United States Department of
Health & Human Services
Office of the Assistant Secretary for Preparedness and Response (ASPR)

Transforming a Medical Countermeasures Enterprise to Meet Long-range National Needs

Incentives, Resources and Opportunities for One Health and Emerging Infectious Disease Efforts

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Pre-Decisional Procurement Sensitive

One Health "Action Plan"

- 1. Joint educational efforts between human medical, veterinary medical schools, and schools of public health and the environment;
- 2. Joint communication efforts in journals, at conferences, and via allied health networks;
- 3. Joint efforts in clinical care through the assessment, treatment and prevention of cross-species disease transmission;
- 4. Joint cross-species disease surveillance and control efforts in public health;
- 5. Joint efforts in better understanding of cross-species disease transmission through comparative medicine and environmental research;
- 6. Joint efforts in the development and evaluation of new diagnostic methods, medicines and vaccines for the prevention and control of diseases across species and;
- 7. Joint efforts to inform and educate political leaders and the public sector through accurate media publications.

Emerging Diseases vs. Public Health Emergencies
The Obvious Interfaces with Animal Health

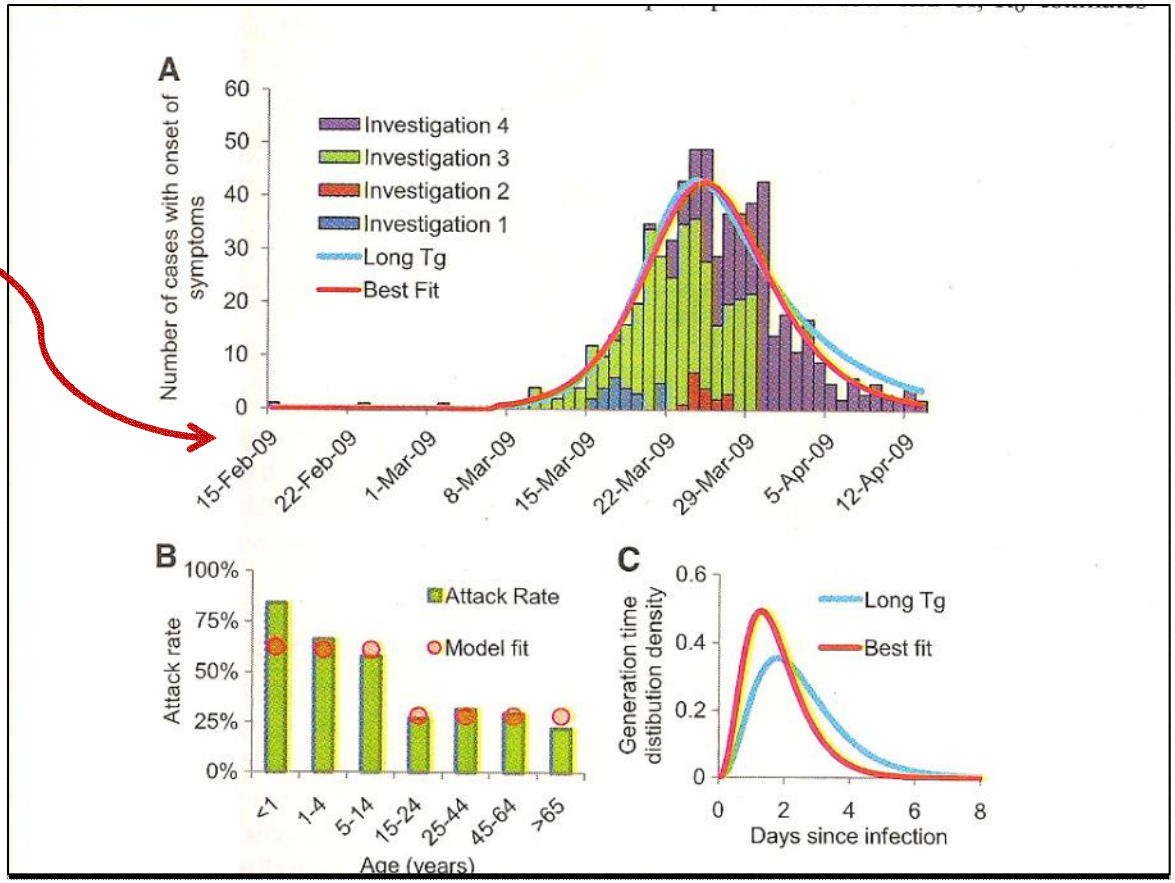
- Most (nearly all) naturally emerging infectious diseases of humans will derive from zoonotic backgrounds
- Most (nearly all) agents on the current threat or select agent lists have derived from zoonotic origins
- Many of the biggest or most challenging viral disease outbreaks are zoonotic (avian influenza, Chikungunya, etc.)
- Most of the drugs, vaccines and diagnostics that will be approved for use for EID and biodefense will rely on animal models for efficacy
- Many of the issues we face with loss of medical countermeasure value due to antibiotic resistance (hence need for new investments) may be linked to agricultural practices

Are there opportunities for collaborative efforts here ?
Yup….

NOVEL 2009 H1N1 VIRUS ORIGIN ?

Photo: Erich Schlegel/Rapport/Newscom

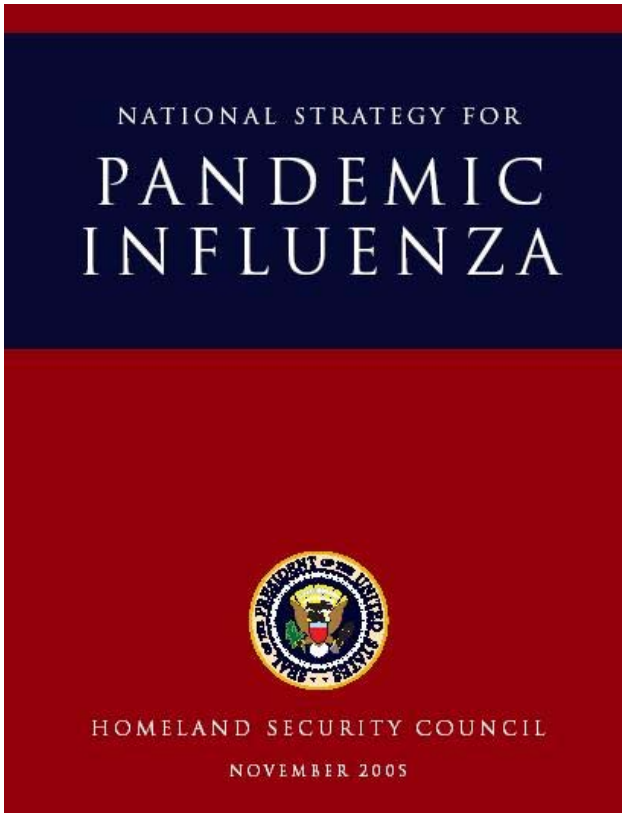
While he may have been the first recognized case, a molecular clock model of the mutation rate in the HA gene suggests a possible common ancestor around 12 January 2009

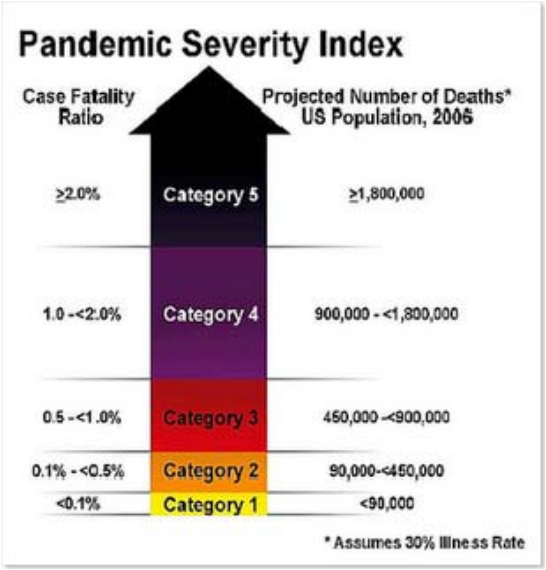


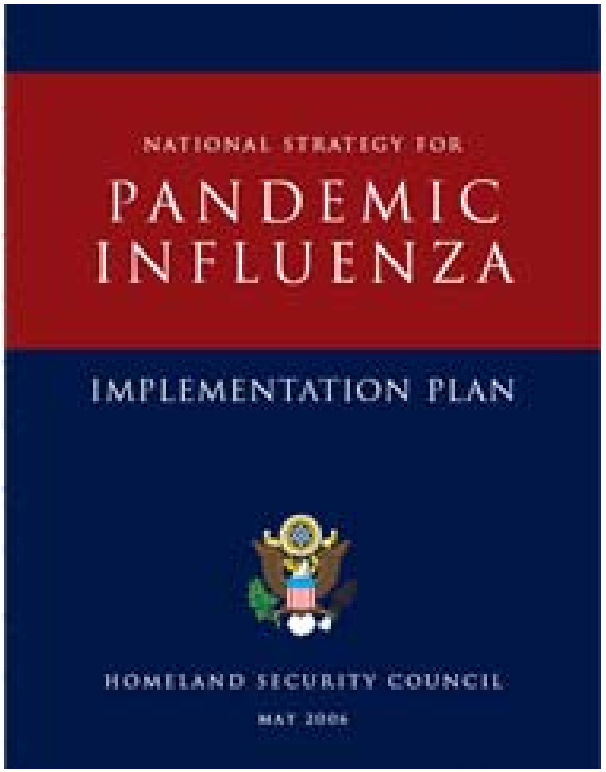
From Fraser, et al., Science, Vol 324 19 June 2009, pg. 1557-1561

