



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

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# **Advanced Development of New Influenza Vaccines**

**Biomedical Advanced Research and Development Authority (BARDA)**

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# 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?*)

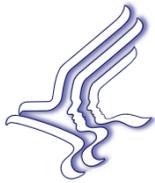
*National Strategy for Pandemic Influenza (Nov 2005) and HHS Pandemic Influenza Plan (Nov 2005) [www.pandemicflu.gov](http://www.pandemicflu.gov)*



# Integrated Portfolio Approach: Pandemic Influenza



	Vaccines	Antivirals	Diagnostics/ Respiratory Devices
Advanced Development	Cell-based Antigen-sparing Recombinant & Molecular	IV Antivirals	<u>Diagnostics</u> Point of Care; Clinical Lab Next Generation <u>Ventilators</u>
Stockpiling & Acquisitions	H5N1 Pre-Pandemic Vaccine	Federal & State Stockpiles IV Antivirals: EUA	Masks & Respirators
Infrastructure Building	Egg-based Supply Retrofit Mfg Facilities New Mfg Facilities		



# 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



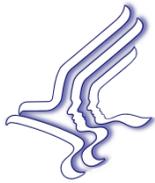


# Antigen-sparing Vaccine Technologies: BARDA Initiatives



- **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

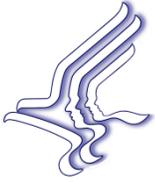




# Improving Influenza Vaccine Manufacturing: BARDA Initiatives



- **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