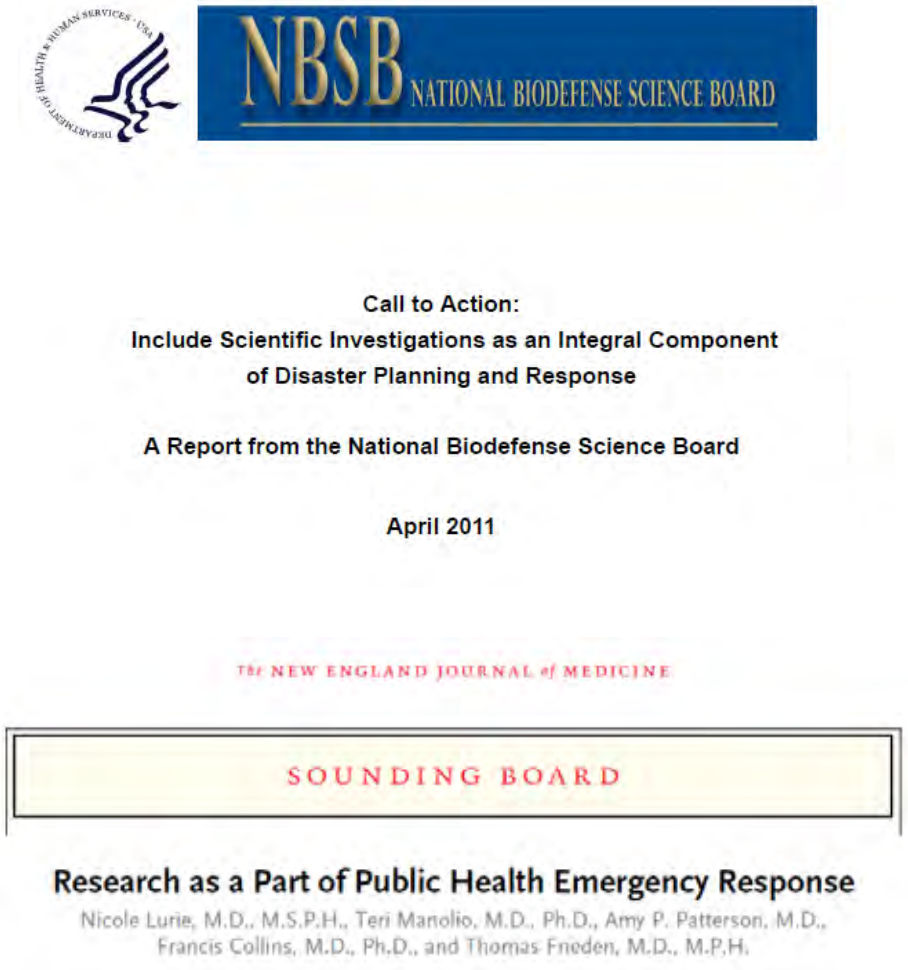
Monitoring and Assessment: FDA's Role

Robert W. Fisher

07 January 2016

Why the focus on science response?


NBSB NATIONAL BIODEFENSE SCIENCE BOARD

Call to Action:
Include Scientific Investigations as an Integral Component of Disaster Planning and Response

A Report from the National Biodefense Science Board

April 2011

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Research as a Part of Public Health Emergency Response

Nicole Lurie, M.D., M.S.P.H., Teri Manolio, M.D., Ph.D., Amy P. Patterson, M.D., Francis Collins, M.D., Ph.D., and Thomas Frieden, M.D., M.P.H.

