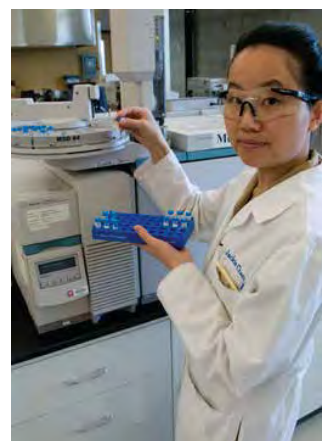


FDA Medical Countermeasures Initiative (MCMi)
Protecting National Health and Security

www.fda.gov/medicalcountermeasures

MCMi Program Update

Fiscal Year 2015



**U.S. FOOD & DRUG
ADMINISTRATION**

Message from Luciana Borio, MD, Acting Chief Scientist, and RADM Carmen T. Maher, MA, BSN, RN, RAC, Acting Assistant Commissioner for Counterterrorism Policy

We are pleased to present the Food and Drug Administration (FDA) Medical Countermeasures Initiative (MCMi) program update for our fifth year of operations.¹ As we have since MCMi was launched in 2010, FDA continues our ongoing work to advance the development and availability of medical countermeasures to protect against chemical, biological, radiological, and nuclear (CBRN) threats. This report covers these activities including medical countermeasure (MCM)-related regulatory science and legal and policy actions.

In August 2015, a delegation from the U.S. government, including representatives from FDA, the National Institutes of Health, and the Biomedical Advanced Research and Development Authority, met in Liberia with representatives from Guinea, Liberia, Sierra Leone, Ivory Coast, Mali, and the World Health Organization, to advance the fight against Ebola. We were honored to be accompanied on this trip by a dedicated FDA cross-agency team.

We were impressed by the commitment of meeting participants and inspired by the individuals running the clinical trials for Ebola vaccines, the common protocol study of Ebola therapeutics, and a study of Ebola survivors. The toll of the disease was evident from both a human and economic perspective—one healthcare worker explained his personal commitment to vaccine development as a result of losing 13 of his family members.

Defeating this epidemic is an achievement that was made possible by the tremendous hard work, dedication, and unprecedented collaboration of multiple partners across the public and private sectors, supporting the heroic efforts of committed individuals from the affected countries.

However, this will not be the final chapter in the fight against Ebola. We will continue to fight long after the epidemic in West Africa has receded into history. The Ebola epidemic has changed the landscape for global cooperation in the fight against emerging infectious diseases. FDA recognizes that we have a critical role in this new paradigm, and also recognizes the essential role effective regulation plays in the clinical development of medical products needed to respond to emerging threats.

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¹ Fiscal year 2015 covers the period from October 1, 2014, to September 30, 2015.



We also continue to respond to emerging public health threats in an unprecedented way. The tragic Ebola epidemic in West Africa was declared over in early 2016. But we can't lose momentum, especially when it comes to supporting development and testing of new products to combat emerging infectious diseases. And we are not— the FDA has a critical role in helping to facilitate the development, and availability of investigational products for use against emerging infectious diseases. We are committed to working with the global community as we collaborate to rapidly respond to emerging threats, including the current outbreak of Zika virus.²

² For more information about FDA's Zika virus response updates, visit:
<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm>



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FDA's Medical Countermeasures Initiative

Fiscal Year 2015 Program Update

Background

The U.S. Food and Drug Administration (FDA) plays a [critical role](#) in protecting the United States from chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats such as pandemic influenza and Ebola virus disease (EVD). 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.³

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 respond effectively to public health emergencies.⁴ 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 the warfighter. 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.^{5,6}

In 2010, FDA launched its [Medical Countermeasures Initiative](#) (MCMi), 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

³ Medical countermeasures (MCMs) include qualified countermeasures as defined in section 319F–1(a) of the Public Health Service Act (42 USC. § 247d–6a(a)); qualified pandemic or epidemic products as defined in section 319F–3 of the Public Health Service Act (PHS Act) (42 USC. § 247d–6d)), and security countermeasures as defined in section 319F–2(c)(1)(B) of the PHS Act (42 USC § 247d–6b). Some items included in this report, such as traumatic brain injury diagnostics, may not meet the statutory definition of MCMs.

⁴ 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 of Preparedness and Response 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 Department of Defense (DoD), the Department of Veterans Affairs, and the Department of Agriculture.

⁵ See e.g., sections 561 and 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

⁶ For purposes of this document, “approved” refers to “FDA-approved, licensed, or cleared” under sections 505, 510(k), or 515 of the Federal Food, Drug, and Cosmetic Act or of section 351 of the PHS Act.



effective regulatory policies and mechanisms to facilitate timely access to available MCMs, and advancing MCM regulatory science to create the tools that support regulatory decision-making.

In 2013, the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 ([PAHPRA](#)) was enacted.⁷ PAHPRA contains key legal authorities to strengthen the United States' 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 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) 2015.⁸

FY 2015 Medical Countermeasure Resources

FDA obligated \$129.7 million in FY 2015 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 \$112.3 million from its FY 2015 base resources to support CBRN and pandemic influenza-related MCM activities. This funding included \$52.0 million for CBRN preparedness activities, \$35.7 million for pandemic influenza preparedness activities, and \$24.6 million for the MCMi.

Table 1: FY 2015 Resources Obligated to Medical Countermeasure Activities (dollars in millions)		
	FY 15 Actual	FY 15 FTE Actual
CBRN Base Funding	\$52.0	229
Pandemic Influenza Base Funding	\$35.7	158
MCMi Base Funding	\$24.6	80.5
\$170 Million No-Year MCMi Funding	\$6.1	0
Subtotal	\$118.4	467.5
Ebola Supplemental Funding (No-Year)	\$11.3	16.8
Total	\$129.7	484.3

This funding supported 467.5 full-time equivalents (FTEs) as well as a \$1.6 million investment in the MCMi Regulatory Science Program.

⁷ Public Law 113-5, 127 Stat. 161.

⁸ Detailed information on FDA's MCM development and review activities in FY 2011, FY 2012, FY 2013 and FY 2014 can be found in the *MCMi Year 1 Status Report*, *MCMi Year 2 Program Update*, *MCMi Fiscal Year 2013 Program Update*, and *MCMi Fiscal Year 2014 Program Update*, available at <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm270744.htm>



No-Year Funding

FDA received \$170 million, one-time funding from HHS to commence MCMi activities at the end of FY 2010 when the MCMi was launched. In FY 2015, FDA obligated the remaining \$6.2 million of the no-year funding to support MCMi activities.⁹ This funding supported regulatory science projects and infrastructure for the MCMi Regulatory Science Program and other non-payroll MCMi costs (e.g., professional development).

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 spent \$11.3 million of this funding in FY 2015 and anticipates expending the remaining \$13.7 million balance by the end of FY 2016. This funding supported 16.8 FTEs as well as a \$6.9 million investment in regulatory science research to support Ebola response activities.

