Monitoring and Assessment: FDA’s Role

Robert W. Fisher
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Why the focus on science response?

“The conduct of scientific investigations in the midst of a disaster has often been considered a distraction, and has been impaired by the lack of infrastructure and mechanisms for launching scientific studies in a timely and effective fashion.”-NBSB

“Although responses to recent events have typically used the best available science at the time, additional research, done in parallel with and after the response itself, is often essential to address the most pressing knowledge gaps presented by public health emergencies and to ensure that they are addressed by the time another similar disaster strikes.”-Lurie et. al
FDA’s role in PHEMCE

• Medical countermeasures (MCMs) are FDA-regulated products that are used to diagnose, prevent, protect from, or treat conditions associated with chemical, biological, radiological, or nuclear (CBRN) threats or emerging infectious diseases

• FDA ensures that MCMs are safe, effective, and secure
  – Drugs, vaccines, diagnostic tests, personal protective equipment (PPE)

• FDA facilitates the development and availability of critical public health emergency MCMs

• FDA establish policies to safeguard MCMs from adulteration and prevent disruption of supplies as a result of terrorist activities
Traditional Medical Product

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
Traditional R&D vs. PHE

<table>
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<tr>
<th>TRADITIONAL RESEARCH AND DEVELOPMENT</th>
<th>PUBLIC HEALTH EMERGENCY</th>
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Whence Monitoring & Assessment?

• PHE MCMs may have limited safety data and little or no effectiveness data in healthy individuals and in those with the indicated illness or conditions
• Data can be collected post-approval, however:
• There is uncertainty surrounding what potential data collection model will work best during the response to a PHE
FDA support of Monitoring and Assessment

• Regulatory science
  – Intramural challenge grants
  – Extramural grants
    • FDABAA-15-00121; topic areas 2 ("Develop and refine clinical trial designs....") and 7 ("Facilitate development of Medical Countermeasures...")

• Outwardly focused
  – Advice to sponsors/stakeholders
  – Participation in PHEMCE
    • Monitoring and Assessment Integrated Program Team
FDA Regulatory Science

“Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.”
M&A Regulatory science

• Emerging Infectious Diseases (EID) workshop @ NIH, Nov 2015
• Intramural projects on adaptive study designs and data collection
• BAA and extramural awards
  – “Streamlining Countermeasure Data Collection During Public Health Emergencies”, USCIITG
  – “Adverse Events Monitoring and Analysis Pilot Program”, MITRE Corporation
M&A IPT Mission Statement

To establish a **comprehensive, PHEMCE-wide coordinated** capability to monitor and assess MCM use (safety, compliance, clinical benefit) through **data collection and analysis** during and after an emergency event to **enable assessment and decision-making during** both present and future public health responses

“Everything in place the day before we need it!”
M&A IPT activities to date

• Developed the concept of a “network-of-networks” for data collection during a PHE
• Received consensus for a CRO hub coordination role and overarching data collection for the “network-of-networks”
• Received initial buy-in from existing networks as potential participants in the “network-of-networks”
• Developed a framework for the initial (adaptive) study design to use in PHE (based on Ebola experience)
Influenza Antiviral

Issues:
- Infrastructure
- Drug Request
- Drug shortage decision-making
- Communication

SNS vs. VMI vs. MFG-owned

Issues:
- Who receives drug?
- SAE reporting
- Medication errors

Drug Tracking/Distribution (CDC/FDA/BARDA/MFG)

MCM Request

Issues: Leverage/utilize other networks?
- Study design – Qs and challenges
- Cost/resources for proposed studies?
- No common protocol or CRF
- Data collection; those not receiving drug?
- Who does the data analysis/auditing?
- Define best outcomes for hosp. patients
- Can we measure EUA drug effectiveness?
- How long for IRB approval?
- Who owns the data?

CRO

Common clinical protocols
Common CRFs
Informed Consent

IRB approval

Data and specimen collection

Data analysis/ownership

Expanded Data Collection in subset of population (USG: NIH/CDC/BARDA/FDA, External: USCIIT/JHU/MFG)

Studies (Observational/Expanded Access/RCTs)

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Common CRFs
Informed Consent

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@FDA_MCMi
Resources

• MCMi Regulatory Science program

• Extramural research funding and current projects

• Animal Rule information and guidance

• MCMi news and events (workshops, etc.)
  – [http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm](http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm)