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

HHS Efforts to Improve the Influenza Vaccine Production Enterprise

Briefing to

The President's Council of Advisors on Science and Technology

March 8, 2011

Purpose

To provide a progress update on PCAST recommendations regarding pandemic influenza

- ***Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of the Pandemic Influenza*** **(August 2010)**

- ***Report to the President on U.S. Preparations for 2009-H1N1 Influenza*** **(August 2009)**

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Overview of PCAST Recommendations

- **Actions with Short-term Impact (1-3 years)**
  - Accelerating the identification of new pandemic threats
  - Shortening time for availability of virus strains, potency and sterility testing
  - Establishing a fill-finish manufacturing network

- **Actions with Longer-term Impact (2-10 years)**
  - Advancing cell culture and recombinant vaccine technologies
  - Accelerating clinical research on live attenuated vaccines
  - Supporting adjuvant development and licensure
  - Supporting basic immunology research on influenza
  - Expanding domestic vaccine manufacturing infrastructure
  - Developing flexible investment strategies
  - Implementing a new management structure for enterprise oversight

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Develop Diagnostics to Identify New Threats

- **HHS (CDC, BARDA, NIH, FDA) and DoD collaborating to improve diagnostic tools and surveillance systems**
  - "Better tests, better guidance, better practice"

- **Testing capability priorities include**
  - Multi-target influenza PCR (MT-PCR)
  - Rapid influenza immunity testing (RIIT)
  - Antiviral resistance influenza testing (ARIT)
  - Rapid virus characterization testing (RVCT)
  - Laboratory and hospital influenza testing (LIT)
  - Point-of-care influenza testing (POC-IT)

- **BARDA is advancing innovative platform technologies**
  - Centrifugal RT-PCR technology
  - Combination PCR and mass spectroscopy-based multiplex testing

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Shorten Time to Manufacture, Test, & License Influenza Vaccines

- **Collaborations underway between BARDA, CDC, NIH, FDA and industry partners to**
  - Develop high production yield vaccine virus seed strains
  - Develop faster and better ways to produce reagents and measure vaccine potency
  - Develop faster ways to measure vaccine sterility

- **Accomplishments / Initiatives**
  - FDA has approved Novartis Rapid Milliflex sterility test
  - FDA/CBER and CDC have begun comparative studies for the calibration of potency reagents using mass spectrometry
  - NIH undertaking an initiative on virus optimization and potency reagent production
  - BARDA awarded contracts for optimization of synthetic vaccine candidate virus seeds and a novel rapid digital sterility test in September 2010

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Establish a Fill-Finish Manufacturing Network

- **BARDA contracted with several non-influenza vaccine manufacturers to fill/finish 2009H1N1 vaccine**
- **BARDA has completed a detailed survey of domestic CMOs & FDA-licensed vaccine manufacturers to assess fill finish capacities**
- **BARDA is developing a solicitation to**
  - Establish a fill-and-finish network for all medical countermeasures, including influenza vaccine
  - Develop a network to harmonize tracking systems from manufacturers to end users through bar coding
  - Develop a product tracking system from manufacturer to patient
- **Release of draft solicitation anticipated in 2Q2011, with release of a final solicitation anticipated by 3Q2011**

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Develop Adjuvants

- **NIH supports discovery & early development of many adjuvants for influenza vaccines**
- **BARDA has awarded multiple contracts to develop adjuvants for use with influenza vaccines**
  - Novartis - MF59
  - GSK - ASO3
  - sanofi pasteur – AFO3
  - Intercell - LT adjuvant patch
  - Protein Sciences - GLA
- **NIH and BARDA have supported numerous clinical trials, including a novel mix-and-match study, of adjuvants coupled with pH1N1, H5, and other avian strains**
- **BLAs for adjuvented influenza vaccines anticipated in 2011**

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Develop Next-Generation Vaccine Technologies

- **Mammalian Cell-based Technologies**
  - BARDA supporting development of seasonal and pandemic influenza vaccines grown in cell culture
  - BARDA anticipates U.S. licensure of first cell-based influenza vaccines in 2012
  - BARDA has supported four manufacturers (Novartis, Baxter, GSK, MedImmune) since 2006 to make cell-based vaccines for U.S. markets