Patient "Zero" from La Gloria, Veracruz, Mexico

Flu was here…And We Had Prepared





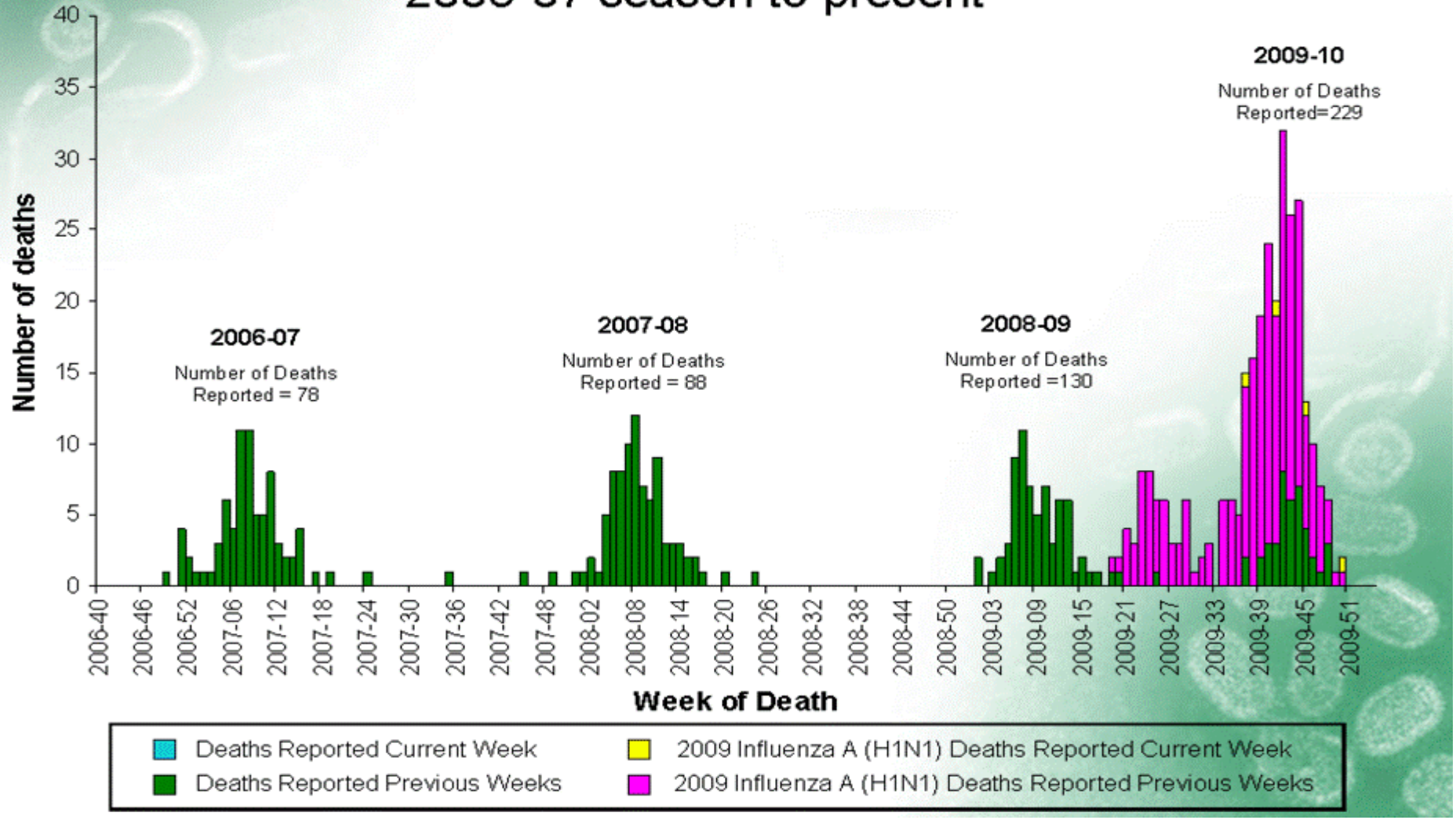


FLUVIEW

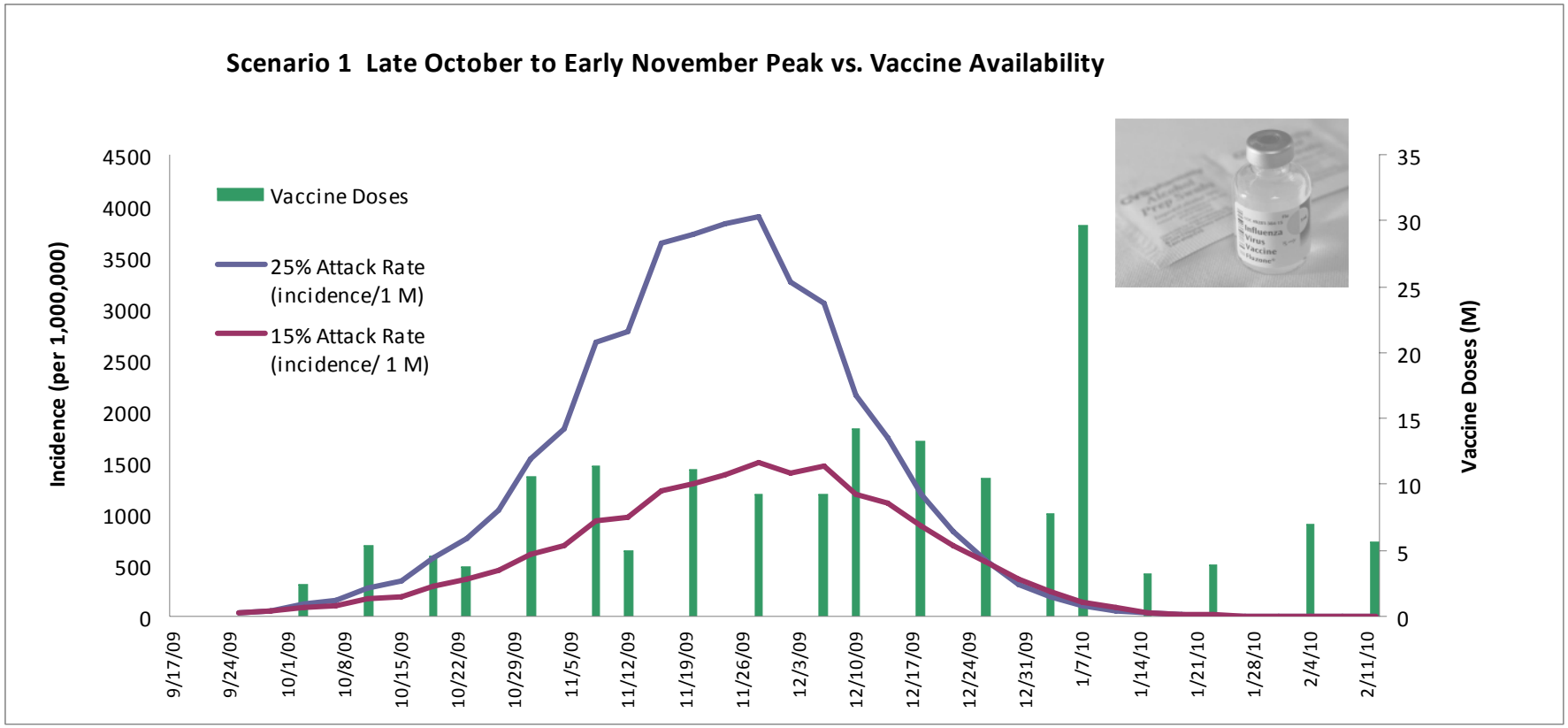
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

