MCMi

FDA's Medical Countermeasures Initiative
Year-1 Status Report — September 2011

— Protecting National Health and Security

US Department of Health and Human Services
Food and Drug Administration

Foreword

FDA launched its Medical Countermeasures Initiative (MCMi) in August 2010 in response to a comprehensive, year-long review of the Public Health Emergency Medical Countermeasures Enterprise, ordered by Department of Health and Human Services (HHS) Secretary Sebelius, to assess the our nation's readiness for future public health emergencies. The review also answered a charge by President Obama to improve our nation's capacity to respond faster and more effectively to chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats—such as pandemic influenza.

To enable FDA to immediately commence work on MCM activities, in September 2010, HHS authorized the transfer of $170 million to FDA from funding appropriated to the Public Health and Social Services Emergency Fund for MCMi. However, the $170 million was initially restricted to activities related to preparing for and responding to an influenza pandemic. Consequently, FDA could not initially implement the broad MCMi program it envisioned; it was limited to funding only regulatory science proposals or infrastructure investments that enhanced preparedness for pandemic influenza. To remove the restriction, the Administration asked Congress to enact legislation to allow FDA to also use the $170 million to address chemical, biological, radiological, and nuclear (CBRN) threats. Congress enacted this change on April 14, 2011,[1] enabling FDA to begin supporting the full scope of CBRN and pandemic influenza threats.

Despite this initial complication, and the uncertain budgetary climate, FDA's MCMi has achieved substantial progress during its first year. This *Year-1 Status Report* briefly summarizes achievements to date and outlines key next steps. FDA will provide more detail on MCMi, its goals, and specific activities in a forthcoming five-year strategic plan.

[1] On April 14, 2011, Congress passed a bill to fund the Federal Government through a full-year Continuing Resolution. On April 15, 2011, President Obama signed Public Law 112-010.

FDA's Medical Countermeasures Initiative (MCMi) Year-1 Status Report

Summary

Launched in August 2010, FDA's Medical Countermeasures initiative (MCMi) has three key goals:

- Enhance FDA's product review and approval processes for the highest priority MCMs and related technologies
- Build the necessary science base for MCM regulatory review and identify clear, efficient regulatory pathways for developing critical MCMs
- Modernize the legal, regulatory, and policy framework to facilitate MCM development and ensure an effective public health response

Following a review of the nation's Public Health Medical Countermeasure Enterprise (Enterprise) by the Secretary of the Department of Health and Human Services (HHS), FDA's Office of Counterterrorism and Emerging Threats (OCET) was asked to manage the implementation of MCMi, including providing additional support to FDA medical product centers in their MCM-related activities. MCMi is building on programs already under way at FDA, with the goal of further supporting the development and approval[2] of MCMs and national preparedness and response to a possible public health emergency. It is critical to make sure that regulatory requirements are clear and that MCM product developers obtain the support they need, especially at the earliest stages of product development, to gather the data necessary for a determination of MCM safety and efficacy.

One of FDA's first tasks was to work closely with the HHS Assistant Secretary for Preparedness and Response (ASPR) to establish MCM priorities for the program and begin formalizing them into a five-year strategic plan for MCMi. The strategic plan, which will be released this coming autumn, lays out in more detail the background of MCMi, initiative goals, and specific activities.[3]

Achieving MCMi goals requires extensive internal coordination (e.g., among FDA's medical product centers, the Office of Regulatory Affairs, other FDA offices) and substantial external

[2] For purposes of this document, *approval* refers to "FDA-approval, licensure, or clearance" under sections 505, 510(k), or 515 of the Federal Food, Drug, and Cosmetic Act or of section 351 of the Public Health Service Act.

[3] For more on FDA's MCMi, see the MCMi web site.

collaboration (e.g., among Federal partners, including other HHS agencies (ASPR, BARDA, CDC),[4] the Department of Defense (DoD), the Department of Homeland Security (DHS); academia; and State and local responders). One of the challenges FDA has faced during its first year has been building the staff and infrastructure to manage this essential program — particularly staff with expertise in MCM development, evaluation, and approval. We can report that FDA has been able to attract a number of exceptionally qualified individuals and has established the administrative framework to implement the budgetary and management components of the initiative.

