Federal Capabilities Needed to Monitor/Assess MCMS Used in Public Health Emergencies – An Initial Framework

Engagement with the NASEM Standing Committee for CDC Center for Preparedness and Response

Issue

- There is a need to monitor how MCMs (therapeutics, vaccines, and diagnostics) used during public health emergencies under appropriate regulatory access mechanisms, such as Emergency Use Authorizations, are performing under real world conditions, inclusive of safety/effectiveness and (for diagnostics) clinical sensitivity/specificity.
- This would include evaluating the MCM performance over time against a potentially evolving threat agent (to inform distribution, mitigate against escape mutants, etc)

Approach

- A group of federal subject matter experts considered representative MCMs used in the COVID-19 response in various regulatory categories representing a range of MCM types, settings, and populations and noted how safety/efficacy data was collected post-FDA authorization/approval/clearance (including any gaps/issues arising)
- These included both pharmaceutical MCMs (vaccines and therapeutics) and diagnostics (including point-of-care and lab-based)
- A series of questions was considered for each MCM (provided in backup slides)

Initial DRAFT List of Critical Federal Capabilities

- An initial DRAFT list of critical monitoring/assessment federal capabilities were developed in three categories:
  - Capabilities effectively used during the COVID-19 response that should be maintained for future public health emergencies
  - Capabilities to be developed in advance of the next public health emergency
  - Capabilities that will be needed during the next public health emergency

Federal Capabilities in Monitoring/Assessment Effectively Used During COVID-19 Response

- Food and Drug Administration (FDA) shared resources on the COVID-19 Evidence Accelerator, which connects various real-world data streams to evaluate effectiveness of treatments (https://www.evidenceaccelerator.org/).
- FDA Real-World Evidence Program (https://www.fda.gov/media/120060/download).
- Harmonization of vaccine development protocols/FDA guidance on development to ensure standardization of data collected during development (to inform monitoring/assessment after deployment)

Federal Capabilities in Monitoring/Assessment Effectively Used During COVID-19 Response (cont)

- Early engagement of industry partners to allow for vigorous coordination
- National Institutes of Health Rapid Acceleration of Diagnostics comparative evaluation of diagnostics
- CDC Vaccine Adverse Event Reporting System (VAERS)
- CDC v-safe After Vaccination Health Checker / v-safe COVID-19 Vaccine Pregnancy Registry
- CDC Vaccine Safety Datalink (VSD)

Monitoring and Assessment Capabilities to be Developed Pre-Incident

General

- Federal MCM development contracts should include (perhaps with a public health trigger):
  - Data use agreements (DUAs)
  - Data sharing agreements
- Definition of leads/roles and responsibilities among key stakeholders (e.g. (FDA, manufacturers, Biomedical Advanced Research and Development Authority, CDC)
- Ability to scale up or down as needed should be included in federal contracts

Diagnostic Development/Assessment Capabilities

- Pre-identified Department/Agency lead(s) for initial diagnostic reagent production
- Prepositioned Material Transfer Agreements/DUAs/contract vehicles:
  - Processes for getting reference materials to private manufacturers (e.g. viral stocks, reference panels) to support scale up of diagnostics
  - Requirements for manufacturers to provide (at cost) tests for comparative USG evaluation
  - Processes for receiving diagnostics at USG labs for comparative evaluation
  - Agreements to consult with federal authorities regarding manufacturing reduction decisions
- Pre-developed specificity panels for diagnostics
- Pre-positioned protocols , pre-identified clinical trial networks, and related infrastructure (including IT systems, experts, encryption protocols) to support federal comparative evaluation in real world sensitivity/specificity over time
- Clarity on the opportunities/limitations around use of Stafford Act funding during an emergency for development and validation of diagnostics

Charging/Standing Up an Interagency Coordinating Body

- Comprised of Departments/Agencies with monitoring and assessment pre-event planning and exercising roles and responsibilities as well as responsibilities during and after responses
- Work to develop plans and systems to support standardization, integration and interoperability of data streams/sources resulting from pharmaceutical MCM & diagnostic use during an emergency to inform data-driven decision making
- Work with jurisdictions to identify minimum acceptable data sets and common variables that all jurisdictions will report on MCM performance (to inform safety/efficacy and sensitivity/specificity evaluations)
- Identify and/or determine the parameters for new system(s) that would be used for aggregation of this data in an emergency
- Develop MOUs across Departments/Agencies detailing the system(s) to be used and how the data would be integrated and shared during an emergency