CDC Centers for Disease Control and Prevention

Number of Influenza-Associated Pediatric Deaths by Week of Death: 2006-07 season to present



Estimating Disease Arrival vs. Vaccine Arrival



Modeling performed in collaboration between University Of Pittsburg, MIDAS Group and ASPR, HHS

Image: http://cdn.wn.com/ph/img/30/cf/0efac6fd727691d08da92b33c623-grande.jpg **, June 2010**

HHS Medical Countermeasure Enterprise Review: Charge from Secretary Sebelius

- On 1 December 2009, Secretary Sebelius charged the ASPR to lead a comprehensive review of the public health medical countermeasure Enterprise to be completed by 31 March 2010
- "in order to get the 21st-century countermeasures we need to keep us safe, we don't just need 21st-century technology. We also need 21st-century financial, legal, and regulatory frameworks that create incentives for companies to build these advanced countermeasures."
- The ultimate goal of this review is a modernized countermeasure production process with more promising discoveries, more advanced development, more robust manufacturing, better stockpiling, and more advanced distribution practices. . . we want to create a system that can respond to any threat at any time. The kind of system that is so dependable and comprehensive that it deters potential bioterrorism attacks and makes our enemies say, "It's not worth the effort."
- look for the fastest ways to move to new technologies that quickly produce countermeasures that are more dependable and robust. Not just for flu and not just for infectious diseases, but for all the public health threats we face today.

http://www.hhs.gov/secretary/speeches/sp20091201.html

Answering President Obama's Directive

" …we are launching a new initiative that will give us the capacity to respond faster and more effectively to bio-terrorism or an infectious disease – a plan that will counter threats at home, and strengthen public health abroad. "