FY 2015 Objectives, Activities, and Achievements

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 development of and access to safe, effective, and quality MCMs to counter high-priority CBRN and emerging infectious disease threats, as well as MCMs to support the warfighter. FDA pursues this objective through a variety of activities including:

- Providing regulatory advice, guidance, and technical assistance to sponsors developing investigational MCMs for CBRN or emerging threat indications, to help clarify requirements for approval
- Reviewing MCM marketing applications and approving those that meet standards for safety, efficacy, and quality
- 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 mechanism

⁹ FDA expended \$49.5 million of the \$170 million 2010 no-year funding during FY 2011, \$54.5 million during FY 2012, \$53.1 million during FY 2013, and \$6.7 million during FY 2014. FDA spent the remaining \$6.2 million balance of the \$170 million in FY 2015.



- 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 high-priority MCMs
- [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 FDA [laws and policies](#) adequately support 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 medical countermeasure mission

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In 2015, FDA approved the first MCM to increase survival in patients exposed to myelosuppressive doses of radiation

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The following sections provide detail on achievements in FY 2015 with respect to these activities.

Medical Countermeasure Approvals

During FY 2015, FDA continued to review marketing applications for MCMs against CBRN and emerging infectious disease threats and to approve applications that met standards for safety, efficacy, and quality. FDA approved the majority of MCM marketing applications under review¹⁰ in FY 2015 (**Appendix 1**).

In the area of MCMs to treat diseases caused by CBRN threats, FDA approved ciprofloxacin for adults and children to treat or prevent pneumonic and septicemic plague,¹¹ and Avelox (moxifloxacin) for adults to treat pneumonic and septicemic plague, and to prevent plague in

¹⁰ “Under review” indicates that a marketing application has been submitted to FDA for approval by the product’s sponsor.

¹¹ Ciprofloxacin labeling for this indication reads for “treatment of plague, including pneumonic and septicemic plague, due to *Yersinia pestis* and prophylaxis for plague in adults and pediatric patients from birth to 17 years of age.”



adult patients.¹² FDA also approved Anthrasil (Anthrax Immune Globulin Intravenous (Human)) to treat adults and children with inhalational anthrax, in combination with appropriate antibacterial drugs. In addition, FDA approved Neupogen (filgrastim) for adults and children to increase survival in patients acutely exposed to myelosuppressive doses of radiation, which would be expected to occur after a radiological or nuclear event. All of these indications were approved under the [Animal Rule](#).^{13,14}

With regard to all-hazards preparedness, FDA approved the Ahead 200 device, which analyzes a patient's electroencephalograph (EEG) using a sensor attached to a smartphone to provide an interpretation of the structural condition of the patient's brain after a head injury at the point of care. This device can help rapidly identify patients who may have traumatic brain injury, as would be expected to occur after detonation of an improvised explosive device. FDA also cleared Burn Resuscitation Decision Support, a desktop software application developed by the U.S. Army to provide clinical decision support for calculating hourly fluid needs post-burn injury.

In the area of diagnostics for CBRN threats, FDA cleared modifications to a gamma phage lysis *Bacillus anthracis* assay, which changed the *B. anthracis* positive control from the specified Pasteur strain (a biological select agent) to the Sterne strain¹⁵ (a non-listed agent), and reduced the logistical burdens of imposing the use of a select agent strain without compromising assay performance.

In the area of re-emerging threats, FDA cleared three modifications to a *Bordetella pertussis* assay: a change to the sample preparation, addition of an acceptable specimen collection and transport system, and addition of an optional sample pre-treatment to neutralize the interfering activity of biological substances found in the nasopharynx (upper part of the throat) of some patients.

¹² Moxifloxacin labeling for this indication reads for "treatment of plague, including pneumonic and septicemic plague, due to susceptible isolates of *Y. pestis* and prophylaxis of plague in adult patients."

¹³ Under the Animal Rule, when human challenge studies would not be ethical and field trials after accidental or intentional exposure have not been feasible, FDA may grant marketing approval based on adequate and well-controlled animal studies when the results of those studies establish that the drug or biological product is reasonably likely to produce clinical benefit in humans. Demonstration of the product's safety in humans is still necessary (see 21 CFR 314.600--650 for drugs and 21 CFR 601.90--95 for biological products).

¹⁴ More information is available in Appendix 1: FY 2015 Medical Countermeasure Approvals, and at: Drugs@FDA: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>, Biologics Products & Establishments: <http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm>, and Medical Device Databases: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm>

¹⁵ More information about the Sterne strain of *B. anthracis* is available from CDC at: http://www.cdc.gov/nczved/divisions/dfbmd/diseases/anthrax_sterne/



In the area of pandemic influenza preparedness, FDA approved the first intravenous antiviral drug for influenza, Rapivab (peramivir injection), for the treatment of acute uncomplicated influenza in adults.

FDA also approved two new influenza tests—both multiplexed devices for the detection of influenza viruses and other respiratory viral and bacterial pathogens. In addition, FDA granted a CLIA waiver for a rapid, instrument-based molecular test for the detection of influenza A and influenza B from nasal swab specimens.¹⁶ This is the first molecular influenza assay to receive a CLIA waiver. FDA also cleared modifications to five previously cleared influenza detection (*in vitro* diagnostic, or IVD) devices to include additional specimen types and labeling changes 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.

Five additional marketing applications for new MCMs or new MCM indications were under review in FY 2015, the reviews for which 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.¹⁷

Supporting an Adequate Supply of Medical Countermeasures

FDA continued efforts to support the establishment and sustainment of an adequate supply of MCMs during FY 2015. 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 expiration date. FDA laboratory personnel test and evaluate drugs submitted for shelf-life extension to assure

¹⁶ All facilities in the United States that perform clinical laboratory testing on human specimens are regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). A CLIA-waived test is an FDA-cleared test that has been granted waived status from the CLIA requirements. These tests are typically simple to use with low risk for an incorrect result when performed by non-laboratory personnel.

¹⁷ For updated information about MCM approvals after the FY 2015 reporting period, visit the MCMi News and Events page at: <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm>



stability and quality before a shelf-life extension is granted. In FY 2015, as a result of SLEP testing that assured drug stability and quality, FDA granted shelf-life extensions for 2,000 lots (batches) of MCM drugs. In addition, on September 3, 2015, FDA issued a memo to state and local public health and first responder stakeholders regarding expiry date extensions of certain lots of doxycycline hyclate 100mg capsules stockpiled for public health preparedness and response purposes.¹⁸

Another way FDA worked to ensure an adequate supply of MCMs in FY 2015 was by conducting post-marketing current good manufacturing practices (cGMP) inspections for facilities that produce MCMs to ensure that these products were produced under cGMP and to help identify and resolve any issues that could potentially lead to a shortage due to manufacturing issues.¹⁹

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.²⁰



FDA also works to resolve MCM shortages as quickly as possible when they occur. In FY 2015, FDA continued to collaborate with U.S. government partners and the product manufacturer of auto-injectors used for the treatment of nerve agent and insecticide poisoning to help prevent shortages of these products after quality issues identified in the manufacturing process resulted in a subset of product being out-of-specification (i.e., having an insufficient quantity of active drug product). FDA reviewed applicable scientific data and determined that, if properly stored, certain auto-injectors could be used beyond their original labeled expiration date for a period specified by FDA, to help ensure that the nation's warfighters and first responders continue to have ready access to these products.²¹ FDA also provided information on such [expiry dating extensions](#) to international military and public health partners to assist them in their

¹⁸ The memo is available at:

<http://www.fda.gov/downloads/Drugs/EmergencyPreparedness/BioterrorismAndDrugPreparedness/UCM462484.pdf>

¹⁹ 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.

