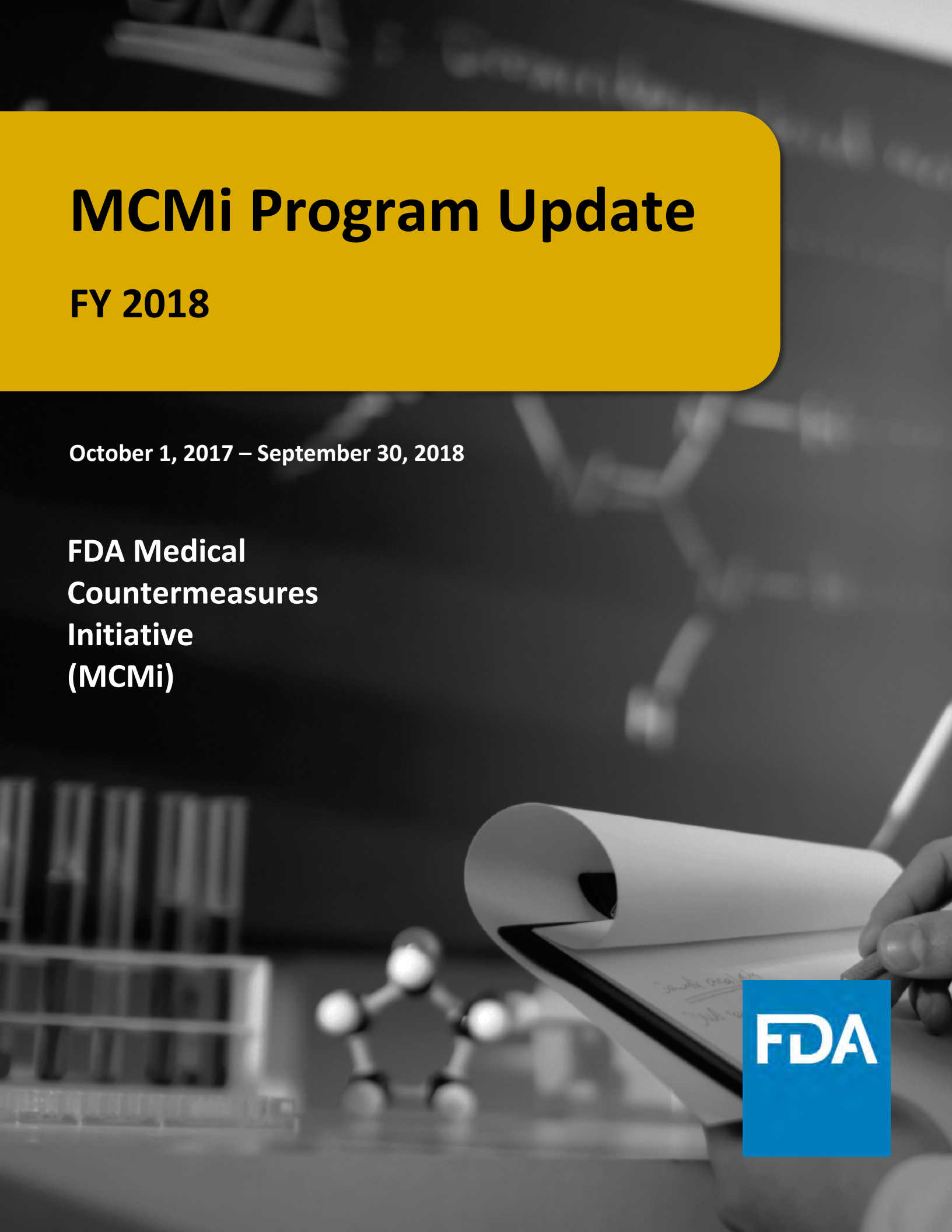

MCMi Program Update

FY 2018

October 1, 2017 – September 30, 2018

FDA Medical Countermeasures Initiative (MCMi)

FDA

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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, or Enterprise) to build and sustain the MCM

[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 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.

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 Enterprise 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.

In 2013, the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) was enacted.[5] PAHPRA contains key legal authorities to strengthen U.S. preparedness for public health emergencies involving CBRN agents and emerging infectious disease threats. PAHPRA also codified many of the activities already ongoing at FDA under the MCMi Program to foster the development and availability of MCMs as well as created new authorities to enable FDA to more effectively support preparedness and response efforts. PAHPRA requires FDA to issue an annual report detailing its MCM activities. This report responds to that requirement for fiscal year (FY) 2018 (October 1, 2017 – September 30, 2018).[6]

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[2] The Enterprise is a coordinated, interagency partnership that fosters the MCM programs necessary to improve public health emergency preparedness as well as to prevent and mitigate the adverse health consequences associated with CBRN threats and emerging infectious diseases. The Enterprise is led by the Office of the Assistant Secretary for Preparedness and Response (ASPR) and includes three primary HHS internal agencies: the Centers for Disease Control and Prevention (CDC), FDA, and the National Institutes of Health (NIH). Key interagency partners are: the Department of Homeland Security (DHS), the DoD, the Department of Veterans Affairs, and the Department of Agriculture (USDA).

[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), or 515 of the FD&C Act or section 351 of the PHS Act.

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

[6] Detailed information on FDA's MCM development and review activities covering FY 2011-2017 can be found at: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm270744.htm

FY 2018 Resources for MCM Activities

FDA obligated $113.2 million in FY 2018 to support CBRN and pandemic influenza-related MCM activities (Table 1). These resources comprised a combination of base funding and no-year funding.

Base Funding

FDA obligated $107.3 million from its FY 2018 base resources to support CBRN and pandemic influenza-related MCM activities. This funding included $46.9 million for CBRN preparedness activities, $35.8 million for pandemic influenza preparedness activities, and $24.6 million for the MCMi Program.

This funding supported 472.7 full-time equivalents (FTEs) as well as a $1.6 million investment in the MCMi Regulatory Science Program.

Table 1: FY 2018 resources obligated to MCM activities (dollars in millions)

(blank cell)	FY 18 Estimate	FY 18 FTE Estimate
CBRN Base Funding	$46.9	226
Pandemic Influenza Base Funding	$35.8	163
MCMi Base Funding	$24.6	81
Subtotal	*$107.3*	*470*
Ebola Supplemental Funding (No-Year)	$0.5	0
Emerging Health Threats Funding (No-Year)	$3.6	2.7
Transfer from No-Year HHS Pandemic Influenza Funding	$1.8	0
Total	**$113.2**	**472.7**

No-Year Funding

In FY 2015, FDA received $25 million in emergency supplemental, no-year funding to support activities related to responding to the Ebola epidemic in West Africa including conducting medical product review and funding regulatory science research to help expedite the development and availability of medical products for Ebola. FDA reprogrammed $5 million of the Ebola supplemental funding to support Zika virus response activities and spent $0.5 million of those funds in FY 2018; this funding supported targeted regulatory science research to support the development and regulatory review of Zika virus MCMs.[7]

In FY 2017, FDA received $3.8 million from remaining balances in HHS supplemental pandemic influenza appropriations to support influenza A (H7N9) preparedness activities. FDA obligated $1.8 million of this funding in FY 2018 to support targeted regulatory science research required to support the development and assessment of MCMs (see **Table 4** for examples).

In FY 2017, FDA received $10 million in supplemental, no-year funding to prevent, prepare for, and respond to emerging health threats (EHTs) and obligated $1.8 million of those funds. In FY 2018, FDA obligated $3.6 million of EHT funds, supporting 2.7 FTEs and $2.8 million in regulatory science research to support emerging threat response activities.

[7] FDA obligated $20 million of the Ebola supplemental funding to support Ebola response activities in FY 2015 - FY 2016. FDA obligated $1.6 million of the $5 million Ebola supplemental funding repurposed to Zika virus response in FY 2016, $2.9 in FY 2017and obligated the remaining $0.5 million in FY 2018.

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 2018 with respect to these activities.

[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); 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).

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 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

Medical Countermeasure Approvals

During FY 2018, 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 2018 (see **Appendix 1: FY 2018 Medical Countermeasure Approvals**).[10]

All-hazards preparedness

To support national burn care preparedness, FDA cleared the ReCell Autologous Cell Harvesting Device, which is intended to reduce the amount of skin harvesting required relative to conventional treatment of burn injuries. Development of this device was supported by a Biomedical Advanced Research and Development Authority (BARDA) contract, including execution of clinical trials and regulatory submission activities.

To address traumatic brain injury, FDA approved the first blood test to evaluate mild traumatic brain injury (mTBI), commonly referred to as concussion, in adults. FDA reviewed and authorized the Banyan Brain Trauma Indicator for marketing in less than six months as part of the Breakthrough Devices Program. FDA's review team worked closely with the test developer and the DoD to expedite review of this test, to enable it to be commercially marketed in the continental U.S. and in foreign U.S. laboratories that service the American military.

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

To support smallpox preparedness, FDA approved TPOXX (tecovirimat), the first drug with an indication for treatment of smallpox. Because human smallpox disease (caused by variola virus) was declared eradicated decades ago, clinical trials in naturally occurring disease are not currently possible; however, concerns remain that the virus could potentially be used as an agent of bioterrorism. TPOXX was approved under the Animal

> FDA approved the first drug with an indication for treatment of smallpox

[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*: http://www.accessdata.fda.gov/scripts/cder/daf/, *Biologics Products & Establishments*: http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm, and *Medical Device Databases*: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm

Rule, which allows findings from adequate and well-controlled animal efficacy studies to serve as the basis of an FDA approval when it is not feasible or ethical to conduct efficacy trials in humans. TPOXX also was awarded the first material threat MCM Priority Review Voucher (PRV), described in more detail on page 43. In addition, FDA approved a Biologics License Application (BLA) supplement for the ACAM2000 Smallpox (Vaccinia) Vaccine, Live, to include updates to the package insert and medication guide, with new CDC contact information.

For chemical nerve agent preparedness, FDA approved a 2 milligram (mg) atropine auto-injector for the treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity as well as organophosphorous or carbamate insecticides in adults and pediatric patients weighing over 90 pounds (generally over 10 years of age).[11] In addition, FDA approved Seizalam (midazolam intramuscular injection) for the treatment of status epilepticus in adults.[12]

For radiological/nuclear (rad/nuc) emergency preparedness, FDA approved a new indication for Leukine (sargramostim) to increase survival of adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome, or H-ARS). Leukine is the third FDA-approved MCM that is indicated to increase survival in patients exposed to myelosuppressive doses of radiation.