President Barack Obama, State of the Union Address, 2010

Pandemic Influenza vs. Biodefense Pathogens

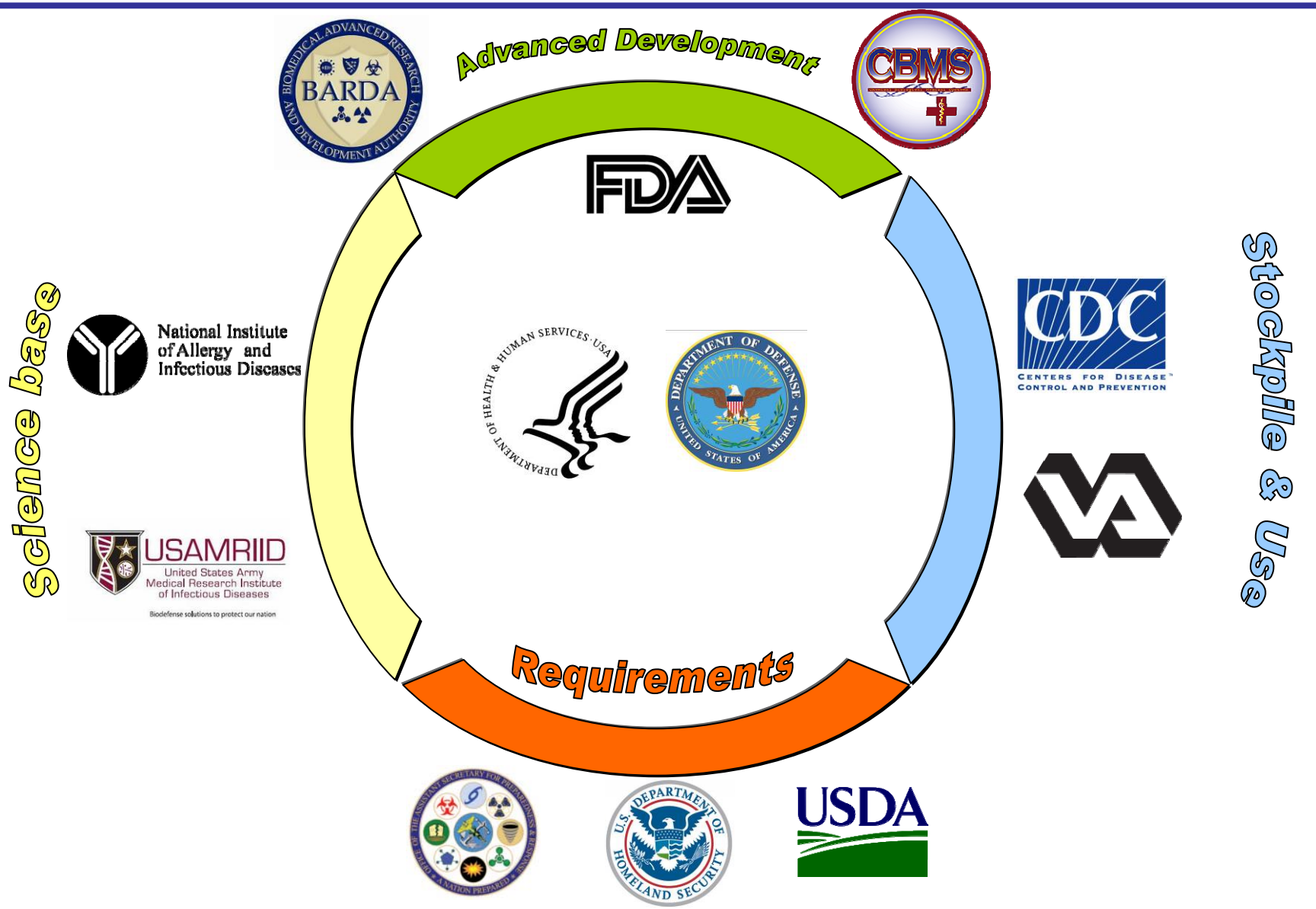
Same as Influenza

- Unpredictable Onset
- Emergency Scenarios Rely on Federal Government procurement and distribution system (SNS)
- Needs more advanced technology development for agile, faster product
- Requires a well-developed public health infrastructure and response at State/Local/Tribal levels
- Place heavy demands on Emergency Room and Hospital Services
- Needs Advanced Planning to develop range of responses and responsibilities

Different than Influenza

- Heavy reliance on vaccine for H1N1 vs. potentially a therapeutic for biodefense pathogen
- Lack of large, mature, commercial sector for product manufacture
- Lack of significant investor community
- More difficult regulatory pathway
- Many more potential threats
- No Warning or ramp up time
- Lack of public “understanding” of the impacts
- Cases generally more concentrated in time and space
- Unfamiliar

Organizations Contributing to the Public Health Emergency Medical Countermeasure Enterprise



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Scoping the Challenge

Define, Design, Develop, Deliver and Dispense Medical Countermeasures to reduce the adverse health consequences of public health emergencies