Despite the fiscal restrictions and budgetary uncertainties of the initial months (see the Foreword), FDA has made substantial progress this first year. The following sections provide specific examples of year-1 activities. Highlights include the following:

- Establishing Action Teams, which are working to identify and help resolve challenges and overcome hurdles in the MCM regulatory development pathway.
- Reaching out through public meetings, workshops, and other interactions with relevant stakeholders to identify specific projects that will advance regulatory science for MCM development, reduce regulatory uncertainties, and expand communication among relevant agencies and between the agencies and prospective MCM developers.
- Evaluating and approving funding for intramural regulatory science projects designed to address identified MCM gaps; enhance FDA's capacity to review, monitor, and assess MCMs; and prepare and respond to public health emergencies.
- Launching the external portion of its regulatory science research program through public outreach and issuing a public request for information (RFI).[5]
- Establishing an FDA team to identify statutory, regulatory, and policy areas that could be modernized to facilitate MCM development as well as the nation's ability to prepare for and respond to a public health emergency.
- Proposing legislative changes that would facilitate the use of MCMs.

[4] BARDA is the Biomedical Advanced Research and Development Authority (BARDA); CDC is the Centers for Disease Control and Prevention.

[5] Request for Information (RFI): FDA Medical Countermeasures Initiative Regulatory Science Program, available at http://grants.nih.gov/grants/guide/notice-files/NOT-FD-11-001.html

Specific Examples of Progress to Date

With the launch of MCMi, FDA announced an Action Plan containing a three-pillar approach. Select achievements and examples of additional activities for each pillar are highlighted here.

Pillar 1: Enhance FDA's product review and approval processes for the highest priority MCMs and related technologies

- Established ***MCMi Action Teams.*** FDA is fully engaged with its Enterprise partners — including ASPR, BARDA, CDC, and DoD — to stay abreast of MCM priorities and requirements. FDA is establishing Action Teams based on those priorities and in alignment with investments in medical countermeasure programs:
  - Action Team on multiplex in vitro diagnostic tests: The goal of this Action Team is to identify and help resolve scientific, legal, regulatory, and policy gaps inhibiting the development of multiplex in vitro diagnostic tests. Such diagnostics could be used to test for multiple pathogens simultaneously, providing invaluable information when responding to a public health emergency.
  - Action Team on therapies for radiation sickness: Acute radiation syndrome occurs when the entire body — or the majority of it — receives a high dose of radiation as would be expected to occur after a radiological or nuclear event. The goal of this Action Team is to support the development and approval of candidate MCMs to treat acute radiation syndrome. The scope of the Action Team is also being expanded to address radiation biodosimetry, which is a high-priority for facilitating an effective response to a radiological or nuclear event.
- Developing a ***memorandum of understanding (MOU)*** to facilitate information sharing with Enterprise partners. Action Teams must collaborate extensively with Federal partners in the Enterprise (e.g., DoD, DHS, other HHS agencies), including the sharing privileged information.
- Scheduled and planning ***three workshops*** to obtain scientific and public input on the regulation of complex in vitro diagnostic tests (September 2011), on development and evaluation of next-generation smallpox vaccines (September 2011), and on MCMs for pediatric populations (winter 2012).
- Established ***CDC/FDA Strategic Leadership*** group, which holds quarterly meetings for threat-based prioritization of regulatory and preparedness issues.
- Working to identify ***regulatory gaps to support effective use*** of stockpiled MCMs, with a focus on at-risk populations, especially the pediatric population.
- Continuing and expanding FDA's MCMi professional development program to include ***threat briefings by relevant experts*** to make sure FDA reviewers are fully aware of the threats (and therefore the risks) as they conduct risk–benefit analyses on MCM products.

Pillar 2: Build the necessary science base for MCM regulatory review and identify clear, efficient regulatory pathways for developing critical MCMs

- Launched a ***rigorous regulatory science program*** for MCMs. Established a Steering Committee comprising Enterprise partners to peer review FDA's intramural MCMi Regulatory Science research program and ensure alignment with Enterprise priorities. More than 80 intramural research projects have been identified to date for funding, and $43.4 million has been allocated as of August 2011 to FDA centers to implement MCMi projects in 9 key topic areas[6] (see text box for some examples).

Examples of Select Regulatory Science Projects Identified for Funding

- **Develop a model to generalize active pharmaceutical ingredient (API) classes to facilitate the development of pediatric oral formulations**
- **Develop accelerated methods to screen key drugs at point of entry or distribution to verify identity and quality of products**
- **Develop new technologies to rapidly and accurately detect adventitious agents in biologics, raw materials (i.e., cell substrates), and their manufacturing intermediates**
- **Develop methods to assess added value of novel vaccine adjuvants to the quality of immune responses against pandemic influenza**
- **Develop web/smart phone-based, real-time active surveillance application for use to support pharmacovigilance and medical device adverse event reporting in a pandemic/CBRN emergency**

- Sponsored an ***IOM workshop*** in March 2011 as an initial effort to begin building an extramural regulatory science program.[7] Gathered input, recommendations, and ideas to help inform the MCM regulatory science program; developed and issued a ***request for information (RFI)*** (issued August 22, 2011) as a follow-up to the IOM meeting to lay the foundation for the extramural component of the MCMi regulatory science program.[8]
- Provided dedicated resources to launch a program to ***qualify animal models***. The Animal Model Qualification Program will enable the product-neutral evaluation and qualification of animal models for a specific context of use. This project complements animal model development programs at the National Institutes of Health (NIH) and the

[6] Key topic areas include animal models; biomarkers; immunology; MCM product quality; risk communication; radiation injury protection; in vitro diagnostics; health informatics; emergency medical equipment.

