for transfusion are stored frozen and need to be thawed before being transfused. This significantly limits use in remote areas without freezers and other support equipment, including places where the military may be deployed. Dried plasma products do not need to be stored frozen and can be reconstituted and administered quickly. By developing guidance on this topic, FDA hopes to

[52] Follow MCMi on Twitter at: **https://twitter.com/FDA_MCMi**

[53] Also see *FDA/DoD Collaborations* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-dod-collaborations**

expedite the development and approval of safe and effective dried plasma products.[54]

- Approved Dsuvia, a sublingual (under the tongue) formulation of sufentanil that's delivered through a disposable, pre-filled, single-dose applicator, for use in adults in certified medically supervised health care settings, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. FDA has made it a high priority to make sure U.S. soldiers have access to treatments that meet the unique needs of the battlefield, including when intravenous administration is not possible for the treatment of acute pain related to battlefield wounds.[55]
- Granted a variance request submitted by the Army Blood Program for the use of cold stored platelets in theater, to help the military treat severely injured warfighters suffering from traumatic bleeding on the battlefield. The issuance of this variance clears the way for platelets, a key blood component, to be refrigerated and stored for up to 14 days prior to treating bleeding patients when conventional platelet products are not available or their use is not practical.[56]
- Continued regular meetings of the DoD-FDA PL 115-92 Chemical MCM Workgroup to support the development of nerve agent MCMs.

On November 2, 2018, FDA and DoD **signed an MOU** setting forth the framework for the ongoing partnership and the creation of a robust program that can better serve the health care needs of American military personnel.[57, 58] This MOU builds upon the work of both agencies to foster and prioritize the efficient development of safe and effective medical products intended to save the lives of American service members.

---

[54] The draft guidance is available at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-development-dried-plasma-products-intended-transfusion**. Also see *FDA In Brief: FDA issues draft guidance on the development of dried plasma products intended for transfusion* at: **https://www.fda.gov/news-events/fda-brief/fda-brief-fda-issues-draft-guidance-development-dried-plasma-products-intended-transfusion**

[55] For more information, see *Statement from FDA Commissioner Scott Gottlieb, M.D., on agency's approval of Dsuvia and the FDA's future consideration of new opioids* at: **https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-agencys-approval-dsuvia-and-fdas-future-consideration**

[56] Also see the DoD news release *FDA Action Makes Blood Product More Accessible to Warfighters in Combat* at: **https://mrdc.amedd.army.mil/index.cfm/media/news_releases/2019/blood_product_more_accessible**

[57] *MOU Concerning Coordination with FDA Regarding DoD Medical Product Development and Assessment* (MOU 225-19-01), available at: **https://www.fda.gov/about-fda/domestic-mous/mou-225-19-001**

[58] Also see *FDA and DoD formalize collaboration to advance medical products in support of American military personnel*, available at: **https://www.fda.gov/news-events/press-announcements/fda-and-dod-formalize-collaboration-advance-medical-products-support-american-military-personnel**

MEDICAL COUNTERMEASURE REGULATORY SCIENCE

In FY 2019, FDA continued to implement the **MCMi Regulatory Science Program** through both intra- and extramural collaborative research, as well as through partnerships with U.S. government agencies, academia, and industry.[59]

MCMs often present unique and complex challenges with respect to developing the data necessary to support public health, clinical, and regulatory decision-making. For example, many of the high-priority threats for which MCMs are being developed do not occur naturally to an extent that would support the conduct of field efficacy studies in humans, and it is not ethical to conduct human challenge studies with threat agents that would pose unacceptable risks to study volunteers. In these situations, efficacy data from animal studies may be used if the results can reasonably be extrapolated to expected human use.

> FDA regulatory science helps translate new technologies into safe, effective MCMs

The challenges are even more complex when it comes to developing MCMs for use in specific populations, such as children or pregnant women. For example, ethical evaluation of the participation of children in clinical trials depends on both the level of risk and the prospect of direct benefit to the participant. Thus, in some circumstances it may not be ethical to conduct certain types of clinical trials in the pediatric population to obtain data that can be used for approving pediatric indications for MCMs—such as safety or dosing information—and FDA may rely on the extrapolation of efficacy data from adult populations, along with information and experience the agency has with the use of a particular class of product (e.g., monoclonal antibodies for use in the pediatric population) to the extent permitted by law.[60]

The goal of the MCMi Regulatory Science Program is to develop tools, standards, and approaches to assess MCM safety, efficacy, quality, and performance, and to help translate cutting-edge science and technology into innovative, safe, and effective MCMs, including for specific populations.

FDA has established a broad and robust intra- and extramural research portfolio under the MCMi Regulatory Science Program to meet its goals in these priority research areas.[61] To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with U.S. government (USG) MCM priorities, FDA established a Steering Committee for Advancing MCMi Regulatory Science—with representatives from NIH, CDC, BARDA, and DoD—that evaluates MCMi Regulatory Science Program research proposals for scientific/technical merit and feasibility as well as for alignment with PHEMCE priorities. FDA continually engages with USG stakeholders to maintain an MCMi Regulatory Science Program that actively addresses current regulatory science gaps.

MCM-related **regulatory science research tools** funded (or partially funded) by FDA are avail-

---

[59] Many projects described in this section are preliminary and/or exploratory in nature. Listing a project does not imply any determination with regard to utility in public health, clinical, or regulatory decision-making.

[60] For example, pharmacokinetic modeling was the basis for pediatric labeling of the monoclonal antibody raxibacumab, approved in 2012 to treat inhalational anthrax, in combination with appropriate antibacterial drugs, and for prophylaxis of inhalational anthrax when alternative therapies are not available or are not appropriate. Label information is available at: **https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125349s000lbl.pdf**

[61] Intramural FDA MCM regulatory science is funded through a competitive challenge grant process. Extramural MCM regulatory science is funded primarily through a Broad Agency Announcement (BAA) (*Food and Drug Administration Broad Agency Announcement for the Advanced Research and Development of Regulatory Science*). More information is available at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/intramural-research** and **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/extramural-research**

Box 3: **Priority research areas supported under the MCMi Regulatory Science Program**
Identifying, developing, and qualifying **drug development tools,** such as animal models and immune biomarkers, to assess safety and efficacy of MCMs
Developing and qualifying **predictive models** and *in vitro* assays (e.g., microphysiological systems) to complement the use of *in vivo* animal models to assess safety and efficacy of MCMs
Validating **NGS-based IVD platforms**
Developing **reference materials** (e.g., standardized challenge pools) related to CBRN threat agents and emerging infectious diseases to facilitate development of MCMs
Assessing the **performance, design, and reuse** of emergency medical equipment including personal protective equipment (PPE)
Enhancing **emergency preparedness and response capabilities**, including risk communication and tracking, and evaluating the safety and clinical benefit of MCMs used during public health emergencies
Advancing broadly applicable, **commercially ready tools**, technologies, and platforms that can improve the manufacturing efficiency, consistency, and quality of MCMs

able at no charge to help MCM researchers advance their products, and help FDA reviewers evaluate MCM products for approval.[62]

In FY 2019, FDA took a new step to help advance the development of novel treatments for TBI with the qualification of a medical device development tool. In March 2019, FDA qualified the OsiriX CDE Software Module[63] from the **TBI Endpoints Development Initiative**. This is the third qualification of a medical device development tool (**MDDT**) by FDA, and the first of a biomarker test tool type. A biomarker test is a lab test or instrument used to detect or measure an indicator of biologic processes or pharmacologic responses to a treatment. This qualification provides a tool for more efficient development of devices in a critical area of medicine–TBI treatment.[64]

FDA also continued work to build and maintain a national capability to **monitor and assess MCMs** after they are dispensed or administered in response to a CBRN threat or emerging infectious disease. In FY 2019, FDA continued collaboration with Harvard Pilgrim Health Care to explore how the Sentinel System—an active surveillance system that uses routine querying tools and pre-existing electronic healthcare data from multiple sources to monitor the safety of regulated medical products—may inform study protocols for MCM safety and effectiveness and to provide a valuable baseline for comparison during a public health emergency. In collaboration with CDER and Harvard Pilgrim, the FDA Office of Counterterrorism and Emerging Threats (OCET) launched a new methods activity to determine whether the Sentinel System detects evidence of residual confounding in the association between influenza antiviral(s) and influenza complications in observational studies.[65]

---

[62] A list of tools is available at: **https://.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/regulatory-science-research-tools**

[63] For more information, see *MDDT Summary of Evidence and Basis of Qualification Decision for Oisrix CDE Software Module* at: **https://www.fda.gov/media/120973/download**

[64] For more information, see *FDA In Brief: FDA takes new step to help advance the development of novel treatments for traumatic brain injury with the qualification of a medical device development tool*, at: **https://www.fda.gov/news-events/fda-brief/fda-brief-fda-takes-new-step-help-advance-development-novel-treatments-traumatic-brain-injury** and *How the FDA Uses Science to Speed Medical Device Innovation* at: **https://.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/how-fda-uses-science-speed-medical-device-innovation**

[65] For more information, see *Examining the Ability to Conduct Influenza Antiviral Effectiveness Studies in Sentinel by Improving*

FY 2019 MCMi Regulatory Science program activities are included in ***Table 4***.