Complex array of naturally-occurring and intentional threats

PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURES ENTERPRISE
PHEMCE

Diverse population

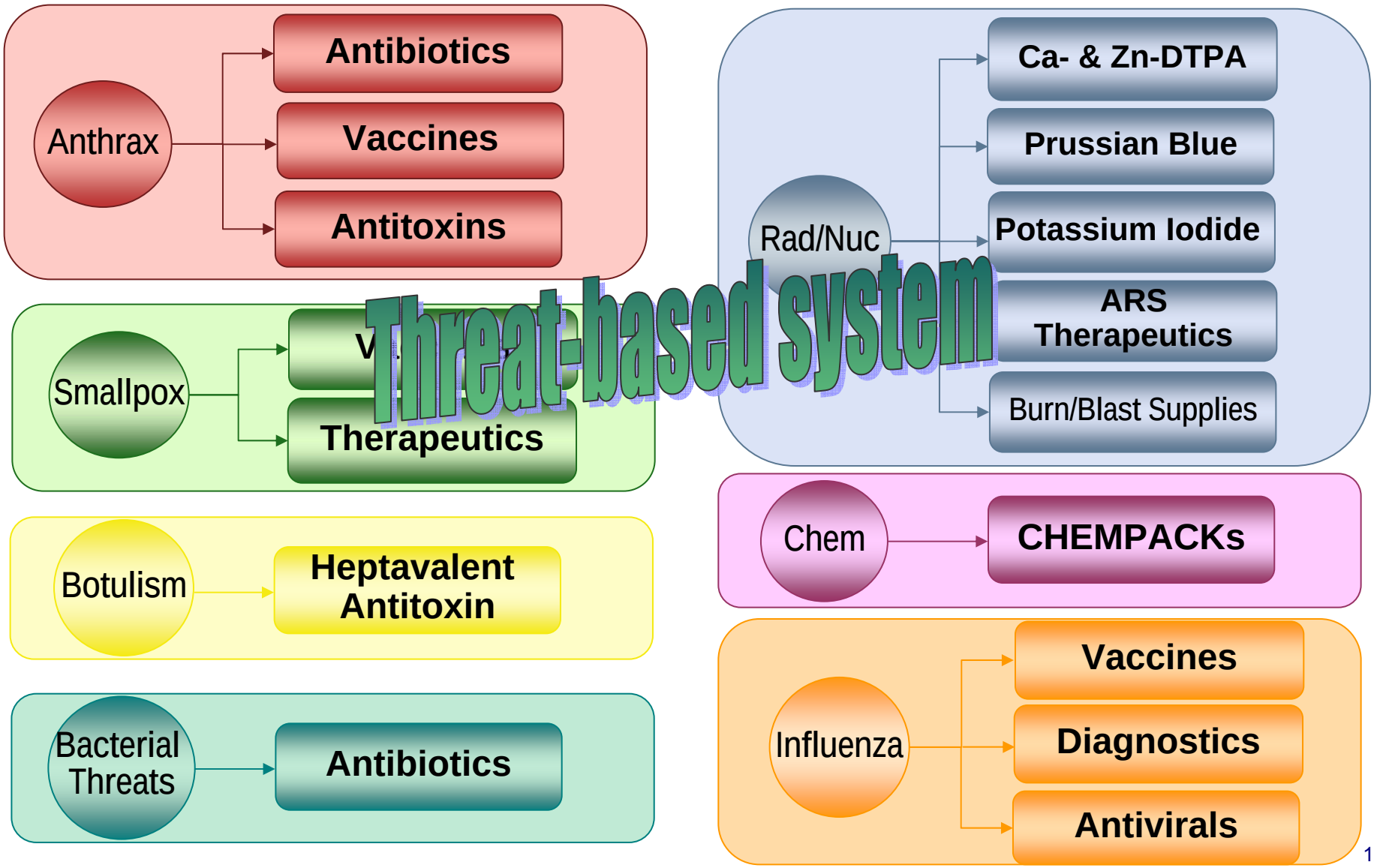
Lengthy, risky and expensive product development; innovative partnerships with industry

Prioritize programs to effectively address mission goals

Strategies & dependencies for effective use

Medical Countermeasures as National Security Assets

Who Gets What? When and How?



Themes from Stakeholders on MCME Needs

- Institute a single, unified enterprise management structure
- Facilitate improved end-to-end partnering (in federal agencies)
- Provide greater transparency for product requirements
- Incorporate end-user needs into end product design
- Develop Target Product Profiles
- Incentivize “multi-use” agents (platforms)
- Empower program managers
- Help create commercial market for MCM products
- Simplify the IP system and improve patent length to 20 years
- Use public private partnerships to encourage more investment by private sector
- Create technical centers of excellence (for advanced development)
- Commit to multi-year funding of CBRN/pan flu products

http://www.iom.edu/Reports/2010/The-Public-Health-Emergency-Medical-Countermeasures-Enterprise.aspx

The MCME Draft Review - Vision

"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 MCME Review

Key attributes of a forward looking strategy

- Investments in products and capabilities that address clearly defined current threats and future, unknown threats
- Embrace nimble, multi-use technologies and platforms
- Increased investment in regulatory science and FDA engagement
- Establish new mechanisms for public-private partnerships
- Be more creative in helping inexperienced companies meet goals by various mechanisms
- Integrate activities and governance structure into a unified oversight

Capability-based system

The MCME Review - Key Initiatives

- **Major investment in upgrading science capacity at FDA**
  - Provide initial $170 M for FDA Regulatory Research
  - Optimize the Regulatory Review Process for Sponsors
    - Focused Action Teams, Regulatory Science Plans
  - Tackle difficult regulatory framework issues with other HHS and interagency partners (EUA, Animal Rule, etc.)
- **Establish Center(s) for Excellence in Advanced Development and Manufacturing**
- **Expand the Product Pipeline at NIAID – Concept Acceleration Program**
- **Address immediate needs for influenza**
  - Potency testing, sterility testing, optimized virus seed backbone
- **Establish a Strategic Investment Fund to increase investments in commercial ventures with multi-use potential**

