FDA Medical Countermeasures Initiative (MCMi)
Protecting National Health and Security

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MCMi Program Update

Fiscal Year 2017

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U.S. FOOD & DRUG
ADMINISTRATION

Message from RADM Denise Hinton, Chief Scientist and Michael Mair, MPH, Acting Assistant Commissioner for Counterterrorism Policy

It is with great pride that we present the Medical Countermeasures Initiative (MCMi) Program Update for Fiscal Year (FY) 2017, which highlights the many notable achievements the Food and Drug Administration (FDA or Agency) has made to advance the development and availability of medical countermeasures (MCMs)—such as drugs, vaccines, and diagnostic tests—to protect the Nation from chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats such as pandemic influenza and Zika Virus.

FY 2017 marked another incredibly active year for FDA under the MCMi Program as part of the Agency's mission to protect and promote public health. These efforts include advancing cutting-edge regulatory science and ensuring that our regulatory processes are as modern and efficient as possible as part of advancing safe and effective MCMs, to using the full breadth of our authorities to enable timely access to available MCMs when they are needed, to supporting the national and international response to the Zika virus epidemic in the Americas, to forging new partnerships to help address global public health preparedness and response challenges.

FDA staff continue to tirelessly work to help protect the Nation from threats we may face

FDA takes seriously our responsibility to help drive and foster innovation as part of protecting public health and national security. The accomplishments over FY 2017—and success in the work that lies ahead—depends on the dedicated staff at FDA who continue to tirelessly work to help protect the Nation from the threats we may face and to promote public health both on the home front and around the world. We are honored to work with such dedicated staff and to share the significant achievements and continued progress the Agency has made in the pursuit of protecting the Nation's health and security.

FY 2018 is already shaping up to be another very active year under the MCMi Program. In January 2018, the Agency launched enhanced engagements with the U.S. Department of Defense (DoD) under a joint program to prioritize the efficient development of safe and effective medical products intended for U.S. military personnel. We are committed to closely working with our colleagues at DoD to support the needs of U.S. military personnel and look forward to continued enhanced collaborations in these important endeavors.

To stay informed of progress under the MCMi throughout the year, sign up to receive email alerts or follow us on Twitter @FDA_MCMi.

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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 assessing 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 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. FDA supports the Enterprise and DoD by providing subject-matter expertise in MCM development and by providing scientific and regulatory input to inform MCM 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]

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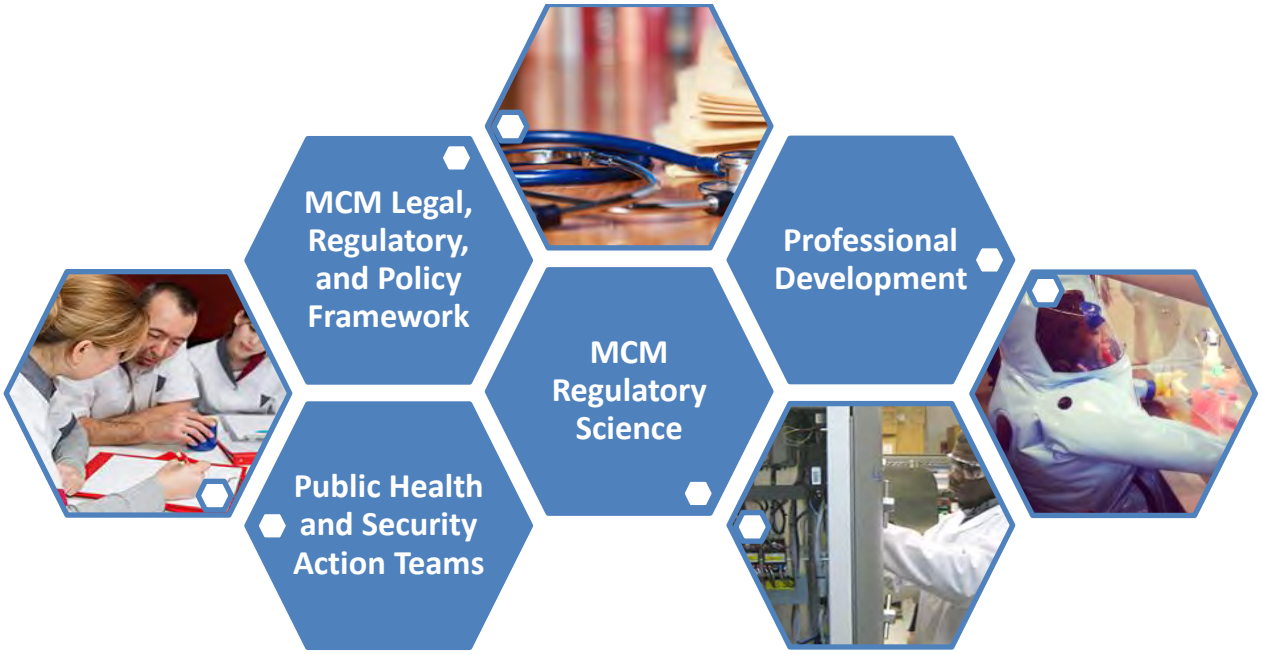
[1] MCMs include qualified countermeasures as defined in section 319F–1(a)(2)(A) of the Public Health Service Act (PHS Act) (42 USC. § 247d–6a(a))(2)(A); qualified pandemic or epidemic products as defined in section 319F–3(i)(7) of the PHS Act (42 USC. § 247d–6d(i)(7)), and security countermeasures as 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. Inclusion of such examples is not intended as comprehensive reporting on Agency activities related to these topics.

[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.

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) 2017.[6]

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

[6] Detailed information on FDA's MCM development and review activities for covering fiscal years 2011-2016 can be found under MCMi Program reports and annual program updates at: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm270744.htm

FY 2017 Resources for Medical Countermeasures Activities

FDA obligated $115.7 million in FY 2017 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 $109.2 million from its FY 2017 base resources to support CBRN and pandemic influenza-related MCM activities. This funding included $48.3 million for CBRN preparedness activities, $36.3 million for pandemic influenza preparedness activities, and $24.6 million for the MCMi Program.

Table 1: FY 2017 resources obligated to MCM activities (dollars in millions)

(blank cell)	FY 17 Actual	FY 17 FTE Actual
CBRN Base Funding	$48.3	226
Pandemic Influenza Base Funding	$36.3	163
MCMi Base Funding	$24.6	81
Subtotal	*$109.2*	*470*
Ebola Supplemental Funding (No-Year)	$2.9	2.1
Emerging Health Threats Funding (No-Year)	$1.8	2.2
Transfer from No-Year HHS Pandemic Influenza Funding	$1.8	0
Total	**$115.7**	**474.3**

This funding supported 470 full-time equivalents (FTEs) as well as a $1.6 million investment in the MCMi Regulatory Science Program.

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 $2.9 million of those funds in FY 2017; this funding supported targeted regulatory science research to support the development and regulatory review of Zika virus MCMs, and 2.1 full-time equivalent FTEs.[7]

[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 and anticipates obligating the remaining $0.5 million in FY 2018.

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 2017 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. This funding supported 2.2 FTEs and $1.2 million in regulatory science research to support emerging threat response activities.

FY 2017 Objectives, Activities, and Achievements

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 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
- ✓ **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 enable 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

Objectives and Activities

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, as well as MCMs to support American military personnel.[8]

The following sections provide detail on achievements in FY 2017 with respect to these activities.

Medical Countermeasure Approvals

During FY 2017, FDA continued to review marketing applications for MCMs against CBRN and emerging infectious disease threats and approve safe and effective medical countermeasures. FDA approved the majority of MCM marketing applications under review[9] in FY 2017 (see **Appendix 1: FY 2017 Medical Countermeasure Approvals**).[10]

With regard to all-hazards preparedness, FDA cleared the Mirragen Advanced Wound Matrix, a product designed to be packed into wounds to control fluid loss, for treatment of acute and chronic wounds.

In the area of MCMs to treat diseases or conditions caused by CBRN threats, FDA approved a Biologics License Application (BLA) supplement for the ACAM2000 Smallpox (Vaccinia) Vaccine, Live, to include additional instructions in the package insert on how to handle the reconstituted vaccine and to change the product labeling in accordance with the guidance for industry, *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex*.[11]

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[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).

[9] "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

[11] This guidance, issued in 2014, is available at: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm342872.pdf

In the area of diagnostics for CBRN threats, FDA granted a request from BioFire Defense, LLC, for the Evaluation of the Automatic Class III Designation for the FilmArray NGDS Warrior Panel, which is the first molecular diagnostic device to assess the presence of *B. anthracis, C. burnetii, F. tularensis, Y. pestis*, Ebola, and Marburg virus DNA directly from sputum or blood collected from patients suspected of exposure to these agents. FDA also approved a U.S. Centers for Disease Control and Prevention (CDC) *Rickettsia* Real-Time PCR Assay intended for the qualitative detection and differentiation of *R. rickettsii* and *R. prowazekii* DNA extracted from the venous whole blood samples of individuals with signs or symptoms of infection and epidemiological risk factors consistent with exposure. FDA also granted a request from the CDC for the Evaluation of Automatic Class III Designation for the Variola virus Real-Time PCR Assay, which is the first molecular assay to assess the presence of Variola virus DNA directly from patient samples. The Variola assay was designed to increase sensitivity and specificity, to replace the Variola virus-specific test previously deployed to Laboratory Response Network (LRN) laboratories. CDC has deployed the assay reagents and verification panels to qualified labs through the LRN, enhancing U.S. government preparedness efforts to quickly detect and respond to a biological attack.

