FDA Medical Countermeasures Initiative

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BARDA Industry Day
The USA is at war with determined, well organized and well funded terrorist organizations worldwide.

Our Homeland faces serious threats, especially from bioterrorism.

USG has responsibility for upgrading public health preparedness.

The Threat

- Bombings & Armed Attacks
- Toxic Industrial Chemicals
- Radioactive Dispersal Devices (RDD)
- Biological Agents

The Pandemic and All-Hazards Preparedness Act  (P.L. 109 – 417, December 2006)

BARDA manages advanced development and procurement programs for vaccines, drugs and biologics-based therapeutics and diagnostics for CBRN threats, pandemic influenza, and emerging infectious diseases.

Programs are supported by:

Advanced Research and Development
Project BioShield Special Reserve Fund
Pandemic Influenza appropriations
From MCM Requirements to USG Asset
HHS Public Health Emergency
Medical Countermeasures Enterprise (Enterprise)

National Biodefense Science Board

NIH
BARDA
BARDA & CDC
CDC
CDC & DHS
CDC & ASPR/OPEO

Research and Development
Advanced Development
Acquisition
Storage/Maintenance
Biosurveillance/Detection
Deployment
Utilization
Looking Back: USG Efforts to Date

• Federal civilian biodefense funding has been estimated to exceed $54B between FY 2001-2010
• Nation lacks range of MCMs listed in the HHS Public Health MCM Enterprise Plan
• 2009 H1N1 influenza pandemic highlighted U.S. vulnerability
  – Lag time between event detection and MCM availability
  – “Maybe We’re Not so Ready for a Pandemic After All” – Wpost October 23, 2009
• Probability of successfully developing required MCM as low as 12 percent
Dec 2009: Secretary Requests MCM Review

• Lessons learned from 2009 H1N1 response and from post-9/11 MCM enterprise

• Impediments to MCM development, including science and financial challenges
  • Broad input from IOM, NBSB, industry, public health leaders

• Improve processes, policies, infrastructure required to develop, approve, and stockpile MCMs
  • “[T]o get the 21\textsuperscript{st} century countermeasures, we don’t just need 21\textsuperscript{st} century technology. We also need 21\textsuperscript{st} century financial, legal, and regulatory frameworks…”
PHARMACEUTICAL DEVELOPMENT
Regulatory Access to Unapproved Products

- Emergency Use IND (21CFR 312.36)
- Treatment Use IND/IDE (21 CFR312.35)
- Emergency Use Authorization (EUA)
Criteria for EUAs, E-INDs, INDs, and FDA-approved Prescription Products  

<table>
<thead>
<tr>
<th>EUA, in General (and for Peramivir)</th>
<th>EIND</th>
<th>IND</th>
<th>FDA-Approved Prescription Product</th>
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</thead>
<tbody>
<tr>
<td><strong>Access</strong></td>
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<tr>
<td>Broad or restricted according to the letter of authorization (peramivir: seriously ill, hospitalized patients)</td>
<td>Single patient with serious illness or immediately life-threatening condition</td>
<td>Limited to clinical trials or expanded access</td>
<td>By prescription</td>
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<tr>
<td><strong>Use</strong></td>
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<td>According to the conditions of authorization (peramivir: intravenous administration in a hospital)</td>
<td>Limited to single patient</td>
<td>Limited to clinical trials or expanded access</td>
<td>According to labeling and practice of medicine</td>
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<tr>
<td><strong>Efficacy requirements</strong></td>
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<td>Reasonable to believe based on totality of scientific evidence, including adequate and well-controlled trials as available (peramivir: benefit observed in patients with acute, uncomplicated influenza)</td>
<td>Rationale for intended use, risk from treatment should be no greater than risk from disease or condition</td>
<td>No efficacy requirements, but safety data from animal studies are needed</td>
<td>Substantial evidence based on adequate and well-controlled clinical trials</td>
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<tr>
<td><strong>Prescriber safety reporting</strong></td>
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<tr>
<td>According to the conditions of authorization (peramivir: mandatory)</td>
<td>Required per IND regulations</td>
<td>Required per IND regulations</td>
<td>Voluntary MedWatch reporting</td>
</tr>
<tr>
<td><strong>Informed consent</strong></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Approval by institutional review board</strong></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
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Regulatory Pathways for Medical Countermeasures

• For Drugs and Biologics
  Animal Rule Approach
  – Regulations: 21 CFR 601.90-95 (biologics)
  21 CFR 314.600-650 (drugs)

• For Diagnostics and Devices
  – Traditional Regulatory Approach
    Animal Rule does not “technically” apply to devices.
    CDRH flexibility and innovation
“FDA has not been able to fulfill its implicit national security mission, in large part because of a lack of resources...It is imperative for America’s health and progress for FDA to be provided adequate resources to bring its regulatory science into the 21st century...Doing so will greatly enhance the FDA’s ability to support MCM development and licensing.”
• January 2010: State of the Union Address
  – “[W]e are launching a new initiative that will give us the capacity to respond faster and more effectively to bioterrorism or an infectious disease – a plan that will counter threats at home and strengthen public health abroad.”
    - President Obama
Review Calls for New Federal Approach to Medical Countermeasures

HHS Secretary releases review and recommendations driven by pandemic flu experience
MCM Review Recommendations

1. Enhance MCM regulatory science (FDA)
2. Foster flexible manufacturing
   - New platforms for product development and manufacturing
   - Advanced development core services partnerships
3. Expand the product translation pipeline
4. Advance influenza vaccine development/manufacturing
5. Establish strategic investment firm for innovation
FDA MCM Action Plan: 3 Pillars

1. Enhance the MCM Review Process
2. Advance MCM Regulatory Science
3. Optimize Legal, Regulatory, and Policy Approaches to MCM Development and Use

Objective:
FDA to strengthen regulatory evaluation and facilitate MCM development
(1) Enhancing the Review Process

• Establish Public Health & Security Action Teams (PHSATs)
  – Multidisciplinary teams to tackle the range of regulatory, scientific and policy issues facing MCM development and approval
  – Highly interactive engagement with MCM Enterprise
  – Develop “Regulatory Science Plan” for each MCM project
  – Provide clear development pathways based on best possible science
  – Ensure consistent approaches & best review practices
(2) Advancing Regulatory Science for MCM Development

- Increase FDA capacity to help address unmet regulatory science needs for highest priority MCMs and new technologies
  - Explore solutions to complex scientific regulatory problems
  - Identify situations in which the application of new science could simplify or speed product development and improve the FDA regulatory processes for MCMs
  - Regulatory science agenda responsive to regulatory review needs
  - Support for FDA interdisciplinary inter-center and USG collaborative programs; partnerships and collaborations between FDA and others
(3) Optimizing the Legal and Policy Framework

• Ensure that laws and regulations support preparedness and response
  – Conduct review of strengths and weaknesses of current approaches
  – Where needed, FDA will develop and make recommendations for any statutory changes that might be required to achieve goal of improving emergency preparedness and response

• Examine needs and feasibility for new or modified approaches such as pre-EUAs, “restricted” or “conditional licenses”

• Address needs of non-Federal public health partners
  – e.g. Shelf-life extension of State-held stockpiles

• Examine limitations of and alternatives to Animal Rule
“Our Nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease.”
The Guiding Principle

Seasonal & Pandemic Influenza Preparedness

All Hazards Preparedness

Emerging Diseases Preparedness

CBRN Preparedness