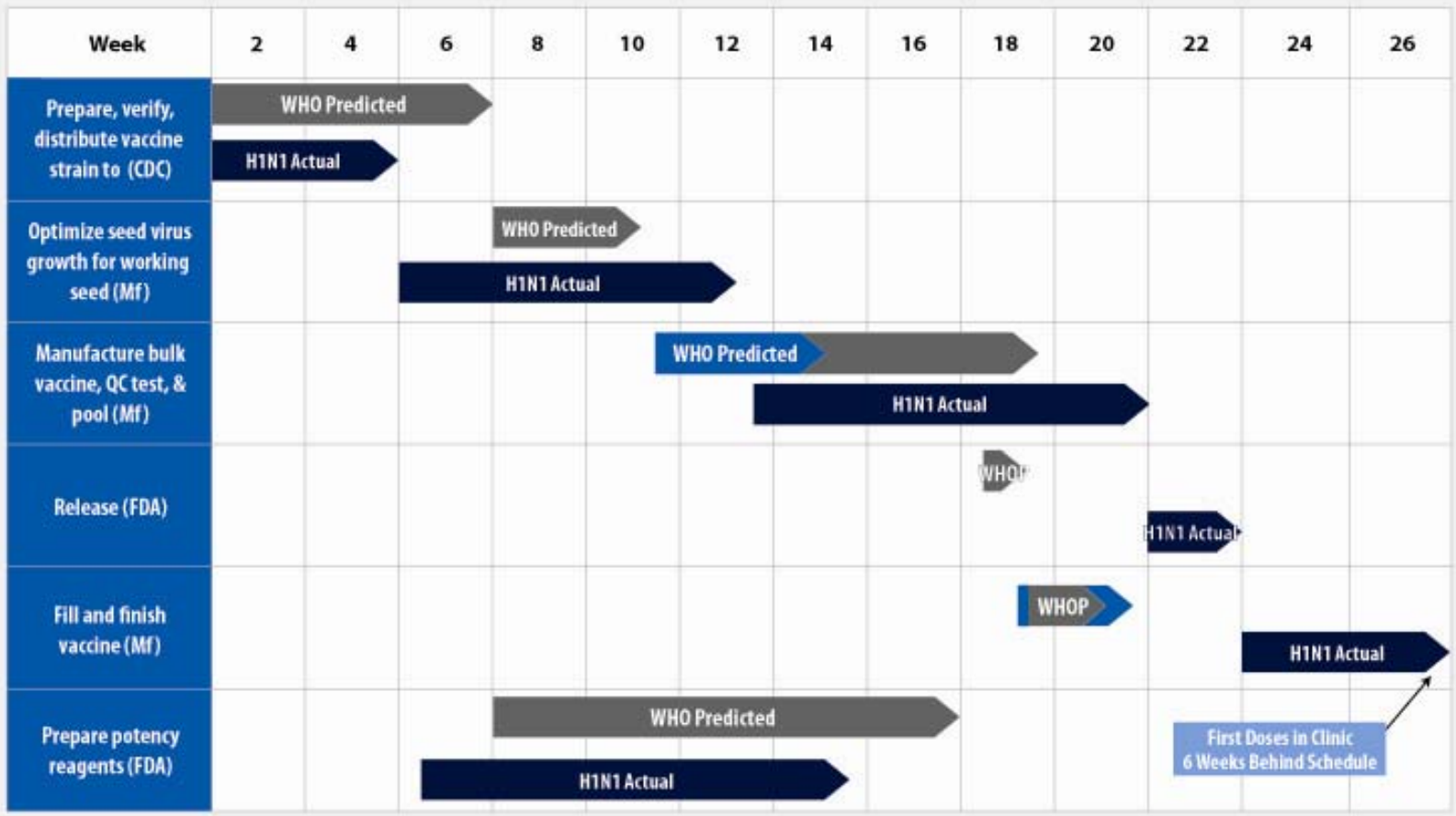
Center(s) of Excellence for Advanced Development and Manufacturing (ADM)

- Separate but complementary facilities to be established by BARDA and DOD
- Provides “core services” capabilities to USG-contracted sponsors of advanced development MCM efforts
- Focused on biologics
- Provides surge capability for influenza vaccine production or similar pandemic needs
- Designed to permit multiple, modular, flexible production methods
- Based on a Public Private Partnership model
- Encouraging consortia of experienced pharmaceutical organizations with academia or other similar partnering
- IP assurances will be established for all parties
- Potential for further business arrangements between consortium & sponsor
- Level of time commitment to government-requested products depends on initial investment ratios between USG and entity
- Solicitation will be issued shortly

Concept Acceleration Program

- **NIAID-based program**
- **Aimed at incubating discovery or early technology for cross over to advanced development**
- **Hire dedicated staff for technology / discovery scouting**
- **Active engagement with entrepreneurs and scientists to nurture early programs**
- **Expanded access to NIH-provided core services**
  - Clinical trials network, reagent repositories, animal model development, etc.
- **Directed funding to continue maturing the concept**

2009 H1N1 Vaccine Production Timeline: Delayed Delivery of First Doses



NOTE: This production time line shows time to first doses of inactivated influenza vaccine; time to release of first doses of LAIV was 21 weeks.