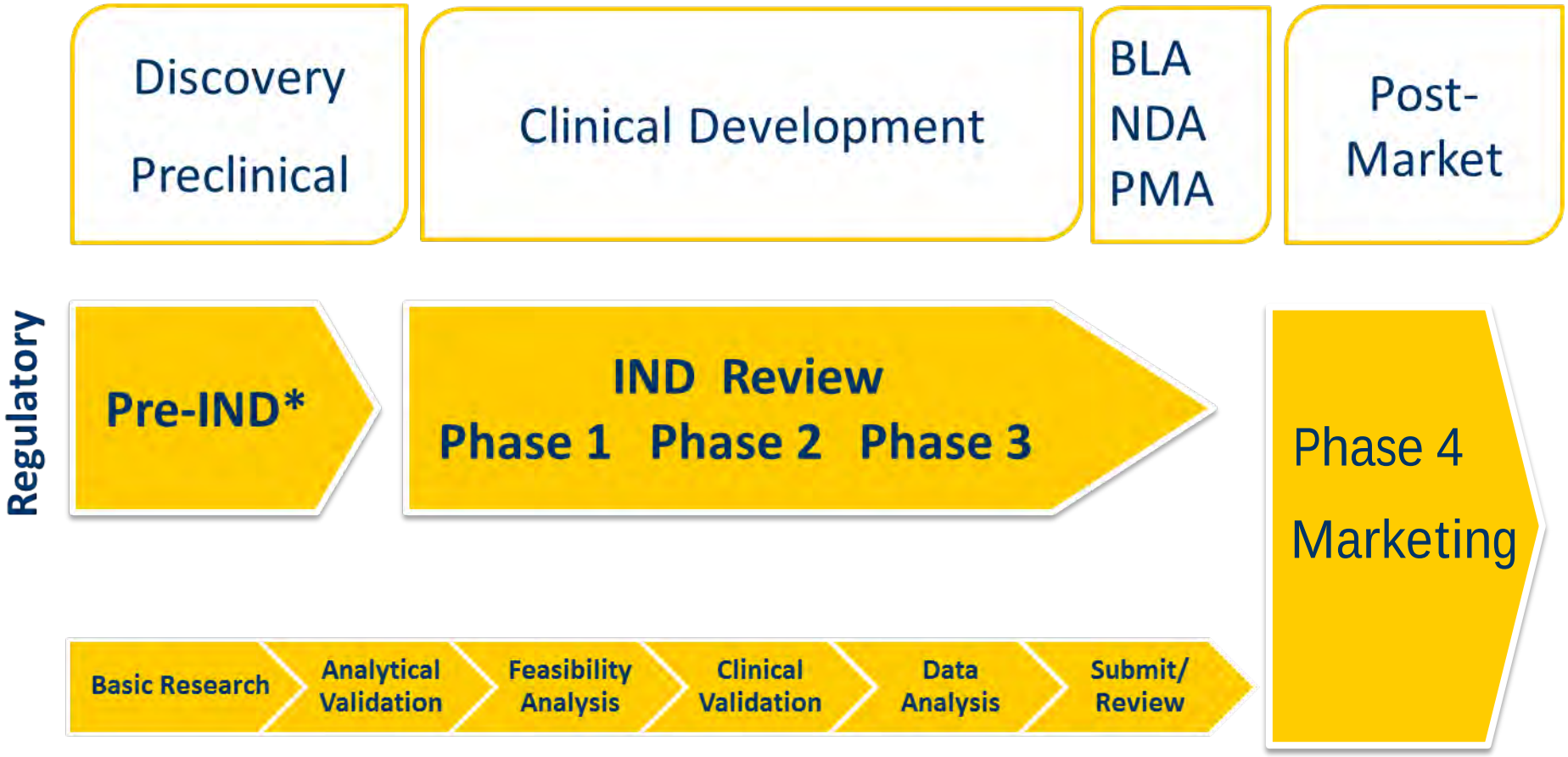
"The conduct of scientific investigations in the midst of a disaster has often been considered a distraction, and has been impaired by the lack of infrastructure and mechanisms for launching scientific studies in a timely and effective fashion."-NBSB

"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



* Pre-submission for medical devices

Traditional R&D vs. PHE

TRADITIONAL RESEARCH AND DEVELOPMENT	PUBLIC HEALTH EMERGENCY

• Intent – Generalizable Knowledge
• Planned/Deliberate
• Well controlled clinical trials
• Smaller numbers of individuals
• Stepwise progression/single product
• Careful decision making/time
• Strict oversight and monitoring
  • Informed Consent/Process
  • IRB Review and Approval
  • Adverse event reporting
	• Intent – respond and mitigate
	• Unplanned/Unexpected
	• Chaos or controlled chaos
	• Large numbers of individuals
	• Simultaneous administration/multiple products
	• Rapid decision making/response
	• Little or no tracking/monitoring
	  • Lack of primary provider oversight/interaction
	• Limited reporting or information dissemination