²⁰ 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.

²¹ For the latest updates on expiry dating extensions for auto-injectors, see <http://www.fda.gov/Drugs/DrugSafety/ucm376367.htm>



determinations about whether they should extend the shelf life of their stockpiled auto-injectors produced by the same manufacturer. Meanwhile, FDA continued to work with the product manufacturer to help rectify the quality issues in its manufacturing process so production of new product can be resumed.

Enabling Access to Available Medical Countermeasures Under FDA’s Emergency Use Authorization²²

During FY 2015, FDA continued to work with Enterprise partners, including DoD, and product sponsors to enable access to available MCMs when necessary. 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 specified CBRN agent or agents if certain statutory criteria are met.²³ In FY 2015, FDA issued nine EUAs for diagnostic tests for Ebola virus as well as re-issued an EUA for an Ebola diagnostic test initially issued in FY 2014. FDA also issued EUAs for diagnostic tests for Enterovirus D68 (EV-D68) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV).²⁴

In addition to issuing EUAs when necessary, FDA also works to ensure that the U.S. government is as prepared as possible to deploy MCMs that may need to be used under an EUA. To facilitate the issuance of EUAs, 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.²⁵ During FY 2015, 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, and nuclear threats. During FY 2015 FDA provided feedback to sponsors on eight pre-EUAs for Ebola diagnostic tests and two pre-EUAs for MERS-CoV diagnostic tests.

²² Section 564 of the FD&C Act

²³ Under the Project BioShield Act of 2004 [PL 108-276], which was amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 [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].

²⁴ For more about EUAs see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm>

²⁵ Pre-EUA packages contain 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.



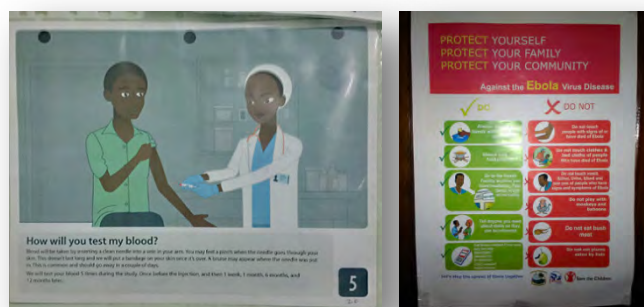
Responding to Emerging Public Health Threats

In FY 2015, FDA continued its intense efforts to support the international response to the Ebola epidemic in West Africa, which emerged in 2014. Throughout the epidemic response, 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 to respond to the epidemic.

In addition, FDA continued similar activities to respond to the MERS-CoV outbreak, which was first noted in the Middle East in 2012 with subsequent importations by international travel into a number of other countries.

Key [FDA response activities](#) included:

- 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 regular contact with drug, vaccine, device, and 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
- Helping design and set up clinical trials for establishing the safety and efficacy of investigational products for the treatment and/or prevention of life-threatening emerging infectious diseases, including Ebola
- Enabling access to investigational MCMs—when necessary—through an appropriate mechanism such as under an EUA or under expanded access mechanisms (e.g., FDA enabled access to investigational MCMs under Emergency Investigational New Drug (eIND) applications to treat Ebola patients in the United States during the period of the Ebola epidemic before clinical trials were established, when the clinical circumstances warranted)



Informed consent and Ebola prevention signs in Liberia. Photos: Kristian Roth, PhD, FDA



- Issuing EUAs for diagnostic tests for MERS-CoV, EV-D68, and EVD (see **Appendix 2** for a list of current EUAs)
- 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, and false product claims, and taking appropriate action when necessary to protect consumers²⁶

Throughout the Ebola epidemic, 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. For example, in August 2015 FDA coordinated in a meeting in



Images from FDA's August 2015 delegation to Liberia. 1) JFK hospital, where an Ebola survivor study is being conducted (left), 2) the Redemption Center Ebola treatment facility (top right), and 3) delegates at the meeting.

Photos: Elizabeth Sadove, JD (1 and 2), and Kristian Roth, PhD (3), FDA

²⁶ View the latest updates on FDA's Ebola response at <http://www.fda.gov/ebola>



Liberia with representatives from the U.S. government (FDA, the National Institutes of Health (NIH), and BARDA), Guinea, Liberia, Sierra Leone, Ivory Coast, Mali, and WHO to provide technical assistance that may help West African regulators make decisions regarding the next steps for specific investigational products for Ebola.

Agreements established in FY 2014 and FY 2015 between FDA and its international counterparts have helped information-sharing and collaboration during the West Africa Ebola epidemic, and have better prepared the international regulatory community to respond to future public health emergencies. For example, in February, March, and September 2015, FDA entered into [reciprocal agreements](#) with, respectively, the Liberian Medicines and Health Products Regulatory Authority (LMHRA), the Pharmacy Board of Sierra Leone (PBSL), and the Ministry of Public Health and Hygiene of Guinea (MSHP) as part of cooperative regulatory activities to help facilitate communication on medical products used, or proposed to be used, for Ebola-related purposes.^{27,28,29}

Facilitating Medical Countermeasure Development

Action Teams

Under the MCMi, FDA established multidisciplinary Public Health and Security Action Teams (Action Teams) as necessary to advance priority MCMs 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 2015.

Multiplex and Microbial Sequencing *In Vitro* Diagnostics Action Team – This Action Team continued its work to facilitate the development of multiplex and microbial DNA sequencing-based *in vitro* diagnostic (IVD) tests. Such diagnostics could be used to test for multiple pathogens simultaneously from a single clinical specimen, providing valuable information when responding to a public health emergency. Key activities during FY 2015 included:

- Continuing a 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

²⁷ FDA and LMHRA reciprocal agreements, signed in FY 2015 (PDF, 821 KB):

<http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM441392.pdf>

²⁸ FDA and PBSL reciprocal agreements, signed in FY 2015 (PDF, 702 KB):

<http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM441396.pdf>

²⁹ FDA and MSHP reciprocal agreements, signed in FY 2015 (PDF 364 KB):

<http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM461832.pdf>



reference databases that will be critical to developers seeking to validate their candidate multiplex IVD tests

- Continuing to facilitate the population of a publicly available and accessible [database](#) for regulatory-grade microbial genomic reference sequences ([FDA-ARGOS](#)), established in FY 2014, through NBCI. The sequencing 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 project³⁰
- 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
- Continuing an information exchange with the CDC [Laboratory Response Network](#) (LRN) and the DHS regarding implementation of Public Health Actionable Assay validation strategies for characterization of biothreat assays for LRN use
- 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)



The lab manager oversees sample extraction, library construction and sequencing activities for the FDA-ARGOS project, a collaboration with the University of Maryland. Photo: University of Maryland, Institute for Genome Sciences

³⁰ As part of this project, FDA set up collaborations to acquire the following prospective samples: 1) clinical isolates from Children's Hospital and George Washington University in Washington, D.C., to enhance diversity of GenBank, 2) biothreat and near-neighbor isolates/gDNA from USAMRIID/CRP, 3) Ebola isolates/gDNA from Public Health Canada/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 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 events. Key activities during FY 2015 included:

- Supporting the development of an ARS Questions and Answers guidance to help sponsors develop products for ARS indications under the Animal Rule
- Supporting the issuance of [draft guidance for Radiation Biodosimetry Devices](#) (PDF, 379 KB), and its continued development toward finalization³¹
- Providing input to BARDA and NIAID on the development of MCMs for Gastrointestinal Acute Radiation Syndrome (GI-ARS)
- Providing FDA reviewers with training and information on the latest scientific research on acute and long-term radiation effects in non-human primates (NHPs), medical management during/after radiological and nuclear mass casualty incidents, and the current status of the PHEMCE MCM monitoring and assessment team

Warfighter Action Team – FDA continued this Action Team’s efforts to facilitate the development and regulatory assessment of MCMs and related technologies primarily to support the warfighter and trauma victims. Key FY 2015 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
- Providing assistance to the DoD on 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 subjects³²
- Working to establish 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

³¹ Draft guidance published December 2014, available at:
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM427866.pdf>

³² Minimal risk research is research in which the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. See, 45 CFR 46.303(d).



FDA also participated in the Military Health System Research Symposium August 17-20, 2015, and provided expert speakers on topics including traumatic brain injury, digital health, physiological monitoring, and the regulatory review process for MCMs, to help facilitate interagency coordination.

Regulatory Advice and Guidance

During FY 2015, FDA continued to provide regulatory advice and guidance to sponsors and applicants of MCMs and our federal partners funding MCM development, to help foster the development and availability of various MCMs. FDA provides regulatory advice and guidance through a variety of mechanisms including direct engagement with sponsors and applicants, issuing [guidance documents](#), and holding [Advisory Committee](#) meetings and public workshops.

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

FDA has established policies and procedures for conducting formal meetings with product sponsors or applicants.³³ Formal meetings are held—as needed—at the request of a product sponsor or applicant, and requests for meetings are granted unless there is a substantive reason for denying the request (e.g., the product for which the meeting is requested is not sufficiently developed to warrant the type of meeting sought).³⁴ When FDA denies a request for a meeting, the sponsor or applicant is provided feedback on steps required to warrant a meeting.

The Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) categorize formal meetings with product sponsors and applicants as Type A, B,

³³ See for example, *Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM437431.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>

³⁴ Formal meetings may also be rescheduled or cancelled based on criteria described in FDA guidance.



and C. Type A meetings are meetings to help an otherwise stalled product development program proceed (such as a dispute resolution meeting, a meeting to discuss a clinical hold,³⁵ and a Special Protocol Assessment meeting³⁶).

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, under the draft guidance [Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products](#) (PDF, 336 KB), issued in March 2015.

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.).

Table 2. FY 2015 Formal Meetings Between CBER/CDER and Medical Countermeasure Sponsors or Applicants		
Meeting Type	CBER	CDER
Type A	0	2
Type B	33	9
Type C	15	10
Total	48	21

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. In FY 2015, CBER held 48 formal meetings with MCM sponsors or applicants, and 6 other (non-PDUFA) meetings, and CDER held 21 formal meetings (**Table 2**) and 10 other (non-PDUFA) meetings.

The Center for Devices and Radiological Health (CDRH) categorizes its formal meetings with product sponsors as Pre-Submission (Pre-sub) and 510(k)/Premarket Approval (PMA) Submission issues. 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.

³⁵ A clinical hold is an order issued by FDA to a product sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. See 21 CFR 312.42 for more information on clinical holds.

³⁶ For more information on Special Protocol Assessments see *Guidance for Industry – Special Protocol Assessment* available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080571.pdf>



CDRH received and reviewed 30 Pre-sub applications for MCM diagnostic devices in FY 2015. FDA provided extensive written feedback on these submissions, and many of the 26 sponsors declined additional formal follow-up meetings after receiving this information. Submission issue meetings are 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 2015, CDRH held 15 formal meetings with MCM sponsors or applicants (**Table 3**), and provided written feedback for 22 MCM sponsors.

Moreover, FDA has significant interactions with MCM sponsors and applicants outside of the formal meeting process to address issues and provide assistance. For example, CDRH has established an Interactive Review Process to facilitate the efficient and timely review and evaluation of premarket submissions and pre-EUA submissions through increased interaction between FDA and sponsors, including the exchange of scientific and regulatory information.³⁷

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.³⁸ FDA did not receive any written RMP requests in FY 2015.

Table 3. FY 2015 Formal Meetings Between CDRH and Medical Countermeasure Sponsors or Applicants	
Meeting Type	CDRH
Pre-Submission	15
Submission	0
Total	15

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.

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

³⁸ Under PAHPRA, MCMs eligible for RMPs are security countermeasures with respect to which the Secretary of HHS has entered into a procurement contract under section 319F-2(c) of the PHS Act (42 USCS § 247d-6b(c)); or MCMs with respect to which BARDA has provided funding under section 319L of the PHS Act (42 USCS § 247d-7e) for advanced research and development. (FD&C Act Sec. 565(f); 21 U.S.C. § 360bbb-4(f)). The Director of BARDA, in consultation with the Commissioner of FDA, prioritizes which eligible MCMs may receive RMPs if resources are not available to establish RMPs for all eligible MCMs for which requests are submitted.



In addition to its direct work with MCM sponsors and applicants, FDA also issues guidance documents that help foster MCM development and availability.³⁹ Guidance documents issued during FY 2015 directly related or applicable to MCMs policies or regulatory issues include:

- [Draft Guidance for Industry and FDA Staff: Premarket Notification Requirements Concerning Gowns Intended for Use in Health Care Settings](#) (PDF, 355 KB) – to describe FDA’s premarket regulatory requirements and the performance testing needed to support liquid barrier claims for gowns intended for use in health care settings⁴⁰
- [Draft Guidance for Industry and FDA Staff: Radiation Biodosimetry Devices](#) (PDF, 379 KB) – to facilitate study designs to establish the analytical and clinical performance characteristics of radiation biodosimetry MCM devices⁴¹
- [Content of Premarket Submissions for Management of Cybersecurity in Medical Devices](#) (PDF, 324 KB) – to strengthen the safety of medical devices, this final guidance recommends that manufacturers consider cybersecurity risks as part of the design and development of a medical device, and submit documentation to the FDA about the risks identified and controls in place to mitigate those risks^{42,43}

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 2015 include:

- October 21-22, 2014 – [Collaborative Approaches for Medical Device and Healthcare Cybersecurity](#) – A workshop to identify cybersecurity challenges to medical devices and strategies to address those challenges to strengthen medical device cybersecurity (co-hosted by HHS and DHS)
- December 12, 2014 – [Immunology of Protection from Ebola Virus Infection](#) – A workshop to discuss important aspects of Ebola virus and vaccine immunology to inform

³⁹ 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))

⁴⁰ This guidance was finalized in FY 2016 (December 9, 2015). Final guidance is available at:

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM452804.pdf>

⁴¹ Draft guidance is available at:

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM427866.pdf>

⁴² Final guidance is available at:

<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm356190.pdf>

⁴³ October 1, 2014 FDA news release about this guidance:

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm416809.htm>



future clinical, scientific, and regulatory decision-making related to vaccines against Ebola (co-sponsored by FDA, NIH, DoD, CDC, and BARDA)

- February 20, 2015 – [Optimizing FDA’s Regulatory Oversight of Next-Generation Sequencing Diagnostic Tests](#) – A workshop to discuss and receive feedback on FDA’s regulatory approach to diagnostic tests for human genetics or genomics using next-generation sequencing (NGS) technology
- May 12, 2015 – The FDA [Vaccines and Related Biological Products Advisory Committee](#) met to discuss the development and licensure of Ebola vaccines
- May 27-28, 2015 – The [FDA Science Forum](#) highlighted the cutting-edge science conducted at FDA, including MCM-related regulatory science topics
- August 21, 2015 – [M-CERSI Symposium on Biomarkers in Drug Development](#) – A one-day symposium for scientists and researchers from industry, academia, and FDA to gain perspective on biomarker development and application of biomarkers in preclinical and clinical research, including evidentiary considerations for biomarker use in drug development, hosted by the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)
- September 28, 2015 – [Promoting Semantic Interoperability of Laboratory Data](#) – A workshop to receive and discuss input from stakeholders regarding proposed approaches to promoting the semantic interoperability of laboratory data between *in vitro* diagnostic devices and database systems, including laboratory information systems and electronic health records (co-hosted by CDC and the National Library of Medicine (NLM))

Collaborations

During FY 2015, 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 65 standing 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 from threat assessment to requirements setting to product development to procurement, stockpiling, and utilization.



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

Medical Countermeasure Regulatory Science

In FY 2015, 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.

MCMs often present unique and complex challenges with respect to developing the data necessary to support regulatory decision-making. For example, many of the high-priority threats for which MCMs are being developed do not occur naturally to an extent that would support the conduct of field efficacy studies in humans, and it is not ethical to conduct human challenge studies with threat agents.⁴⁴ 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 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

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The MCMi
Regulatory Science
Program helps
translate cutting-
edge technology
into innovative,
safe, and effective
medical
countermeasures

• • •

⁴⁴ High-priority threats identified by the Enterprise for which medical countermeasures 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 2015 PHEMCE Strategy and Implementation Plan for more information at <http://www.phe.gov/Preparedness/mcm/phemce/Documents/2015-PHEMCE-SIP.pdf> (see Box 1, page 8).



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).⁴⁵

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. Priority research areas being supported under the MCMi Regulatory Science Program include:

- 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 next-generation 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 activities related to responding to the Ebola epidemic in West Africa, including medical product review and regulatory science research to help expedite the development and availability of medical products for Ebola

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.⁴⁶ To ensure that the MCMi Regulatory Science Program is appropriately targeted and coordinated with U.S. government MCM priorities, FDA established a Steering Committee for Advancing MCMi Regulatory Science—which includes representatives from NIH, CDC, BARDA, and DoD—

⁴⁵ 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

⁴⁶ Intramural FDA medical countermeasure regulatory science is funded through a competitive challenge grant process. Extramural medical countermeasure 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/ucm391617.htm>



that evaluates MCMi Regulatory Science Program research proposals for scientific/technical merit and feasibility as well as for alignment with Enterprise priorities.

FY 2015 MCMi Regulatory Science program activities included:

- 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^{47,48}
- [Mapping immune responses](#) to certain biothreat agents and MCMs in humans and animal models to create species-specific immune function maps⁴⁹
- Improving animal models to evaluate serious adverse events related to use of the smallpox vaccine and therapies to counteract these complications⁵⁰
- Expanding a database of regulatory-grade nucleic acid sequences to include antimicrobial-resistant organisms
- Developing and characterizing a repository of antimicrobial-resistant strains and panels to be made publicly available for developers of diagnostics and therapies to identify and treat antimicrobial-resistant bacteria, in collaboration with CDC. The [FDA-CDC Antimicrobial Resistance Isolate Bank website](#) containing available information on strains and panels was recently launched as a pilot to allow interested stakeholders to order isolates. So far, CDC has fulfilled and processed 43 orders for panels upon request by various organization types including diagnostic and pharmaceutical companies and public health departments
- Developing a mobile device (e.g., smartphone) application for reporting adverse events associated with MCMs to FDA, including an in-depth MCMs module
- Cataloging the most likely and serious difficulties that may complicate emergency administration of MCMs, and [developing communication strategies](#) to help ensure appropriate public use of life-saving MCMs in emergency situations⁵¹

⁴⁷ The project was funded under the extramural MCMi regulatory science program. For more information see Organs-On-Chips for Radiation Countermeasures at <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm364491.htm>

⁴⁸ Studies with organs-on-chips are not considered adequate replacement for animal efficacy studies required under the Animal Rule at this time.

⁴⁹ The project was funded under the extramural MCMi regulatory science program. For more information see Cross Species Immune Reference at <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm332539.htm>

⁵⁰ Additional information is available in the *Journal of Virology*: <http://jvi.asm.org/content/89/6/3295.short>

⁵¹ This project was funded under the extramural MCM regulatory science program. For more information see Ensuring Appropriate Public Use of Medical Countermeasures through Effective Emergency Communication at



- Investigating [decontamination and reuse](#) of respirators in public health emergencies, and [optimizing respirator decontamination](#) to ensure supplies for emergency preparedness⁵²
- 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 States⁵³
- Establishing a model to estimate pediatric pharmacokinetics for antibacterial and antiviral MCMs
- Developing Ebola reference materials including antibodies and nucleic acids
- Developing improved animal models to study filovirus immune responses
- Evaluating new methods and tools to assess potency and the quality of the immune response to influenza vaccines that include adjuvants
- Evaluating whether currently used protective-garment testing methods are adequate to measure penetration of Ebola virus, and identifying alternative garment testing methods that may predict Ebola penetration without use of live Ebola virus and high-containment facilities
- Working on approaches to novel clinical trial designs to speed advancement of promising MCMs for emerging infectious diseases such as Ebola⁵⁴
- Expanding FDA's database of regulatory-quality sequences to include filoviruses like Ebola, as well as organisms associated with co-morbidities
- Improving understanding of immunology-based diagnostic and potency assays for Ebola, including use under challenging field conditions
- Monitoring Ebola virus genomic drift and potential impacts on MCMs

<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm400865.htm>

⁵² These projects were funded under the extramural MCM regulatory science program. For more information see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm412725.htm> and <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm414974.htm>

⁵³ This project was funded under the extramural MCM regulatory science program. For more information see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm414015.htm>

⁵⁴ Information about Ebola clinical trials, including vaccine and therapeutic trials, developed with the Partnership for Research on Ebola Virus in Liberia (PREVAIL) is available at: <http://www.nih.gov/news-events/news-releases/study-ebola-survivors-opens-liberia>



FDA also expanded and sustained MCM regulatory science collaborations in FY 2015. For example FDA:

- Sponsored the third 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., Animal Biosafety Level 3 and 4) laboratories used to support product approval under the Animal Rule
- Supported the [Animal Model Qualification Program](#), which provides a mechanism for the evaluation of product-independent animal models for use in drug and biological product development under the Animal Rule⁵⁵
- Established and continue to expand a publicly available, well-curated reference database of regulatory-grade sequences from diverse microorganisms. This database, called FDA dAtabase for Regulatory Grade micrObial Sequences (FDA-ARGOS), will be critical to developers seeking to validate their candidate high-throughput sequencing-based IVD assays. This database is being hosted by NCBI⁵⁶
- Continued collaborations with DARPA on regulatory science research for the development of innovative regulatory tools, such as biomimetic models, as well as to support their 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 the National Institute of Standards and Technology (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

⁵⁵ For more information on FDA's Animal Model Qualification Program see <http://www.fda.gov/drugs/developmentapprovalprocess/drugdevelopmenttoolsqualificationprogram/ucm284078.htm>

⁵⁶ NCBI BioProject 231221 (FDA-ARGOS): <http://www.ncbi.nlm.nih.gov/bioproject/231221>





Course instructors, in black shirts, work with attendees at the 2015 Achieving Data Quality and Integrity in Maximum-Containment Laboratories course. In its third year, this week-long training was filled to capacity, and included international attendees.

Photos: April Finnen, FDA



Medical Countermeasure Regulatory Policy

During FY 2015, FDA continued efforts to ensure that [U.S. laws, regulations, and policies](#) enable 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 availability of MCMs. FY 2015 activities included:

- Continuing efforts to implement [PAHPRA authorities](#) 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.⁵⁷ Implementation efforts have focused on:
 - Developing a draft guidance on Emergency Use Authorization of Medical Products and Related Authorities, which, when finalized, will replace the current guidance, Emergency Use Authorization of Medical Products (July 2007) and Emergency Use Authorization Questions and Answers (April 2009)

⁵⁷ For more information on PAHPRA's MCM provisions see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm346195.htm>



- Establishing a Memorandum of Understanding (MOU) with CDC for developing and issuing Emergency Use Instructions (EUI)
- Drafting emergency dispensing orders for doxycycline and ciprofloxacin for anthrax preparedness (utilizing section 564A authorities)
- Drafting a guidance on doxycycline expiry dating extension for state and local public health stakeholders
- Finalizing the 2014 revised draft guidance [Product Development Under the Animal Rule](#) (PDF, 563 KB)⁵⁸
- Working with [state and local](#) public health authorities and responders and public health NGOs to support MCM preparedness and response capabilities at the state and community levels, including responding to numerous EUA- and other emergency use-related inquiries and participating in multiple national-level workshops and meetings on legal preparedness, FDA's roles in MCM distribution and dispensing, and enactment of PAHPRA⁵⁹
- Sustaining support for and [participation](#) in the annual Public Health Preparedness Summit convened by the National Association of County and City Health Officials (NACCHO)
- Sustaining support for and participation in the Institute of Medicine's (IOM) [Forum on Medical and Public Health Preparedness for Catastrophic Events](#), 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
- Working with the WHO to establish a framework for sharing MCMs during public health emergencies, with a focus on an operational framework for deployment of smallpox vaccine



⁵⁸ This guidance was finalized in FY 2016 (October 27, 2015).

⁵⁹ 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>



- Supporting and participating in FDA’s Global Health Security agenda and strategy, as well as other HHS-led efforts related to global MCM policies
- Continuing to work with appropriate partners to develop and propose new approaches for addressing legal, regulatory, and policy challenges associated with the development and use of specific MCMs. Examples of areas where FDA provided policy assistance include:
 - Issues related to MCM development that are unique to the warfighter
 - Issues related to expiration dating that are unique to MCMs and to public health stakeholders
 - Approaches to data collection on MCMs used during public health emergencies
 - Issues related to use of expanded access and EUA mechanisms to make available unapproved MCMs for investigational Ebola products in FY 2015
 - MCM import and export issues during emergency responses and to support preparedness for international events, with a focus on export issues related to the Ebola response in FY 2015
 - Issues related to information disclosure and liability protections
 - FDA expectations for ensuring data quality and integrity for certain studies in animals to support approval under the Animal Rule
 - FDA expectations for qualification of animal models under the Animal Model Qualification Program
 - Enhanced flexibility to conduct minimal risk research in support of product development
 - Harmonizing multi-jurisdictional regulation of certain personal protective equipment
 - Issuing guidance clarifying and describing the premarket regulatory requirements for gowns regulated under 21 CFR 878.4040⁶⁰
 - Establishing an MOU to support NIH and BARDA’s challenge incentive for development of diagnostics for antimicrobial-resistant pathogens⁶¹

⁶⁰ This guidance was finalized in FY 2016 (December 9, 2015). Final guidance is available at: <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM452804.pdf>

⁶¹ More information about this challenge is available in the September 9, 2015 Federal Register notice at: <https://www.federalregister.gov/articles/2015/09/09/2015-22690/announcement-of-public-consultation-on-antimicrobial-resistance-rapid-point-of-care-diagnostic-test>



Professional Development

FDA launched a Medical Countermeasure [Professional Development Program](#) under the MCMi 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. Key activities of the MCMi Professional Development Program during FY 2015 included:

- **MCMi Lecture Series:** These [lectures](#), presented by highly respected leaders in their fields, broaden the understanding of the policies, procedures, and U.S. governmental preparedness and response framework for FDA reviewers who are assessing MCM applications. FDA held 4 lectures in this series during FY 2015 with 698 attendees, 17 of whom received continuing education (CE) credits.⁶²
- **Foundations for Preclinical Review Lecture Series:** This is a monthly lecture series 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 both internal and external invited experts in the field. FDA held 8 lectures in this series during FY 2015 with 612 attendees, 89 of whom received CE credits.
- **MCM 101:** On September 21-22, 2015, FDA offered its first MCM 101 course designed to inform FDA staff on challenges specific to the development, approval, and monitoring/assessment of MCMs and to identify FDA's role and tools applicable to resolving these issues. In its first year, 56 FDA employees attended this two-day course.⁶³



⁶² For more about MCMi lectures see

<http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMiProfessionalDevelopmentActivities/ucm399895.htm>

⁶³ PAHPRA provides key legal authorities to sustain and strengthen national preparedness for public health emergencies involving CBRN agents, as well as emerging infectious disease threats. PAHPRA also codifies and builds on FDA's ongoing efforts to enhance review processes and advance regulatory science. New provisions (PAHPRA section 304) focus on FDA's interactions with government and industry working to develop MCMs, including by ensuring that FDA personnel are appropriately involved in interagency activities related to MCM advanced research and development, and that those who are involved in review of applications for MCMs have sufficient background information, training, and expertise (sec. 565(b)(3)(B) of the FD&C Act).



- **Conference Support:** FDA supported 32 staff to attend 6 MCM-related external conferences during FY 2015.
- **Georgetown University Certificate Program on Biohazardous Threat Agents and Emerging Infectious Diseases:** This 12-credit, online, graduate-level [certificate program](#) is available to FDA staff involved in MCM activities to learn more about the science behind and impact of biothreat agents and emerging diseases. At successful course completion, participants receive a Certificate in Biohazardous Threat Agents and Emerging Diseases. Three FDA staff graduated in FY 2015 and one staff member is currently enrolled in the program.⁶⁴

⁶⁴ For more about additional MCM education opportunities see <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMiProfessionalDevelopmentActivities/ucm400029.htm>



Appendix 1: FY 2015 Medical Countermeasure Approvals

FY 2015 Medical Countermeasure Approvals			
Medical Countermeasure ⁶⁵	Sponsor/Applicant	Key Dates	Indication
Biologics⁶⁶			
Anthraxisil (Anthrax Immune Globulin Intravenous (Human))	Cangene Corporation	<ul style="list-style-type: none"> Submitted 07/25/2014 Approved 03/24/2015 	For the treatment of adult and pediatric patients with inhalational anthrax, in combination with appropriate antibacterial drugs. (FDA news release)
Drugs⁶⁷			
Avelox (moxifloxacin)	Bayer Healthcare Pharmaceuticals, Inc.	<ul style="list-style-type: none"> Submitted 07/08/2014 Approved 05/08/2015 	New indication approved for the treatment of plague in adults, including pneumonic and septicemic plague, due to susceptible isolates of <i>Yersinia pestis</i> , and prophylaxis for plague in adults. (FDA news release)
Cipro (ciprofloxacin)	Bayer HealthCare Pharmaceuticals, Inc.	<ul style="list-style-type: none"> Submitted 04/02/2014 (tablets, oral suspension, and injection in flexible containers for IV infusion) and 08/04/2014 (injection for IV) Approved 02/02/2015 	New indication approved for the treatment of plague, including pneumonic and septicemic plague, due to <i>Yersinia pestis</i> and prophylaxis for plague in adults and pediatric patients from birth to 17 years of age.

⁶⁵ Includes medical countermeasures approved, licensed, or cleared by FDA in FY 2015 (October 1, 2014 – September 30, 2015).

⁶⁶ Additional information about biologics products can be found at:

<http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm>

⁶⁷ Additional information about drug products can be found by searching the Drugs@FDA database at:

<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>



FY 2015 Medical Countermeasure Approvals			
Medical Countermeasure ⁶⁵	Sponsor/Applicant	Key Dates	Indication
Neupogen (filgrastim)	Amgen, Inc.	<ul style="list-style-type: none"> Submitted 09/30/2014 Approved 03/30/2015 	New indication approved to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome). (see also: FDA Approves Radiation Medical Countermeasure)
Rapivab (peramivir injection)	BioCryst	<ul style="list-style-type: none"> Submitted 12/19/2013 Approved 12/19/2014 	For the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days. (FDA news release)
Devices⁶⁸			
Ahead 200	Brainscope Company, Inc.	<ul style="list-style-type: none"> Received 12/22/2014 Cleared 05/15/2015 	Using commercial smartphone hardware, the Ahead 200 records and analyzes a patient's EEG using a custom sensor attached to the handheld to provide an interpretation of the structural condition of the patient's brain after head injury.
Alere I Influenza A&B Test (direct nasal swab only)	Alere Scarborough, Inc.	<ul style="list-style-type: none"> Received 06/09/2014 Cleared 06/13/2014 CLIA waiver granted 01/05/2015 	A rapid, instrument-based molecular test for the detection of influenza A and influenza B from nasal swab specimen. FDA granted the first waiver to allow a nucleic acid-based test to be used in a greater variety of health care settings. The test was previously only available for use in certain laboratories. (FDA news release)

⁶⁸ 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>



FY 2015 Medical Countermeasure Approvals			
Medical Countermeasure ⁶⁵	Sponsor/Applicant	Key Dates	Indication
Alere I Influenza A&B, Alere I Instrument, Alere I Influenza A&B Control Swab Kit	Alere Scarborough, Inc.	<ul style="list-style-type: none"> Received 06/01/2015 Cleared 07/28/2015 	A previously 510(k)-cleared rapid molecular IVD test utilizing an isothermal nucleic acid amplification technology for the qualitative detection and discrimination of influenza A and B viral RNA in direct nasal swabs and nasal or nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. This 510(k) was to also include testing of nasal and nasopharyngeal swab samples that have been eluted into viral transport media (VTM).
Alere I Instrument, Alere I Influenza A&B	Alere Scarborough, Inc.	<ul style="list-style-type: none"> Received 06/23/2015 Cleared 07/16/2015 	A previously cleared 510(k) for a rapid molecular IVD test utilizing an isothermal nucleic acid amplification technology for the qualitative detection and discrimination of influenza A and B viral RNA in nasal swabs from patients with signs and symptoms of respiratory infection. This 510(k) is for a labeling change adding the assay type selection for the Alere™ I assay software update.
BD Veritor System for the Rapid Detection of Flu A+B	Becton Dickinson and Co.	<ul style="list-style-type: none"> Received 05/15/2015 Cleared 06/10/2015 	A previously 510(k)-cleared and CLIA-waived instrument-based antigen detection test using direct respiratory tract swab samples. This special 510(k) was to update the analytical reactivity section of the Instructions for Use (IFU) with additional influenza strains.
BD Veritor System for the Rapid Detection of Flu A+B (Laboratory Kit)	Becton Dickinson and Co.	<ul style="list-style-type: none"> Received 05/15/2015 Cleared 06/08/2015 	A previously 510(k)-cleared instrument-based antigen detection test using liquid respiratory samples. This special 510(k) was to update the analytical reactivity section of the IFU with additional influenza strains.



FY 2015 Medical Countermeasure Approvals			
Medical Countermeasure ⁶⁵	Sponsor/Applicant	Key Dates	Indication
Burn Resuscitation Decision Support – Clinical	Surgeon General, Department of the Army	<ul style="list-style-type: none"> Received 2/14/2014 Cleared 12/23/2014 	Clinical decision support for calculating hourly fluid needs post burn injury (desktop software application).
FilmArray Respiratory Panel (RP)	BioFire Diagnostics, Inc.	<ul style="list-style-type: none"> Received 10/27/2014 Cleared 02/17/2015 	Multiplexed nucleic acid test for Flu A, Flu A/H1, Flu A/H3, A/2009H1, Flu B, and other respiratory viruses and atypical bacterial agents, and <i>Bordetella pertussis</i> .
Gamma Phage Lysis Assay for the Identification of <i>Bacillus Anthracis</i>	Surgeon General, Department of the Army	<ul style="list-style-type: none"> Received 12/18/2014 Cleared 04/16/2015 	The previously cleared 510(k) was for a lytic phage assay specific for the detection of <i>Bacillus anthracis</i> . The modification presented in this special 510(k) consisted of changing the <i>B. anthracis</i> positive control from the specified Pasteur strain, to the Sterne strain.
Simplexa Flu A/B & RSV Direct and Simplexa Flu A/B and RSV Positive Control Pack	Focus Diagnostics, Inc.	<ul style="list-style-type: none"> Received 08/25/2014 Cleared 12/05/2014 	Previously 510(k)-cleared for use on the 3M Integrated Cycler instrument for the <i>in vitro</i> qualitative detection and differentiation of influenza A virus, influenza B virus, and respiratory syncytial virus (RSV) RNA in nasopharyngeal swabs (NPS) from human patients with signs and symptoms of respiratory tract infection in conjunction with clinical and epidemiological risk factors. This 510(k) was to update the analytical reactivity section of the IFU with additional influenza strains.
Verigene Respiratory Pathogens Flex Nucleic Acid Test (RP Flex)	Nanosphere, Inc.	<ul style="list-style-type: none"> Received 12/23/2014 Cleared 09/04/2015 	A new multiplexed assay intended for use on the Verigene instrument for the <i>in vitro</i> qualitative detection and differentiation of influenza A virus, A/H1, A/H3, influenza B virus, and other respiratory viral and bacterial pathogens in nasopharyngeal swabs (NPS) from human patients with signs and symptoms of respiratory tract infection, in conjunction with clinical and epidemiological risk factors.