In the area of pandemic influenza preparedness, FDA approved an expanded indication for peramivir injection (Rapivab) to include treatment of children ages 2 years and older with acute uncomplicated influenza, who have been symptomatic for no more than two days. This is the first new influenza antiviral available for children in more than 10 years. FDA also approved expanded indications to extend the age range of use of FluLaval and FluLaval Quadrivalent influenza vaccines to include children 6 to 35 months of age; and to extend the Afluria Quadrivalent influenza vaccine for use in persons 5 years and older. FDA also approved a new indication to include a quadrivalent formulation (Flublok Quadrivalent), for use in persons 18 years of age and older and to include the data from the confirmatory clinical study to verify and describe the clinical benefit of Flublok (trivalent formulation) in persons 50 years of age and older. The FLUARIX quadrivalent influenza vaccine indication was also expanded to include clinical data to support harmonization of the monovalent bulk manufacturing process with the monovalent bulk manufacturing process used for the FLUARIX trivalent influenza vaccine at the company's Dresden manufacturing facility.

FDA also approved nine new influenza tests and approved modifications to four previously approved influenza detection *in vitro* diagnostic (IVD) devices to, for example, include additional specimen types, redesign primers and probes, streamline manufacturing, increase instrument throughput, update the limitations section of the labeling, and revise labeling to add results of testing new strains of influenza viruses. These steps forward in influenza treatments 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.

On January 12, 2017, FDA issued a Final Order reclassifying rapid influenza virus antigen detection test systems intended to detect influenza virus directly from clinical specimens that had been regulated as class I into class II with special controls and into a new device classification regulation. One of the special controls associated with the new regulation is a requirement for manufacturers of these tests to conduct annual reactivity testing with contemporary (circulating) influenza strains. FDA collaborated with CDC to develop a test panel of influenza viruses, which is made available to manufacturers by CDC annually at no cost.

Six additional marketing applications for new MCMs or new MCM indications were under review in FY 2017; 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.[12]

Supporting an Adequate Supply of Medical Countermeasures

FDA continued efforts to support the establishment and sustainment of an adequate supply of MCMs during FY 2017. 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 2017, as a result of SLEP testing that assured drug stability and quality, FDA granted shelf-life extensions for 2,020 lots (batches) of MCM drugs.

Another way FDA worked to ensure an adequate supply of MCMs in FY 2017 was by conducting post-marketing current good manufacturing practices (cGMP) inspections for facilities that

[12] For updated information about MCM approvals after the FY 2017 reporting period, visit the MCMi News and Events page at: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm

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.[13]

To help ensure an adequate supply of MCMs for potential anthrax emergencies, FDA published a draft guidance for government (including state, local, tribal, and territorial (SLTT)) public health and emergency response stakeholders, *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles* (PDF, 226 KB). Issued in April 2017, this document, when finalized, will provide recommendations to government stakeholders on testing (i.e., outside of SLEP) that can be conducted to extend the shelf life (i.e., expiration date) under the FD&C Act of their stockpiled doxycycline tablets and capsules for public health emergency preparedness and response purposes for an anthrax emergency.[14]

In addition, FDA continued efforts to better secure the drug supply chain to protect consumers from counterfeit or substandard drugs, including MCMs. For example, FDA obtained spectral data on foreign-manufactured, FDA-approved MCM drugs and added that information to its spectral library, which will help facilitate the prevention of the introduction of counterfeit or substandard MCM drugs into the supply chain by providing a reference standard.[15]

FDA also works to resolve MCM shortages as quickly as possible when they occur. In FY 2017, 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 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 that U.S. military personnel and first responders continue to have ready access to these products.[16] FDA also provided information (some publicly posted) on such expiry dating extensions to international military and public health partners to assist

[13] 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.

[14] On September 20, 2017, FDA presented a webinar through CDC for stakeholders to discuss drug product expiry date extensions, background for issuing the draft guidance, specific doxycycline products for which the final guidance will apply and recommended protocol for testing, and the process for requesting and receiving an authorized extension from FDA. A recording of this webinar and responses to questions raised during the webinar are available at: https://www.train.org/cdctrain/course/1073481/. The webinar helps to inform development of the final guidance.

[15] Spectral data provides information about the molecular make-up of compounds, such as drugs, and can be used to help identify counterfeit MCMs, or MCMs that do not meet quality objectives.

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

them in their determinations about whether they should extend the shelf life of their stockpiled auto-injector products produced by the same manufacturer. Meanwhile, FDA continued to work with the product manufacturer so production of new product could be resumed.

Enabling Access to Available Medical Countermeasures Under FDA's Emergency Use Authorization Authority[17]

During FY 2017, FDA continued to work with Enterprise partners, including DoD, and product sponsors to enable access to available MCMs when necessary.[18] One way FDA does this is by issuing Emergency Use Authorizations (EUAs), which allow 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 a CBRN agent or agents if certain statutory criteria are met (see **Appendix 2: Current Emergency Use Authorizations** for a list of current EUAs).[19] In FY 2017, FDA issued 8 EUAs for diagnostic tests to detect Zika virus and/or diagnose Zika virus infection (in addition to 12 similar Zika EUAs issued in FY 2016[20]), and granted 16 amendments to address clarifications or updates to the EUA labeling or Fact Sheets for Patients or Health Care Providers or modifications, such as addition of authorized specimen types, extraction methods, and/or detection instruments, that require review of supporting scientific data.

As the result of an extensive and complex multi-year, intra- and inter-agency effort to address manufacturing challenges related to auto-injectors, FDA issued an EUA in FY 2017 enabling the emergency use of an auto-injector MCM to maintain preparedness for chemical threats. This EUA is critical in supporting both American military personnel and first responder preparedness goals for a nerve agent emergency. FDA worked closely with HHS in drafting the HHS Secretary's supporting EUA determination and declaration (which were required for issuance of the EUA), as well as a Public Readiness and Emergency Preparedness (PREP) Act declaration,

[17] Section 564 of the FD&C Act

[18] This support includes numerous activities including availability of pre-IND consultations for drug development proposals, and pre-EUA discussions, if appropriate, when product technology is sufficiently mature and generalizable (and need among potential U.S. users sufficiently widespread) to justify an HHS determination and declaration.

[19] 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.

[20] FDA authorized 20 Zika diagnostic tests for emergency use—14 NAT-based tests to diagnose acute infections and 5 serological tests to assess potential exposure to Zika virus—during FY 2016 and FY 2017. One Zika diagnostic EUA was subsequently revoked by FDA, at the request of the manufacturer. For additional information, see: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm#eua

which provides important liability protections for nerve agent countermeasures. After issuing the EUA and receiving additional data, FDA amended the EUA to authorize use of pediatric strengths.

In addition to issuing EUAs when necessary, FDA has developed a pre-EUA submission process 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.[21] During FY 2017, FDA continued to work with CDC, the Biomedical Advanced Research and Development Authority (BARDA), DoD, and industry on pre-EUA activities for MCMs against a diverse array of threats including smallpox, anthrax, pandemic influenza, Ebola virus, Zika virus, chemical and nuclear threats. For example, during FY 2017 FDA provided feedback to sponsors on 39 pre-EUAs for Zika diagnostic tests.[22]

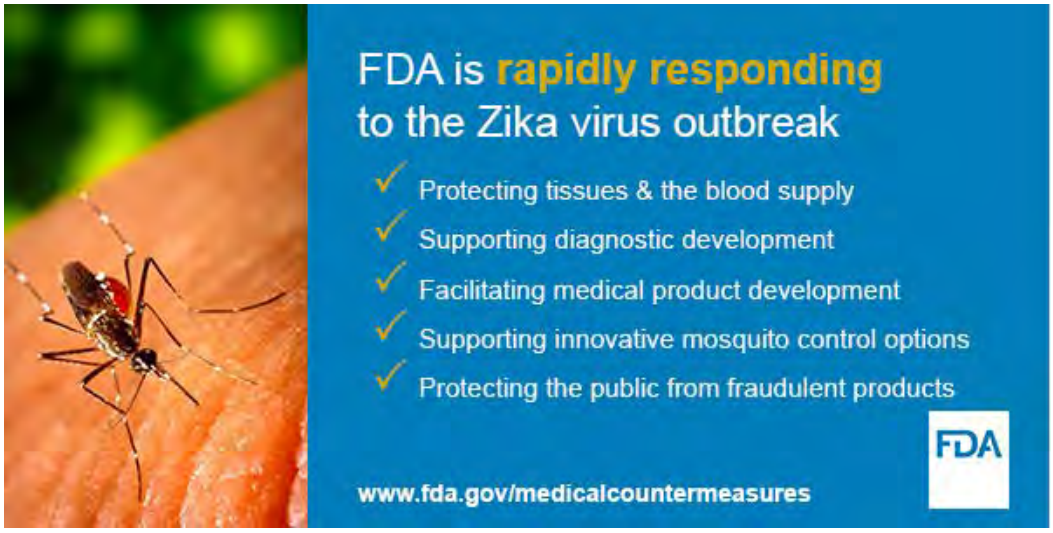
Responding to Emerging Infectious Disease Public Health Threats

In FY 2017, FDA actively supported the national and international response to Zika virus and continued to support the international response to the Ebola epidemic in West Africa.

Throughout the epidemic responses, FDA has worked proactively with U.S. government partners, medical product developers, and international partners (including the World Health Organization (WHO) and international regulatory counterparts) providing scientific and regulatory advice to help facilitate the development and availability of MCMs. For example, during FY 2017, FDA held 8 pre-Investigational New Drug (IND) meetings for Zika vaccines and reviewed 6 Zika vaccine INDs from 13 different sponsors.

[21] 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 in the development of conditions of authorization, fact sheets, and other documentation needed for an EUA in advance of an emergency.

[22] HHS. *Determination and Declaration Regarding Emergency Use of In Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection*. 81 Fed. Reg. 10878 (March 2, 2016). On February 26, 2016, the HHS Secretary determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves Zika virus.



In addition, FDA continued similar activities to respond to the Middle East Respiratory Syndrome coronavirus (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.

Throughout these response activities, FDA has worked to establish and maintain good lines of communication with regulatory authorities in the affected countries to enable technical and information exchange, and to make sure that the needs of the affected countries are understood and addressed.

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/tissue-based products (HCT/Ps) for transplantation, including informing collection establishments of CDC-identified potential increased Zika virus risk to blood and tissue safety in certain U.S. locations
- ✓ Developing **Zika Virus RNA reference materials** that were distributed to manufacturers to validate nucleic acid-based diagnostic tests and blood screening testing methods
- ✓ Making available a **panel** to aid in the regulatory evaluation of serological tests for the detection of recent Zika virus infection
- ✓ Improving FDA's ability to detect performance issues with EUA diagnostic assays by activating a **new mailbox** (CDRH-EUA-Reporting@fda.hhs.gov) that can be used by clinical laboratories that have a concern about the performance of an EUA diagnostic assay to contact FDA directly, in addition to contacting the assay manufacturer
- ✓ Enabling **access to investigational MCMs**—when necessary—through an appropriate mechanism such as under an expanded access protocol or under an EUA, including provisions for access to therapeutics and vaccines during a 2017 Ebola outbreak in the Democratic Republic of the Congo
- ✓ **Issuing EUAs** for diagnostic tests for Zika and EVD and for a treatment against chemical nerve agent threats
- ✓ Addressing issues related to the **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, distribution of misbranded/counterfeit products

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 2017.

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 2017 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-ARGOS), established in FY 2014, through NCBI. A contract was awarded to the Institute of Genomic Sciences at the University of

Maryland to sequence and deposit additional genus-diverse and public health need isolates. Approximately 2,000 isolates will be sequenced as part of the FDA-ARGOS project. This database is being expanded to generate 150 high-quality, nearly complete draft genome sequences of mosquito-borne viral pathogens, including Zika virus sequences.[23] In FY 2017, FDA initiated reference genome sequencing for 25 microbial constituents as part of the FDA-ARGOS project.

- ✓ 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.

- ✓ Continuing collaboration with NIST to 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. Activities this year included the release of four microbial genomic DNA standards, development of mixed-pathogen DNA standard research material, and the Standards for Pathogen Detection for Biosurveillance and Clinical Applications Workshop.

- ✓ 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).

[23] 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 U.S. Army Medical Research Institute of Infectious Diseases (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

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 2017 included:

- ✓ Supporting development of an *ARS Questions and Answers* guidance to help sponsors develop products for ARS indications under the Animal Rule.
- ✓ Facilitating interaction with rad/nuc government funding agencies (NIAID, BARDA, and others) and strengthening FDA rad/nuc preparedness activities.
- ✓ Discussing regulatory strategies for MCM development for radiation-induced coagulopathy, with emphasis on assessing effectiveness.
- ✓ Providing FDA reviewers with training and information on the latest scientific research related to gastrointestinal (GI)-ARS and lung-ARS to enable appropriate regulatory decisions.

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 2017 activities included:

- ✓ Meeting with the U.S. Army Medical Research and Materiel Command (MRMC), the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD), and the Defense Threat Reduction Agency (DTRA) to discuss regulatory and scientific issues.
- ✓ 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.[24]
- ✓ Establishing 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. This program has begun, and two DoD laboratory experts are currently being cross-trained in regulatory review at FDA.

[24] 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).

- ✓ Providing technical assistance to the Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) effort to support DoD's acquisition and fielding of a clinical test and evaluation capability for development of therapeutic MCMs being developed by DoD.

- ✓ Responding to DoD questions concerning use of the approved MCM nerve agent pretreatment pyridostigmine bromide.

- ✓ Working closely with DoD staff to develop and execute a scientific meeting to discuss the state of the science of oxygen carrier products, and ensuring that relevant FDA blood product experts participated in discussions. The Oxygen Carrier State of the Science Meeting was held February 6-8, 2017.

Regulatory Advice and Guidance

During FY 2017, 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 the *Federal Register* of March 11, 2015 (80 FR 12822), FDA published a notice announcing the availability of a draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (Revision 2). The revised draft guidance updates the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants* (Revision 1) and, when finalized, will represent the Agency's current thinking on the

topic.[25] Formal meetings are held—as needed—at the request of a product sponsor or applicant, and requests for meetings are granted unless there is a substantive reason for denying the request (e.g., the product for which the meeting is requested is not sufficiently developed to warrant the type of meeting sought).[26] 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,[27] and a Special Protocol Assessment meeting[28]).

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)/Biologics License Application (BLA) meetings). 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 draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (PDF, 156 KB), issued in December 2017.

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-Prescription Drug User Fee Act (PDUFA) meetings such as meetings on a sponsor's compliance status or follow-up on post-marketing commitments.

[25] See for example, *Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* 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* available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

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

[27] 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.

[28] For more information on Special Protocol Assessments see *Draft Guidance for Industry – Special Protocol Assessment* available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm498793.pdf

In FY 2017, CBER held 40 formal meetings with MCM sponsors or applicants (including one Pre-Submission meeting), and CDER held 40 formal meetings (Table 2) and 5 other (non-PDUFA) meetings.

Table 2: FY 2017 formal meetings between CBER/CDER and MCM sponsors or applicants

Meeting Type	CBER	CDER
Type A	2	1
Type B	24	11
Type C	13	28
Total	**39**	**40**

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.

Table 3: FY 2017 formal meetings between CDRH and MCM sponsors or applicants*

Meeting Type	CDRH
Pre-Submission	15
Submission	0
Total	**15**

**The number of formal meetings included in this table does not include most Zika-related meetings, such as pre-EUA meetings.*

CDRH reviewed 23 Pre-subs and 29 Submissions (marketing applications) for MCM medical devices in FY 2017. 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 were 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 2017, CDRH provided written feedback for 23 MCM Pre-subs or Submission applications and held 15 formal Pre-sub and 0 formal Submission meetings with MCM sponsors or applicants (Table 3).

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.[29] In FY 2017, CDRH reviewed and provided written feedback on 41 pre-EUAs and 9 EUAs and held 36 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 product sponsor or applicant can be delineated.[30] FDA did not receive any written RMP requests in FY 2017.

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

In addition to its direct work with MCM sponsors and applicants, FDA also issues guidance documents that help foster MCM development and availability.[31] Guidance documents issued during FY 2017 directly related or applicable to MCMs policies or regulatory issues are listed in **Appendix 3: MCM-Related Guidance Issued in FY 2017**. FDA held webinars for industry to discuss many of the guidance documents issued in FY 2017, including a 2017 FDA/CDC webinar on extending expiration dates of stockpiled doxycycline for anthrax preparedness.[32]

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 2017 are listed in **Appendix 4: Key MCM-Related Meetings Held in FY 2017**. In addition to these FDA-hosted meetings, FDA

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[29] 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

[30] 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.

[31] Guidance documents are documents prepared for FDA staff, applicants/sponsors, 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))

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

experts continued to participate in and present at a wide variety of other meetings, workshops, and conferences. [33,34]

Collaborations

During FY 2017, FDA continued to collaborate extensively with Enterprise and DoD partners to foster the development and availability of MCMs. FDA provided subject matter expertise and technical assistance to 66 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.[35]

As just one example of interagency collaboration with DoD, FDA participated in the Military Health System Research Symposium in August 2017. For this annual event, FDA provides expert speakers on topics including traumatic brain injury, digital health, physiological monitoring, and the regulatory review process for MCMs, to help facilitate interagency coordination.