Table 4: MCMi Regulatory Science Program activities in FY 2019

CBRN
Developing models of radiation damage in lung, gut, and bone marrow **organs-on-chips** and then using these models to test candidate MCMs to treat such damage. In FY 2019, FDA completed an expansion pilot study to analyze differences in sex-specific responses to radiation.[66] Additionally, FDA awarded a **new contract** to continue development of human organ chip models including comparative studies against existing *in vivo* human/animal data, to determine performance specifications necessary to qualify organ chip models for applications in MCM development
Exploring nanopore technology to enhance detection and tracing of *Clostridium botulinum* and *Escherichia coli* contamination
Testing and comparing how effective different antibacterial drugs are against melioidosis acquired by different routes of exposure in nonclinical modeling
Providing recommendations for radiation biodosimetry device pre-EUA submissions
Conducting exploratory analysis of 3D printing of biologics to support development of MCMs for burn/blast and radiation-induced injuries
Developing microphysiological systems (MPS) as tools to support MCM development
Developing immunoassays for rapid and sensitive detection of ricin, botulinum, and abrin toxins in novel formats
Emerging threats (e.g., Ebola and Zika)
Expanding a **database of reference-grade nucleic acid sequences** for emerging threats, to include viruses such as Ebola and Zika, and antimicrobial-resistant pathogens
Distributed **Zika virus RNA reference materials** to manufacturers seeking EUA for nucleic acid-based diagnostic tests for Zika virus
Distributed **Zika serological reference panel** to manufacturers seeking EUA for serological diagnostic tests specific for detection of recent Zika virus infection
Providing Zika test developers with study recommendations for Zika nucleic acid-based diagnostic tests and Zika serological assay premarket submissions
Continuing to support improvement of small animal models for emerging threats (e.g., Ebola and Zika)
Conducting survivor studies to better understand Ebola's after-effects, to help find new treatments. In September 2019, FDA awarded a contract modification to conduct additional nonclinical studies in collaboration with NIAID, to develop innovative tools for Ebola research
Identifying target peptide sequences for a Zika IgM diagnostic device
Exploring antibody responses following Zika virus infection or vaccination in humans, to help support development of effective vaccines and serodiagnostics

Confounding Control at: **https://www.sentinelinitiative.org/sentinel/methods/examining-ability-conduct-influenza-antiviral-effectiveness-studies-sentinel**

[66] FDA contracts HHSF223201310079C and HHSF223201820398A/0001 were supported by OCET, in conjunction with the FDA Office of Women's Health (OWH).

Applying advanced transcriptomic analysis (the study of all messenger RNA from the genes of an organism) to **compare responses to Ebola virus disease in humans and in animals**, to help identify biomarkers of Ebola, and expected disease outcomes
Studying **antibody responses** to an investigative Ebola vaccine, which may guide development and evaluation of effective countermeasures
In collaboration with DoD, working to better understand the **microbial pathogenesis** of Ebola, Marburg, Rift Valley fever, Crimean Congo hemorrhagic fever, Chikungunya, and Zika viruses
Conducting the largest Ebola virus and host gene expression (i.e., transcriptomics) study to date, using the latest sequencing technologies, including single-cell sequencing methods, to **assess how Ebola virus evolves and spreads** within the body[67]
Developing a **unique biobank** of clinical Ebola samples from over 2,500 participants, including investigational Ebola vaccinees and Ebola survivors, to characterize the durability and correlates of vaccine-induced and natural immunity to Ebola virus disease (EVD)
Pandemic influenza
Demonstrating the ability of a universal influenza vaccine candidate to **reduce the transmission of influenza virus** in mice, even though this vaccine does not completely block infection by the virus[68]
Public health emergency preparedness and response
Optimizing respirator decontamination to ensure supplies for emergency preparedness. In FY 2019, this project led to the first American Society for Testing and Materials (ASTM) **consensus standard** for ultraviolet germicidal irradiation (UVGI) surface decontamination
Developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during a public health emergency through a **collaboration** with the Society of Critical Care Medicine's Discovery, the Critical Care Research Network, and critical care physicians at 20 hospitals throughout the U.S.
Exploring how the Sentinel System may **inform study protocols** for MCM safety and effectiveness, and provide a baseline for comparison during a public health emergency
Continuing support of the **CDC & FDA Antibiotic Resistance (AR) Isolate Bank**
Exploring MCM capabilities within the FDA Real-Time Application for Portable Interactive Devices (RAPID) system, including the real-time collection, transfer, analysis, and bi-directional communication of MCM product information and safety and effectiveness data

[67] The MCMi Program awarded this contract in FY 2018; work began in FY 2019.

[68] These findings are important because they suggest the vaccine could both protect recipients and reduce transmission—even when virus strains emerge with differing envelope proteins, a type of change, that when it occurs, can make existing influenza vaccines less effective. Also see, in *Vaccine: Reduction of influenza virus transmission from mice immunized against conserved viral antigens is influenced by route of immunization and choice of vaccine antigen*, available at: **https://doi.org/10.1016/j.vaccine.2018.06.051**

FDA also expanded and sustained MCM regulatory science collaborations in FY 2019. For example, FDA:

- Sponsored the seventh installment of a **week-long training course** with the University of Texas Medical Branch (UTMB) to provide training on best practices to ensure the quality and integrity of data generated in maximum-containment (i.e., biosafety level (BSL)-3 and -4) laboratories used to support product approval under the **Animal Rule**,[69] and in April 2019 launched a pilot version of a new **clinical course**, Achieving Data Quality and Integrity in Clinical Trials Involving High-Consequence Pathogens. To date, 395 individuals have attended these courses.[70]
- Continued collaborations with the Defense Advanced Research Projects Agency (DARPA) on regulatory science research for the development of innovative regulatory tools, such as biomimetic models, and the National Interagency Confederation for Biological Research (NICBR) to help develop synchronized scientific interaction among federal partners to enhance public health, medical research, and biotechnology development.
- Continued collaborations with the **Bill and Melinda Gates Foundation** on the development and evaluation of home-use influenza diagnostic tests and other common goals to improve public health by stimulating and fostering medical product innovation and enabling medical product development, including MCMs.
- Continued collaborations with the National Aeronautics and Space Administration (NASA) on regulatory science research to develop and provide MCMs to support human space exploration.
- Serves as one of 14 voting representatives on the HHS Tick-Borne Disease Working Group, established under Section 2062 of the 21st Century Cures Act (Cures Act) [PL 114-255]. The working group is developing recommendations on how to address the growing incidences of diseases transmitted by ticks.
- Continued collaborating and meeting with CDC, BARDA, NIH, DoD, the U.S. Department of Agriculture (USDA), Environmental Protection Agency (EPA), U.S. Geological Survey (USGS), and the Department of Homeland Security (DHS) to help develop a national strategy on vector-borne diseases to develop a comprehensive national system to detect, prevent, and respond to these threats. This is a sustained effort to address significant challenges and reverse the upward trends in illness, suffering, and death from vector-borne diseases.
- Worked with NIH and USDA to support publication of **Reducing Administrative Burden for Researchers: Animal Care and Use in Research** (PDF, 824 KB). Published in August 2019, the report describes the recommenda-

---

69 Before a medical product can be approved by FDA, the sponsor must prove the product's safety and its efficacy. FDA has regulations commonly known as the Animal Rule that allow, under very limited circumstances, FDA to grant approval of a drug or biological product based of effectiveness demonstrated in adequate and well-controlled efficacy studies in animal models of the human disease or condition of interest, when the results of those studies establish that the product is reasonably likely to produce clinical benefit in humans. The product sponsor must still demonstrate the product's safety in humans. The Animal Rule can be used only for drug and biological products that are intended to prevent or reduce serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological, or nuclear substances when (1) it has not been feasible to study the product's effectiveness definitively in natural, accidental, or hostile occurrences of the disease or condition and (2) it would not be ethical to induce the disease or condition in human volunteers for study purposes, and if a proposed countermeasure cannot be approved through other existing regulatory pathways. Also see Animal Rule Information at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/animal-rule-information**

70 For more information about these courses, see the *Health Security* article, *A Cross-Disciplinary Training Program for the Advancement of Medical Countermeasures*, at: **https://www.liebertpub.com/doi/10.1089/hs.2019.0032**

tions of the Cures Act, section 2034(d) Working Group and decisions of the agencies.

FDA continues to create and support programs to advance the development and review of MCMs that will be regulated under the Animal Rule. For example, in FY 2019 FDA:

- Worked with the **Critical Path Institute** and the Clinical Data Interchange Standards Consortium (**CDISC**) to develop electronic data standards for the natural history and efficacy studies conducted in animals that support Animal Rule applications.
- Continued to support the **Animal Model Qualification Program**, which provides a mechanism for the evaluation of product-independent animal models for use in drug and biological product development under the Animal Rule.
- Developed and posted a Compliance Program for the Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies on the **Bioresearch Monitoring Program (BIMO) Compliance Programs web page**. This compliance program provides instructions for the inspection of nonclinical laboratories conducting Animal Rule-specific studies.[71] Inspections of these studies are conducted to verify, to the extent practicable, the quality and integrity of the data contained in the final reports of the Animal Rule-specific studies submitted to FDA.

ADVANCED MANUFACTURING

Advanced manufacturing can accelerate therapy development, rapidly scale manufacturing capabilities for vaccines and other MCMs, as well as shorten supply chains to increase manufacturing resilience. In conjunction with government and industry partners, FDA is committed to supporting innovations in advanced manufacturing as outlined in the Cures Act and the **FDA 2018 Strategic Policy Roadmap**.