[7] See Advancing Regulatory Science for Medical Countermeasure Development — A Workshop, available at http://www.iom.edu/Activities/Research/DrugForum/2011-MAR-29.aspx.

[8] The RFI can be accessed on the MCMi web site.

US Biomedical Advanced Research and Development Authority (BARDA) located in ASPR.

- Began implementing ***IT enhancements*** and supercomputing capabilities to simulate the effect of MCMs on the body and accelerate medical product development.
- Established an ***MOU with the DoD's Defense Advanced Research Projects Agency (DARPA)*** to collaborate on regulatory science research in support of innovative regulatory tools, such as biomimetic models, that can be used in development and approval of MCMs.

Pillar 3: Modernize and optimize the legal, regulatory, and policy framework to facilitate MCM development and ensure an effective public health response

- Established an ***FDA policy team*** that initially analyzed existing statutory framework for making MCMs available in emergency circumstances. Based on this analysis, FDA ***developed proposals*** that were incorporated into HHS's legislative package as part of the reauthorization of the Pandemic and All Hazards Preparedness Act (PAHPA).[9] The changes provide enhanced clarity and flexibility for emergency use authorization (EUA) of MCMs prior to a CBRN event to enhance rapid deployment, better facilitate pre-event planning and positioning of medical products, and clarify that certain actions taken in preparation for or during an emergency will not violate FDA laws and regulations. FDA's recommendations were part of the HHS proposals that were incorporated into the House's PAHPA reauthorization bill.[10]
- Developed and issued an **EUA for doxycycline** for post-exposure prophylaxis, with the goal of supporting pre- and post-event preparedness activities for mass distribution and dispensing in an anthrax event.[11] The EUA supports anthrax planning and preparation activities under Executive Order 13527.
- Established an ***FDA work group*** that is assisting the ASPR Division of International Health Security in the development of policy and operational framework to facilitate international sharing of MCMs during public health emergencies.
- Provided assistance to HHS/BARDA with respect to a feasibility assessment for expanding the existing ***shelf-life extension program (SLEP)*** to include State and/or local assets. Under the SLEP program, FDA tests and evaluates certain drugs in Federal stockpiles to see if they maintain their quality beyond their labeled expiration dates so that their shelf lives can be extended.
- Hosted a meeting of ***State and local public health preparedness officials*** and their legal counsel in December 2010 to share information on legal issues, including FDA's legal and regulatory role, related to emergency preparedness and response.

---

[9] Pandemic and All Hazards Preparedness Act of 2006, P.L. 109-417, 120 STAT. 2831 (Dec. 19, 2006).

[10] Pandemic and All-Hazards Preparedness Reauthorization Act of 2011, HR 2404, 112th Cong., 1st Sess. (2011).

[11] See Doxycycline Mass Dispensing EUA Information on FDA's web site.

Next Steps

FDA will continue to build on existing programs while identifying new areas of focus, including supporting development of medical products and technologies deemed the highest priority by the Enterprise. Planned key activities include:

- Continue to participate in collaborations, partnerships, and other efforts to develop new tools (e.g., qualified animal models, innovative in silico assays) to support MCM development.
- Develop new regulatory science capabilities to enable FDA to apply innovative approaches to the regulatory process to improve MCM development timelines and success rates.
- Expand the number of staff who are specifically qualified to review and approve MCM applications.
- Continue to establish Action Teams for high-priority MCMs and related technologies to, among other things, enable a more robust and interactive review process and to support development of platform technologies to enhance MCM manufacturing capability.
- Continue FDA's MCM professional development program and threat briefings to increase the expertise of review staff relevant to medical products that can counter CBRN threat agents.
- Improve ability to predict and mitigate shortages in MCM drug, biologics, and devices (including in vitro diagnostics and emergency medical equipment) during public health emergencies.

Assuming consistent and continuous resources, this coming fiscal year (2012) will see substantial progress in the MCM regulatory science program, especially in the areas of extramural research and establishment of strategic partnerships with industry, academia, and Enterprise partners. These partnerships will enable FDA to leverage cutting edge science and apply innovative approaches to the regulatory process, improving MCM development timelines and success rates.