For viral encephalitis preparedness, FDA approved a BLA supplement for IXIARO Japanese Encephalitis Virus Vaccine, Purified, Inactivated, Adsorbed, to include data from studies which included a long-term pediatric study, and to approve recommendation of a booster dose at least 11 months after completion of the primary vaccination series for individuals over 17 years of age who are at risk of continued exposure or re-exposure to Japanese encephalitis virus.[13]

Diagnostics and screening tests for CBRN threats and emerging diseases

To protect the blood supply and human cell, tissue and cellular and tissue-based products (HCT/Ps) from Zika, FDA approved the cobas Zika nucleic acid test for use on the cobas 6800/8800 systems, for the direct detection of Zika virus RNA in human plasma. This test—the

[11] Two additional strengths (0.5 mg and 1 mg) of the atropine auto-injector manufactured by Rafa Laboratories Ltd. are available under EUA: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#nerveagents

[12] For additional information, including BARDA and DoD support for this product, see from HHS ASPR *FDA approval of anti-seizure drug provides a new tool for protecting Americans during a chemical attack* at: https://www.phe.gov/ASPRBlog/pages/BlogArticlePage.aspx?PostID=319

[13] Viral encephalitis pathogens, including Japanese encephalitis, are classified as Category B threat agents, the second-highest priority category organisms of U.S. national security concern. https://emergency.cdc.gov/agent/agentlist-category.asp

first approved test to screen Zika virus in blood donations—is intended for use to screen donor samples in plasma from individual human donors, including donors of whole blood and blood components, and for use to screen organ and tissue donors when donor samples are obtained while the donor's heart is still beating.

For Middle East Respiratory Syndrome Coronavirus (MERS-CoV) preparedness, FDA cleared the FilmArray RP2/RP2plus Control Panel, for the simultaneous qualitative detection and identification of nucleic acids from MERS-CoV and multiple common viral and bacterial respiratory pathogens in nasopharyngeal swabs obtained from individuals meeting MERS-CoV clinical and/or epidemiological criteria.

To detect non-variola[14] orthopoxvirus DNA, including vaccinia, cowpox, monkeypox, and ectromelia viruses at varying concentrations, FDA cleared the CDC's Non-variola Orthopoxvirus Real-time PCR (polymerase chain reaction) Primer and Probe Set, for the *in vitro* qualitative detection of non-variola orthopoxvirus DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Laboratory Response Network (LRN) laboratory.

Pandemic influenza preparedness

FDA approved an expanded indication for Fluarix Influenza Virus Vaccine, to extend the age range to include children 6 to 35 months of age. FDA also approved BLA supplements for three other influenza vaccines to include updates to the package insert to include, for example, revised contact information for adverse event and pregnancy outcome reporting, pregnancy registry enrollment, and to comply with the Pregnancy and Lactation Labeling Rule, in addition to approvals for annual strain changes.

FDA also approved three new influenza tests and approved modifications to seven previously approved influenza detection *in vitro* diagnostic (IVD) devices to, for example, include additional specimen types, address software modifications, 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.

[14] Because variola virus, the historical cause of smallpox, is no longer found in nature but several related orthopoxvirus species can cause disease with some overlapping manifestations, a test for non-variola orthopoxvirus DNA can help to distinguish whether a particular sample contains orthopoxvirus DNA that is not variola.

Additional marketing applications in progress

Ten additional marketing applications for new MCMs or new MCM indications were under review in FY 2018; 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.[15]

Supporting an Adequate Supply of Medical Countermeasures

FDA continued efforts to support the establishment and sustainment of an adequate supply of MCMs during FY 2018. 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 2018, as a result of SLEP testing that assured drug stability and quality, FDA granted shelf-life extensions for approximately 2,100 lots (batches) of MCM drugs.

[15] For updated information about MCM approvals after the FY 2018 reporting period, visit *MCMi News and Events*: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm

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. For example, FDA issued a memo (PDF, 286 KB) to government public health and emergency response stakeholders extending the expiration date of five specific lots of doxycycline hyclate 100 mg capsules held in strategic stockpiles for anthrax emergency preparedness and response purposes.[16] FDA authorized these extensions based on the first request FDA received from a government stakeholder under the draft guidance for extending the expiration dating of doxycycline held in strategic stockpiles.[17] These extensions apply to the same lots of doxycycline that are properly held by any other government stakeholders.

FDA approved an auto-injector for chemical nerve agent preparedness, supporting adequate MCM supplies

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 2018, 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, and determined that, if properly stored, certain lots of this manufacturer's auto-injector products held for emergency use could be used beyond the original labeled expiration date for a period specified by FDA, to help ensure ready access to these products. Based on its review of scientific data, FDA also identified certain lots that are no longer useable and, therefore, should be properly disposed of.[18]

FDA also responded to numerous 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. As noted above, in FY 2018, FDA approved a 2 mg atropine auto-injector, for the treatment of poisoning by susceptible organophosphorous nerve agents

[16] For more information, see *Expiration date extensions of certain lots of doxycycline hyclate capsules*: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm619289.htm

[17] FDA. *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Draft Guidance for Government Public Health and Emergency Response Stakeholders.* April 2017. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM554506.pdf

[18] For the latest updates on expiry dating extensions for chemical nerve agent auto-injectors, see: http://www.fda.gov/Drugs/DrugSafety/ucm376367.htm

having cholinesterase activity as well as organophosphorous or carbamate insecticides in adults and pediatric patients weighing over 90 pounds.[19]

Another way FDA worked to ensure an adequate supply of MCMs in FY 2018 was 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 they're manufactured—whether they're 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.[21]

[19] For more information about the approved 2 mg Rafa Atropine Auto-Injector, see the product label: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/212319s000lbl.pdf As noted above, the pediatric strengths (0.5 mg and 1 mg) of this product continue to be available for emergency use under an EUA: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#nerveagents

[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/InternationalPrograms/Agreements/ucm598735.htm

Enabling Access to Medical Countermeasures Under FDA's Emergency Use Authorization Authority[22]

During FY 2018, FDA continued to work with Enterprise 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]

[22] Section 564 of the FD&C Act

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

[24] Under the Project BioShield Act of 2004 [PL 108-276], which was amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) [PL 113-5], the Secretary of HHS has the authority to authorize the "emergency use" of MCMs in emergencies under certain terms and conditions [21 USCS § 360bbb-3]. The authority to issue EUAs was delegated to the FDA Commissioner. Section 564 of the FD&C Act was also amended by the 21st Century Cures Act of 2016 [PL 114-255] and Public Law 115-92 (2017).

In July 2018, FDA issued an EUA to enable the emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma for the treatment of hemorrhage or coagulopathy of U.S. military personnel during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. [25]

FDA issued an EUA for freeze-dried plasma to support American military personnel

In FY 2018, FDA amended the Rafa Atropine Auto-Injector EUA to clarify that the authorized product may be administered through clothing and include changes to Rafa-planned manufacturing processes. The EUA provides access to dosages that have not been approved (i.e., 0.5 mg and 1 mg pediatric strengths). FDA also reissued the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay H7N9 influenza EUA, and amended 8 Zika virus diagnostic EUAs upon request from the product manufacturers to add additional instruments or specimen types or make clarifications.

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 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.[26] During FY 2018, FDA continued to work with government partners and industry on pre-EUA activities for MCMs against a diverse array of threats.

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]

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[25] For more information, see the FDA news release: *FDA takes action to support American military personnel by granting an authorization for freeze-dried plasma product to enable broader access while the agency works toward approval of the product*: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612893.htm

[26] 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.

[27] An EUA issued on November 9, 2018 uses the new templates. See the DPP Ebola Antigen System fact sheet for healthcare providers at: https://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM625570.pdf

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. Emerging infectious disease response activities in FY 2018 included:

Ebola

FDA continued to support the international response to Ebola outbreaks in Africa, which emerged in West Africa in 2014 and re-emerged in the Democratic Republic of the Congo (DRC) in 2017 and 2018.[28] For example, FDA:

- ✓ Continued to work closely with interagency partners, medical product developers, the World Health Organization (WHO), and international regulatory counterparts to help advance response efforts including supporting the evaluation, use, and export of investigational therapeutics and vaccines in the ongoing Ebola outbreak, as well as earlier ones. For example, FDA provided advice on development of a clinical trial protocol to compare several investigational Ebola therapeutics.
- ✓ Continued to work with manufacturers of authorized Ebola diagnostics to make rapid tests available, as well as advance these products toward market approval.
- ✓ Sought a permanent injunction against a company selling unapproved hand sanitizers that claimed to prevent infections from pathogens including Ebola.

Zika

FDA also continued to actively support the national and international response to Zika virus. In FY 2018, FDA activities included:

- ✓ Approved the cobas Zika test, the first test for screening Zika virus in blood donations, and the Procleix Zika Virus Assay, a qualitative nucleic acid test for the detection of Zika virus RNA in individual plasma specimens obtained from volunteer donors of whole blood and blood components for transfusion.

FDA approved the first test for screening Zika virus in blood donations

[28] Also see: *Statement from FDA Commissioner Scott Gottlieb, M.D., on federal preparedness and FDA's response efforts to the Ebola virus outbreak in the Democratic Republic of Congo*: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609275.htm

- ✓ Issued revised guidance (PDF, 222 KB) on the testing of donated blood and blood components for Zika virus, to allow testing of pooled donations, which is usually more cost effective and less burdensome for blood establishments.[29]

- ✓ Continued to work with Zika diagnostic manufacturers to amend EUAs, and help advance Zika diagnostics toward market approval.

- ✓ Posted new tables detailing performance characteristics of Zika virus (ZIKV) diagnostic tests (assays) currently available for use under EUA: Table 1: Molecular ZIKV EUA Assays - Performance Characteristics (PDF, 200 KB); and Table 2: Molecular ZIKV EUA Assays - Key Characteristics (PDF, 247 KB). The tables include information about analytical sensitivity, along with other performance characteristics determined during EUA evaluation.

MERS-CoV

FDA continued similar activities to respond to the MERS-CoV outbreak, which was first noted 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; one new MERS-CoV IVD test was cleared in FY 2018.

[29] Also see: *FDA in Brief: FDA announces revised guidance on the testing of donated blood and blood components for Zika virus*: https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm612702.htm

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 diagnostics that have not yet met requirements for full marketing clearance

Issuing EUAs for a diagnostic test for H7N9 influenza (re-issuance), and a freeze-dried plasma product to enable broader access to support American military personnel

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 multidisciplinary 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 2018.

Microbial Sequencing and Multiplex In Vitro Diagnostics Action Team

This Action Team continued its work to make available a vetted, validated, and curated database of high-quality genomic sequence data for MCM and clinically significant bacterial pathogens 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 2018 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).[30] In FY 2018, FDA initiated reference genome sequencing

[30] 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 http://www.ncbi.nlm.nih.gov/bioproject/231221

for 500 microbial constituents. The FDA-ARGOS database generates and publishes regulatory-grade microbial genomes, which enable ID-NGS developers to perform *in silico* validation of their workflows. 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 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.[31] 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.