- **Recombinant Technologies**
  - NIH/NIAD is supporting early development of more than 13 recombinant-based influenza vaccines and multiple unviersal vaccines
  - BARDA is supporting development of multiple recombinant influenza vaccines (Protein Sciences [2009], Novavax [2011], VaxInnate [2011])
  - Contract awards require contractors to provide first doses within 12 weeks and 50 million doses within 6 months

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Develop Live-Attenuated Virus Vaccines

- **BARDA is supporting development of cell-based LAIV vaccines and alternative LAIV vaccines (St. Petersburg)**
- **NIAID has had a CRADA with MedImmune since 2005 to develop LAIVs for all 15 influenza virus subtypes and to evaluate them in preclinical and clinical studies**
- **NIAID is supporting research on prime-boost approaches to enhance the immunogenicity of LAIV vaccines in cases where the vaccine alone is only weakly immunogenic (e.g., H5N1)**
- **Development of LAIV in multidose vials and regulatory framework for pandemic usage is needed**

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Study Basic Immunology of Influenza

- **NIAID supports a large portfolio of basic immunology studies, focused on**
  - Human immune responses to vaccines and infectious diseases
  - Identifying better correlates of immune protection and adverse events
  - Using this knowledge to advance vaccine development and perhaps lead to a “universal influenza vaccine”

- **Two major NIAID initiatives that study influenza infection and vaccines are**
  - *Human Immunology Project Consortium* (launched 2010) to provide state-of-the-art analyses of innate and adaptive immune responses to infection and vaccination
  - *Modeling Immunity for Biodefense,* which supports the development of new and improved models to advance the study of immunology or immune-based therapies

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Build Domestic Vaccine Manufacturing Infrastructure

- **BARDA partnered with sanofi pasteur and MedImmune to retrofit domestic bulk and fill finish vaccine manufacturing facilities used to make 2009 H1N1 vaccine**

- **BARDA partnered with Novartis to build a new state-of-the-art cell-based vaccine manufacturing facility (NC) with capacity to make 150M doses in 6 months**

- **Centers for Innovation in Advanced Development and Manufacturing**
  - Will provide core advanced development and manufacturing services for CBRN MCMs as well as influenza vaccine manufacturing surge capacity
  - Will provide training for biopharmaceutical manufacturing workforce
  - Synopsis released March 2, 2011

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Change the Way We Do Business

- **Medical Countermeasure Strategic Investor**
  - Non-profit, government-financed venture capital entity that will support the development of strategic public health technologies, including multi-use platforms and products
  - Will provide critical financial and business services for small companies

- **FDA Action Teams & Regulatory Science**

- **HHS Governance**
  - Single governance system for all countermeasures
  - Early coordination of all agency partners (and DoD)

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Reflections on H1N1: Science Response

- **HHS implemented many of recommendations from August 2009 PCAST Report on H1N1, including**
  - Expanding surveillance systems to monitor the spread of H1N1
  - Accelerating fill-finish of 2009-H1N1 vaccine
  - Establishing clear guidelines on use of antiviral drugs
  - Making IV antiviral drug peramivir available under EUA

- **Planning scenario based on modeling used in PCAST report generated a great deal of sensationalized reporting**

- **H1N1 and other recent events (Haiti, Deepwater Horizon) underscore the need for a robust "science response" capability**
  - National Biodefense Science Board to provide recommendations on needed infrastructure

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Conclusion: Challenges & Opportunities

- **HHS is committed to improving its overall response capabilities for pandemic influenza and all other threats. Distribution and utilization of pandemic MCMs will become the critical choke points.**
  - Development of real science and industry based solutions will be required to benefit from increased product manufacturing surge capacity.
- **Safe and effective vaccines and MCMs will continue to be a critical part of our national response**
- **The PHEMCE Review will lead to significant improvements in our capabilities, public-private partnerships, and business model**
- **We are making significant advances in developing next-generation technologies and platforms to address pandemic influenza, but maintaining program budgets, capabilities, and focus will be a challenge in coming years**

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