> FDA signed a cooperative agreement (CRADA) with a national public private partnership for biopharmaceutical innovation called NIIMBL

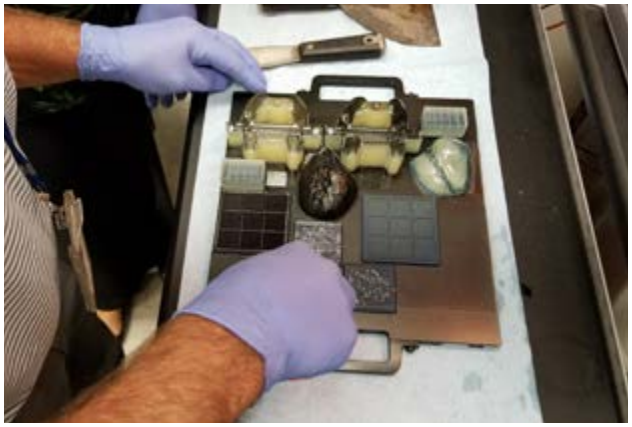
In July 2019, for example, FDA signed a Cooperative Research and Development Agreement (CRADA) with the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). NIIMBL is a **Manufacturing USA** public private partnership (PPP) dedicated to advancing biopharmaceutical manufacturing innovation and workforce development. The CRADA allows FDA to collaborate with biotech stakeholder NIIMBL members, accelerating Agency and industry adoption of biotech innovations. FDA actively engages with other PPPs, many of which are **Manufacturing USA Institutes**, including **America Makes**, **BioFabUSA**, and **NextFlex**, to proactively address regulatory challenges presented by advanced manufacturing technologies, including continuous manufacturing. In addition to PPPs, FDA

[71] The Animal Rule-specific studies are the natural history studies that define the animal model in which the efficacy of an investigational drug or biological product will be tested, the adequate and well-controlled animal efficacy studies intended to provide the primary evidence of effectiveness to support marketing approval of the product, and the pharmacokinetic and/or pharmacodynamic studies in animals used to select a dose and regimen in humans.

is engaging with industry and government consortia, such as the **4D Bio**[3] consortium of the Uniformed Services University, Naval Research Laboratory, and Walter Reed National Military Medical Center, dedicated to bringing advanced technologies and therapies to military personnel.

Since 2015, FDA has been working with BARDA to advance innovations in manufacturing for BARDA-supported MCMs, including those manufactured in HHS Centers for Innovation in Advanced Development and Manufacturing (**HHS-CIADM**) facilities. In addition, FDA coordinated with DoD on the opening of its DoD Medical Countermeasures Advanced Development and Manufacturing (**MCM ADM**) facility, and continues to support ongoing operations. These innovations in manufacturing technology will help enable rapid ramp-up of manufacturing capabilities for vaccines and other MCMs to respond to emerging threats and other public health emergencies, such as pandemic influenza. These technologies could also accelerate the development of therapies for orphan diseases by improving the cost-efficiency of small-scale manufacturing processes, and enable manufacturing process and standards development for emerging therapies including cell and gene-therapies, supporting goals of the Cures Act.

In December 2017, FDA became the first regulator worldwide to provide a comprehensive technical framework to advise manufacturers creating medical products on 3D printers, by issuing the guidance ***Technical Considerations for Additive Manufactured Medical Devices***. To date, FDA has cleared more than 125 3D-printed medical devices and has approved a **3D-printed drug**. Since releasing this guidance, FDA has worked closely with America Makes on a Standards Roadmap for 3D printing. FDA's continued interaction with stakeholder groups, including the Department of Veterans Affairs Innovation Network is facilitating advanced 3D-printed solutions that are reaching civilian and military patients.



The Office of the Chief Scientist's Committee for the Advancement of Clinical and Scientific Education (CACSE) held a course for FDA staff in September 2018 to help reviewers recognize how additive manufacturing technologies fit within the regulatory framework. In addition, FDA's in-house, cross-center 3D printing core research facilities enable FDA scientists to develop scientific standards for 3D-printed medical products, conduct research on the effects of 3D printing on drug product quality and performance, and identify critical aspects of processes and controls that affect the safety and performance of **devices**.

To support innovation in this field, FDA has led the world in advancing efforts to provide a comprehensive regulatory framework to manufacturers and a more effective pathway to getting state-of-the-art medical products into the hands of patients and health care providers. Examples include CDER's **Emerging Technology Program**, which provides opportunities for early engagement regarding innovative approaches to pharmaceutical product design or manufacturing. Under this program, FDA has approved five regulatory applications that used continuous manufacturing technologies for commercial drug product production. The new **CBER Advanced Technology Team** was also started to promote communication between CBER and prospective innovators/developers of advanced manufacturing technologies.

In August and **September** 2018, FDA awarded five grants, using Cures Act authorities, to institutions of higher education and nonprofit organizations to study and recommend improvements for the continuous manufacturing of drugs and biological products, as well as similar innovative monitoring and control techniques. In addition, in September 2019, CBER awarded three contracts solicited through an FDA Broad Agency Announcement (BAA) to explore novel applications of continuous manufacturing processes for more complex biologic products, such as vaccines, and cell and gene therapies.

MEDICAL COUNTERMEASURE REGULATORY POLICY

During FY 2019, FDA continued efforts to ensure that the FDA **legal, regulatory and policy** framework enables the application of advances in regulatory science to the regulatory review process and adequately supports preparedness for and response to CBRN and emerging infectious disease threats by facilitating the development and availability of MCMs. In addition to addressing policy aspects of those activities described generally throughout this document (see ***Box 1***), examples of FDA advancing policy-specific efforts in FY 2019, as discussed in more detail in other sections, include:

- 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 and for certain DoD-related threat agents.
- Supporting an adequate supply of MCMs through efforts to extend the shelf life of certain MCMs outside of SLEP, utilizing authorities under section 564A(b) of the FD&C Act.
- Leading or providing policy subject matter input to FDA MCM-related collaborations, including with DoD under PL 115-92.
- Clarifying regulatory issues around building frameworks for conducting clinical trials during public health emergencies.
- Participating in interagency emergency preparedness exercises, including the HHS Crimson Contagion Exercise Series, which focused on a pandemic involving a novel strain of influenza, and the DHS/Federal Emergency Management Agency (FEMA) Shaken Fury Exercise,[72] which involved issues related to the import of foreign medical products for a domestic response.

FDA also continued to develop and propose new approaches for addressing legal, regulatory, and policy challenges associated with the development and use of MCMs. For example, FDA is:

- Continuing work to harmonize the multi-jurisdictional regulation of certain PPE that may be used during public health emergencies, such as pandemic influenza.
- Continuing to address issues related to information disclosure and liability protections related to MCM products.
- Identifying and developing new legislative proposals, providing technical assistance on others' legislative proposals, supporting MCM-related congressional testimony, and providing technical support for passage and implementation of the **Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019** (PAHPAIA) (PL 116-22) (PDF, 320 KB), which reauthorizes and modifies programs related to public health emergency preparedness and response.[73]
- Leading development of or providing policy input to MCM-related guidance documents issued in FY 2019 (***Appendix 3: MCM-Re-***

[72] For more information about this exercise, see from FEMA, *Shaken Fury 2019*, at: **https://www.fema.gov/shaken-fury-2019**

[73] For more information on PAHPAIA, see *MCM-Related Counterterrorism Legislation* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/mcm-related-counterterrorism-legislation**

lated Guidance Issued in FY 2019), key meetings and workshops (***Appendix 4: Key MCM-Related Meetings Held in FY 2019***), and information for stakeholders about key MCM-related **authorities**.

- Working with CDC and the Centers for Medicare and Medicaid Services (CMS) to leverage the expertise of each agency to collaborate on and address issues related to the implementation of EUA diagnostic tests in clinical and public health laboratories during public health emergencies. The Tri-Agency Task Force for Emergency Diagnostics (TTFED) was formally launched in February 2019.[74]
- Supporting development of the **U.S. Health Security National Action Plan: Strengthening Implementation of the International Health Regulations** (PDF, 2.1 MB) based on the 2016 Joint External Evaluation (JEE), containing hundreds of cross-sectoral activities to better prepare the U.S. to prevent, detect, and respond to public health emergencies. HHS/ASPR led the coordination of the plan's development, working closely with the National Security Council (NSC) and more than 40 U.S. government departments and agencies, including FDA, to identify key activities and ensure long-term support for its implementation.
- Drafted **memoranda of understanding** (MOUs) to provide frameworks for FDA collaborations.

During FY 2019, FDA continued working to implement several additional MCM-related provisions of the **Cures Act**, which was signed into law in December 2016. Specifically, the Cures Act amended the FD&C Act to establish a program for awarding (PRVs) to encourage development of material threat MCMs. FDA developed a draft guidance[75] that provides to internal and external stakeholders answers to questions

74 For more information, see *Information for Laboratories Implementing IVD Tests Under EUA* at: **https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/information-laboratories-implementing-ivd-tests-under-eua**

75 When final, this guidance will represent the Agency's current thinking on this subject.

FDA has received on material threat **MCM PRVs**. FDA issued this **draft guidance** in January 2018, to explain to internal and external stakeholders how FDA intends to implement the material threat MCM PRV program. On September 25, 2019, FDA issued a **notice** establishing the FY 2020 user fees for MCM PRVs.[76]

The Cures Act also amended the FD&C Act to allow FDA to harmonize human subject protections laws with other federal agencies by allowing for waivers of informed consent for minimal risk studies. In November 2018, FDA **proposed to amend** its regulations to implement these provisions and add an exception to informed consent requirements for certain FDA-regulated clinical investigations that present no more than minimal risk to human research participants.[77]

In addition, throughout FY 2019, FDA continued work to implement Public Law 115-92, enacted in December 2017, which amended FDA's EUA authorities to allow for emergency uses of medical products for threats in addition to CBRN agents, to include other agents that may cause or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces.

FDA also continues to work with DoD to implement Public Law 115-92's provisions for enhanced engagements to expedite development and FDA's review of products to diagnose, treat, or prevent serious or life-threatening diseases or conditions facing American military personnel.

PROFESSIONAL DEVELOPMENT

> The MCMi Program trained 700+ FDA staff on MCM-related issues and technologies in FY 2019

FDA launched the MCMi **Professional Development Program** during FY 2011 to ensure that FDA scientists are informed about CBRN threats and associated health impacts as they conduct benefit-risk analyses on MCMs, and that FDA scientists can meet the regulatory challenges posed by new areas of science and technology in the area of MCM development.

In FY 2019, FDA continued efforts to launch a new program designed to train recent pre- and post-doctoral scientists and physicians in research disciplines relevant to FDA's mission. Although the traineeship program is not limited to traineeships involving MCMs, it advances MCMi Program goals to improve and advance MCM science and train reviewers in MCM review processes.

Additional key activities in FY 2019 included:

MCMi Lecture Series

These lectures, presented by highly respected leaders in their fields, broaden understanding of the policies, procedures, and U.S. governmental preparedness and

---

[76] See *Fee for Using a Material Threat Medical Countermeasure Priority Review Voucher in Fiscal Year 2019* (84 FR 51597, September 30, 2019).

[77] The Notice of Proposed Rule Making can be found at: **https://www.federalregister.gov/documents/2018/11/15/2018-24822/institutional-review-board-waiver-or-alteration-of-informed-consent-for-minimal-risk-clinical**. For more information, see FDA's guidance *IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects* at: **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/irb-waiver-or-alteration-informed-consent-clinical-investigations-involving-no-more-minimal-risk**

response framework for FDA reviewers who are assessing MCM applications. FDA held 5 lectures in this series during FY 2019 with a total of 490 attendees.

Foundations for Preclinical Review Lecture Series

These lectures focus on preclinical scientific and technical issues of importance to MCM reviewers, since many MCMs are developed under the Animal Rule. Presentations cover topics that address a new procedure or infrastructure change and are targeted to FDA staff reviewing preclinical information in medical product applications. FDA held 5 lectures in this series during FY 2019 with a total of 216 attendees.

MCMi Intramural Research Lecture Series

This new lecture series, initiated in May 2019, brings together the FDA research community to engage with FDA scientists supported by the MCMi Intramural Regulatory Science Program to share ideas and knowledge, and inspire continued advancement in MCM regulatory science. These sessions are designed for an FDA audience, including scientists involved in the review of medical product applications. FDA held 5 lectures in this series during FY 2019.

APPENDIX 1: FY 2019 MEDICAL COUNTERMEASURE APPROVALS

Medical Countermeasure[78]	Applicant	Key Dates	Indication
Biologics and Drugs[79]			
Afluria and **Afluria Quadrivalent** Influenza Vaccines (2)	Seqirus Pty Ltd.	• Submitted October 31, 2017 • Approved October 4, 2018	BLA supplements extend the indication for use in persons 6 through 59 months of age. Afluria Quadrivalent was first approved in the U.S. in August 2016, for adults 18+ and helps protect against two influenza A strain viruses and two B strain viruses. (**approval letter**)
DENGVAXIA Dengue Tetravalent Vaccine, Live	Sanofi Pasteur, Inc.	• Submitted August 31, 2018 • Approved May 1, 2019	For the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3, and 4. Dengue Tetravalent Vaccine, Live is approved for use in individuals 9 through 16 years of age with laboratory-confirmed previous dengue infection and living in endemic areas. *Also see: **First FDA-approved vaccine for the prevention of dengue disease in endemic regions*** (**approval letter**)
Fluzone Quadrivalent Influenza Virus Vaccine	Sanofi Pasteur, Inc.	• Submitted March 30, 2018 • Approved January 23, 2019	BLA supplement to include the use of a 0.5 mL single dose presentation of Fluzone Quadrivalent formulation in children 6 to <36 months of age. (**approval letter**)
JYNNEOS Smallpox and Monkeypox Vaccine, Live, Non-Replicating	Bavarian Nordic A/S	• Submitted October 25, 2018 • Approved September 24, 2019	For the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection. *Also see: **FDA approves first live, non-replicating vaccine to prevent smallpox and monkeypox*** (**approval letter**)
Xofluza (baloxavir marboxil)	Genentech, Inc.	• Submitted April 24, 2018 • Approved October 24, 2018	For the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours. *Also see: **FDA approves new drug to treat influenza*** (**approval letter**)

[78] Includes MCMs approved, licensed, or cleared by FDA in FY 2019 (October 1, 2018 - September 30, 2019).

[79] For products (biologics) regulated by CBER, additional information can be found at: **https://www.fda.gov/vaccines-blood-biologics/biologics-products-establishments**; for products (drugs and biologics) regulated by CDER, additional information can be found at: **http://www.accessdata.fda.gov/scripts/cder/daf/**

Devices[80]			
Acucy Influenza A&B Test with the Acucy System	Sekisui Diagnostics, LLC	• Received July 26, 2018 • Cleared December 17, 2018	Rapid qualitative test for the detection of influenza A and B, composed of a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasal and nasopharyngeal swabs. (**decision summary**) (**CLIA Waiver Decision Summary**)
ADVIA Centaur Zika test	Siemens Healthcare Diagnostics Inc.	• Received June 14, 2019 • Cleared July 17, 2019	For *in vitro* diagnostic use in the qualitative detection of IgM antibodies to the Zika virus in human serum and plasma (potassium EDTA or lithium heparin) specimens using the ADVIA Centaur XP and ADVIA Centaur XPT systems. (**decision summary**)
BrainScope TBI (Model: Ahead 400)	Brainscope Company, Inc.	• Received November 21, 2018 • Cleared February 19, 2019	A multi-modal, multi-parameter assessment indicated for use as an adjunct to standard clinical practice to aid in the evaluation of patients who have sustained a closed head injury within the past 72 hours (3 days), are between the ages of 18-85 years, have a Glasgow Coma Scale (GCS) score of 13-15 (including patients with concussion /mTBI), and are being considered for a head CT. BrainScope TBI should not be used as a substitute for a CT scan. (**decision summary**)
BrainScope TBI (Model: Ahead 500)	Brainscope Company, Inc.	• Received March 29, 2019 • Cleared September 11, 2019	A multi-modal, multi-parameter assessment indicated for use as an adjunct to standard clinical practice to aid in the evaluation of patients who have sustained a closed head injury, and have a GCS score of 13-15 (including patients with concussion/mTBI) injury visible on head CT. (**decision summary**)
CDC influenza A and B multiplex nucleic acid assays (7)	Centers for Disease Control and Prevention	• Received February 12, 2019 • Cleared March 27, 2019	For indications including qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens, for the presumptive identification of virus in patients who may be infected with influenza A subtype A(H5) (Asian lineage) from viral RNA in human respiratory specimens and viral culture in conjunction with clinical and epidemiological risk factors, and to provide epidemiologic information for surveillance of circulating influenza viruses. (**decision summary**)
Dome Electrode	Coapt, LLC	• Received February 21, 2019 • Cleared April 4, 2019	Intended for non-invasive use with recording and monitoring equipment of EMG. (**decision summary**)

[80] Additional information about device approvals can be found in Medical Devices Databases: **https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases**, including the 510(k) Premarket Notification Database: **https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm**