- ✓ 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.

- ✓ Continuing a collaboration with the Defense Advanced Research Projects Agency (DARPA) to support its Diagnostics on Demand (DxOD)/Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program.

- ✓ Sustaining an interactive collaboration with the DoD on the development of its Next-Generation Diagnostic System (NGDS) to replace the Joint Biological Agent Identification and Diagnostic System (JBAIDS).

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

Warfighter Action Team

This Action Team 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 2018 activities included:

- ✓ Establishing 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** on page 32 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, and visiting DoD research facilities to learn more about their development priorities and the unique conditions military healthcare professionals face when treating the warfighter.
- ✓ Assisting the DoD with potential approaches for addressing the unique challenges in conducting studies or making MCMs available for the warfighter. Focus areas include traumatic brain injury, hemorrhage, nerve agents, and research that involves minimal risk to human subjects.[32]
- ✓ Continuing a formal fellowship program between FDA and the 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.
- ✓ Participating in the Military Health System Research Symposium (August 2018). FDA provided expert speakers on topics including traumatic brain injury, auto-injector regulation, blood product regulation, and the regulatory review process for MCMs, to help facilitate interagency coordination.

[32] 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).

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 2018 included:

- ✓ Facilitating interaction with rad/nuc preparedness government funding agencies (NIAID, BARDA, and others) and strengthening FDA rad/nuc preparedness activities.
- ✓ Discussing regulatory strategies to expedite product development for radiation-induced thrombocytopenia, a condition characterized by low blood platelet count.
- ✓ Providing FDA reviewers with training and information on the latest scientific research related to gastrointestinal (GI)-acute radiation syndrome (ARS), lung-ARS, and cutaneous radiation injury to enable appropriate regulatory decisions.
- ✓ Assisting BARDA with development of radiation biodosimetry medical devices and discussing regulatory and scientific issues.
- ✓ Enhancing interactions between NIAID and FDA to discuss cellular therapy products for treatment of radiation injuries and connecting NIAID with the INitial Targeted Engagement for Regulatory Advice on CBER ProducTs (INTERACT).
- ✓ Establishing a new web page, which was published in FY 2018, Radiological and Nuclear Emergency Preparedness Information from FDA.

Regulatory Advice and Guidance

During FY 2018, 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 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 the Center for Biologics Evaluation and Research (CBER), see FDA's guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* (Revision 1). In December 2017, FDA published a revised draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (PDF, 156 KB). 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.[33] 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

[33] 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/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm590547.pdf and *Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff* (September 2017) available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

product for which the meeting is requested is not sufficiently developed to warrant the type of meeting sought).[34] 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,[35] and a Special Protocol Assessment (SPA) meeting[36]).

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, 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 2018, CBER held 31 formal meetings with MCM sponsors or applicants, and CDER held 30 formal meetings (Table 2) and 15 other (non-PDUFA) meetings.

Table 2: FY 2018 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	1	1
Type B	20	14
Type C	10	15
Total	**31**	**30**

[34] Formal meetings may also be rescheduled or canceled based on criteria described in FDA guidance.
[35] 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.
[36] For more information on Special Protocol Assessments see *Guidance for Industry – Special Protocol Assessment* (April 2018) available at : https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm498793.pdf

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 62 Pre-subs and 19 Submissions (marketing applications) for MCM medical devices in FY 2018. 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 2018, CDRH provided written feedback for 66 MCM Pre-sub or Submission applications and held 43 formal Pre-sub and 0 formal Submission meetings with MCM sponsors or applicants (**Table 3**).

Table 3: FY 2018 formal meetings between CDRH and MCM sponsors or applicants

Meeting Type	CDRH
Pre-Submission	43
Submission	0
Total	**43**

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.[37] In FY 2018, CDRH reviewed and provided written feedback on 30 pre-EUAs and 10 EUAs and held 11 pre-EUA and EUA meetings.

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

[37] For more information on the Interactive Review Process see *Types of Communication During the Review of Medical Device Submissions - Guidance for Industry and Food and Drug Administration Staff* available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM341948.pdf

product sponsor or applicant can be delineated.[38] FDA did not receive any written MCM-related RMP requests in FY 2018.

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. To improve the efficiency and effectiveness of oversight over biologics manufacturing, in January 2018, FDA issued a direct final rule that amends the general biologics regulations to remove outdated requirements and help eliminate inconsistencies and duplicative processes—specifically, how frequently the FDA is inspecting certain facilities and the actual duties of the inspector.

In FY 2018, FDA issued indication-specific guidance to assist developers of MCMs for smallpox and anthrax

In addition to its direct work with MCM sponsors and applicants, FDA also issues guidance documents that help foster MCM development and availability.[39] Guidance documents issued during FY 2018 directly related or applicable to MCMs policies or regulatory issues are listed in **Appendix 3: MCM-Related Guidance Issued in FY 2018**. In FY 2018, FDA issued a final guidance (PDF, 115 KB) to assist sponsors in the development of new drugs for the prophylaxis of inhalational anthrax,[40] and a revised draft guidance (PDF, 120 KB) to assist sponsors in all phases of development of antiviral drugs for the treatment or prevention of smallpox (variola virus) infection. FDA held webinars for industry to discuss many of the guidance documents issued in FY 2018, with topics including final guidances on NGS-

[38] 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.

[39] 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))

[40] Also see: *FDA In Brief: As part of a longstanding program encouraging the development of medical countermeasures; new FDA policy promotes innovation to thwart inhalational anthrax*: https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm608629.htm

based tests, optimizing vaccine study data submissions, and FDA's MedWatch adverse event reporting program.[41]

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 2018 are listed in **Appendix 4: Key MCM-Related Meetings Held in FY 2018**. 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. [42,43]

In FY 2018, FDA continued to improve communication with product sponsors, offering new resources including an online tutorial to guide sponsors through the orphan designation process (which is sometimes sought by MCM developers), and a new fillable form (PDF, 3.18 MB) to make the orphan designation submission process easier for sponsors to complete designation requests, and more efficient for FDA to review. FDA also launched the new INTERACT meeting program to facilitate early interactions between sponsors and CBER staff.[44]

In addition, in August 2018, FDA launched a new pilot program to advance innovative clinical trial designs, as part of the agency's broader program to modernize drug development and promote innovation in drugs targeted to unmet needs. Drug and biologic companies that participate in the Complex Innovative Designs Pilot Meeting Program will have additional opportunities to meet with agency staff to discuss the use of novel complex innovative trial designs (CID) for their clinical development programs. Examples of topics that may arise in the discussion of complex innovative trial designs include the use of seamless trial designs, modeling and simulations to assess trial operating characteristics, the use of biomarker enriched populations, complex adaptive designs, Bayesian models and other benefit-risk determinations, and other novel designs. The new program will help solidify the science used to support these novel approaches and promote their adoption in drug development programs where these trial constructs can advance innovation.[45]

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[41] For additional examples, see this list of CDRH medical device webinars and stakeholder calls: http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm411063.htm

[42] A list of MCM-related events by year is available in the *MCMi Events Archive*: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm372288.htm

[43] Where available, MCM-related legal and policy presentations given by FDA staff can be found at: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411508.htm and MCMi regulatory science presentations can be found at: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm534276.htm

[44] Also see: *FDA In Brief: FDA announces program to enhance early communications with biological product developers*: https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm611534.htm

[45] Sponsors may submit meeting requests for the pilot program through June 30, 2022.

Collaboration and Communication

During FY 2018, FDA continued to collaborate extensively with Enterprise and DoD (more on page 32) partners to foster the development and availability of MCMs. FDA provided subject matter expertise and technical assistance to 67 standing interagency and Enterprise- 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 is also supporting development and 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, 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.

Other key collaborations in FY 2018 include:

Final order exempting certain N95 respirators from premarket notification requirements

FDA and CDC's National Institute for Occupational Safety and Health (NIOSH) share regulatory oversight of N95 respirators. In a final order released on May 16, 2018, FDA exempted certain N95s from premarket notification [510(k)] requirements, and executed a Memorandum of Understanding (MOU) with NIOSH. The final order and MOU streamline the regulation of N95s to help manufacturers easily identify, understand, and work to meet marketing requirements, and help ensure the availability of safe and effective medical products, particularly during times of increased demand, such as a public health emergency. This final action will also decrease regulatory burden on the medical device industry and eliminate costs required to comply with certain Federal regulations.

NASA MOU

In September 2018, FDA and the National Aeronautics and Space Administration (NASA) signed an MOU to provide mutual support to biomedical research and development on drugs, biologics, and medical devices for space exploration missions as well as for MCM development, such as for radiation-induced human health risks.

Bill and Melinda Gates Foundation MOU

In FY 2017, FDA and the Gates Foundation signed an MOU to establish a framework to facilitate collaboration to carry out common goals to improve public health by stimulating and fostering medical product innovation and enabling medical product developmemt, including MCMs. In FY 2018, FDA and the Gates Foundation continued collaborations under this MOU across a broad range of topics including developing over-the-counter influenza diagnostics, identifying immune correlates of protection for vaccines of public health significance, and developing animal models to support the evaluation of vaccines.

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,[46] as well as other HHS-led efforts related to global MCM policies.
- ✓ Implementing CBER-WHO Cooperative Agreements[47] 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.

[46] "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

[47] For example, *CBER-WHO Cooperative Agreement: Supporting Influenza Vaccine Introduction to Low-Middle Income Countries* (http://www.fda.gov/BiologicsBloodVaccines/InternationalActivities/ucm342894.htm); for more about CBER's WHO Cooperative Agreements, see: http://www.fda.gov/biologicsbloodvaccines/internationalactivities/whoengagements/ucm274213.htm

- 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 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.

Enhancing communication

In FY 2018, FDA also worked to enhance communication related to MCM preparedness and response by continuing ongoing outreach activities (e.g., MCMi email newsletter and various presentations), and publishing new web pages to centralize information on topics including smallpox, radiological and nuclear emergency preparedness, and antimicrobial resistance.

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 the 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, the 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 expedite its review of priority DoD medical products in a manner similar to products under the breakthrough 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.[48]

[48] Also see: *FDA/DoD Collaborations*: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm592560.htm and the January 16, 2018 FDA news release *FDA and DoD launch program to expedite availability of medical products for the emergency care of American military personnel*: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592581.htm

Related to FDA-DoD ongoing and frequent collaborations, in FY 2018, FDA:

- ✓ Granted an EUA for emergency use of Pathogen-Reduced Leukocyte-Depleted Freeze-Dried Plasma, at DoD's request.
- ✓ Approved an atropine auto-injector as an MCM for chemical nerve agent exposure. This drug-device product was developed in partnership[49] with the Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense, and was approved six months ahead of the DoD's product development schedule.
- ✓ Following a priority review, approved the first prophylaxis indication for a new malaria drug in over 18 years, tafenoquine (Arakoda). This drug was developed in partnership with the U.S. Army Medical Research and Materiel Command (USAMRMC).
- ✓ Established with DoD 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.[50] This 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.

