Advanced Development of New Influenza Vaccines

Biomedical Advanced Research and Development Authority (BARDA)

Robert C Huebner, Ph.D.
Deputy Director, Influenza Division
HHS/ASPR/BARDA
U.S. Pan Flu MCM Strategic Current & Possible New Policy Goals before H1N1

- **Vaccines**
  - Goal #1: Establish and maintain a dynamic pre-pandemic influenza vaccine stockpile available for 20 M persons (2 doses/person) or more persons depending on vaccine mfg. capacity & results of dose-sparing adjuvant studies and prime-boost immunization studies: H5N1 vaccine stockpiles
  - Goal #2: Provide pandemic vaccine to all U.S. citizens within 6 months of a pandemic declaration: pandemic vaccine (600 M doses)

- **Antivirals**
  - Goal #1: Provide influenza antiviral drug stockpiles for pandemic treatment of 25% of U.S. population (75 M treatment courses) and federal share of antivirals for outbreak prophylactic usage as a community mitigation measure as shared responsibility
  - Goal #2: Provide influenza antiviral drug stockpiles for strategic limited containment at onset of pandemic (6 M treatment courses)

- **Diagnostics**
  - Goal #1: Develop new high-throughput laboratory, point-of-care (POC), and home detection influenza diagnostics for pandemic influenza virus detection

- **Other Countermeasures**
  - Goal #1: Develop and acquire other MCMs including syringes/needles, masks/respirators, ventilators, antibiotics, & other supplies (Pneumococcal & Streptococcal Vaccines?)

*National Strategy for Pandemic Influenza (Nov 2005) and HHS Pandemic Influenza Plan (Nov 2005) [www.pandemicflu.gov](http://www.pandemicflu.gov)*
**Integrated Portfolio Approach: Pandemic Influenza**

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Cell-based Influenza Vaccines: BARDA Initiatives

• Robust, flexible, and scalable less vulnerable manufacturing platform for influenza vaccines
• Awarded 6 contracts ($1.3 B) in 2005-06 for advanced development of cell-based seasonal & pandemic influenza vaccines towards US licensure
  – commitment for domestic manufacturing surge capacity of 150 M doses in 6 mos. of pandemic onset
• Novartis, Baxter, sanofi pasteur, GSK, Solvay, MedImmune
• Two manufacturers have completed Phase 3 clinical studies & expected to submit BLAs in 2011-2012
• Two manufacturers in early stage development
• Two manufacturers down-selected in 2009
Antigen-sparing Vaccine Technologies: BARDA Initiatives

- Adjuvants, immunostimulating molecules, provide dose-sparing effects, cross-strain protection, and enhanced immunity to vaccines

- Awarded 3 contracts in 2007 ($133 M) for advanced development of pandemic influenza vaccines with adjuvants towards US-licensure
  - Novartis, GSK, Intercell
  - One manufacturer is completing Phase 3 clinical studies & expected to submit BLA in 2011
  - One manufacturer completed Phase 2 clinical studies and another program is on hold pending clinical re-evaluation

- Awarded 3 contracts ($250M) to perform clinical trials of H1N1 vaccines that included the evaluation of H1N1 formulations using adjuvants
  - Novartis, GSK, sanofi pasteur

- Mix-n-Match program with NIH
  - H1N1 program with sanofi pasteur antigen and GSK adjuvant completed
  - H5N1 program with sanofi pasteur antigen and GSK/Novartis adjuvant
    - IND filed December 2010 and clinical testing started Q2 2011
Recombinant-based Influenza Vaccines:
BARDA Initiatives

- Recombinant & molecular technologies may provide vaccine sooner with less dependence on influenza virus strain properties
- US-licensure with commitment for domestic manufacturing surge capacity of 50M doses in 6 mos. of pandemic onset & initial lot release in 12 weeks consistent with PCAST and MCM Review recommendations
- Recombinant I RFP awarded one contract in June 2009 for advanced development of recombinant-based seasonal & pandemic influenza vaccines towards US-licensure
  - Protein Sciences Corporation ($155M)
    - purified HA protein from baculovirus-derived insect cells
    - Completing Phase 3 clinical studies and filed BLA
- Two additional contracts were awarded with Recombinant II RFP in February 2011
  - Novavax ($97M base/$179M with options)
    - Insect cell-based expression of influenza VLPs
    - Phase 2 clinical trial completed
  - VaxInnate ($118M base/$196M with options)
    - Bacterial expression of influenza HA-flagellin fusion proteins
    - Phase 1 clinical study has been completed
Improving Influenza Vaccine Manufacturing: BARDA Initiatives

• Lessons of the 2009 H1N1 pandemic - AAR, PCAST, MCR
  — Need to develop virus vaccine strains optimized for high production yields in eggs and cells
  — Need to utilize vaccine manufacturing technologies independent of influenza virus growth and purification
  — Lot release of H1N1 vaccine was impacted adversely by availability of potency assay reagents & sterility testing
  — Need to leverage Interagency collaboration

• HHS Initiatives – NIH, CDC, FDA, BARDA, Industry
  — Optimize influenza virus vaccine strains for high production yield
    • Three years - $26.9M
    • Contract with Novartis/JCVI awarded September 2010
  — Develop improved potency assay standards and methods
    • Three years - $31.2M
  — Develop rapid sterility assays
    • Four years - $4.85M
    • Contact with RMB awarded September 2010
Future Directions

• Focus on sustainable technologies that will allow more rapid production and release of influenza vaccines (shorten 6 months target to 4 months)
  – Licensure of cell-based influenza vaccines
  – Licensure of influenza vaccines using antigen sparing technologies
  – Introduction of improved productivity vaccine candidates
  – Introduction of new testing technology to allow more rapid release of influenza vaccines
  – Licensure of recombinant/molecular-based influenza vaccines that do not require virus replication for vaccine production
  – Sustainability is key