EyeBOX	Oculogica, Inc	• Received December 22, 2017 • Approved December 28, 2018	Intended to measure and analyze eye movements as an aid in the diagnosis of concussion within one week of head injury in patients 5 through 67 years of age in conjunction with a standard neurological assessment of concussion. A negative EyeBOX classification may correspond to eye movement that is consistent with a lack of concussion. A positive EyeBOX classification corresponds to eye movement that may be present in both patients with or without concussion. (**De Novo decision summary**)
EyeBOX	Oculogica, Inc.	• Received May 2, 2019 • Cleared July 31, 2019	Intended to measure and analyze eye movements as an aid in the diagnosis of concussion (mTBI) within one week of head injury in patients 5 through 67 years of age in conjunction with a standard neurological assessment of concussion. A negative EyeBOX classification may correspond to eye movement that is consistent with a lack of concussion. A positive EyeBOX classification corresponds to eye movement that may be present in both patients with or without concussion. (**decision summary**)
FilmArray Pneumonia Panel	BioFire Diagnostics, LLC	• Received April 13, 2019 • Cleared November 9, 2019	Multiplexed nucleic acid test intended for use with FilmArray, FilmArray 2.0, or FilmArray Torch systems for the simultaneous detection and identification of multiple respiratory viral (including influenza A and influenza B) and bacterial nucleic acids, as well as select antimicrobial resistance genes. Cleared for use with sputum-like and BAL-like specimens for the qualitative reporting of atypical bacteria, viruses and antimicrobial resistance gene panel targets and semi-quantitative reporting of bacteria. (**decision summary**)
FilmArray Pneumonia Panel Plus	BioFire Diagnostics, LLC	• Received May 18, 2018 • Cleared November 15, 2018	Multiplexed nucleic acid test intended for use with FilmArray, FilmArray 2.0, or FilmArray Torch systems for the simultaneous detection and identification of nucleic acids from Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and multiple respiratory viral (including influenza A and influenza B) and bacterial nucleic acids, as well as select antimicrobial resistance genes. Cleared with addition of sputum-like and (bronchoalveolar lavage) BAL-like specimens, additional instrumentation and semi-quantitative reporting of certain bacteria panel targets. (**decision summary**)
FilmArray Pneumonia/ Pneumonia Plus Control	Maine Molecular Quality Controls, Inc.	• Received February 5, 2019 • Cleared May 3, 2019	For *in vitro* diagnostic use as external assayed quality control materials to monitor the qualitative amplification, detection, and identification steps of the laboratory nucleic acid test, FilmArray Pneumonia Panel/Pneumonia plus Panel on the FilmArray Systems. (**decision summary**)

FluChip-8G Influenza A+B Assay	InDevR, Inc.	• Received September 12, 2018 • Cleared April 22, 2019	A multiplex RT-PCR *in vitro* diagnostic test intended for the qualitative detection and differentiation of seasonal influenza A/H3N2, seasonal influenza A/H1N1pdm09, and "non-seasonal" influenza A subtypes other than seasonal H1N1pdm09 or H3N2. The assay is also intended for the qualitative detection and differentiation of the genetic lineage of human influenza B viruses as B/Victoria or B/Yamagata. (**decision summary**)
ImPACT	imPACT Applications, Inc.	• Received May 8, 2018 • Cleared October 20, 2018	Intended for use as a computer-based neurocognitive test battery to aid in the assessment and management of concussion. ImPACT is a neurocognitive test battery that provides health care professionals with objective measure of neurocognitive functioning as an assessment aid and in the management of concussion in individuals ages 12-59. (**decision summary**)
Modified BrainScope One	Brainscope Company Inc.	• Received July 3, 2018 • Cleared December 19, 2019	A multi-modal, multi-parameter assessment indicated for use as an adjunct to standard clinical practice to aid in the evaluation of patients who have sustained a closed head injury within the past 72 hours (3 days), are between the ages of 18-85 years, have a GCS score of 13-15 (including patients with concussion/mTBI), and are being considered for a head CT. BrainScope One should not be used as a substitute for a CT scan. (**decision summary**)
Phoenix	US Bionics, Inc.	• Received November 14, 2018 • Cleared April 17, 2019	Orthotically fits to the lower limbs and trunk. The device is intended to enable individuals with spinal cord injury at levels T4 to L5 to perform ambulatory functions in rehabilitation institutions in accordance with the user assessment and training certification program. This device is not intended for sports or stair climbing. (**decision summary**)
QIAstat-Dx Respiratory Panel	QIAGEN GmbH	• Received December 21, 2018 • Cleared May 18, 2019	Multiplexed nucleic acid test intended for use with QIAstat-Dx system for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs eluted in Universal Transport Media. Targets include Influenza A, Influenza A H1, Influenza A H3, Influenza A H1N1/pdm09, and Influenza B. (**decision summary**)
Quantum Blood and IV Fluid Infusion Warmer	Life Warmer, Inc.	• Received July 3, 2018 • Cleared January 28, 2019	Indicated for warming blood, blood products, and intravenous solutions prior to administration in adult patients. It is intended to be used by health care professionals in hospital, clinical, field, and transport environments to help prevent hypothermia. (**decision summary**)
Sense System With IBT Electrodes	Infinite Biomedical Technologies, LLC	• Received August 6, 2018 • Cleared October 5, 2018	To be used exclusively for external prosthetic fittings of upper limbs. (**decision summary**)

Silverlon Wound Contact, Burn Contact Dressings	Argentum Medical, LLC	• Received February 14, 2019 • Cleared July 18, 2019	Expanded indication for this first-of-its-kind wound contact dressing to include management of certain injuries caused by exposure to sulfur mustard vapor, commonly known as mustard gas. (**decision summary**)
Trilogy Evo Universal Ventilator	Respironics, Inc.	• Received May 2, 2018 • Cleared July 18, 2019	Cleared with new features such as auto-PEEP, and CO2 monitoring. (**decision summary**)
ZIKV Detect 2.0 IgM Capture ELISA	InBios International, Inc.	• Received December 26, 2018 • Cleared May 23, 2019	To detect Zika virus IgM antibodies in human blood. *Also see*: ***FDA authorizes marketing of first diagnostic test for detecting Zika virus antibodies*** (**decision summary**)

APPENDIX 2: CURRENT EMERGENCY USE AUTHORIZATIONS[81]

Year	MCM	Requestor
Anthrax [*Bacillus anthracis*]		
2008	Doxycycline hyclate 100 mg oral tablets (in National Postal Model home & workplace kits)	HHS (ASPR/BARDA)
2011[a]	All oral formulations of doxycycline (mass dispensing)	HHS (CDC)
Novel Influenza A (H7N9) Virus		
2013[f]	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	HHS (CDC)
2014	Lyra Influenza A Subtype H7N9 Assay	Quidel Corporation
2014	A/H7N9 Influenza Rapid Test	Arbor Vita Corporation
Middle East Respiratory Syndrome Coronavirus [MERS-CoV]		
2013[b]	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	HHS (CDC)
2015[d]	RealStar MERS-CoV RT-PCR Kit U.S.	altona Diagnostics GmbH
Ebola Virus		
2014[b]	DoD EZ1 Real-time RT-PCR Assay	DoD
2014[c,g]	iCDC Ebola VP40 rRT-PCR Assay	HHS (CDC)
2014[c,g]	CDC Ebola NP rRT-PCR Assay	HHS (CDC)
2014[c]	BioFire Defense FilmArray NGDS BT-E Assay	BioFire Defense
2014[g]	BioFire Defense FilmArray Biothreat-E test	BioFire Defense
2014[b]	RealStar Ebolavirus RT-PCR Kit 1.0	altona Diagnostics GmbH
2014	LightMix Ebola Zaire rRT-PCR Test	Roche Molecular Systems, Inc.
2015	Xpert Ebola Assay	Cepheid
2016	Idylla Ebola Virus Triage Test	Biocartis NV
2018[g]	DPP Ebola Antigen System	Chembio Diagnostic Systems, Inc.

[a] To be terminated after issuance of doxycycline emergency dispensing order, cGMP waiver, and CDC EUI (sec. 564A of the FD&C Act)
[b] Re-issued in 2014, [c] Re-issued in 2015, [d] Re-issued/amended in 2016, [e] Re-issued/amended in 2017, [f] Re-issued/amended in 2018, [g] Re-issued/amended in 2019

[81] Chart is current as of December 31, 2019. **View the latest EUAs**. Dates listed in this table refer to the calendar year. Chart continues on next page.

Enterovirus D68		
2015	CDC Enterovirus D68 2014 Real-time RT-PCR Assay	HHS (CDC)
Zika Virus		
2016[d,e,f,g]	CDC Zika Immunoglobulin M (IgM) Antibody Capture Enzyme-Linked Immunosorbent Assay (Zika MAC-ELISA)	HHS (CDC)
2016[d,e]	CDC Trioplex Real-time RT-PCR Assay (Trioplex rRT-PCR)	HHS (CDC)
2016[d,e]	Zika Virus RNA Qualitative Real-Time RT-PCR	Quest Diagnostics Infectious Disease, Inc.
2016[d,e]	RealStar Zika Virus RT-PCR Kit U.S.	altona Diagnostics GmbH
2016[d,e,f]	Aptima Zika Virus assay	Hologic, Inc.
2016[e]	Zika Virus Real-time RT-PCR Test	Viracor Eurofins
2016[d]	VERSANT Zika RNA 1.0 Assay (kPCR) Kit	Siemens Healthcare Diagnostics Inc.
2016	Sentosa SA ZIKV RT-PCR Test	Vela Diagnostics USA, Inc.
2016	Zika Virus Detection by RT-PCR Test	ARUP Laboratories
2016[e]	Abbott RealTi*me* ZIKA	Abbott Molecular, Inc.
2016	Zika ELITe MGB Kit U.S.	ELITechGroup Inc. Molecular Diagnostics
2017	Gene-RADAR Zika Virus Test	Nanobiosym Diagnostics, Inc.
2017[e,f,g]	LIAISON XL Zika Capture IgM II	DiaSorin Incorporated
2017	TaqPath Zika Virus Kit	Thermo Fisher Scientific
2017	CII-ArboViroPlex rRT-PCR Assay	Columbia University
2017[f,g]	DPP Zika IgM Assay System	Chembio Diagnostic Systems, Inc.
Nerve Agents		
2017[e,f]	Atropine Auto-Injector	HHS (CDC)
Freeze Dried Plasma		
2018	Pathogen-Reduced Leukocyte-Depleted Freeze Dried Plasma	DoD