[49] Some products are considered relevant to FDA-DoD interactions if they are the subject of applications submitted by commercial entities but developed with certain kinds of substantive DoD support.

[50] *MOU Concerning Coordination with FDA Regarding DoD Medical Product Development and Assessment* (MOU 225-19-01), available at: https://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm624949.htm

Medical Countermeasure Regulatory Science

In FY 2018, 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.[51]

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.[52]

[51] 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.

[52] 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: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125349s000lbl.pdf

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 ***in silico* predictive models** (e.g., microphysiological systems) and *in vitro* assays 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 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

The goal of the MCMi Regulatory Science Program is to develop the 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.[53] To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with 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 Enterprise priorities. FDA continually engages with our USG stakeholders to maintain an MCMi Regulatory Science Program that actively addresses current regulatory science gaps.

FY 2018 MCMi Regulatory Science program activities are included in **Table 4**.

[53] 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 http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391600.htm and https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391318.htm

Table 4: MCMi Regulatory Science Program activities in FY 2018

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 September 2018, FDA expanded this study to analyze differences in sex-specific responses to radiation[54])
Exploring nanopore technology to enhance detection and tracing of *Clostridium botulinum* and *Escherichia coli* contamination
Testing and comparing how effective different antibiotics 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
Emerging threats (e.g., Ebola and Zika)
Expanding a database of reference-grade nucleic acid sequences for emerging threats, to including viruses such as Ebola and Zika, and antimicrobial-resistant pathogens
Developing and validating assays for Ebola that can be utilized outside of specialized, high-containment Biosafety Level 4 (BSL-4) laboratories
Distibuted Zika virus RNA reference materials (developed in FY 2017) to manufacturers seeking EUA for nucleic acid-based diagnostic tests for Zika virus
Distributed Zika serological reference panel (developed in FY 2017) 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 develop improved small animal models for Ebola and Zika
Developing bioassays and identifying potential markers of disease progression by evaluating cellular factors affecting Ebola virus surface glycoprotein-mediated cell fusion under BSL-2 conditions
Exploring alternative garment testing methods to determine optimum test equipment and conditions for assessing personal protective equipment (PPE) to predict Ebola penetration without use of live Ebola virus and high-containment facilities
Supporting field laboratory testing of Ebola antibodies in Sierra Leone, improving field laboratory capacity in Liberia, and coordinating clinical testing for rare African viruses in Uganda

[54] FDA contract HHSF223201820398A/0001 was awarded by the FDA Office of Counterterrorism and Emerging Threats (OCET), in conjunction with the FDA Office of Women's Health (OWH).

Conducting survivor studies to better understand Ebola's after-effects, to help find new treatments; in April 2018 FDA awarded a contract modification to conduct nonclinical studies for bridging data between human clinical samples and animal models

Sponsoring nonclinical research studies to help inform FDA recommendations regarding potential transmission of Zika virus via organs and tissues

Identifying target peptide sequences for a Zika immunoglobulin M (IgM) diagnostic device

Exploring antibody responses following Zika virus infection or vaccination in humans, to help support development of effective vaccines and serodiagnostics

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

Developing a rapid and sensitive assay to assess antibody response to Ebola virus vaccine without using the virus

Developing a new mouse model to help explore the potential activity of Zika virus vaccines and therapeutics, providing a platform for potentially improving and expediting studies to understand the causes and effects (pathology) of the Zika virus

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[55]

Pandemic influenza

Evaluating the use of chimeric viruses to improve production of influenza B vaccines

Addressing potential bottlenecks in the production of seasonal and pandemic influenza vaccines by developing novel alternative methods to measure influenza vaccine

Public health emergency preparedness and response

Optimizing respirator decontamination to ensure supplies for emergency preparedness[56]

Developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during a public health emergency through a collaboration with the the Society of Critical Care Medicine's Discovery, the Critical Care Research Network, and critical care physicians at 20 hospitals throughout the U.S.

Developing phantom-based test methods for evaluation of near-infrared diagnostic devices for traumatic brain injury (TBI) and cerebral monitoring

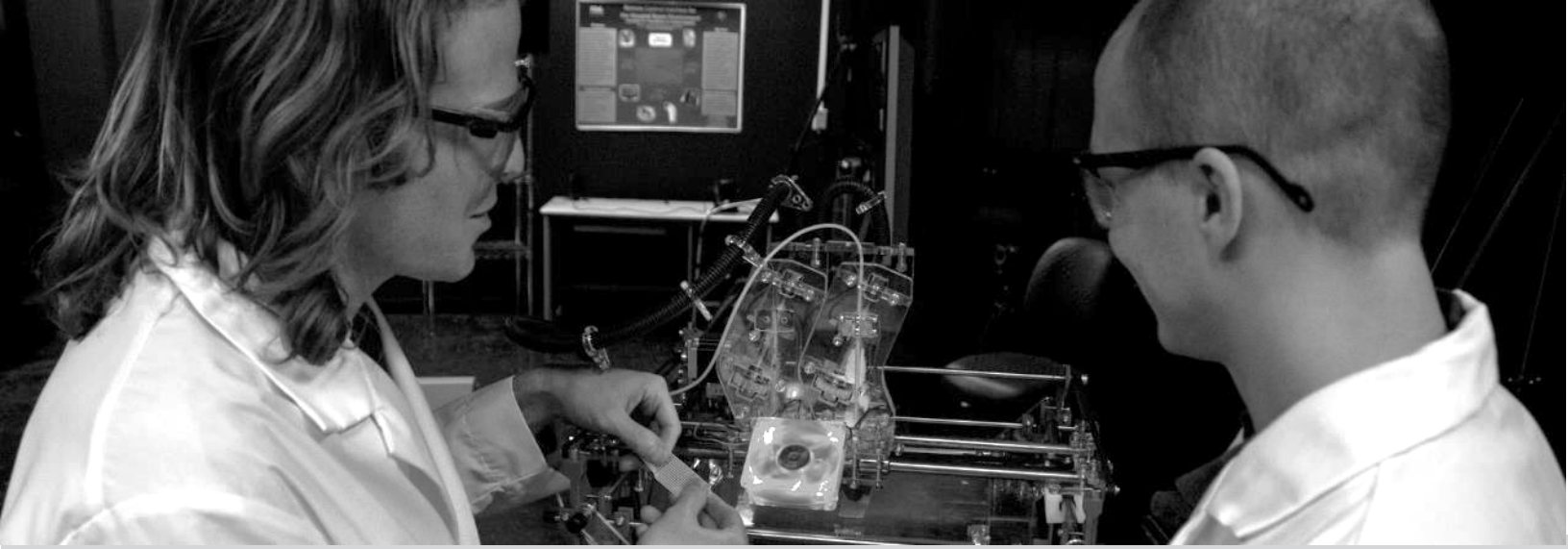
[55] The MCMi Program awarded this contract, and work began, in FY 2018.
[56] On October 2, 2017, BARDA announced a new contract that builds on this work, to advance the development of respirators that can be re-used up to 100 times. See: https://www.phe.gov/Preparedness/news/Pages/reusable-respirator-2Oct2017.aspx

Developing techniques for the preclinical evaluation of physiological closed-loop controlled supportive therapy devices, particularly related to the computational patient model
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
Developing the CDC & FDA Antibiotic Resistance (AR) Isolate Bank
Developing tools for risk assessment of critical quality attributes of antiviral drug products using physiologically based pharmacokinetic modeling approaches
Developing 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
Continuing to explore potential lessons from animal models for understanding pharmacokinetics of MCMs used during pregnancy for influenza and CBRN threats
Exploring the use of microphysiological systems to evaluate human-specific toxicity of MCMs *in vitro*
Designing a blood supply model to help public health officials effectively plan strategies to minimize any disruption of the blood supply should blood collection efforts be reduced as a result of an emergency

FDA also expanded and sustained MCM regulatory science collaborations in FY 2018. For example, FDA:

- ✓ Sponsored the sixth installment of a program 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., BSL-3 and -4) laboratories used to support product approval under the Animal Rule.
- ✓ Supported 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.
- ✓ Continued collaborations with DARPA on regulatory science research for the development of innovative regulatory tools, such as biomimetic models, in addition to supporting its DxOD/ADEPT program, 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.

In addition, FDA published a new web page, Regulatory Science Research Tools, which lists information about MCM-related regulatory science tools funded (or partially funded) by FDA—and available at no charge—to help MCM researchers advance their products, and help FDA reviewers evaluate MCM products for approval.



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. In July 2018, for example, FDA and BARDA co-sponsored a workshop, Continuous Manufacturing for the Modernization of Pharmaceutical Production to discuss the business and regulatory concerns associated with adopting continuous manufacturing techniques to produce biologics (e.g., enzymes, monoclonal antibodies, and vaccines) and discuss specific challenges for process integration across the manufacturing system. FDA representatives also actively participate in ongoing public-private partnerships such as the Manufacturing USA Institutes, including America Makes, BioFabUSA and the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), to proactively address regulatory challenges presented by advanced manufacturing technologies, including continuous manufacturing.

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.

FDA has cleared more than 100 3D-printed medical devices, and a 3D-printed drug

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 *3D Printing of Medical Devices, and Technical Considerations for Additive Manufactured Medical Devices* (PDF, 619 KB). FDA continues work to provide a more comprehensive regulatory pathway that keeps pace with those advances, and helps facilitate efficient access to safe and effective innovations that are based on these technologies. For example, burn patients could be treated with their own new skin cells 3D printed directly onto their burn wounds.[57] FDA has cleared more than 100 3D-printed medical devices and has approved a 3D-printed drug.

The Office of the Chief Scientists'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. One example has been 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.

In August and September 2018, FDA awarded a total of eight 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.

[57] Also see: *Statement by FDA Commissioner Scott Gottlieb, M.D., on FDA ushering in new era of 3D printing of medical products; provides guidance to manufacturers of medical devices*: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587547.htm

Medical Countermeasure Regulatory Policy

During FY 2018, 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 2018, 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.
- ✓ 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.

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:

- ✓ Working 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.

- ✓ Working with CDC and the Centers for Medicare and Medicaid Services (CMS) to better coordinate the implementation of EUA IVD assays by providing strategy, oversight, and technical advice.

- ✓ Conducting message testing to improve understandability of communications on IVD tests used during an emergency.

- ✓ Identifying and developing new legislative proposals in anticipation of the reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA), and supporting MCM-related congressional testimony.[58]

- ✓ Leading development of or providing policy input to MCM-related guidance documents issued in FY 2018 (**Appendix 3: MCM-Related Guidance Issued in FY 2018**) and key meetings and workshops (**Appendix 4: Key MCM-Related Meetings Held in FY 2018**).

During FY 2018, FDA continued working to implement several additional MCM-related provisions of the Cures Act, which was signed into law on December 13, 2016. Many provisions of the law will facilitate development of MCMs. The MCMi Program is implementing provisions to support emergency preparedness and response capabilities for public health emergencies involving CBRN and emerging infectious disease threats, and to foster the development of MCMs.

The Cures Act amended the FD&C Act to authorize FDA to establish a program for awarding PRVs to encourage development of material threat MCMs. FDA developed a draft guidance that provides to internal and external stakeholders answers to questions FDA has received on material threat MCM priority review vouchers (PRVs). FDA issued this draft guidance (PDF, 148 KB) in January 2018, to explain to internal and external stakeholders how FDA intends to implement the material threat MCM PRV program. On October 2, 2017, FDA issued a notice establishing the FY 2018 user fees for MCM PRVs .[59] In July 2018, FDA issued the first MCM priority review voucher.[60] In addition, in August 2018, FDA added four tropical diseases to the

[58] See, for example, *Facing 21st Century Public Health Threats: Our Nation's Preparedness and Response Capabilities, Part I*: https://www.fda.gov/NewsEvents/Testimony/ucm592774.htm

[59] See *Fee for Using a Material Threat Medical Countermeasure Priority Review Voucher in Fiscal Year 2018* (82 FR 45859, October 2, 2017).

[60] MCM priority review vouchers issued are listed on this FDA web page: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm566498.htm#prv

list of diseases eligible for a tropical disease PRV, under the previously existing tropical disease PRV program, to encourage drug development in areas of unmet need.[61]

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.[62]

In addition, throughout FY 2018, FDA worked 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 biological, chemical, radiological, or nuclear agent(s), to include other agents that may cause or are otherwise associated with, an imminently life-threatening and specific risk to the U.S. military forces. Leveraging this expanded authority, FDA issued an EUA to allow for the emergency use of a freeze dried plasma product (see page 14) for DoD.

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. For example, FDA and DoD established the DoD-FDA PL 115-92 Chemical MCM Workgroup to support the development of nerve agent auto-injector products for the warfighter.

[61] FDA added Lassa fever, chikungunya virus disease, rabies, and cryptococcal meningitis to the list of diseases eligible for a tropical disease PRV. Viral hemorrhagic fevers including Lassa are Category A high-priority organisms. For more about potential bioterrorism agents by category, see from CDC: https://emergency.cdc.gov/agent/agentlist-category.asp

[62] 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/RegulatoryInformation/Guidances/ucm566474.htm

Professional Development

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 2018, 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 2018 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 response framework for FDA reviewers who are assessing MCM applications. FDA held 9 lectures in this series during FY 2018 with 1,133 attendees, and a total of 88 continuing education (CE) credits.

The MCMi Program trained more than 2,000 FDA staff on MCM-related issues and technologies in FY 2018

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 2 lectures in this series during FY 2018 with 191 attendees, and a total of 11 CE credit hours awarded.

Hot Topics Lecture Series

Hot Topics is a series of timely scientific presentations to help inform FDA staff about technologies and issues that may impact MCM development. These sessions are designed for an FDA audience, including scientists involved in the review of medical product applications, and include a variety of expert speakers from industry, academia, and government. FDA held 5 lectures in this series during FY 2018, with 815 attendees.

Appendix 1: FY 2018 Medical Countermeasure Approvals

Medical Countermeasure[63]	Applicant	Key Dates	Indication
Biologics and Drugs[64]			
ACAM2000 Smallpox (Vaccinia) Vaccine, Live	Sanofi Pasteur Biologics LLC	• Submitted June 6, 2017 • Approved November 22, 2017	BLA supplement to include updates to the package insert and the medication guide with new CDC contact information. (approval letter)
Atropine Auto-Injector (2 mg)	Rafa Laboratories, Ltd.	• Submitted June 27, 2018 • Approved July 9, 2018	For the treatment of poisoning by susceptible organophosphorous nerve agents having cholinesterase activity as well as organophosphorous or carbamate insecticides in adults and pediatric patients weighing over 90 lbs [41 kg] (generally over 10 years of age). (approval letter)
Fluarix Quadrivalent Influenza Virus Vaccine	GlaxoSmithKline Biologicals	• Submitted March 15, 2017 • Approved January 11, 2018	BLA supplement to extend the age range to include children 6 to 35 months of age. (approval letter) *Note: additional BLA supplements for this product were also approved in 2018.*

[63] Includes MCMs approved, licensed, or cleared by FDA in FY 2018 (October 1, 2017 - September 30, 2018).
[64] For products (biologics) regulated by CBER, additional information can be found at: http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm; for products (drugs and biologics) regulated by CDER, additional information can be found at: http://www.accessdata.fda.gov/scripts/cder/daf/

Medical Countermeasure[63]	Applicant	Key Dates	Indication
Flublok Quadrivalent Influenza Vaccine	Protein Sciences Corporation	• Submitted December 19, 2017 • Approved April 4, 2018	BLA supplement to revise the package insert to include revised contact information for adverse event and pregnancy outcome reporting, and for pregnancy registry enrollment. (approval letter)
Flucelvax Quadrivalent Influenza Vaccine	Seqirus, Inc.	• Submitted January 12, 2018 • Approved June 20, 2018	BLA supplement to revise the package insert to comply with the Pregnancy and Lactation Labeling Rule, and to include changes to Section 6 of the package insert based on post-marketing reports. (approval letter)
FluMist Influenza Vaccine Live, Intranasal	MedImmune, LLC	• Submitted November 10, 2017 • Approved May 15, 2018	BLA supplement to revise the package insert to comply with the Pregnancy and Lactation Labeling Rule. (approval letter)
IXIARO, Japanese Encephalitis Virus Vaccine, Purified, Inactivated, Adsorbed	Valneva Austria GmbH	• Submitted June 16, 2017 • Approved April 13, 2018	BLA supplement to include data from studies including a long-term pediatric study, and to approve recommendation of a booster dose at least 11 months after completion of the primary vaccination series for individuals <17 years of age who are at risk of continued exposure or re-exposure to Japanese encephalitis virus. (approval letter)
Seizalam (midazolam injection)	Meridian Medical Technologies, Inc.	• Submitted November 16, 2017 • Approved September 14, 2018	For the treatment of status epilepticus in adults. (approval letter)
TPOXX (tecovirimat)	SIGA Technologies, Inc.	• Submitted December 8, 2017 • Approved July 13, 2018	For the treatment of patients with human smallpox disease caused by variola virus. (approval letter) *Also see: FDA approves the first drug with an indication for treatment of smallpox*

Medical Countermeasure[63]	Applicant	Key Dates	Indication
Devices[65]			
Accula Flu A/Flu B Test	Mesa Biotech, Inc.	• Received June 2, 2017 • Cleared February 6, 2018	New molecular IVD test utilizing PCR and lateral flow technologies for the qualitative, visual detection and differentiation of influenza A and influenza B viral RNA. (decision summary)
Alere BinaxNOW Influenza A & B Card 2, Alere Reader	Alere Scarborough, Inc.	• Received July 11, 2018 • Cleared August 8, 2018	Software modification to mitigate a low-frequency failure mode associated with detectable but not visible dark spots within the Influenza A test line due to non-specific binding. (decision summary)
Alere BinaxNOW Influenza A & B Card 2, Alere Reader, and Alere BinaxNOW Influenza A & B Card 2 Control Swab Kit	Alere Scarborough, Inc.	• Received November 13, 2017 • Cleared December 13, 2017	Software modification to allow the reader to operate in "walk-away" mode. (decision summary)
Alere I Influenza A & B, Alere I Strep A, Alere I RSV, and Alere I Influenza A & B 2	Alere Scarborough, Inc.	• Received December 26, 2017 • Cleared January 26, 2018	Algorithm modification to mitigate issues with false invalid results. (decision summary)
Banyan Brain Trauma Indicator (BTI)	Banyan Biomarkers, Inc.	• Received August 29, 2017 • Cleared February 14, 2018	The first blood test to evaluate mild traumatic brain injury (mTBI), commonly referred to as concussion, in adults. (decision summary)
BD Veritor System for Rapid Detection of Flu A + B CLIA waived kit	BD	• Received February 20, 2018 • Cleared March 20, 2018	Package insert update to add a new performance table and related explanations in the Clinical Performance section. (decision summary)

[65] Additional information about device approvals can be found in Medical Devices Databases: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm, including the 510(k) Premarket Notification Database: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm

Medical Countermeasure[63]	Applicant	Key Dates	Indication
BioSign Flu A+B	Princeton BioMeditech Corp.	• Received August 9, 2018 • Cleared September 18, 2018	Revised package insert to reflect a reorganization of the Clinical Performance section, based on an additional clinical study conducted during the 2017 – 2018 influenza season. (decision summary)
CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel: Influenza B Lineage Genotyping Kit	CDC	• Received July 2, 2018 • Cleared July 30, 2018	Device modification to add three additional options of nucleic acids extraction instrument and extraction method combinations. (decision summary)
cobas Zika, Nucleic acid test for use on the cobas 6800/8800 systems	Roche Molecular Systems, Inc.	• Received April 7, 2017 • October 5, 2017	For the direct detection of Zika virus RNA in human plasma. Intended for use to screen donor samples for Zika virus RNA in plasma samples from individual human donors, including donors of whole blood and blood components, and for use to screen organ and tissue donors when donor samples are obtained while the donor's heart is still beating. (approval letter from CBER) *Also see: FDA approves first test for screening Zika virus in blood donations*
ER-REBOA Catheter	Prytime Medical	• Submitted September 15, 2017 • Cleared November 8, 2017	Modified labeling to remove the pregnancy contraindication, to add a warning to protect the fetus if medical imaging is used, and to address minor clarifications. The ER-REBOA Catheter is intended for temporary occlusion of large vessels and blood pressure monitoring including patients requiring emergency control of hemorrhage. (decision summary)

Medical Countermeasure[63]	Applicant	Key Dates	Indication
FilmArray RP2/RP2plus Control Panel	BioFire Diagnostics, LLC	• Received October 4, 2017 • Cleared November 24, 2017	For the simultaneous qualitative detection and identification of nucleic acids from MERS-CoV and multiple common viral and bacterial respiratory pathogens in nasopharyngeal swabs obtained from individuals meeting MERS-CoV clinical and/or epidemiological criteria. (approval letter)
Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set	CDC	• Received May 7, 2018 • Cleared September 20, 2018	For the *in vitro* qualitative presumptive detection of non-variola orthopoxvirus DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a LRN reference laboratory. The assay detects non-variola orthopoxvirus DNA, including vaccinia, cowpox, monkeypox, and ectromelia viruses at varying concentrations. (decision summary)
Power Infuser	ZOLL Medical Corporation	• Received June 5, 2018 • Cleared July 18, 2018	Made a material change to the tubing used in the Crystalloid/ Colloid Cartridge and Blood Cartridge. The previous material, DEHP Tygon tubing (S-40-HL Manufactured by Saint Gobain) is no longer available. The Power Infuser is intended for continuous or intermittent administration of therapeutic and clinically appropriate intravenous (IV) fluids, blood, and packed red blood cells through clinically acceptable access points, by medical, paramedical and emergency medical personnel (including military) in the field and in pre-hospital and hospital environments. (decision summary)