WHOP = World Health Organization Predicted

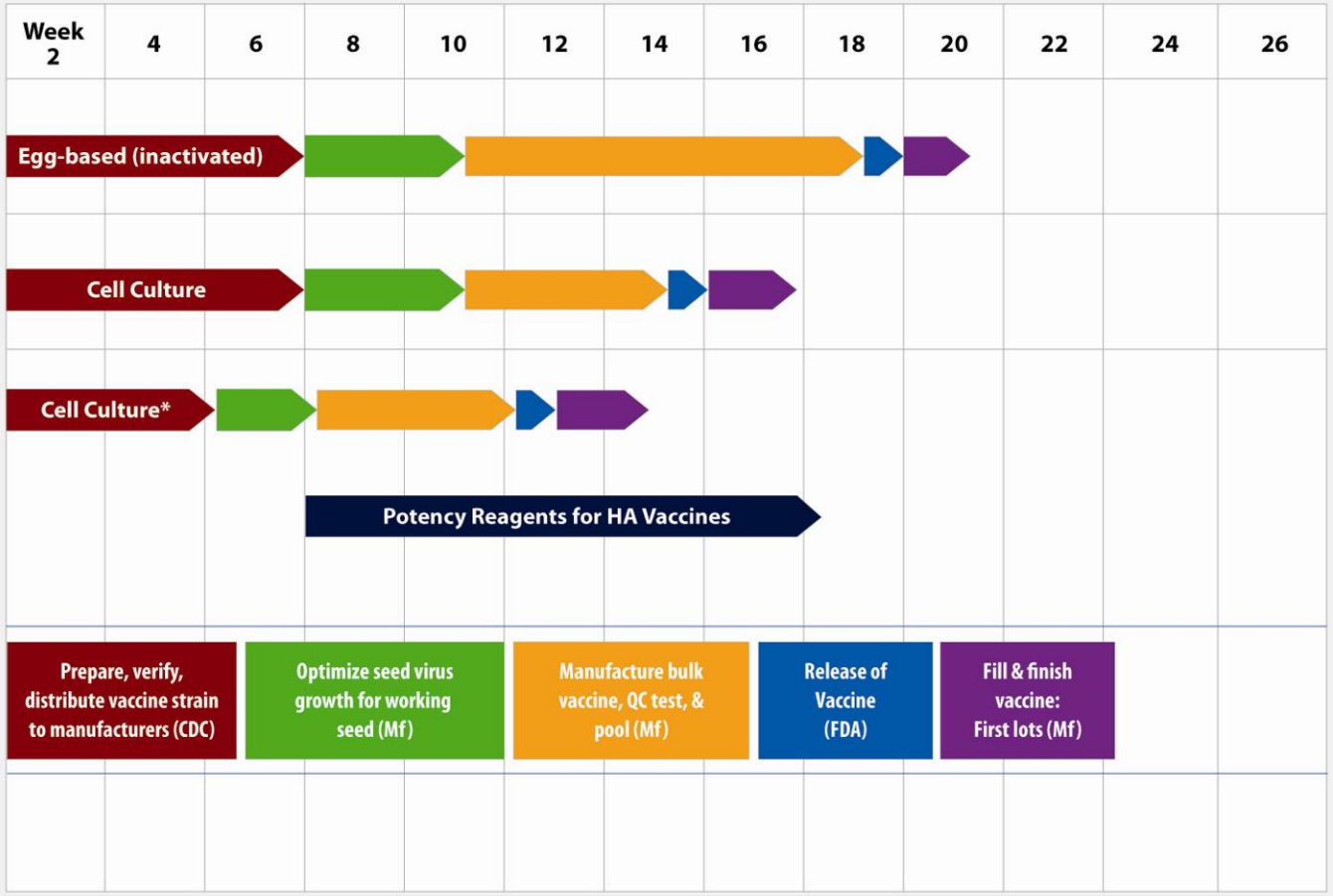
Accelerate Influenza Vaccine Production

- **Collaborative effort between CDC, NIH, BARDA, FDA**
- **Speed process to optimize seed viruses for vaccine production**
  - Combinatorial genetic approaches to optimize gene constellations for new seed stocks
- **Modernize Potency Testing**
  - Alternative methods will be analyzed such as isotopic dilution mass spectrometry, Surface Plasmon Resonance, etc
  - Optimize, validate and apply immune-capture isotope dilution MS methods
- **Modernize Sterility Testing**
  - Evaluate a variety of rapid microbial contamination systems such as but not limited to Growth Direct System, Scan RDI, etc. for sterility testing of biological products CDC commitment
  - Validate new sterility methods for specificity, robustness, ruggedness and repeatability

Effects of Recommended Actions on Delivery of Pandemic Influenza Vaccines

Recommended Change	Estimated Time Required to Make the Change	Effects on Time to First Dose	Effects on Bulk Production until Demand Satisfied	Alternative Uses in Other Medical Countermeasures
Increased Surveillance	1-3 years	Moves the starting line forward by weeks or more	None	Yes
Faster Production of Optimal Vaccine Seed	1-2 years	Up to several weeks	Up to several weeks (if more efficient virus growth)	No
Modernized Sterility Tests	1-2 years	Approximately 1 week	None	Yes
Improved Generation of Potency Reagents	1-2 years	Avoids possible delay of up to several weeks	None	Possibly
Expanded and Streamlined Fill and Finish Procedures	1-3 years	Slight	Up to weeks	Yes

Production Timelines for Egg and Cell Culture Inactivated Vaccines



*Assumes an additional and expected reduction in time to prepare and optimize seed viruses.

Strategic Investor

- **Provide funding incentives and business acumen to businesses with technologies or platforms that produce benefit to Government needs, while also producing commercial value to partner**
- **Evaluate similar programs**
  - In-Q-Tel (Intelligence Community)
  - OnPoint (Army)
  - Red Planet (NASA)
- **Not for profit, independent management company**
- **Aimed at providing expert business assistance**
- **Potential for funding from other private syndicated sources**

Summary

- The Medical Countermeasure Enterprise Review addresses gaps in the ability of the USG to the increase the product pipeline, lower risks for commercial partners and begin to develop a capabilities-based rather than threat-based strategy for medical defense
- As the initiatives move from ideas to established programs there are opportunities to have robust partnering across disciplines to harness expertise in moving toward a capability-based response system for all infectious disease hazards