FDA continued to work with SLTT public health authorities and responders and public health 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.[36] FDA continues to participate in multiple national-level workshops and meetings on legal preparedness. For example, FDA continues to sustain support for and participate in:

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

[34] 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

[35] In FY 2017, FDA created a new web page about MCM monitoring and assessment activities, available at: https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm561377.htm

[36] For a list of MCM-related legal and policy presentations, publications and Q&As, see http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411508.htm

- ✓ The annual Public Health Preparedness Summit convened by the National Association of County and City Health Officials (NACCHO)

- ✓ The NASEM Health and Medicine Division 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

Several key collaborations in FY 2017 include:

- ✓ Reaffirming an MOU with DARPA to promote collaboration and provide a mechanism for sharing certain non-public information[37]
- ✓ Signing an MOU with the Bill and Melinda Gates Foundation, 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 development, including MCMs[38]
- ✓ With NIH, creating a template to help facilitate the regulatory review process for NIH-funded clinical trial protocols. This template will help investigators prepare protocols that contain all the information necessary to enable efficient and timely review by Institutional Review Boards (IRB) as well as comply with FDA regulations.

In addition to working with federal, SLTT and non-government organizations (NGOs), FDA continued to work with international partners such as WHO to foster the development and availability of MCMs.

Agreements established in FY 2017 (and in previous years) between FDA and its international counterparts have helped information-sharing and collaboration, and have better prepared the international regulatory community to respond to future public health emergencies. In August 2017, FDA signed a new commitment allowing FDA and the European Commission's Directorate-General for Health and Food Safety (DG SANTE) and the European Medicines Agency (EMA) to share full inspection reports as part of cooperative law enforcement or cooperative regulatory activities.[39]

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[37] This MOU was signed June 1, 2017, replacing a previous agreement signed in 2012.
[38] This MOU was signed June 27, 2017.
[39] The reciprocal confidentiality commitments, which benefit a wide range of FDA operations potentially including MCMs, were signed on August 23, 2017, and are available at: https://www.fda.gov/InternationalPrograms/Agreements/ConfidentialityCommitments/ucm573683.htm and https://www.fda.gov/InternationalPrograms/Agreements/ConfidentialityCommitments/ucm573684.htm

Additional 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 and strategy, as well as other HHS-led efforts related to global MCM polices. For example, in FY 2017, FDA participated in the International Health Regulations (IHR) (2005) Joint External Evaluation of the United States, a voluntary, collaborative process to assess a country's capacity under the IHR to prevent, detect, and rapidly respond to public health threats whether occurring naturally or due to deliberate or accidental events.

- ✓ Implementing CBER-WHO Cooperative Agreements[40] to advance global access to safe and effective vaccines and build capacities for the import, registration, and emergency use of prequalified MCMs.

- ✓ 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 that allows the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large-scale crisis

    - Coalition for Epidemic Preparedness Innovations (CEPI) - CEPI is an innovative partnership between public, private, philanthropic and civil organizations that aims to stop future epidemics by developing new vaccines

[40] 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

- 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 between regulatory agencies to encourage submission of regulatory dossiers and evaluation of the submitted information on potential new medicines to address emerging public health threats

Medical Countermeasure Regulatory Science

In FY 2017, 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.[41]

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

[41] 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. For example, studies with organs-on-chips are not considered adequate replacement for animal efficacy studies required under the Animal Rule.

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.

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 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).[42]

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.

[42] 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 biomarkers to evaluate products for safety and efficacy, and using protein engineering to stabilize vaccine proteins)
- ✓ Developing **methods to assess MCM product quality** and related product release assays
- ✓ Validating **NGS-based IVD platforms**
- ✓ Assessing the **performance** of emergency medical equipment
- ✓ 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
- ✓ Supporting regulatory science research in response to **public health emergencies** including the Ebola epidemic in West Africa, and the Zika outbreak in multiple countries (including the U.S. and its territories), to help expedite the development and availability of medical products to treat, prevent, and detect these viruses (for example: genome sequencing; developing and validating assays, reference materials, and biomarkers; conducting nonclinical testing; developing animal models; supporting field laboratory testing; and studying antibody responses)

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.[43] To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with U.S. government (USG) MCM priorities, FDA established a Steering Committee for

[43] 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 (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

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 in a timely manner.

FY 2017 MCMi Regulatory Science program activities are included in **Table 4**.

Table 4: MCMi Regulatory Science Program activities in FY 2017

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
Developing assays that can detect low levels of botulism neurotoxin in food
Examining the utility of thermal processes for inactivating *Staphylococcal* enterotoxin B in milk
Testing and comparing how effective different antibiotics are against melioidosis acquired by different routes of exposure
Providing recommendations for radiation biodosimetry device pre-EUA submissions
Emerging Threats (e.g., Ebola and Zika)[44]
Expanding a database of reference-grade nucleic acid sequences to include antimicrobial-resistant organisms as well as Ebola- and Zika-related sequences
Developing and validating assays for Ebola that can be utilized outside of specialized, high-containment Biosafety Level 4 (BSL-4) laboratories
Developing Zika virus RNA reference materials that were distributed to manufacturers to validate nucleic acid based diagnostic tests and blood screening testing methods
Making available a Zika serological reference panel to aid in the regulatory evaluation of serological tests for the specific detection of recent Zika virus infection
Providing Zika test developers with study recommendations for Zika nucleic acid-based diagnostic tests and Zika serological assay Pre-Market submissions
Continuing the development of improved small animal models for Ebola and Zika

[44] Also see a regulatory science poster, Strengthening Regulatory Science to Support Development and Approval of Medical Countermeasures for Ebola, presented at the Hemorrhagic Fever Viruses conference in Santa Fe, NM in December 2016, available at: https://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/UCM532855.pdf

Table 4: MCMi Regulatory Science Program activities in FY 2017

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
Evaluating alternative garment testing methods that may predict Ebola penetration without use of live Ebola virus and high-containment facilities
Developing a toolkit to assess efficacy of Ebola vaccines and therapeutics
Supporting field laboratory testing of Ebola antibodies in Sierra Leone
Conducting survivor studies to better understand Ebola's after-effects, to help find new treatments; in September 2017, FDA modified this contract to apply the technology used for the Ebola project to gather critical information about the nature of Zika virus infection
Sponsoring nonclinical research studies to help inform FDA recommendations regarding potential transmission of Zika virus via organs and tissues[45]
Identifying target peptide sequences for a Zika immunoglobulin M (IgM) diagnostic device
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[46]
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
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
Developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during a public health emergency through a collaboration with the United States Critical Illness and Injury Trials Group (USCIITG) and critical care physicians at 20 hospitals throughout the United States

[45] Two awards were made in FY 2016 (a contract and a grant); work began in FY 2017.
[46] The MCMi Program awarded a contract to complete this work in FY 2017.

Table 4: MCMi Regulatory Science Program activities in FY 2017

Developing phantom-based test methods for evaluation of near-infrared diagnostic devices for traumatic brain injury (TBI) and cerebral monitoring
Developing techniques for the preclinical evaluation of physiological closed-loop controlled supportive therapy devices, particularly related to the computational patient model
Developing ways to leverage the FDA Sentinel Initiative infrastructure for monitoring and assessment of MCMs by evaluating the Sentinel System capability to collect and analyze MCM data and determining the utility of administrative and claims data in assessing MCM safety and effectiveness
Developing an FDA/CDC antimicrobial resistant isolates 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

FDA also expanded and sustained MCM regulatory science collaborations in FY 2017. For example, FDA:

- ✓ Sponsored the fifth 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.[47]

- ✓ 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.

- ✓ Established and continued to expand a publicly available, well-curated reference database of regulatory-grade microbial sequences from diverse microorganisms. This database, FDA-ARGOS, will be critical to developers seeking to validate their candidate high-throughput sequencing-based IVD assays. The FDA-ARGOS database was expanded to include Ebola-related sequences in 2015 and Zika-related sequences in 2016.

- ✓ 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.

- ✓ Collaborated with NIST to produce sequence-based microbial challenge materials for diagnostic tests; two clinical (CDRH FDA-ARGOS) and two environmental (FDA Center for Food Safety and Nutrition (CFSAN)) isolates were selected, sourced, and advanced to the NIST reference material production pipeline.

[47] Also see a poster, Measuring the Success of the UTMB-FDA Course: Achieving Data Quality and Integrity in Maximum Containment Laboratories, presented at the Military Health System Research Symposium in August 2017 in Kissimmee, FL, available at: https://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/UCM576389.pdf

Ensure that U.S. laws, regulations, and policies help support preparedness and response for potential CBRN and emerging disease threats

Medical Countermeasure Regulatory Policy

During FY 2017, FDA continued efforts to ensure that the FDA regulatory and policy framework enables the application of advances in regulatory science to the regulatory review process and adequately support 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 2017, 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 and/or providing policy subject matter input to FDA MCM-related collaborations

- ✓ Clarifying regulatory issues around building frameworks for conducting clinical studies during public health emergencies

FDA 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 personal protective equipment 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
- ✓ Establishing an FDA training program to, among other things, support training for MCM development
- ✓ Working with CDC and the Centers for Medicare and Medicaid Services (CMS) to better coordinate the implementation of EUA *in vitro* diagnostic assays by providing strategy, oversight, and technical advice
- ✓ Identifying and developing new legislative proposals in anticipation of the reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA)
- ✓ Leading development of or providing policy input to MCM-related guidance documents issued in FY 2017 (**Appendix 3: MCM-Related Guidance Issued in FY 2017**) and key meetings and workshops (**Appendix 4: Key MCM-Related Meetings Held in FY 2017**)

Among the key MCM-related guidance documents listed in **Appendix 3**, two in particular reflect FDA policy recommendations related to implementation of FDA's MCM emergency use authorities:

- ✓ FDA finalized the guidance *Emergency Use Authorization of Medical Products and Related Authorities.*[48] This guidance informs industry and government sponsors and other stakeholders of FDA's general recommendations and procedures for issuance of EUAs under section 564 of the FD&C Act, implementation of the emergency use authorities in section 564B of the FD&C Act, and reliance on the governmental pre-positioning authority in section 564B of the FD&C Act.