Medical Countermeasure[63]	Applicant	Key Dates	Indication
QuickVue Influenza A+B	Quidel Corporation	• Received February 5, 2018 • Cleared February 13, 2018	Manufacturing modification to improve product consistency and performance. Updated package insert to add new clinical performance data, remove old data, remove nasal aspirate and nasal wash specimens from the list of claimed upper respiratory specimen types, and add the relevant up-to-date FDA-recommended warning and limitation statements. (decision summary)
RECELL Autologous Cell Harvesting Device	Avita Medical Americas, LLC	• Received September 28, 2017 • Cleared September 20, 2018	For the treatment of acute thermal burn wounds in patients 18 years of age and older. (approval letter from CBER)
Xpert Xpress Flu, Xpert Nasopharyngeal Sample Collection Kit, Xpert Nasal Sample Collection Kit, GeneXpert Xpress II, and GeneXpert Xpress IV	Cepheid	• Received May 26, 2017 • Cleared December 19, 2017	New multiplex nucleic acid assay that detects and differentiates influenza A and influenza B through nucleic acid extraction, amplification, and detection using real-time RT-PCR. (decision summary)
Xpert Xpress Flu/RSV, Xpert Nasopharyngeal Sample Collection Kit, Xpert Nasal Sample Collection Kit, GeneXpert Xpress II, and GeneXpert Xpress IV	Cepheid	• Received January 25, 2018 • Cleared July 24, 2018	New application for a multiplex nucleic acid assay that detects and differentiates influenza A, influenza B and respiratory syncytial virus (RSV) through nucleic acid extraction, amplification, and detection using real-time RT-PCR. (decision summary)

Medical Countermeasure[63]	Applicant	Key Dates	Indication
Xpert Xpress Flu, Xpert Nasopharyngeal Sample Collection Kit, Xpert Nasal Sample Collection Kit, GeneXpert Dx Systems (GX-I, GX-II, GX-IV, GX-XVI), GeneXpert Infinity-48S System, and GeneXpert Infinity-80 System	Cepheid	• Received May 17, 2018 • Cleared August 15, 2018	To implement a new software version, and expand the intended use claim to include nasal swab specimens as an additional cleared specimen type. (decision summary)
XSTAT 30, 1-Pack	RevMedx, Inc.	• Submitted March 1, 2018 • Cleared May 18, 2018	The submission included a change to the XSTAT 30 applicator. XSTAT 30 is an expandable, multi-sponge wound dressing used to control severe, life-threatening bleeding from wounds in areas where a tourniquet cannot be placed (such as the groin or armpit) in battlefield and civilian trauma settings. (decision summary)

Appendix 2: Current Emergency Use Authorizations[66]

Year	MCM	Requester
Anthrax [*Bacillus anthracis*]		Blank
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		Blank
2014[b]	DoD EZ1 Real-time RT-PCR Assay	DoD
2014[c]	CDC Ebola VP40 rRT-PCR Assay	HHS (CDC)
2014[c]	CDC Ebola NP rRT-PCR Assay	HHS (CDC)
2014[c]	BioFire Defense FilmArray NGDS BT-E Assay	BioFire Defense
2014	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
2015[g]	OraQuick Ebola Rapid Antigen Test – whole blood	OraSure Technologies, Inc.
2016[d,g]	OraQuick Ebola Rapid Antigen Test – cadaveric oral fluid	OraSure Technologies, Inc.
2016	Idylla Ebola Virus Triage Test	Biocartis NV
2018	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

[66] Chart is current as of March 25, 2019, including one Ebola EUA issued in FY 2019. View the latest EUAs. Dates listed in this table refer to the calendar year. Chart continues on next page.

Year	MCM	Requester
Enterovirus D68		Blank
2015	CDC Enterovirus D68 2014 Real-time RT-PCR Assay	HHS (CDC)
Zika Virus		Blank
2016[d,e,f]	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[e]	xMAP MultiFLEX Zika RNA Assay	Luminex Corporation
2016[e,f]	ZIKV Detect 2.0 IgM Capture ELISA	InBios International, 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*m*e 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]	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[e]	ADVIA Centaur Zika test	Siemens Healthcare Diagnostics Inc.
2017[f]	DPP Zika IgM Assay System	Chembio Diagnostic Systems, Inc.
Nerve Agents		Blank
2017[e,f]	Atropine Auto-Injector	HHS (CDC)
Freeze Dried Plasma		Blank
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 2018[67]

Date	Guidance Type	Guidance Name	Purpose
October 3, 2017	Final (update)	Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers (PDF, 180 KB)	Provides information for industry, researchers, physicians, institutional review boards (IRBs), and patients about the implementation of FDA's regulation on expanded access to investigational drugs for treatment use under an IND.
October 4, 2017	Final	Guidance for Industry #236 – Clarification of FDA and EPA Jurisdiction over Mosquito-Related Products (PDF, 85 KB)	Provides information on FDA and U.S. Environmental Protection Agency (EPA) jurisdiction over the regulation of mosquito-related products, including those produced through the use of biotechnology. The FDA will continue to have jurisdiction over mosquito-related products that are intended to prevent, treat, mitigate, or cure a disease (including by an intent to reduce the level, replication, or transmissibility of a pathogen in mosquitoes).
October 12, 2017	Draft	Format and Content of a REMS Document (PDF, 166 KB)	Describes a new recommended format for a REMS document, based on extensive stakeholder feedback. On January 29, 2018, FDA also launched a new set of web pages that aims to provide a one-stop source for general information about REMS programs.

[67] 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: https://www.fda.gov/RegulatoryInformation/Guidances/default.htm

Date	Guidance Type	Guidance Name	Purpose
October 25, 2017	Draft	Breakthrough Devices Program (PDF, 257 KB)	This program is intended to help patients have more timely access to devices and breakthrough technologies that provide for more effective treatment or diagnosis for life-threatening or irreversibly debilitating diseases, for which no approved or cleared treatment exists or that offer significant advantages over existing approved or cleared alternatives. This guidance describes the policies that the agency intends to use to implement the program.
October 25, 2017	Final	Deciding When to Submit a 510(k) for a Change to an Existing Device (PDF, 1 MB)	To help manufacturers decide when to submit a new 510(k) for a change to an existing device that was cleared through the 510(k) process or wsa granted a De Novo approval.
October 25, 2017	Final	Deciding When to Submit a 510(k) for a Software Change to an Existing Device (PDF, 585 KB)	To assist industry in determining when a software (including firmware) change to a medical device may require a manufacturer to submit and obtain FDA clearance of a new premarket notification (510(k)).
November 17, 2017	Draft	Expedited Programs for Regenerative Medicine Therapies for Serious Conditions (PDF, 131 KB)	Describes the expedited programs avialable to sponsors of regenerative medicine therapies for serious conditions, under section 506(g) of the Cures Act.
November 28, 2017	Final	Pediatric Information for X-ray Imaging Device Premarket Notifications (PDF, 672 KB)	Outlines the information that should be provided in premarket notification submissions (510(k)s) and device labeling for X-ray imaging devices that are indicated for pediatric populations or general use X-ray imaging devices for which considerable pediatric application is anticipated.
December 5, 2017	Final	Technical Considerations for Additive Manufactured Medical Devices (PDF, 619 KB)	Provides a comprehensive technical framework to advise manufacturers creating medical products on 3D printers. *Also see: Statement by FDA Commissioner Scott Gottlieb, M.D., on FDA ushering in new era of 3D printing of medical products*

Date	Guidance Type	Guidance Name	Purpose
December 8, 2017	Draft	Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act (PDF, 547 KB)	Provides FDA's current thinking regarding the amended device definition (Section 3060(a) of the Cures Act) and the resulting effect the amended definition has on FDA's guidances related to medical device software.
December 8, 2017	Draft	Clinical and Patient Decision Support Software (PDF, 461 KB)	Provides clarity on the scope of FDA's regulatory oversight of (1) clinical decision support software intended for healthcare professionals, and (2) patient decision support software intended for patients and caregivers who are not healthcare professionals.
December 15, 2017	Draft	The Least Burdensome Provisions: Concept and Principles (PDF, 513 KB)	Intended to accurately reflect Congress' intent by describing the guiding principles and recommended approach for FDA staff and industry to facilitate consistent application of least burdensome principles.
December 18, 2017	Draft	Drug Products, Including Biological Products, that Contain Nanomaterials (PDF, 235 KB)	Provides recommendations to industry engaged in developing human drug products in which a nanomaterial is present in the finished dosage form, including recommendations regarding investigational, premarket, and post-market submissions for these products.
December 18, 2017	Draft	Investigational *In Vitro* Diagnostics (IVDs) Used in Clinical Investigations of Therapeutic Products (PDF, 731 KB)	Assists sponsors of clinical investigations of therapeutic products that also include investigational IVDs, and IRBs that review such investigations in complying with the IDE regulation.
December 18, 2017	Draft	Replacement Reagent and Instrument Family Policy for *In Vitro* Diagnostic Devices (PDF, 615 KB)	Updates and clarifies the policy for a manufacturer's application of an assay that was previously cleared for use based on performance characteristics with a specified instrument, to an additional instrument that was previously cleared or that is a member of an instrument family from which another member has been previously cleared.

Date	Guidance Type	Guidance Name	Purpose
December 20, 2017	Final	Medical Device Accessories - Describing Accessories and Classification Pathways (PDF, 449 KB)	Provides guidance about the regulation of accessories to medical devices. This guidance is intended to describe FDA's policy concerning the classification of accessories and to discuss the application of this policy to devices that are commonly used as accessories to other medical devices.
December 22, 2017	Draft	Chemistry, Manufacturing, and Controls (CMC) Changes to an Approved Application: Certain Biological Products (PDF, 252 KB)	Assists applicants and manufacturers of certain licensed biological products in determining which reporting category is appropriate for a change in CMC information to an approved BLA. The updated guidance applies to certain biological products licensed under the PHS Act, including IVDs licensed under BLAs.
December 29, 2017	Final	Best Practices for Communication Between Investigational New Drug Application Sponsors and the Food and Drug Administration (PDF, 191 KB)	Describes best practices and procedures for timely, transparent, and effective communications between IND sponsors and FDA at critical junctures in drug development, which may facilitate earlier availability of safe and effective drugs to the American public. *Also see: FDA In Brief: FDA provides guidance on improving the agency's interactions with product developers to make the drug development process more informed and efficient*
December 29, 2017	Draft	Formal Meetings Between the Food and Drug Administration and Sponsors or Applicants of Prescription Drug User Fee Act Products (PDF, 156 KB)	Provides recommendations to industry on formal meetings between FDA and sponsors or applicants relating to the development and review of drug or biological products.