[d] Re-issued/amended in 2016, [e] Re-issued/amended in 2017, [f] Re-issued/amended in 2018, [g] Re-issued/amended in 2019

APPENDIX 3: MCM-RELATED GUIDANCE ISSUED IN FY 2019[82]

Date	Guidance Type	Guidance Name	Purpose
October 12, 2018	Final	Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations (**link**)	The revisions to HHS' Federal Policy for Protection of Human Research Subjects (45 CFR 46, Subpart A; "the Common Rule" or "2018 Requirements") created certain differences between FDA's human subject regulations and HHS' human subject regulations. While FDA intends to undertake rulemaking to harmonize, to the extent practicable and consistent with other statutory provisions, its regulations with the 2018 Requirements consistent with section 3023 of the Cures Act, we recognize the potential for confusion in the interim for sponsors, investigators, and Institutional Review Boards (IRBs) who are involved in both HHS-regulated research and FDA-regulated clinical investigations. This guidance is intended to clarify the impact of certain provisions of the 2018 Requirements on FDA-regulated clinical investigations.
October 16, 2018	Draft	Rare Diseases: Early Drug Development and the Role of Pre-IND Meetings (**link**)	To assist sponsors of drug and biological products for the treatment of rare diseases in planning and conducting more efficient and productive pre-IND meetings.
October 18, 2018	Draft	Content of Premarket Submissions for Management of Cybersecurity in Medical Devices (**link**)	To provide FDA's updated recommendations for the device design, labeling, and documentation to be included in premarket submissions for devices with cybersecurity risks.
October 29, 2018	Draft	Considerations for the Development of Dried Plasma Products Intended for Transfusion (**link**)	To provide recommendations to assist manufacturers in the development of dried plasma products, including recommendations regarding starting materials for the preparation of dried plasma products, manufacturing and product quality, product characterization studies, packaging and reconstitution, clinical studies and devices for manufacturing dried plasma.
November 6, 2018	Draft	Meta-Analyses of Randomized Controlled Clinical Trials to Evaluate the Safety of Human Drugs or Biologic Products (**link**)	To provide guidance to sponsors submitting INDs, new NDAs, BLAs, or supplemental applications on the appropriate use of prospective meta-analyses to assess a product risk. This draft guidance specifically focuses on meta-analyses for evaluating safety data from randomized, controlled trials.

[82] This table includes guidance documents designed to address MCM-specific topics and guidance documents that address more general topics considered to have likely relevance to some aspects of MCM development. It is not intended as a comprehensive list of all guidance documents; some product sponsors may find additional relevant documents on the FDA guidance website at **https://www.fda.gov/regulatory-information/search-fda-guidance-documents**

November 28, 2018	Draft	Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of *In Vitro* Diagnostic Devices (**link**)	To implement section 3057 of the Cures Act, which requires FDA to revise "Section V. Demonstrating Insignificant Risk of an Erroneous Result — Accuracy" of the guidance *Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices* that was issued on January 30, 2008. This draft guidance represents FDA's current thinking regarding the appropriate use of comparable performance between a waived user and a moderately complex laboratory user to demonstrate accuracy.
November 28, 2018	Draft	Recommendations for Dual 510(k) and CLIA Waiver by Application Studies (**link**)	To assist manufacturers in using the Dual 510(k) and CLIA Waiver by Application pathway. It describes study designs for generating data that supports both 510(k) clearance and CLIA waiver. Use of the Dual 510(k) and CLIA Waiver by Application pathway is optional; however, FDA believes this pathway is in many instances the least burdensome and fastest approach for manufacturers to obtain a CLIA waiver in addition to 510(k) clearance for new IVD devices.
December 4, 2018	Draft	Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion (**link**)	To provide recommendations for additional measures to help control the risk of bacterial contamination of room-temperature stored platelets intended for transfusion.
December 12, 2018	Draft	Biomarker Qualification: Evidentiary Framework (**link**)	To provide recommendations on general considerations to address when developing a biomarker for qualification under the Cures Act. Qualification of a biomarker is a determination that within the stated context of use, the biomarker can be relied on to have a specific interpretation and application in drug development and regulatory review.
December 12, 2018	Final	Data Integrity and Compliance With Drug CGMP Questions and Answers (**link**)	To clarify the role of data integrity in CGMP for drugs.
December 18, 2018	Final	Breakthrough Devices Program (**link**)	To describe policies FDA intends to use to implement the new Breakthrough Devices Program, established by the Cures Act. The Breakthrough Devices Program supersedes and combines elements from FDA's Expedited Access Pathway (EAP), which was intended to facilitate the development and expedite review of certain devices that demonstrate the potential to address unmet medical needs, as well as the Priority Review Program, which implemented statutory criteria for granting priority review to PMAs and applied those criteria to other types of premarket submissions for medical devices.

January 17, 2019	Final	Coordinated Development of Antimicrobial Drugs and Antimicrobial Susceptibility Test Devices (**link**)	To minimize time between the approval of new antimicrobial drugs and clearance of antimicrobial susceptibility tests used to determine the potential effectiveness of those drugs; and provide recommendations to the medical device and drug industries on how to work together to facilitate timely clearance of antimicrobial susceptibility test devices by FDA.
January 23, 2019	Final	Labeling for Human Prescription Drug and Biological Products Approved Under the Accelerated Approval Regulatory Pathway (**link**)	To assist applicants in developing the Indications and Usage section of labeling for human prescription drug and biological products approved under the accelerated approval regulatory pathway, specifically indications for drugs approved via accelerated approval on the basis of a surrogate endpoint or a clinical endpoint other than survival or irreversible morbidity.
January 23, 2019	Draft	S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines (**link**)	Prepared under the auspices of the International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use, to recommend international standards for the nonclinical safety studies recommended to support the development of pediatric medicines.
January 23, 2019	Final	Immunogenicity Testing of Therapeutic Protein Products—Developing and Validating Assays for Anti-Drug Antibody Detection (**link**)	To provide recommendations to facilitate industry's development and validation of immune assays for assessment of the immunogenicity of therapeutic protein products during clinical trials. The recommendations for assay development and validation provided in this document apply to assays for the detection of one or more anti-drug antibodies. This document also includes updated information on the development and validation of screening assays, confirmatory assays, titering assays, and neutralization assays, as well as an additional discussion of immunogenicity risk assessment.
January 24, 2019	Draft	REMS Assessment: Planning and Reporting (**link**)	To describe how to develop a REMS Assessment Plan; specifically, how the REMS program goals, objectives, and REMS design may impact the selection of metrics and data sources, which will be used to assess whether the REMS is meeting its risk mitigation goals.
January 24, 2019	Draft	Survey Methodologies to Assess REMS Goals That Relate to Knowledge (**link**)	To provide recommendations to industry on conducting REMS assessment surveys, used to evaluate respondent knowledge of REMS-related information. This guidance discusses general principles and recommendations related to conducting REMS assessment knowledge surveys, including study design, survey instrument development, survey data collection and processing, and data analysis.
February 5, 2019	Final	The Least Burdensome Provisions: Concept and Principles (**link**)	To describe FDA's use of the least burdensome approach to medical device regulation to remove or reduce unnecessary burdens that may delay the marketing of beneficial new products, while maintaining the statutory requirements for clearance and approval.

February 5, 2019	Draft	Principles of Premarket Pathways for Combination Products (**link**)	To present FDA's current thinking on principles for premarket review of combination products, including how to determine which type of premarket submission is appropriate, including new drug applications or abbreviated new drug applications for drug-led combination products; stand-alone or biosimilar biologics license applications for biologic-led combination products, and 510(k), de novo, or premarket approval applications for device-led combination products.
February 26, 2019	Draft	Quality Considerations for Continuous Manufacturing (**link**)	To clarify FDA's current thinking regarding innovative CM approaches and can help resolve potential issues some companies have as they consider implementation.
March 15, 2019	Final	Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products (**link**)	To assist industry in developing enrichment strategies that can be used in clinical investigations intended to demonstrate effectiveness (and in some cases safety) of human drugs and biological products. This guidance defines several types of enrichment strategies, provides examples of potential clinical trial designs, and discusses potential regulatory considerations when using enrichment strategies in clinical trials.
March 15, 2019	Draft	A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers (**link**)	To provide information to sponsors on risk-based approaches to monitoring of investigational studies of human drug and biological products, medical devices, and combinations thereof. This guidance expands on the guidance for industry entitled Oversight of Clinical Investigations—A Risk-Based Approach to Monitoring (August 2013) by providing additional guidance to facilitate sponsors' implementation of risk-based monitoring.
March 25, 2019	Draft	Rare Diseases: Natural History Studies for Drug Development (**link**)	To help inform the design and implementation of natural history studies that can be used to support the development of safe and effective drugs and biological products for rare diseases.
March 26, 2019	Final	Standards Development and the Use of Standards in Regulatory Submissions Reviewed in the Center for Biologics Evaluation and Research (**link**)	To provide CBER recommendations on the use of standards in product development and control as well as the use of such standards in CBER's managed review process.
March 28, 2019	Final	Pediatric Information Incorporated Into Human Prescription Drug and Biological Product Labeling (**link**)	To assist applicants in determining the appropriate placement and content of pediatric information in human prescription drug and biological product labeling as described in the regulations for the content and format of labeling for human prescription drug and biological products.
April 24, 2019	Final	Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles (**link**)	To provide guidance to government stakeholders on testing to extend the shelf life (i.e., expiration date) under the FD&C Act of stockpiled doxycycline tablets and capsules for public health emergency preparedness and response purposes for an anthrax emergency.

May 8, 2019	Draft	Submitting Documents Utilizing Real-World Data (RWD) and Real-World Evidence (RWE) to the FDA for Drugs and Biologics (**link**)	To encourage sponsors and applicants who are using RWD to generate RWE as part of a submission to provide information on their use of RWE to the FDA in a simple, uniform format.
June 6, 2019	Draft	Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs (**link**)	To provide recommendations for more inclusive trial practices, trial designs, and methodological approaches sponsors can take to broaden eligibility criteria and increase enrollment of more diverse populations in clinical trials. Broadening eligibility criteria, when appropriate, maximizes the generalizability of trial results and the ability to understand the therapy's benefit-risk profile across the patient population likely to use the drug in clinical practice, without jeopardizing patient safety.
June 28, 2019	Draft	M10 Bioanalytical Method Validation (**link**)	Developed by the ICH, to describe the various elements and expectations to validate specific tests used to measure the parent and active metabolites of drugs administered in nonclinical and clinical studies submitted in regulatory applications for biological matrices such as plasma, blood, or serum.
July 9, 2019	Final	Risk Evaluation and Mitigation Strategies: Modifications and Revisions Guidance for Industry (**link**)	To provide information on how FDA defines the types of changes to approved REMS, how application holders should submit changes to an approved REMS, and how the FDA will process submissions from application holders for changes to REMS.
July 18, 2019	Final	Submitting Next Generation Sequencing Data to the Division of Antiviral Products (**link**)	Technical Specifications Document, to provide the current thinking of FDA's Division of Antiviral Products in regard to the submission of next-generation nucleotide sequence analysis procedures and data in support of resistance assessments for the development of antiviral drug products. Providing accurate resistance information is imperative for protecting public health to prevent the emergence of novel resistant and cross-resistant viral variants that have the potential to infect others and cause major outbreaks of disease that cannot be controlled by approved drug products.
July 31, 2019	Draft	E8(R1) General Considerations for Clinical Studies (**link**)	Prepared under the auspices of the ICH, to describe internationally accepted principles and practices for the design and conduct of clinical studies of drug and biologic products. In addition, the draft guidance provides an overview of the types of clinical studies that sponsors may perform and data sources they may use during the product's life cycle. The draft guidance intends to promote the quality of the studies submitted to regulatory authorities, while allowing for flexibility.

August 29, 2019	Final	Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions (**link**)	To describe FDA's consideration of uncertainty when determining benefit-risk for certain premarket decisions on medical devices based on the totality of the valid scientific evidence, and outlines a rigorous, methodical approach for the consideration of uncertainty when assessing the benefits and risks of a medical device and for determining when it may be appropriate to shift some data collection from the premarket to the postmarket phase.
August 29, 2019	Final	Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications (**link**)	To describe the principal factors, including uncertainty of benefits and risks, FDA considers when making benefit-risk determinations for certain premarket decisions. Appendices B and C of this guidance are updated with a revised Benefit-Risk Determination Worksheet that incorporates the same factors for benefit-risk determinations described in the guidance. The revised worksheet provides structure to guide and organize the benefit-risk factors and to support consistent decision-making.
September 6, 2019	Final	Acceptance Review for De Novo Classification Requests (**link**)	To explain the procedures and criteria FDA intends to use in assessing whether a request for an evaluation of automatic class III designation (de novo classification request or de novo request) meets a minimum threshold of acceptability and should be accepted for substantive review. This guidance also includes a De Novo Acceptance Checklist and a Recommended Content Checklist.
September 12, 2019	Final	The Special 510(k) Program (**link**)	To describe an optional pathway for certain well-defined device modifications where a manufacturer modifies its own legally marketed device, and design control procedures produce reliable results that can form, in addition to other 510(k) content requirements, the basis for substantial equivalence. This guidance clarifies the types of technological changes appropriate for review as Special 510(k)s.
September 19, 2019	Draft	Safer Technologies Program for Medical Devices (**link**)	A new, voluntary program for certain medical devices and device-led combination products that are reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target an underlying disease or condition associated with morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program.
September 20, 2019	Draft	Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products (**link**)	To provide guidance to sponsors and applicants on interacting with FDA on CID proposals for drugs or biological products. In accordance with the Cures Act mandate (section 3021), this guidance discusses the use of novel trial designs in the development and regulatory review of drugs and biological products, how sponsors may obtain feedback on technical issues related to modeling and simulation, and the types of quantitative and qualitative information that should be submitted for review.

APPENDIX 4: KEY MCM-RELATED MEETINGS HELD IN FY 2019[83]

Date	Type of Event	Event Name	Purpose
October 3, 2018	Public meeting	Vaccines and Related Biological Products Advisory Committee (VRB-PAC) (**link**)	To discuss and make recommendations on the selection of strains to be included in an influenza virus vaccine for the 2019 southern hemisphere influenza season
October 23-24, 2018	Public workshop	FDA & MHRA Good Clinical Practice Work-shop: Data Integrity in Global Clinical Trials – Are We There Yet? (**link**)	To provide FDA CDER and Medicines and Healthcare products Regulatory Agency UK (MHRA) perspectives on the importance of quality management practices on data reliability
November 26, 2018	Public workshop	Workshop with stakeholders on support to quality development in early access approaches (i.e., PRIME, Break-through Thera-pies) (**link**)	To discuss between regulators and industry technical quality challenges and scientific and regulatory approaches that could be used to facilitate development and preparation of robust chemistry, manufacturing, and controls (CMC) data packages, enabling timely access to medicines while providing assurance that patient safety and product quality are not compromised
November 29-30, 2018	Public workshop	Pathogen Reduc-tion Technologies for Blood Safety (**link**)	To foster the development and implementation of pathogen reduction technologies for blood components intended for transfusion
December 2, 2018	Public workshop	Implementation of Signal Detection Capabilities in the Sentinel System (**link**)	To solicit broad stakeholder input on the landscape of meth-odological approaches for signal detection, as well as the opportunities and challenges to implement these approaches in Sentinel's distributed data network, and consider key gover-nance and operational needs for implementing signal detection tools in a hypothesis-free environment
December 11, 2018	Public meeting	Drug Develop-ment Tool Process Under the 21st Century Cures Act and PDUFA VI (**link**)	To solicit public comments on processes related to FDA's Drug Development Tool Qualification programs, which includes Biomarker Qualification Program, Clinical Outcome Assessment Qualification Program, and the Animal Model Qualification Pro-gram (AMQP). The AMQP is a drug development tool program to advance the public availability of product-independent animal models that can be used to support the efficacy testing of multiple investigational MCMs for the same targeted disease or condition being developed under the Animal Rule

[83] This table includes FDA-sponsored meetings intended to address MCM-specific topics, or more general FDA-sponsored meetings that may be relevant to some aspects of MCM development. In some cases, FDA may have provided funding to support certain meetings hosted by others (e.g., NASEM).

March 6-7, 2019	Public meeting	Vaccines and Related Biological Products Advisory Committee (VRB-PAC) (**link**)	To discuss and make recommendations on the selection of strains to be included in the influenza virus vaccines for the 2019 to 2020 influenza season
March 20-21, 2019	Public meeting	Blood Products Advisory Committee (**link**)	To discuss and make recommendations on strategies to reduce the risk of Zika virus (ZIKV) transmission by blood and blood components
March 20-21, 2019	Public workshop	Pathophysiology of Radiation-Induced Lung Injury (no link available)	Co-sponsored by NIH, FDA, and BARDA, to discuss current clinical practices for lung injuries and the available animal models for radiation-induced lung injuries, to understand the relevant indices of lung injury, and to identify gaps in the animal models
March 21-22, 2019	Public workshop	Innovations in Technologies to Extend the Golden Hour (**link**)	Hosted by NIH, DoD, BARDA, and FDA, to propel the development of innovative medical devices for military and civilian trauma and emergency care
March 22, 2019	Public meeting	Vaccines and Related Biological Products Advisory Committee (VRB-PAC) (**link**)	To discuss and make recommendations specifically on the H3N2 strain, in follow-up to a delay by the WHO in recommending H3N2 strain for inclusion in the 2019-2020 seasonal influenza vaccines
April 3-5, 2019	Public workshop	Eleventh Annual Sentinel Initiative Public Workshop (**link**)	To share recent developments within the Sentinel Initiative, provide training on Sentinel System's tools and data infrastructure, and promote engagement and collaboration with patients, industry, and consumers
April 8-10, 2019	Training course	Achieving Data Quality and Integrity in Clinical Trials Involving High Consequence Pathogens (**link**)	New in 2019, a pilot course on achieving data quality and integrity in clinical trials involving high-consequence pathogens, presented in addition to previously existing course on achieving data quality and integrity in maximum-containment laboratories
April 8-12, 2019	Training course	Achieving Data Quality and Integrity in Maximum Containment Laboratories Course (**link**)	To offer a unique opportunity for the regulatory and scientific communities to discuss complex issues in an interactive environment and identify and share best practices for ensuring data quality and integrity in BSL-4 facilities
May 6-7, 2019	Public workshop	Cutaneous Radiation Injuries Workshop (no link available)	Co-sponsored by NIH, FDA, and BARDA, clinical experts in radiation and other skin injuries (e.g., burns, diabetic ulcers and otherwounds) to provide context for methods to assess severity of skin injuries and progression of healing, and describe the preclinical modeling of these injuries and the use ofsuch models in determining efficacy of MCMs to treat radiation-induced skin complications
May 14, 2019	Public workshop	BioCompute Objects: Tools for Communicating NGS Data and Analysis (**link**)	To engage more stakeholders in creating and using BioCompute for NGS and other bioinformatics data analysis communications with FDA