- ✓ FDA published a draft guidance for government, including SLTT public health and emergency response stakeholders, *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles* (PDF, 226 KB). This guidance, when finalized, will support stockpile management efforts, using section 564A(b) of the FD&C Act. See page 8 for additional information.

During FY 2017, FDA worked to implement several MCM-related provisions of the 21st Century Cures Act (Cures Act), which was signed into law on December 13, 2016. Many provisions of the law will facilitate development of MCMs. FDA is implementing three provisions in particular 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. (Also see **Table 5: Implementation of FDA MCM Cures Act provisions in FY 2017**.)

[48] The draft guidance was made available for public comment in April 2016, and was finalized in January 2017, replacing the previous guidance, *Emergency Use Authorization of Medical Products* (July 2007) and *Emergency Use Authorization Questions and Answers* (April 2009). View the guidance at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm

Table 5: Implementation of FDA MCM Cures Act provisions in FY 2017

- ✓ The Cures Act, section 3024, provides enhanced flexibility to conduct minimal risk research in support of product development, by allowing FDA to implement the waiver or alteration of informed consent, including appropriate safeguards to protect the rights, safety, and welfare of human subjects. This action will harmonize with the HHS "Common Rule."[49] This provision was enacted to, among other things, facilitate the conduct of minimal risk studies to advance the development of certain MCMs (e.g., devices under development by the DoD intended to improve combat casualty care).
    - FDA published document for immediate implementation on July 25, 2017, entitled *IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects*. This guidance informs sponsors, investigators, and IRBs that FDA does not intend to object to an IRB waiving or altering informed consent for certain minimal risk clinical investigations when appropriate human subject protection safeguards are met. FDA is currently drafting rulemaking that will codify this provision. We intend to withdraw the guidance when the final rule becomes effective.
- ✓ The Cures Act expanded FDA's MCM emergency use authorities to: (1) allow FDA to authorize emergency use of (i.e., issue EUAs for) unapproved animal drugs or unapproved uses of approved animal drugs under section 564; (2) make applicable other MCM emergency use authorities under section 564A to approved animal drugs; and (3) allow unapproved animal drugs to be held for emergency use under section 564B. In January 2017, FDA's guidance, *Emergency Use Authorization of Medical Products and Related Authorities*, explained that the emergency use authorities and guidance recommendations are now applicable to animal drugs and encouraged interested parties to contact FDA to discuss implementation questions.
- ✓ The Cures Act makes provisions for awarding priority review vouchers (PRVs) that meet the criteria specified by the FD&C Act. 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. FDA issued this draft guidance (PDF, 148 KB) in January 2018. On October 2, 2017 FDA issued a notice establishing the user fees for MCM PRVs .[50]

[49] HHS's *Federal Policy for the Protection of Human Subjects* (56 FR 28001, June 18, 1991) is referred to as the "Common Rule." The Common Rule sets forth requirements for the protection of human subjects involved in research that is conducted or supported by HHS (see 45 CFR 46, Subpart A) and 15 other federal departments and agencies.

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

Develop and maintain a highly qualified MCM workforce to meet the regulatory challenges posed by new science and technology

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.

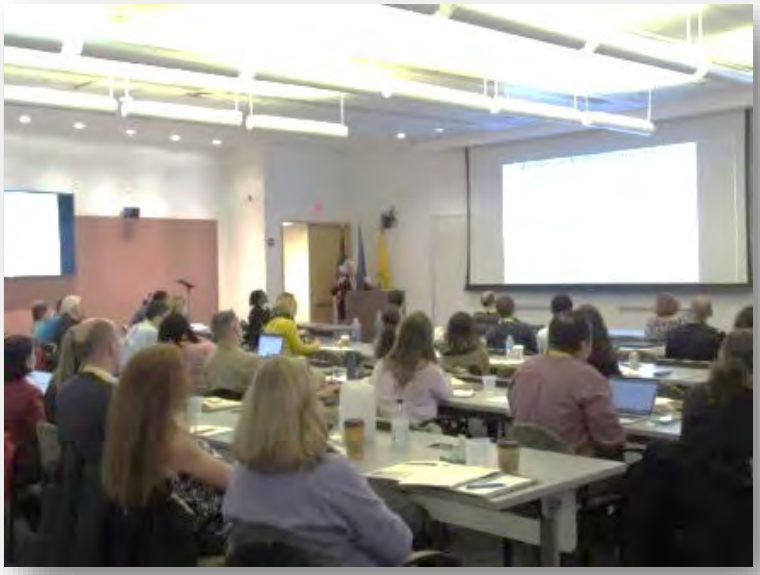
In FY 2017, FDA began efforts to launch a new program designed to train recent pre- and post-doctoral scientists and physicians in research disciplines relevant to FDA's mission. Although the traineeship program is not limited to traineeships involving MCMs, it advances MCMi Program goals to improve and advance MCM science and train reviewers in MCM review processes.

Additional key activities in FY 2017 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 6 lectures in this series during FY 2017 with 337 attendees, 93 of whom received continuing education (CE) credits.

- ✓ **Foundations for Preclinical Review Lecture Series:** These lectures focus on preclinical scientific and technical issues of importance to MCMs, since many MCMs are developed under the Animal Rule. Presentations are designed to educate researchers and reviewers on issues of humane animal care and reproducibility. Speakers include internal and external experts in the field. FDA held 6 lectures in this series during FY 2017 with 330 attendees, 12 of whom received CE credits.

- ✓ **Hot Topics Lecture Series:** Hot Topics is a series of timely scientific presentations and discussions 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 9 lectures in this series during FY 2017, with 1,833 attendees.



WHAT ARE MEDICAL COUNTERMEASURES?

FDA-REGULATED MEDICAL PRODUCTS

Medical countermeasures, or MCMs, are FDA-regulated products that may be used in a PUBLIC HEALTH EMERGENCY stemming from a terrorist attack with or accidental release of a biological, chemical, or radiological/nuclear agent, or a naturally occurring emerging infectious disease.

MCMs

PREVENT
PROTECT AGAINST
TREAT OR
DIAGNOSE

DISEASES OR HEALTH EFFECTS CAUSED BY

CBRN

THREAT AGENTS

CHEMICAL
BIOLOGICAL
RADIOLOGICAL
NUCLEAR

& EMERGING INFECTIOUS DISEASES

EXAMPLES of MCMs

BIOLOGIC PRODUCTS

- Vaccines
- Blood products
- Antibodies

DRUGS

- Antimicrobials
- Chemical threat antidotes
- Treatments for radiation injury

DEVICES

- Diagnostic tests
- Personal protective equipment (PPE)

→ Gloves
→ Respirators/masks
→ Gowns

(continues on next page)

FDA's MCM ROLES [some examples]

FDA IS RESPONSIBLE FOR ASSESSING
SAFETY &
EFFECTIVENESS
OF MCMs
FOR FDA APPROVAL

ACTIVITIES INCLUDE:
- → Review evidence for approval
- → Regulatory science
- → Policy & legal support
- → Professional development

FDA WORKS WITH PARTNERS TO ADVANCE
DEVELOPMENT &
AVAILABILITY
OF MCMs

- → Governments (state, local, territorial, tribal, national, international)
- → Domestic & international organizations
- → Medical & scientific community
- → Industry

+ PHEMCE Public Health Emergency Medical Countermeasures Enterprise (Federal agencies)

TO **PREPARE** FOR & **RESPOND** TO **EMERGING THREATS**

121 **MCMs APPROVED** SINCE 2012*

60+ EUAs SINCE 2005

FDA CAN ISSUE
EMERGENCY USE AUTHORIZATIONS
TO ENABLE **ACCESS** TO MCMs PRIOR TO APPROVAL
(OR FOR UNAPPROVED USES)

FDA ALSO HAS OTHER LEGAL AUTHORITIES TO FACILITATE EMERGENCY ACCESS TO MCMs

FDA MEDICAL COUNTERMEASURES INITIATIVE (MCMi)

MCMi is an FDA-WIDE initiative across FDA product centers (including CBER, CDER, and CDRH) and offices to coordinate MCM development, preparedness, and response, led by the Office of Counterterrorism and Emerging Threats, in the Office of the Chief Scientist.