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

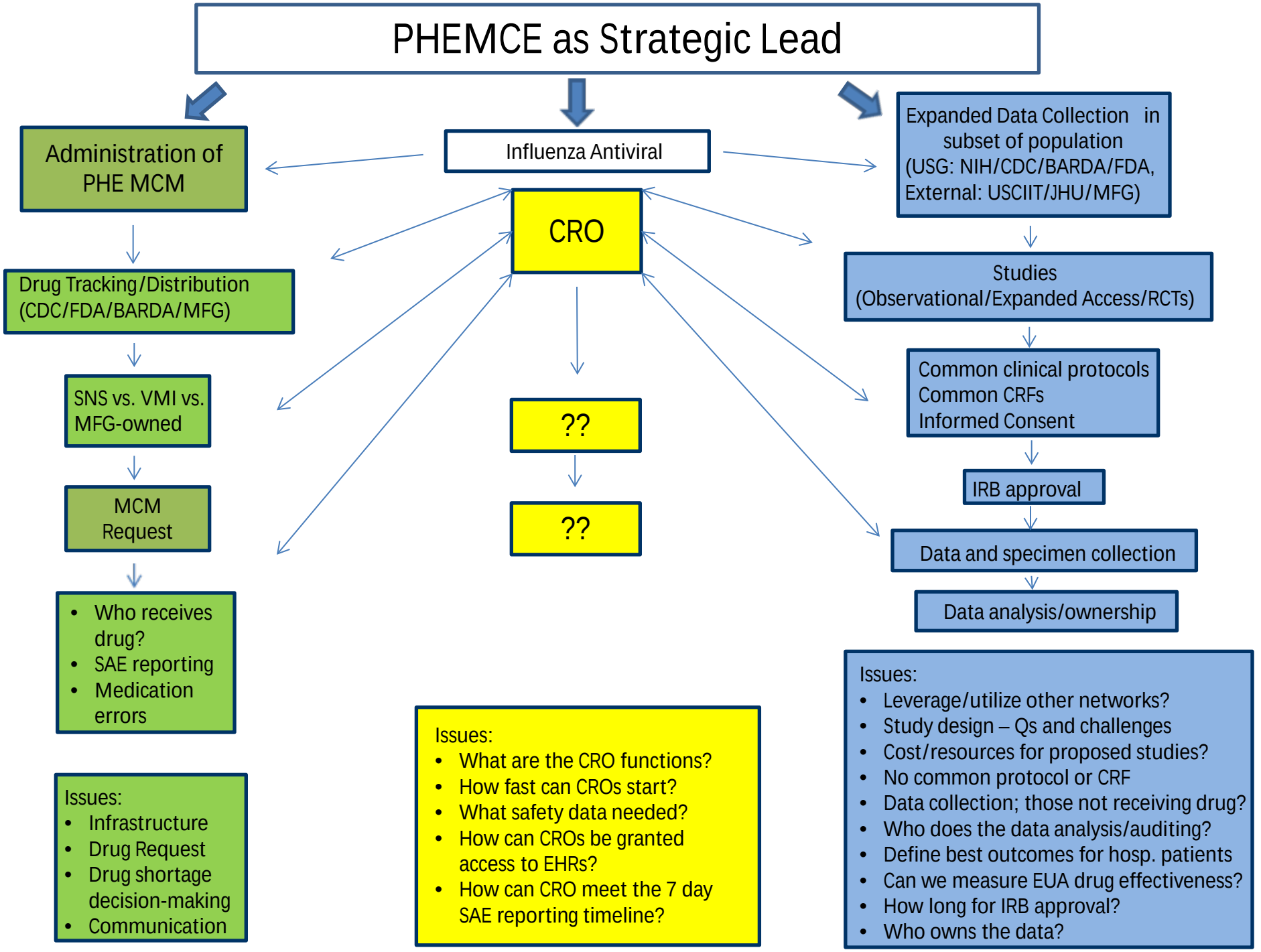
M&A IPT Mission Statement

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)


PHEMCE as Strategic Lead
Administration of PHE MCM
Influenza Antiviral
Expanded Data Collection in subset of population (USG: NIH/CDC/BARDA/FDA, External: USCIIT/JHU/MFG)
CRO
Drug Tracking/Distribution (CDC/FDA/BARDA/MFG)
SNS vs. VMI vs. MFG-owned
MCM Request
• Who receives drug?
• SAE reporting
• Medication errors
??
??
Studies (Observational/Expanded Access/RCTs)
Common clinical protocols
Common CRFs
Informed Consent
IRB approval
Data and specimen collection
Data analysis/ownership
Issues:
• Infrastructure
• Drug Request
• Drug shortage decision-making
• Communication
Issues:
• What are the CRO functions?
• How fast can CROs start?
• What safety data needed?
• How can CROs be granted access to EHRs?
• How can CRO meet the 7 day SAE reporting timeline?
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?

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Thank you!

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@FDA_MCMi

Resources

- MCMi Regulatory Science program
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/default.htm
- Extramural research funding and current projects
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391617.htm
- Animal Rule information and guidance
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391604.htm
- MCMi news and events (workshops, etc.)
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm262925.htm