Building a National Capability to Monitor and Assess Medical Countermeasure Use in Response to Public Health Emergencies

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NASEM Workshop

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Public Health Emergencies (PHE)

- 9/11 and Anthrax
- Re-emerging H5N1
- SARS
- H1N1 Pandemic
- Emerging H7N9 Threat
- Measles outbreak
- H7N9
- Zika
- HPAI outbreak
- Ebola
- Japan Earthquake Nuclear Event
- MERS-CoV
- Polio


Chemical + Biological + Radiological + Infectious Diseases

Timeline courtesy of HHS/ASPR
The Problem

The U.S. government has a limited capacity to rapidly collect and analyze PHE medical countermeasure (MCM) safety and effectiveness data, especially during a PHE response.

...now what?
FDA’s MCM Roles

• Facilitating development of and access to MCMs
  – e.g., Animal Rule
• Legal mechanisms (e.g., EUA, IND, IDE, Expanded Access)
• Consumer protection
• Collaboration
• **Monitoring MCM use for safety and effectiveness**
Traditional Medical Product Lifecycle

- Discovery
- Preclinical
- Clinical Development
- BLA/NDA/PMA
- Post-Market

Pre-IND*

IND Review
Phase 1 Phase 2 Phase 3

Phase 4 Marketing

Basic Research Analytical Validation Feasibility Analysis Clinical Validation Data Analysis Submit/Review

* Pre-submission for medical devices
PHE MCM Lifecycle Challenges

- Affected population only available during PHE
- Preclinical only: little/no human data
- No available MCMs
- Pipeline: early R&D
- Postmarketing commitments/requirements
- Human efficacy tests unethical
- Animal Rule
### How is assessment different in a public health emergency?

<table>
<thead>
<tr>
<th><strong>PHE</strong></th>
<th><strong>TRADITIONAL R &amp; D</strong></th>
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<tbody>
<tr>
<td>- Intent – respond and mitigate</td>
<td>- Intent – generalizable knowledge</td>
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<tr>
<td>- Unplanned / unexpected</td>
<td>- Planned / deliberate</td>
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<tr>
<td>- Uncontrolled or no data collection</td>
<td>- Well-controlled clinical trials</td>
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<tr>
<td>- Large numbers of individuals</td>
<td>- Smaller numbers of individuals</td>
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<tr>
<td>- Simultaneous administration / multiple products</td>
<td>- Stepwise progression / single product</td>
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<tr>
<td>- Rapid decision-making / response</td>
<td>- Careful decision-making / time</td>
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<tr>
<td>- Little or no tracking / monitoring</td>
<td>- Strict oversight and monitoring</td>
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<td>- Lack of primary provider oversight / interaction</td>
<td>- Informed consent / process</td>
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<td>- Limited reporting or information dissemination</td>
<td>- IRB review and approval</td>
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<td>- Adverse event reporting</td>
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Preparedness

Data Collection

Possible Threat

Response

Threat Identified

BENEFIT

RISK

Public Health Needs

TRUST

Regulatory Framework

Science

Incident / Event
H1N1

Cases reported in Mexico
April 2009

CDC starts releasing MCMs from SNS
Apr. 21

CDC starts candidate vaccines
Apr. 21

CDC confirms US cases
Apr. 15

US declares PHE
Apr. 26

WHO declares PHEIC
Apr. 25

Discussions well underway:
- Vaccine EUA/lic.
- Vaccine safety
- Antivirals
May 2009

Resistance to oseltamivir & zanamivir found
July 2009

Resistance to oseltamivir & zanamivir found
July 2009

FDA approves 4 H1N1 vaccines
Sept. 2009

Peramivir EUA
Oct. 2009

FDA issues 1st EUAs for flu antivirals & diagnostics
Apr. 27

Vaccine distribution planning well underway
June 2009

Vaccine distribution planning well underway
June 2009

NIH starts clinical trials
July 2009

NIH announces trial results
Sept. 2009

NIH announces trial results
Sept. 2009

ACIP meeting for recommendations
July 2009

ACIP meeting for recommendations
July 2009

Sources:
FDA 2009 H1N1 (Swine) Flu Page (archived)
H1N1 EUAs – Archived Information (FDA)
Historical Information about Device Emergency Use Authorizations (FDA)
CDC 2009 H1N1 Pandemic: Summary Highlights, April 2009 – April 2010 (archived)
Operations for Response

Electronic Health Data

Unstructured/Big Data

Clinical Networks

Photo credits, from top left, clockwise: CDC, FEMA, NIAID, LLNL
Progress to Date

Image courtesy of BARDA
What more can we do?

• EHR capabilities
• Handhelds
• Linking clinical trial networks

• Machine learning
• Social media / crowdsourcing
• “Smart” tech
Our Charge

How do we leverage and coordinate all of this during a PHE response—our only opportunity to collect safety and efficacy data for MCMs?
Resources

• MCM Monitoring and Assessment (new page)
  – https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm561377.htm

• FDA Medical Countermeasures Initiative (MCMi)
  – https://www.fda.gov/medicalcountermeasures

  – https://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm

• PAHPRA (Public Law 113-5)

• MCM emergency use authorities (EUA, etc.)
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