Date	Guidance Type	Guidance Name	Purpose
January 17, 2018	Draft	Material Threat Medical Countermeasure Priority Review Vouchers (PDF, 174 KB)	The Cures Act established a new PRV program to encourage development of material threat MCMs. This draft guidance explains to internal and external stakeholders how FDA proposes to implement its material threat MCM PRV program. *Also see: FDA In Brief: FDA takes steps to spur development of medical countermeasures needed to protect, prepare for emerging threats to public health and national security*
January 29, 2018	Draft	QIDP Designation Questions and Answers (PDF, 390 KB)	Outlines policies and procedures related to the designation of a qualified infectious disease product (QIDP) under the Generating Antibiotic Incentives Now (GAIN) Act.
February 28, 2018	Draft	Standardization of Data and Documentation Practices for Product Tracing (PDF, 170 KB)	Elaborates on the standards for the interoperable exchange of transaction information, transaction history and transaction statements (product tracing information), as required under the Drug Supply Chain Security Act (DSCSA).
February 28, 2018	Draft	Definitions of Suspect Product and Illegitimate Product for Verification Obligations Under the Drug Supply Chain Security Act (PDF, 283 KB)	Describes the FDA's interpretation of terms used in the definitions of "suspect" and "illegitimate" products in the DSCSA to help trading partners meet their verification obligations, which include notifying the FDA.
April 9, 2018	Draft	Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials (PDF, 90KB)	Discusses the ethical and scientific issues when considering the inclusion of pregnant women in clinical trials of drugs and biological products. This draft guidance is intended to advance scientific research in pregnant women, and discusses issues that should be considered within the framework of human subject protection regulations.

Date	Guidance Type	Guidance Name	Purpose
April 11, 2018	Final	E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population (PDF, 354 KB)	Prepared under the auspices of the International Conference on Harmonisation (ICH), this guidance is an addendum to the guidance published in 2000 entitled E11 Clinical Investigation of Medicinal Products in the Pediatric Population. This addendum complements and provides clarification and current regulatory perspective on topics in pediatric drug development.
April 16, 2018	Final	Special Protocol Assessment (PDF, 182 KB)	Provides information about the procedures and general policies adopted by CDER and CBER for SPA. Several protocols are eligible for SPA, including animal efficacy protocols for studies intended to provide primary evidence of effectiveness required for approval or for licensure for products developed under the Animal Rule. *Also see: FDA In Brief: FDA advances policies to bring greater predictability and certainty to the drug development process*
April 27, 2018	Draft	Multiple Function Device Products: Policy and Considerations (PDF, 472 KB)	Explains FDA's regulatory approach and policy for all multiple function device products. Specifically, this guidance clarifies when and how FDA intends to assess the impact of other functions that are not the subject of a premarket review on the safety and effectiveness of a device function subject to FDA review.
May 2, 2018	Final	Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products (PDF, 86 KB)	Revised guidance for establishments that make donor eligibility determinations for donors of HCT/Ps. This update supports the continuation of recommendations to screen living donors of HCT/Ps for risks of infection with ZIKV based on geographic areas with risk.

Date	Guidance Type	Guidance Name	Purpose
May 17, 2018	Final	Institutional Review Board (IRB) Written Procedures (web link)	FDA and the HHS Office for Human Research Protections issued this joint guidance for institutions and IRBs responsible for the review and oversight of human subject research regulated by the FDA and/or conducted or supported by HHS. The new guidance seeks to clarify requirements, reaffirm important human subject protections, and provide consistent recommendations for institutions and IRBs reviewing and overseeing research involving human subjects. *Also see: FDA In Brief: FDA takes new steps to protect human research subjects in clinical trials by helping to ensure requirements on research institutions are consistently and efficiently applied*
May 24, 2018	Final	Anthrax; Developing Drugs for Prophylaxis of Inhalational Anthrax (PDF, 116 KB)	Assists sponsors in the development of new drugs for the prophylaxis of inhalational anthrax. *Also see: FDA In Brief: As part of a longstanding program encouraging the development of medical countermeasures; new FDA policy promotes innovation to thwart inhalational anthrax*
May 31, 2018	Draft	Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management (PDF, 451 KB)	Encourages companies to use innovative manufacturing technologies and processes, making it easier for them to manage post-approval changes across different global markets by reducing unnecessary regulatory burdens and costs.
May 31, 2018	Draft	Recommended Content and Format of Complete Test Reports for Non-Clinical Bench Performance Testing in Premarket Submissions (PDF, 366 KB)	Describes relevant information that should be included in complete test reports for nonclinical bench performance testing provided in a premarket submission (i.e., PMA applications, humanitarian device exemption (HDE) applications, premarket notification (510(k)) submissions, IDE applications and De Novo requests).
June 5, 2018	Draft	Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products (PDF, 184 KB)	Provides recommendations to industry on formal meetings between FDA and sponsors or applicants relating to the development and review of biosimilar or interchangeable biological products regulated by CDER or CBER, under the Biosimilar User Fee Act (BsUFA).

Date	Guidance Type	Guidance Name	Purpose
June 7, 2018	Draft	Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (PDF, 265 KB)	Explains the ways submitters can request feedback from, or a meeting with, FDA regarding potential or planned medical device or device-led combination product submissions. The FDA Q-Submission Program is a system that tracks different types of requests for feedback from or interaction with FDA regarding planned regulatory submissions as well as requests for certain types of formal designations that are not standalone marketing submissions or research authorizations.
June 12, 2018	Draft	Limited Population Pathway for Antibacterial and Antifungal Drugs (PDF, 128 KB)	Outlines the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD), which is intended to encourage the development of certain antibacterial and antifungal drugs to help address the critical public health and patient care concern that has resulted from the current decline in antibacterial drug research and development as serious antibacterial and antifungal drug-resistant infections increase.
July 6, 2018	Final	Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components (PDF, 222 KB)	Explains that, in order to comply with applicable testing regulations, blood establishments must continue to test all donated whole blood and blood components for Zika virus using a nucleic acid test. The revised guidance explains the basis for the FDA's determination that pooled testing of donations using a screening test licensed for such use by the FDA is a sufficient method for complying with these regulations and effectively reducing the risk of Zika virus transmission, unless there is an increased risk of local mosquito-borne transmission of Zika virus in a specific geographic area that would trigger individual donation testing in that location. Alternatively, blood establishments may use an FDA-approved pathogen-reduction device for plasma and certain platelet products. *Also see: FDA announces revised guidance on the testing of donated blood and blood components for Zika virus*

Date	Guidance Type	Guidance Name	Purpose
July 10, 2018	Revised Draft (Revision 1)	Smallpox (Variola Virus) Infection: Developing Drugs for Treatment or Prevention (PDF, 120 KB)	Assists sponsors in all phases of development of antiviral drugs for the treatment or prevention of smallpox (variola virus) infection. This draft guidance addresses nonclinical development, key study design considerations for animal efficacy studies to support potential NDA/BLA submissions under the Animal Rule, and considerations for obtaining a human safety database.
July 18, 2018	Final	Use of Electronic Health Record Data in Clinical Investigations (PDF, 328 KB)	Intended to assist sponsors, clinical investigators, contract research organizations, IRBs, and other interested parties on the use of electronic health record data in FDA-regulated clinical investigations.
September 6, 2018	Draft	Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions (PDF, 616 KB)	Describes FDA's current approach to considering uncertainty in making benefit-risk determinations to support FDA premarket decisions for medical device PMAs, De Novo requests, and HDE applications.
September 20, 2018	Final	Product Identifier Requirements Under the Drug Supply Chain Security Act-Compliance Policy (PDF, 254 KB)	Describes FDA's intention with regard to enforcement of the DSCSA provision requiring manufacturers to begin affixing or imprinting product identifiers on their products beginning November 27, 2017. *Also see: FDA in Brief: FDA advances policies related to bolstering security of drug products in the U.S. supply chain*
September 20, 2018	Draft	Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers (PDF, 363 KB)	Clarifies questions relating to product identifiers that are required by the FD&C Act, as amended by the DSCSA for packages and homogenous cases of certain drug products.

Date	Guidance Type	Guidance Name	Purpose
September 24, 2018	Final	Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics (PDF, 538 KB)	Promotes consistency, predictability, and transparency in the device submission review process when determining substantial equivalence for devices that have different technological characteristics, which do not raise different questions of safety and effectiveness. *Also see: FDA In Brief: FDA takes new steps to enable innovators to more efficiently advance technological characteristics of certain medical devices while ensuring safety of products*

Appendix 4: Key MCM-Related Meetings Held in FY 2018[68]

Date	Type of Event	Event Name	Purpose
October 4, 2017	Public meeting	Vaccines and Related Biological Products Advisory Committee (VRBPAC) (link)	To discuss and make recommendations on the selection of strains to be included in an influenza virus vaccine for the 2018 southern influenza season.
October 24-25, 2017	Public meeting	National Antimicrobial Resistance Monitoring System (NARMS) (link)	Along with partners CDC and USDA, FDA held a public meeting to summarize NARMS progress since the last public meeting in 2014, present recommendations made by the FDA Science Board review of NARMS in 2017, and to explore new possible directions for NARMS within a One Health paradigm.
November 7, 2017	Public meeting	Vaccines and Related Biological Products Advisory Committee (link)	To discuss and make recommendations on the clinical development plan for Pfizer's investigational *Staphylococcus aureus* vaccine intended for pre-surgical prophylaxis in elective orthopedic surgical populations.
November 8-9, 2017	Public workshop	Immune Globulin (IG) Potency in the 21st Century (link)	To discuss new challenges for Industry to meet U.S. potency requirements for IG products and to identify measures to address these challenges.
November 16, 2017	Public hearing	Devices Referencing Drugs (link)	To discuss a potential approach for premarket review of medical devices intended for a new use with an approved, marketed drug when the sponsor for the approved drug does not wish to pursue or collaborate on the new use.

[68] 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 provided funding to support certain meetings hosted by others (e.g., NASEM).