? LEARN MORE OR ASK US

www.fda.gov/medicalcountermeasures

AskMCMi@fda.hhs.gov

FDA U.S. FOOD & DRUG ADMINISTRATION

*Number includes approved MCMs listed in the MCMi annual program update in fiscal years 2012-2017

Appendix 1: FY 2017 Medical Countermeasure Approvals

Medical Countermeasure[51]	Applicant	Key Dates	Indication
Biologics and Drugs[52]			
ACAM2000 Smallpox (Vaccinia) Vaccine, Live	Sanofi Pasteur Biologics LLC	• Submitted November 3, 2016 • Approved May 2, 2017	BLA supplement to include additional instructions in the package insert on how to handle the reconstituted vaccine and to change the product labeling in accordance with the guidance for industry, *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex*. (approval letter)
AFLURIA; Afluria Quadrivalent Influenza Vaccine	Seqirus Pty Ltd.	• Submitted October 31, 2016 • Approved August 31, 2017	Expanded to extend the indication for use in persons 5 years and older. (approval letter)
FLUARIX; FLUARIX Quadrivalent Influenza Vaccine	GlaxoSmithKline Biologicals	• Submitted January 21, 2016 • Approved November 18, 2016	Label expanded to include clinical data to support harmonization of the monovalent bulk manufacturing process at the company's Dresden manufacturing facility. (approval letter)
Flublok Influenza Vaccine	Protein Sciences Corporation	• Submitted December 8, 2015 • Approved October 7, 2016	New indication to include a quadrivalent formulation (Flublok Quadrivalent), for use in persons 18 years of age and older and to include the data from the confirmatory clinical study to verify and describe the clinical benefit of Flublok (trivalent formulation) in person 50 years of age and older. (approval letter)

[51] Includes MCMs approved, licensed, or cleared by FDA in FY 2017 (October 1, 2016 - September 30, 2017).
[52] 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[51]	Applicant	Key Dates	Indication
FluLaval; FluLaval Quadrivalent Influenza Vaccine	ID Biomedical Corporation of Quebec	• Submitted January 27, 2016 • Approved November 18, 2016	Extended the age range of use of FluLaval and FluLaval Quadrivalent to include children 6 to 35 months of age. (approval letter)
Peramivir injection (Rapivab)	BioCryst Pharmaceuticals, Inc.	• Submitted March 24, 2017 • Approved September 20, 2017	Expanded indication to include treatment of children ages 2 years and older with acute uncomplicated influenza, who have been symptomatic for no more than 2 days. (approval letter)
Devices[53]			
3C Patch System	Reapplix ApS	• Received January 3, 2017 • Cleared April 3, 2017	Peripheral blood processing device for wound management. (approval letter from CBER)
FilmArray NGDS Warrior Panel	BioFire Defense, LLC	• Received March 24, 2017 • Cleared June 22, 2017	The first molecular assay to assess the presence of *B. anthracis, C. burnetii, F. tularensis, Y. pestis*, Ebola and Marburg virus DNA directly from sputum or blood collected from patients suspected of exposure to these agents.
FilmArray Respiratory Panel EZ	BioFire Diagnostics LLC	• Received September 10, 2015 • Cleared October 3, 2016	The device is intended for use in detecting 11 viral and three bacterial pathogens associated with respiratory infections from a single patient sample. Clinical trials that were used to gain 510(k) clearance were supported by DTRA.
Mirragen Advanced Wound Matrix	Engineered Tissue Solutions, Inc.	• Received April 15, 2016 • Cleared September 15, 2016	Designed to be packed into wounds to control wound fluids, the device consists of a fully resorbable borate glass matrix comprised of fibers and beads for treatment of acute and chronic wounds.

[53] 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[51]	Applicant	Key Dates	Indication
Rickettsia Real-time PCR Assay	CDC	• Received March 30, 2017 • Cleared June 29, 2017	For the qualitative detection and differentiation of *R. rickettsii* and *R. prowazekii* DNA extracted from the venous whole blood samples of individuals with signs or symptoms of infection and epidemiological risk factors consistent with exposure.
Variola Virus Real-time PCR Assay	CDC	• Received April 14, 2016 • Cleared February 6, 2017	For the qualitative detection of Variola virus DNA in pustular or vesicular clinical specimens collected from individuals with high suspicion of smallpox (based on CDC criteria).
Various Alere influenza assays • Alere i Influenza A&B • Alere i influenza A&B Control Swab Kit • Alere i Instrument	Alere Scarborough, Inc.	• Received November 21, 2016 • Cleared December 21, 2016	For the qualitative detection and discrimination of influenza A and B viral RNA in direct nasal swabs and nasal or nasopharyngeal swabs eluted in viral transport media from patients with signs and symptoms of respiratory infection, in conjunction with clinical and epidemiological risk factors.
Various CDC influenza assays • CDC Human Influenza Virus Real-time RT-PCR Diagnostic Panel • Influenza A/B Typing Kit • CDC Human Influenza Virus Real-time RT-PCR Diagnostic Panel • Influenza A Subtyping Kit • CDC Human Influenza Virus Real-time RT-PCR • Influenza B Lineage Genotyping Kit • CDC Human Influenza Virus Real-time RT-PCR	CDC	• Received July 11, 2017 • Cleared August 9, 2017	For qualitative detection of influenza virus type A or B viral RNA in upper respiratory tract clinical specimens from human patients with signs and symptoms of respiratory infection and/or from viral culture; determination of the subtype of seasonal human influenza A viruses; determination of the genetic lineage of human influenza B viruses; and presumptive identification of virus in patients who may be infected with influenza A subtype A(H5) (Asian lineage).

Medical Countermeasure[51]	Applicant	Key Dates	Indication
Xpert Xpress Flu assay	Cepheid	• Submitted September 2, 2016 • Cleared February 13, 2017	For the *in vitro* qualitative detection and differentiation of influenza A and influenza B viral RNA, using nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection, in conjunction with clinical and epidemiological risk factors.
Xpert Xpress Flu/RSV	Cepheid	• Submitted August 19, 2016 • Cleared February 9, 2017	For the *in vitro* qualitative detection and differentiation of influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA, using nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection, in conjunction with clinical and epidemiological risk factors.

Appendix 2: Current Emergency Use Authorizations[54]

Year	MCM	Requester
Anthrax [*Bacillus anthracis*]		
2008	Doxycycline hyclate 100 mg oral tablets (in National Postal Model home & workplace kits)	HHS (ASPR/BARDA)
2011[a]	All oral formulations of doxycycline (mass dispensing)	HHS (CDC)
Novel Influenza A (H7N9) Virus		
2013[f]	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	HHS (CDC)
2014	Lyra Influenza A Subtype H7N9 Assay	Quidel Corporation
2014	A/H7N9 Influenza Rapid Test	Arbor Vita Corporation
Middle East Respiratory Syndrome Coronavirus [MERS-CoV]		
2013[b]	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	HHS (CDC)
2015[d]	RealStar MERS-CoV RT-PCR Kit U.S.	altona Diagnostics GmbH
Ebola Virus		
2014[b]	DoD EZ1 Real-time RT-PCR Assay	DoD
2014[c]	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	OraQuick Ebola Rapid Antigen Test – whole blood	OraSure Technologies, Inc.
2016 [d]	OraQuick Ebola Rapid Antigen Test – cadaveric oral fluid	OraSure Technologies, Inc.
2016	Idylla Ebola Virus Triage Test	Biocartis NV

[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

(continues on next page)

[54] Chart is current as of May 24, 2018, including EUAs issued in FY 2018. View the latest EUAs.

Year	MCM	Requester
Enterovirus D68		
2015	CDC Enterovirus D68 2014 Real-time RT-PCR Assay	HHS (CDC)
Zika Virus		
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*me* ZIKA	Abbott Molecular, Inc.
2016	Zika ELITe MGB Kit U.S.	ELITechGroup Inc. Molecular Diagnostics
2017	Gene-RADAR Zika Virus Test	Nanobiosym Diagnostics, Inc.
2017	LIAISON XL Zika Capture IgM Assay	DiaSorin Incorporated
2017	TaqPath Zika Virus Kit	Thermo Fisher Scientific
2017	CII-ArboViroPlex rRT-PCR Assay	Columbia University
2017	ADVIA Centaur Zika test	Siemens Healthcare Diagnostics Inc.
2017[f]	DPP Zika IgM Assay System	Chembio Diagnostic Systems, Inc.
Nerve Agents		
2017[e,f]	Atropine Auto-Injector	Rafa Laboratories Ltd.

[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

Appendix 3: MCM-Related Guidance Issued in FY 2017

Date	Guidance Type	Guidance Name	Purpose
December 9, 2016	Final	Drug Supply Chain Security Act Implementation: Identification of Suspect Product and Notification (PDF, 146 KB)	To aid certain trading partners in identifying a suspect product and specific scenarios that could significantly increase the risk of a suspect product entering the pharmaceutical distribution supply chain
December 28, 2016	Final	Postmarket Management of Cybersecurity in Medical Devices (PDF, 1.2 MB)	To inform industry and FDA staff of the Agency's recommendations for managing postmarket cybersecurity vulnerabilities for marketed and distributed medical devices
January 10, 2017	Final	Recommendations for Assessment of Blood Donor Eligibility, Donor Deferral and Blood Product Management in Response to Ebola Virus (PDF, 99 KB)	Notifies blood establishments that FDA has determined Ebola virus to be a transfusion-transmitted infection (TTI) and provides blood establishments that collect blood and blood components for transfusion or further manufacture, including source plasma, with FDA recommendations for assessing blood donor eligibility, donor deferral, and blood product management in the event that an outbreak of Ebola virus disease (EVD) with widespread transmission is declared in at least one country

Date	Guidance Type	Guidance Name	Purpose
January 13, 2017	Final	Emergency Use Authorization of Medical Products and Related Authorities (PDF, 288 KB)	Explains FDA's general recommendations and procedures applicable to the authorization of the emergency use of certain medical products under sections 564, 564A, and 564B of the FD&C Act as amended or added by PAHPRA. Replaces two previous guidance documents: Emergency Use Authorization of Medical Products (July 2007) and Emergency Use Authorization Questions and Answers (April 2009)
January 18, 2017	Draft	Considerations in Demonstrating Interchangeability With a Reference Product Guidance for Industry (PDF, 229 KB)	To assist sponsors in demonstrating that a proposed therapeutic protein product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under section 351(k) of the PHS Act
January 19, 2017	Draft	Regulation of Intentionally Altered Genomic DNA in Animals (PDF, 200 KB)	To clarify FDA's approach to the regulation of intentionally altered genomic DNA in animals, including animals produced through the use of genome editing and genetic engineering (e.g., to help suppress the population of virus-carrying mosquitoes)
January 19, 2017	Draft	Regulation of Mosquito-Related Products (PDF, 74 KB)	Clarifies which mosquito-related products FDA regulates and which such products the Environmental Protection Agency (EPA) regulates, regardless of whether these mosquito-related products are developed using biotechnology

Date	Guidance Type	Guidance Name	Purpose
April 25, 2017	Draft	Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles (PDF, 226 KB)	Provides guidance to government public health and emergency response stakeholders on testing to extend the shelf life (i.e., expiration date) under the FD&C Act of stockpiled doxycycline tablets and capsules for public health emergency preparedness and response purposes for an anthrax emergency
June 30, 2017	Draft	Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy (PDF, 101 KB)	Informs manufacturers and other supply chain stakeholders that although manufacturers are to begin including a product identifier on prescription drug packages and cases on November 27, 2017, the FDA is delaying enforcement of those requirements until November 2018 to provide manufacturers additional time and avoid supply disruptions
July 25, 2017	Final	Institutional Review Board (IRB) Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects (PDF, 218 KB)	Informs sponsors, investigators, IRBs, and other interested parties that FDA does not intend to object to an IRB waiving or altering informed consent requirements, as described in the guidance, for certain minimal risk clinical investigations. In addition, this guidance explains that FDA does not intend to object to a sponsor initiating, or an investigator conducting, a minimal risk clinical investigation for which an IRB waives or alters the informed consent requirements as described in the guidance

Date	Guidance Type	Guidance Name	Purpose
August 2, 2017	Final	Antibacterial Therapies for Patients With an Unmet Medical Need for the Treatment of Serious Bacterial Diseases (PDF, 149 KB)	To assist sponsors in the clinical development of new antibacterial drugs. Specifically, the guidance explains FDA's current thinking about possible streamlined development programs and clinical trial designs for antibacterial drugs to treat serious bacterial diseases in patients with an unmet medical need, including antibacterial drugs that are pathogen-focused
August 9, 2017	Final	Qualification of Medical Device Development Tools - Guidance for Industry, Tool Developers, and Food and Drug Administration Staff (PDF, 174 KB)	Formalizes the Medical Device Development Tools (MDDT) program, which FDA launched as a pilot in 2013. Provides guidance on a voluntary program for qualification of MDDTs for use in evaluating devices subject to regulation by CDRH, to facilitate development and timely evaluation of medical devices by providing a more efficient and predictable means for collecting the necessary information to support regulatory submissions and associated decision-making
August 31, 2017	Final	Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices (PDF, 492 KB)	To clarify how FDA evaluates real-world data to determine whether they are sufficient for generating the types of real-world evidence that can be used in FDA regulatory decision-making for medical devices
September 21, 2017	Draft	Statistical Approaches to Evaluate Analytical Similarity (PDF, 125 KB)	To provide advice on the evaluation of analytical similarity to sponsors interested in developing biosimilar products for licensure under section 351(k) of the PHS Act

Date	Guidance Type	Guidance Name	Purpose
September 25, 2017	Final	Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs (PDF, 118 KB)	Issued by FDA and the HHS Office for Human Research Protections (OHRP) to assist institutions and IRBs in preparing and maintaining minutes of IRB meetings that meet the regulatory requirements for minutes set forth in FDA and HHS regulations. The guidance also provides general recommendations on the type and amount of information to be included in the minutes
September 29, 2017	Final	Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization (PDF, 71 KB)	Provides recommendations to pharmaceutical companies interested in participating in a program involving the submission of chemistry, manufacturing, and controls (CMC) information containing emerging technology to FDA. For purposes of this guidance, emerging technology should be novel in the context of the pharmaceutical and related industries, with the potential to modernize the pharmaceutical manufacturing body of knowledge related to product quality

Appendix 4: Key MCM-Related Meetings Held in FY 2017

Date	Type of Event	Event Name	Purpose
October 14, 2016	Public meeting	Progress Toward Implementing the Product Identification Requirements of the Drug Supply Chain Security Act (DSCSA) (link)	Provided members of the pharmaceutical distribution supply chain and other interested stakeholders an opportunity to share information with FDA about the efforts under way to implement the DSCSA's product identification requirements
November 7-9, 2016	Training course	Clinical Investigator Training Course (link)	Co-sponsored by FDA and University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI), an intensive, three-day course to train clinical investigators in all aspects of clinical studies: preclinical and clinical science, statistical structure of trials, ethical requirements, and regulatory considerations, help foster communication between clinical investigators and FDA, and enhance investigators' understanding of FDA's role in experimental medicine
November 8, 2016	Public workshop	Workshop on Promoting Semantic Interoperability of Laboratory Data (link)	Hosted by FDA, CDC, the National Library of Medicine (NLM) of the NIH, the Office of the National Coordinator for Health Information Technology (ONC), and the Centers for Medicare and Medicaid Services (CMS), to receive and discuss input from stakeholders regarding proposed approaches to facilitate the adoption and implementation of interoperability standards in a manner that enables consistent, accurate, and harmonized descriptions of *in vitro* diagnostic tests and results
November 9-10, 2016	Public hearing	Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (link)	To obtain comments on FDA's regulation of firms' communications about medical products, with a particular focus on firms' communications about unapproved uses of their approved/cleared medical products

Date	Type of Event	Event Name	Purpose
November 17-18, 2016	Public meeting	Blood Products Advisory Committee (link)	The committee met in open session to hear an informational session on Zika virus and blood safety in the United States
December 5, 2016	Public workshop	The Role of Hospitals in Modernizing Evidence Generation for Device Evaluation: Harnessing the Digital Revolution for Surveillance (link)	To explore the critical role of hospitals in the evolution of device surveillance and in creating more robust surveillance capabilities
December 7, 2016	Public workshop	The Sentinel Post-Licensure Rapid Immunization Safety Monitoring (PRISM) System (link)	To describe the Sentinel Initiative and PRISM program, illustrate how PRISM is used by FDA for regulatory responsibilities, and discuss the future direction of PRISM in terms of expansion and further integration into the regulatory review process
February 2, 2017	Public workshop	Ninth Annual Sentinel Initiative Public Workshop (link)	To bring together leading experts and interested stakeholders to discuss the ongoing development of the FDA's Sentinel Initiative, which aims to use electronic health care data for post-market risk identification and analysis of medical product safety
February 8-9, 2017	Public workshop	Identification and Characterization of the Infectious Disease Risks of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps) (link)	To have a scientific discussion of the current methods available for identifying and characterizing infectious disease risks associated with HCT/Ps

Date	Type of Event	Event Name	Purpose
March 1, 2017	Public workshop	Current State and Further Development of Animal Models of Serious Infections Caused by *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (link)	To facilitate the development of narrow-spectrum antibacterial drugs, such as those that are active against only a single species of bacteria that may not occur frequently. When the species occurs infrequently, performing clinical trials can be extremely challenging. Therefore, animal models of infection may be useful to explore the activity of a candidate antibacterial drug and may help to predict whether the drug will be efficacious in humans
March 22, 2017	Public meeting	Improving Efficiency of Public Health Emergency Response Meeting	Meeting organized by the Association of Public Health Laboratories (APHL) to engage CDC, CMS, FDA, and APHL members in a collaborative discussion on approaches to improve the effectiveness of emergency mechanisms and to create appropriate flexibilities for public health laboratories complying with Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulation during a public health emergency to better ensure a coordinated and efficient public health response. In the future, this meeting will be held annually
April 6, 2017	Public workshop	Emerging Tick-Borne Diseases and Blood Safety (link)	To discuss tick-borne pathogens that continue to emerge as threats to blood safety, the effectiveness of current and potential mitigation strategies, and the general approach to decision making on blood safety interventions
April 13, 2017	Public meeting	Antimicrobial Drugs Advisory Committee (link)	To discuss the development of antibacterial drugs that treat a single species of bacteria when the target species infrequently causes infections; examples of such drugs include those that are only active against *P. aeruginosa* or *A. baumanni*
April 13, 2017	Public lecture	Zika Virus Vaccines and Therapeutics (link)	Public learning opportunity, presented as part of the FDA and University of Maryland CERSI lecture series