May 20-22, 2019	Public workshop	Filovirus Animal Nonclinical Group (FANG) Workshop (**link**)	To update the FANG (an interagency working group) and other members of the filovirus community on cross-cutting topics that impact vaccine and therapeutic product development and regulatory approval
June 10, 2019	Public webinar	Financial Incentives for CDER Medical Products (**link**)	To discuss the logistics of priority review vouchers (PRVs), including general information on three FDA priority review voucher programs (including MCM material threat PRVs), and specific information on how to redeem a voucher, what information to submit, and when to pay
July 11-12, 2019	Public workshop	Leveraging Randomized Clinical Trials to Generate Real-World Evidence for Regulatory Purposes (**link**)	To explore key considerations for utilizing randomized designs, such as large simple trials or those that incorporate pragmatic elements, and RWD to generate RWE. Discussion focused on key components of trial design including intervention selection, outcome measurement, blinding, and study population characteristics as well as important regulatory considerations
July 12, 2019	Public meeting	Limited Population Pathway for Antibacterial and Antifungal Drugs (**link**)	To provide a public forum for FDA to listen to comments on the draft guidance for industry, *Limited Population Pathway for Antibacterial and Antifungal Drugs,* that was published in the Federal Register on June 13, 2018
August 6-7, 2019	Public workshop	Developing Medical Countermeasures to Rescue Opioid-induced Respiratory Depression (no link available)	Hosted by NIH, in partnership with BARDA, FDA, and the Defense Threat Reduction Agency (DTRA), to advance current understanding of available models of pharmaceutical-based agents (PBAs)-induced toxicities, specifically with regards to intoxication by synthetic opioids. The development of MCMs relies critically on the availability of well-characterized animal models with defined pathophysiology that allows for effective bridging to humans. Such models and information are essential for the research and development of MCMs to mitigate morbidity and/or prevent mortality
September 11-12, 2019	Public symposium	FDA Science Forum (**link**)	To discuss FDA research, including MCM-related research. Sessions included FDA's approach to prevention and response, including prevention through cybersecurity and promoting medical product and food security rapid response to infectious disease and foodborne pathogen outbreaks, use of the Animal Rule, emergency communication devices, rapid diagnostic tests, and antimicrobial resistance
September 16-17, 2019	Public workshop	Identification and Use of Biomarkers to Advance Development of Preventive Vaccines (**link**)	To exchange information with stakeholders from industry, academia, and government about the scientific, clinical, and regulatory challenges encountered in the identification, characterization, and qualification of biomarkers for use in the development of preventive vaccines for infectious disease indications
September 18, 2019	Public workshop	Implementing FDA's Predictive Toxicology Roadmap: An Update of FDA Activities (**link**)	To highlight work FDA has been doing to support and implement FDA's **Predictive Toxicology Roadmap**, a six-part framework for integrating predictive toxicology methods into safety and risk assessments

APPENDIX 5: ACRONYMS

AMQP	Animal Model Qualification Program
AMR	Antimicrobial resistance
AR	Antibiotic resistance
ASTM	American Society for Testing and Materials
ATCC	American Type Culture Collection
ARMADA	Antibiotic Resistance Monitoring, Analysis, and Diagnostics Alliance
ARS	Acute radiation syndrome
ASPR	Assistant Secretary for Preparedness and Response (HHS)
BAA	Broad Agency Announcement
BAL	Bronchoalveolar lavage
BARDA	Biomedical Advanced Research and Development Authority
BIMO	Bioresearch Monitoring Program
BLA	Biologics License Application
BSL	Biosafety level
CACSE	Committee for the Advancement of Clinical and Scientific Education
CBRN	Chemical, biological, radiological, and nuclear
CBER	FDA Center for Biologics Evaluation and Research
CDC	U.S. Centers for Disease Control and Prevention
CDER	FDA Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
CDRH	FDA Center for Devices and Radiological Health
CEPI	Coalition for Epidemic Preparedness Innovations
cGMP	Current good manufacturing practices
CFR	Code of Federal Regulations
CID	Complex innovative (trial) design
CLIA	Clinical Laboratory Improvement Amendments of 1988
CMC	Chemistry, manufacturing, and controls
CMS	Centers for Medicare and Medicaid Services
CRADA	Cooperative Research and Development Agreement
CRP	Critical Reagents Program
CT	Computerized tomography
DARPA	Defense Advanced Research Projects Agency
DHS	U.S. Department of Homeland Security
DoD	U.S. Department of Defense
DRC	Democratic Republic of the Congo
DTRA	Defense Threat Reduction Agency
EAP	Expedited Access Pathway
EHT	Emerging health threats
EMG	Electromyography
ELISA	Enzyme-linked immunosorbent assay
EPA	Environmental Protection Agency
EUA	Emergency Use Authorization

EVD	Ebola virus disease
FANG	Filovirus Animal Nonclinical Group
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	U.S. Food and Drug Administration
FDA-ARGOS	FDA dAtabase for Regulatory Grade micrObial Sequences
FDASIA	Food and Drug Administration Safety and Innovation Act
FEMA	Federal Emergency Management Agency
FTE	Full-time equivalent
FY	Fiscal year
GCS	Glasgow Coma Scale
GHSA	Global Health Security Agenda
GHSI	Global Health Security Initiative
GloPID-R	Global Research Collaboration for Infectious Diseases Preparedness
H-ARS	Hematopoietic syndrome of acute radiation syndrome
HCT/P	Human cells, tissues, and cellular and tissue-based products
HHS	U.S. Department of Health and Human Services
HHS-CIADM	Department of Health and Human Services Centers for Innovation in Advanced Development and Manufacturing
ICH	International Conference on Harmonisation
ICMRA	International Coalition of Medicines Regulatory Authorities
IDE	Investigational Device Exemption
IgM	Immunoglobulin M
IHR	International Health Regulations
IND	Investigational New Drug
IRB	Institutional Review Board
IVD	*In vitro* diagnostic
JEE	Joint External Evaluation
LLNL	Lawrence Livermore National Laboratory
MCM	Medical countermeasure
MCM ADM	DoD Medical Countermeasures Advanced Development and Manufacturing
MCMi	FDA Medical Countermeasures Initiative
MDR	Multi-drug resistant
MDDT	Medical device development tool
MERS-CoV	Middle East Respiratory Syndrome coronavirus
mg	Milligram
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
mL	Milliliter
MOU	Memorandum of Understanding
MPS	Microphysiological systems
MRA	Mutual Recognition Agreement
mTBI	Mild traumatic brain injury
NACCHO	National Association of County and City Health Officials
NASA	National Aeronautics and Space Administration
NASEM-HMD	National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division
NCBI	National Center for Biotechnology Information
NDA	New Drug Application

NGDS	Next-Generation Diagnostic System
NGO	Non-governmental organization
NGS	Next-generation sequencing
NIAID	National Institute of Allergy and Infectious Diseases
NIAID IRF	National Institute of Allergy and Infectious Diseases – Integrated Research Facility
NICBR	National Interagency Confederation for Biological Research
NIH	U.S. National Institutes of Health
NIIMBL	National Institute for Innovation in Manufacturing Biopharmaceuticals
NIST	National Institute of Standards and Technology
OCET	Office of Counterterrorism and Emerging Threats
OWH	Office of Women's Health
PBA	Pharmaceutical-based agent
PAHPAIA	Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PCR	Polymerase chain reaction
PDUFA	Prescription Drug User Fee Act
PEEP	Intrinsic positive end-expiratory pressure (auto-PEEP)
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
PPE	Personal protective equipment
PPP	Public private partnership
PRV	Priority review voucher
Rad/nuc	Radiological/nuclear
RAPID	Real-Time Application for Portable Interactive Devices
REMS	Risk Evaluation and Mitigation Strategies
RMP	Regulatory Management Plan
RNA	Ribonucleic acid
RWD	Real-world data
RWE	Real-world evidence
SLEP	Shelf-Life Extension Program
SLTT	State, local, tribal and territorial
SNS	Strategic National Stockpile
SPA	Special Protocol Assessment
TBI	Traumatic brain injury
TTFED	Tri-Agency Task Force for Emergency Diagnostics
U.S.	United States
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
USG	United States government
USGS	U.S. Geological Survey
UTMB	University of Texas Medical Branch
UVGI	Ultraviolet germicidal irradiation
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization
ZIKV	Zika virus

Stay Connected

www.fda.gov/MedicalCountermeasures

AskMCMi@fda.hhs.gov

@FDA_MCMi

Email updates

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration

Office of the Commissioner, Office of the Chief Scientist
Office of Counterterrorism and Emerging Threats
10903 New Hampshire Avenue, Silver Spring, MD 20993