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 adjuvanted 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 universal 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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