Monitoring and Assessment Capabilities Needed During the Incident

Data Standards/Strategic Guidance for Data Collection and Reporting

- Leveraging pre-determined minimum data elements and systems agreed upon pre-incident
- Ongoing MCM performance over time as threat evolves
- Standards/guidance to ensure ongoing clinical trial data (e.g. for MCM use in additional populations, need for boosters, continued efficacy against variants) is being provided to federal data systems to inform monitoring/assessment work.
  - Data transferred should be cleaned and vetted
- Mechanisms to leverage data from use of products overseas

Additional Capabilities

- Lab and clinical study capacity (appropriately resourced) to provide comparative and ongoing comparative evaluation of therapeutics/diagnostic real-world performance
- Ability to rapidly develop reference panels and specificity panels and make these widely available to support ongoing validation of diagnostic real world performance
- Ability to collect and make available pooled patient samples (e.g. as raw materials for diagnostic panels/validation; challenge materials for ongoing MCM evaluation)

Initial Consultation Discussion Questions

- At a high level, are these the key capabilities that are needed for this work? Are there any additional ones?
- Should all these capabilities be built/maintained at the federal level (vs in the private sector)?

ADDITIONAL INFORMATION

Questions Considered for Each Pharmaceutical MCM

1. What organization(s) were involved in collecting safety and efficacy data during the COVID-19 response for this MCM? Did roles and responsibilities evolve over time?
2. What type of data was needed to answer specific question (e.g. safety, effectiveness, health outcomes) under a variety of scenarios?
3. How were the existing clinical networks (e.g., clinical trial networks, study/research networks) leveraged for the monitoring and assessment of this MCM? What was effective and what gaps/needs were identified?
4. For this MCM, how was existing surveillance infrastructure (or new methods where necessary) used to collect quality safety and effectiveness data?
5. How was monitoring and assessment data used in real time during the COVID-19 response to provide transparency to the public around the use of this MCM? What worked and what didn't?
6. What legal or administrative issues had to be addressed in using healthcare data? Could any of these be addressed ahead of time in advance of future emergencies?

Questions Considered for Each Pharmaceutical MCM (cont)

7. Was a passive surveillance system used to collect data on this MCM? What were the pros/cons/effective use cases for the various systems used to collect safety and efficacy data (e.g., U.S. government-managed systems, sponsor-managed systems, manufacturer-provided product and safety data outside the U.S.)?
8. What capabilities were used to manage and analyze the data in a coordinated way to inform policymaking and clinical decisions at all levels for this MCM? What worked and what didn't?
9. During an emergency response, it is critical for MCM information to be shared quickly and accurately. How did PHE MCM information flow during the COVID-19 response for this MCM? Did all stakeholders get the information when they needed it? Why or why not?

Questions Considered for Each Diagnostic MCM

1. What organization(s) were involved in collecting sensitivity and specificity data during the COVID-19 response for this MCM? Did roles and responsibilities evolve over time?
2. What type of data were needed to answer specific question (e.g. clinical sensitivity and specificity) under a variety of scenarios?
3. How were the existing clinical networks (e.g., clinical trial networks, study/research networks) leveraged for the monitoring and assessment of this MCM? What was effective and what gaps/needs were identified?
4. For this MCM, how was existing surveillance infrastructure (or new methods where necessary) used to collect quality sensitivity and specificity data?
5. How was monitoring and assessment data used in real time during the COVID-19 response to provide transparency to the public around the use of this MCM? What worked and what didn't?
6. What legal or administrative issues had to be addressed in using healthcare data? Could any of these be addressed ahead of time in advance of future emergencies?

Questions Considered for Each Diagnostic MCM (cont)

7. Was a passive surveillance system used to collect data on this MCM? What were the pros/cons/effective use cases for the various systems used to collect sensitivity and specificity data (e.g., U.S. government-managed systems, sponsor-managed systems, manufacturer-provided product and data outside the U.S.)?
8. What capabilities were used to manage and analyze the data in a coordinated way to inform policymaking and clinical decisions at all levels for this MCM? What worked and what didn't?
9. During an emergency response, it is critical for MCM information to be shared quickly and accurately. How did PHE MCM information flow during the COVID-19 response for this MCM? Did all stakeholders get the information when they needed it? Why or why not?

Joanna M. Prasher, PhD MPH
Senior Advisor Medical Countermeasures
CDC/Center for Preparedness and Response
mex7@cdc.gov

Robert Fisher
Senior Advisor for CBRN and Pandemic Influenza
FDA/Office of the Commissioner/Office of Counterterrorism and Emerging Threats
Robert.Fisher@fda.hhs.gov

Yon Yu, Pharm.D, CAPT, USPHS
Regulatory Affairs and Clinical Guidance Team Lead
CDC/National Centers for Emerging and Zoonotic Infectious Diseases/Division of Preparedness and Emerging Infections
fkb8@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.