FY 2015 Medical Countermeasure Approvals			
Medical Countermeasure ⁶⁵	Sponsor/Applicant	Key Dates	Indication
Xpert Flu/RSV XC Assay	Cepheid	<ul style="list-style-type: none"> Received 07/28/2014 Cleared 11/22/2014 	An automated, multiplex real-time, reverse transcriptase polymerase chain reaction (RT-PCR) assay intended for the <i>in vitro</i> qualitative detection and differentiation of influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA.



Appendix 2: Current Emergency Use Authorizations

Year	MCM	Requester	Status
Anthrax [<i>Bacillus anthracis</i>]			
2008	Doxycycline hyclate 100 mg oral tablets (in National Postal Model home & workplace kits)	HHS (ASPR/ BARDA)	Amended in 2009, 2010, 2011 (Current)
2011	All oral formulations of doxycycline (mass dispensing)	HHS (CDC)	Current ^a
Novel Influenza A (H7N9) Virus			
2013	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	HHS (CDC)	Current
2014	Lyra [™] Influenza A Subtype H7N9 Assay	Quidel Corporation	Current
2014	A/H7N9 Influenza Rapid Test	Arbor Vita Corporation	Current
Middle East Respiratory Syndrome Coronavirus [MERS-CoV]			
2013 ^b	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	HHS (CDC)	Current
2015 ^d	RealStar [®] MERS-CoV RT-PCR Kit U.S.	altona Diagnostics GmbH	Current
Ebola Virus			
2014 ^b	DoD EZ1 Real-time RT-PCR Assay	DoD	Current
2014 ^c	CDC Ebola VP40 rRT-PCR Assay	HHS (CDC)	Current
2014 ^c	CDC Ebola NP rRT-PCR Assay	HHS (CDC)	Current
2014 ^c	BioFire Defense FilmArray NGDS BT-E Assay	BioFire Defense	Current
2014	BioFire Defense FilmArray Biothreat-E test	BioFire Defense	Current
2014 ^b	RealStar [®] Ebolavirus RT-PCR Kit 1.0	altona Diagnostics GmbH	Current
2014	LightMix [®] Ebola Zaire rRT-PCR Test	Roche Molecular Systems, Inc.	Current
2015 ^c	ReEBOV [™] Antigen Rapid Test	Corgenix	Current
2015	Xpert [®] Ebola Assay	Cepheid	Current
2015	OraQuick [®] Ebola Rapid Antigen Test – whole blood	OraSure Technologies, Inc.	Current
2016	OraQuick [®] Ebola Rapid Antigen Test – cadaveric oral fluid	OraSure Technologies, Inc.	Current
Enterovirus D68			
2015	CDC Enterovirus D68 2014 Real-time RT-PCR Assay	HHS (CDC)	Current
Zika Virus			
2016	CDC Zika Immunoglobulin M (IgM) Antibody Capture Enzyme-Linked Immunosorbent Assay (Zika MAC-ELISA)	HHS (CDC)	Current
2016	CDC Trioplex Real-time RT-PCR Assay (Trioplex rRT-PCR)	HHS (CDC)	Current

^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 in 2016.

Note: chart accurate as of publication of this report [April 12, 2016], including EUAs issued in FY 2016.

[View the latest EUAs.](#)



Appendix 3: Acronyms

ADEPT	Autonomous Diagnostics to Enable Prevention and Therapeutics
AMR	Antimicrobial resistance
ATCC	American Type Culture Collection
ARS	Acute Radiation Syndrome
ASPR	Assistant Secretary for Preparedness and Response (HHS)
BARDA	Biomedical Advanced Research and Development Authority
BLA	Biologics License Application
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
CFSAN	FDA Center for Food Safety and Nutrition
cGMP	Current good manufacturing practices
CLIA	Clinical Laboratory Improvement Amendments of 1988
DARPA	Defense Advanced Research Projects Agency
DDT	Drug development tools
DHS	U.S. Department of Homeland Security
DoD	U.S. Department of Defense
DTRA	Defense Threat Reduction Agency
DxOD	Diagnostics on Demand
EEG	Electroencephalograph
eIND	Emergency Investigational New Drug
EUA	Emergency Use Authorization
EV-D68	Enterovirus D68
EVD	Ebola virus disease
FDA	U.S. Food and Drug Administration
FDA-ARGOS	FDA dAtabase for Regulatory Grade micrObial Sequences
FTE	Full-time equivalent
FY	Fiscal year
GI-ARS	Gastrointestinal Acute Radiation Syndrome
HHS	U.S. Department of Health and Human Services
IDE	Investigational Device Exemption
IFU	Instructions for Use
IND	Investigational New Drug
IOM	Institute of Medicine (National Academy of Medicine)
JBAIDS	Joint Biological Agent Identification and Diagnostic System



JPEO-CBD	Joint Program Executive Office for Chemical and Biological Defense
LLNL	Lawrence Livermore National Laboratory
LMHRA	Liberian Medicines and Health Products Regulatory Authority
LRN	CDC Laboratory Response Network
M-CERSI	University of Maryland Center of Excellence in Regulatory Science and Innovation
MCM	Medical countermeasure
MCMi	FDA Medical Countermeasures Initiative
MDR	Multi-drug-resistant
MERS-CoV	Middle East Respiratory Syndrome coronavirus
MSHP	Ministry of Public Health and Hygiene of Guinea
MOU	Memorandum of Understanding
MRMC	U.S. Army Medical Research and Materiel Command
NACCHO	National Association of County and City Health Officials
NCBI	National Center for Biotechnology Information
NGDS	Next-Generation Diagnostic System
NGO	Non-governmental organization
NGS	Next-generation sequencing
NHP	Non-human primate
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
PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PBSL	Pharmacy Board of Sierra Leone
PDUFA	Prescription Drug User Fee Act
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PMA	Premarket Approval
PREVAIL	Partnership for Research on Ebola Virus in Liberia
RMP	Regulatory Management Plan
RNA	Ribonucleic acid
RSV	Respiratory syncytial virus
SLEP	Shelf-Life Extension Program
SNS	Strategic National Stockpile
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USCIITG	United States Critical Illness and Injury Trials Group
UTMB	University of Texas Medical Branch
WHO	World Health Organization





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