Date	Type of Event	Event Name	Purpose
November 30 - December 1, 2017	Public meeting	Blood Products Advisory Committee (link)	To discuss topics including strategies to reduce the risk of transfusion-transmitted Zika virus.
December 4, 2017	Public webinar	CDER Small Business and Industry Assistance (CDER SBIA) Webinar - REMS Integration Initiative: An Overview (link)	To discuss the REMS Integration Initiative, introduce the new REMS document template, and provide an update on REMS Structured Product Labeling (SPL) and the REMS@FDA website.
December 5-6, 2017	Public meeting	Enhanced Drug Distribution Security Under the Drug Supply Chain Security Act (DSCSA) (link)	To provide members of the drug distribution supply chain and other interested stakeholders an opportunity to discuss strategies and issues related to the enhanced drug distribution security provisions of the DSCSA.
February 7-8, 2018	Public workshop	Tenth Annual Sentinel Initiative Public Workshop (link)	To bring the stakeholder community together to discuss a variety of topics on active medical product surveillance.
February 12, 2018	Industry day	Biologics Effectiveness and Safety (BEST) Sentinel Initiative Industry Day (link)	To identify vendors that have the capability and capacity to provide large sources of patient data, enhanced tools, and infrastructure to expand and enhance the current post-market surveillance system, and to allow CBER to publicly communicate its requirements and provide an opportunity for vendors to ask questions.
February 28, 2018	Public meeting	Enhanced Drug Distribution Security Under the Drug Supply Chain Security Act (DSCSA) public meeting (link)	To provide members of the drug distribution supply chain and other interested stakeholders an opportunity to discuss strategies and issues related to the enhanced drug distribution security provisions of the DSCSA.
March 1, 2018	Public meeting	Vaccines and Related Biological Products Advisory Committee (link)	To discuss topics including selection of strains to be included in influenza virus vaccines for the 2018-2019 influenza season.

Date	Type of Event	Event Name	Purpose
March 6-7, 2018	Public meeting	Examining the Impact of Real-World Evidence on Medical Product Development: A Workshop Series – Workshop 2: Practical Approaches (link)	To examine how real-world evidence development and uptake can enhance medical product development and evaluation. This second of three related workshops included in-depth audience discussions and active participation that illuminated the types of data that are appropriate for what specific purposes and suggested practical approaches for data collection and evidence use by developing and working through example use cases.
March 20, 2018	Public meeting	Promoting the Use of Complex Innovative Designs (CID) in Clinical Trials (link)	To facilitate discussion and information sharing about the use of CID in drug development and regulatory decision making and obtain input from stakeholders about the CID pilot program.
March 21-22, 2018	Public meeting	Joint Meeting of the Blood Products Advisory Committee and the Microbiology Devices Panel of the Medical Devices Advisory Committee (link)	To discuss items including an overview of research programs of the Laboratory of Emerging Pathogens, the Laboratory of Bacterial and Transmissible Spongiform Encephalopathy Agents, and the Laboratory of Molecular Virology in the Division of Emerging Transfusion-Transmitted Diseases, Office of Blood Research and Review, CBER.
April 16, 2018	Public workshop	Evaluating Inclusion and Exclusion Criteria in Clinical Trials (link)	To discuss a variety of topics related to eligibility criteria in clinical trials, their potential impact on patient access to investigational drugs, and how they might facilitate the enrollment of a diverse patient population. Other topics addressed include alternative clinical trial designs that may increase enrollment of more diverse patient populations, and opportunities for using data from expanded access trials.
April 23, 2018	Public meeting	Science Board to the FDA (link)	To address items including how FDA can leverage its existing tools and authorities, and work with stakeholders, to better address the complex scientific, public health, and technology challenges it faces today.

Date	Type of Event	Event Name	Purpose
April 23-27, 2018	Training course	Achieving Data Quality and Integrity in Maximum Containment Laboratories (link)	FDA-sponsored course offering 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 1, 2018	Public meeting	Antimicrobial Drugs Advisory Committee (link)	To discuss NDA 208627 for tecovirimat, submitted by SIGA Technologies Inc., for the proposed indication of the treatment of smallpox disease caused by variola virus in adults and pediatric patients.
May 8, 2018	Public webinar	CDER SBIA Webinar: Optimizing Your Study Data Submissions to FDA: Office of Vaccines Research and Review (OVRR) Data Submission (link)	To provide an overview of recent updates made to FDA's Study Data Technical Conformance Guide (PDF, 581 KB).
June 22, 2018	Public meeting	Blood Products Advisory Committee (link)	To hear presentations on FDA CBER research programs including the Laboratory of Emerging Pathogens, Laboratory of Bacterial and Transmissible Spongiform Encephalopathy Agents, and Laboratory of Molecular Virology, in the Division of Emerging Transfusion-Transmitted Diseases, Office of Blood Research and Review.
June 25-26, 2018	Public symposium	2018 Center for Biologics Evaluation and Research (CBER) Science Symposium (link)	To discuss scientific topics related to the regulation of biologics, and highlight science conducted at CBER by showcasing how scientific research informs regulatory decision-making. Topics include emerging and re-emerging diseases, and new technologies.
July 17-18, 2018	Public meeting	Examining the Impact of Real-World Evidence on Medical Product Development: Application (link)	To examine how real-world evidence development and uptake can enhance medical product development and evaluation. This third of three related workshops examined and suggested approaches for operationalizing the collection and use of real-world evidence.

Date	Type of Event	Event Name	Purpose
July 18-19, 2018	Public meeting	Blood Products Advisory Committee (link)	To discuss and provide advice regarding bacterial risk control strategies for blood collection establishments and transfusion services to enhance the safety and availability of platelets for transfusion.
July 30-31, 2018	Public workshop	Continuous Manufacturing for the Modernization of Pharmaceutical Production: A Workshop (link)	Hosted by the NASEM Board on Chemical Sciences and Technology, and sponsored by FDA and BARDA, to discuss the business and regulatory concerns associated with adopting continuous manufacturing techniques to produce biologics, such as enzymes, monoclonal antibodies, and vaccines.
August 13-14, 2018	Public meeting	Pediatric Medical Device Development (link)	To identify strategies to enhance the medical device ecosystem to cultivate development and innovation of devices that serve the unique needs of pediatric populations.
August 21-22, 2018	Public workshop	Development of Non-Traditional Therapies for Bacterial Infections (link)	To discuss preclinical development, early stage clinical trials, and phase 3 clinical trial designs to evaluate safety and efficacy of non-traditional therapies intended to serve as primary or adjunctive therapy to existing antibacterial drugs (e.g., preclinical and clinical development of several types of non-traditional therapies, including monoclonal antibodies, immunomodulators, lysins, and other non-traditional therapies).
September 4, 2018	Public hearing	Facilitating Competition and Innovation in the Biological Products Marketplace (link)	To discuss FDA's approach to enhancing competition and innovation in the biological products marketplace, including by facilitating greater availability of biosimilar and interchangeable products.
September 12, 2018	Public hearing	FDA's Predictive Toxicology Roadmap (link)	To obtain comments on how to foster the development and evaluation of emerging toxicological methods and new technologies and incorporate them into regulatory review.

Date	Type of Event	Event Name	Purpose
September 14, 2018	Public workshop	Advancing the Development of Pediatric Therapeutics 5: Advancing Pediatric Pharmacovigilance (link)	To provide a forum to gather information on the latest developments in pediatric pharmacovigilance from the perspective of various stakeholders and to expand the conversation to include the utility and challenges of emerging pharmacovigilance tools, including specific challenges associated with pediatric data tools.

Appendix 5: Acronyms

ADEPT	Autonomous Diagnostics to Enable Prevention and Therapeutics
AMR	Antimicrobial resistance
AR	Antibiotic resistance
ATCC	American Type Culture Collection
ARS	Acute radiation syndrome
ASPR	Assistant Secretary for Preparedness and Response (HHS)
BAA	Broad Agency Announcement
BARDA	Biomedical Advanced Research and Development Authority
BEST	Biologics Effectiveness and Safety
BLA	Biologics License Application
BSL	Biosafety level
BsUFA	Biosimilar User Fee Act
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
CDRH	FDA Center for Devices and Radiological Health
CE	Continuing education
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
CRP	Critical Reagents Program
DARPA	Defense Advanced Research Projects Agency
DHS	U.S. Department of Homeland Security
DNA	Deoxyribonucleic acid
DoD	U.S. Department of Defense
DRC	Democratic Republic of the Congo
DSCSA	Drug Supply Chain Security Act

DTRA	Defense Threat Reduction Agency
DxOD	Diagnostics on Demand
EHT	Emerging health threats
EPA	Environmental Protection Agency
EUA	Emergency Use Authorization
EVD	Ebola virus disease
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
FTE	Full-time equivalent
FY	Fiscal year
GAIN	Generating Antibiotic Incentives Now Act
GHSA	Global Health Security Agenda
GHSI	Global Health Security Initiative
GI-ARS	Gastrointestinal acute radiation syndrome
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
HDE	Humanitarian Device Exemption
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
IG	Immune globulin
IgM	Immunoglobulin M
IHR	International Health Regulations
IND	Investigational New Drug
INTERACT	INitial Targeted Engagement for Regulatory Advice on CBER ProducTs
IRB	Institutional Review Board
IV	Intravenous
IVD	*In vitro* diagnostic
JBAIDS	Joint Biological Agent Identification and Diagnostic System
LLNL	Lawrence Livermore National Laboratory
LPAD	Limited Population Pathway for Antibacterial and Antifungal Drugs
LRN	Laboratory Response Network

MCM	Medical countermeasure
MCM ADM	DoD Medical Countermeasures Advanced Development and Manufacturing
MCMi	FDA Medical Countermeasures Initiative
MDR	Multi-drug resistant
MERS-CoV	Middle East Respiratory Syndrome coronavirus
mg	Milligram
MOU	Memorandum of Understanding
MRA	Mutual Recognition Agreement
mTBI	Mild traumatic brain injury
NACCHO	National Association of County and City Health Officials
NARMS	National Antimicrobial Resistance Monitoring System
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
NICBR	National Interagency Confederation for Biological Research
NIH	U.S. National Institutes of Health
NIIMBL	National Institute for Innovation in Manufacturing Biopharmaceuticals
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
OCET	Office of Counterterrorism and Emerging Threats
OVRR	Office of Vaccines Research and Review
OWH	Office of Women's Health
PAHPA	Pandemic and All-Hazards Preparedness Act
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PCR	Polymerase chain reaction
PDUFA	Prescription Drug User Fee Act
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
PPE	Personal protective equipment
PRV	Priority review voucher

QIDP	Qualified infectious disease product
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
RSV	Respiratory syncytial virus
SBIA	Small Business and Industry Assistance
SLEP	Shelf-Life Extension Program
SLTT	State, local, tribal and territorial
SNS	Strategic National Stockpile
SPA	Special Protocol Assessment
SPL	Structured Product Labeling
TBDWG	Tick-Borne Disease Working Group
TBI	Traumatic brain injury
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
U.S.	United States
USG	United States Government
UTMB	University of Texas Medical Branch
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization
ZIKV	Zika virus

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