Date	Type of Event	Event Name	Purpose
April 24-28, 2017	Training course	Achieving Data Quality and Integrity in Maximum Containment Laboratories (link)	FDA and UTMB collaborate to provide an annual training course on how to meet good laboratory practice (GLP) requirements in high and maximum biocontainment security level laboratory facilities
May 17-19, 2017	WHO consultation	Consultation on Options to Improve Regulatory Preparedness to address Public Health Emergencies	To determine needs for further development of the Emergency Use Approval and Listing mechanisms[55] established through the WHO prequalification programme, and to develop consensus on options to improve regulatory preparedness to address public health emergencies and agreement on tools to be developed, used and promoted by WHO to assist member states
May 18-19, 2017	Public workshop	Cybersecurity of Medical Devices: A Regulatory Science Gap Analysis (link)	Hosted by FDA, the National Science Foundation (NSF) and DHS Science and Technology, to examine opportunities for FDA engagement with new and ongoing research, catalyze collaboration among health care and public health stakeholders to identify regulatory science challenges, discuss innovative strategies to address those challenges, and encourage proactive development of analytical tools, processes, and best practices by the stakeholder community to strengthen medical device cybersecurity
May 31 – June 1, 2017	Public meeting	FDA Science Forum (link)	To highlight the breadth and depth of cutting-edge science FDA conducts and demonstrate how FDA's scientific research informs regulatory decision-making. The Forum included MCM-related sessions

[55] For more information, see *Emergency Use Assessment and Listing Procedure (EUAL) for candidate medicines for use in the context of a public health emergency*, at: http://www.who.int/medicines/news/EUAL-medicines_7July2015_MS.pdf?ua=1

Date	Type of Event	Event Name	Purpose
June 6-7, 2017	Public workshop	Building a National Capability to Monitor and Assess Medical Countermeasure Use in Response to Public Health Emergencies (link)	Hosted by NASEM-HMD, with funding from FDA, to discuss the roles and efforts of the federal government and relevant stakeholders who have an interest in building and maintaining a national MCM monitoring and assessment (M&A) capability for public health emergencies; discuss federal M&A efforts and opportunities for future work in areas including electronic health record capabilities, big data, clinical networks, and operations for response; and help inform the development of strategic MCM M&A plans for public health emergencies
July 10, 2017	Training course	Sentinel Training at FDA (link)	To provide an overview of data that are and are not available in the Sentinel Distributed Database, the Sentinel Common Data Model, and a description of the distributed tools available to work with the data. This seminar will help those in attendance understand the kinds of questions that can be asked using health care claims data generally and within the Sentinel System specifically
July 10-11, 2017	Public workshop	Bacteriophage Therapy: Scientific and Regulatory Issues (link)	Hosted by FDA and NIH/NIAID, to exchange information with the medical and scientific community about the regulatory and scientific issues associated with bacteriophage therapy
August 15-16, 2017	Public workshop	NIST-FDA-DHS Standards for Pathogen Detection for Biosurveillance and Clinical Applications Workshop (link)	To present state-of-the-art pathogen detection technologies, primarily related to sequencing, emphasizing the need for standards relevant to the clinical diagnostic and biothreat detection stakeholder communities
August 23, 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

Date	Type of Event	Event Name	Purpose
September 8, 2017	Public workshop	Pediatric Trial Design and Modeling: Moving into the Next Decade (link)	To review current best practices in designing pediatric drug development trials using the knowledge and tools available; discuss problems and potential solutions presently encountered with pediatric drug development trials; and discuss strategies related to design and evaluation that have the best chance of facilitating and optimizing the use of pediatric drug development trials to achieve the labeling of products for pediatric indications
September 13, 2017	Public workshop	A Framework for Regulatory Use of Real-World Evidence (RWE) (link)	To discuss a variety of topics related to the use of real-world data and evidence in drug development and regulatory decision-making, including an update on FDA's implementation of the Cures Act's provisions related to RWE and the development of a framework for tackling challenges related to RWE's regulatory acceptability
September 13, 2017	Public workshop	Antimicrobial Susceptibility and Resistance: Addressing Challenges of Diagnostic Devices (link)	To discuss scientific and regulatory challenges associated with the efficient development of traditional devices for antimicrobial susceptibility testing (AST) and molecular or novel diagnostic technologies for the detection of antimicrobial resistance markers. Specifically, this workshop addressed the new regulatory solutions to some of these challenges created by the Cures Act

Date	Type of Event	Event Name	Purpose
September 20, 2017	Training event	Extending Expiration Dates of Stockpiled Doxycycline: Overview of FDA Guidance Webcast (link – free account may be required to view)	Hosted by FDA and CDC's Division of Strategic National Stockpile, for federal, state, and local government public health and emergency response stakeholders, non-governmental organizations, and laboratory representatives who have an interest in the process for extending the shelf life of stockpiled doxycycline for anthrax preparedness, to discuss drug product expiry date extensions, background for issuing the draft guidance, specific doxycycline products for which the guidance applies and recommended protocol for testing, and the process for requesting and receiving an authorized extension from FDA

Appendix 5: Acronyms

ADEPT	Autonomous Diagnostics to Enable Prevention and Therapeutics
AMR	Antimicrobial resistance
APEC	Asia Pacific Economic Cooperation
APHL	Association of Public Health Laboratories
ATCC	American Type Culture Collection
ARS	Acute radiation syndrome
ASPR	Assistant Secretary for Preparedness and Response (HHS)
AST	Antimicrobial susceptibility test
BARDA	Biomedical Advanced Research and Development Authority
BLA	Biologics License Application
BSL	Biosafety level
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
CERSI	Center of Excellence in Regulatory Science and Innovation
CFSAN	FDA Center for Food Safety and Nutrition
cGMP	Current good manufacturing practices
CFR	Code of Federal Regulations
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
DG SANTE	Directorate-General for Health and Food Safety (European Commission)
DHS	U.S. Department of Homeland Security
DNA	Deoxyribonucleic acid
DoD	U.S. Department of Defense
DSCSA	Drug Supply Chain Security Act
DTRA	Defense Threat Reduction Agency
DxOD	Diagnostics on Demand
EHT	Emerging Health Threats
EID	Emerging infectious disease
EMA	European Medicines Agency
EPA	Environmental Protection Agency

EUA	Emergency Use Authorization
EUAL	Emergency Use Assessment and Listing (a World Health Organization procedure)
EVD	Ebola virus disease
FDA	U.S. Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA-ARGOS	FDA dAtabase for Regulatory Grade micrObial Sequences
FTE	Full-time equivalent
FY	Fiscal year
GHSA	Global Health Security Agenda
GI-ARS	Gastrointestinal acute radiation syndrome
GloPID-R	Global Research Collaboration for Infectious Diseases Preparedness
GLP	Good laboratory practices
HCT/P	Human cells, tissues, and cellular and tissue-based products
HHS	U.S. Department of Health and Human Services
ICMRA	International Coalition of Medicines Regulatory Authorities
IDE	Investigational Device Exemption
IHR	International Health Regulations
IND	Investigational New Drug
IRB	Institutional Review Board
IVD	*In vitro* diagnostic
JBAIDS	Joint Biological Agent Identification and Diagnostic System
JEE	Joint External Evaluation
JMEDICC	Joint Mobile Emerging Disease Intervention Clinical Capability
JPEO-CBD	Joint Program Executive Office for Chemical and Biological Defense
LLNL	Lawrence Livermore National Laboratory
LRN	Laboratory Response Network
M&A	Monitoring and assessment
MCM	Medical countermeasure
MCMi	FDA Medical Countermeasures Initiative
MDDT	Medical Device Development Tools program
MDR	Multi-drug-resistant
MERS-CoV	Middle East Respiratory Syndrome coronavirus
MOU	Memorandum of Understanding
MRMC	U.S. Army Medical Research and Materiel Command
NACCHO	National Association of County and City Health Officials
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
NIST	National Institute of Standards and Technology
NLM	National Library of Medicine
NSF	National Science Foundation
OHRP	Office for Human Research Protections (HHS)
ONC	Office of the National Coordinator for Health Information Technology
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
PEP	Post-exposure prophylaxis
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS Act	Public Health Service Act
PMA	Premarket Approval
PRISM	Post-Licensure Rapid Immunization Safety Monitoring
PRV	Priority review voucher
Rad/nuc	Radiological/nuclear
RAPID	Real-Time Application for Portable Interactive Devices
REMS	Risk Evaluation and Mitigation Strategies
RMP	Regulatory Management Plan
RWE	Real-world evidence
SLEP	Shelf-Life Extension Program
SLTT	State, local, tribal and territorial
SNS	Strategic National Stockpile
TBI	Traumatic brain injury
TTI	Transfusion-transmitted infection
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
USCIITG	United States Critical Illness and Injury Trials Group
USG	United States Government
UTMB	University of Texas Medical Branch
WHO	World Health Organization

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