Pandemic Influenza Countermeasures Program

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Vaccines

- Goal #1: Establish and maintain a dynamic pre-pandemic influenza vaccine stockpile available for 20 M persons (2 doses/person) or more 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 (or less) months of a pandemic declaration: pandemic vaccine (600 M doses)

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- 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 & other supplies

National Strategy for Pandemic Influenza (Nov 2005) and HHS Pandemic Influenza Plan (Nov 2005)  www.pandemicflu.gov
## Integrated Portfolio Approach: Pandemic Influenza

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<tr>
<th>Advanced Development</th>
<th>Vaccines</th>
<th>Antivirals</th>
<th>Diagnostics/Respiratory Devices</th>
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<td></td>
<td>Cell-based, Antigen-sparing, Recombinant, Manufacturing Initiative</td>
<td>New Antiviral Drugs RFP I &amp; II</td>
<td>Diagnostics Point of Care; Clinical Lab Next Generation Ventilators</td>
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<tr>
<td>Stockpiling &amp; Acquisitions</td>
<td>H5N1 Pre-Pandemic Vaccine, Adjuvants, &amp; H1N1 Response</td>
<td>Federal &amp; State Stockpiles IV Antivirals: EUA</td>
<td>Masks &amp; Respirators</td>
</tr>
<tr>
<td>Infrastructure Building</td>
<td>Egg-based Supply Retrofit Mfg Facilities New Mfg Facilities International Mfg Facilities</td>
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</tbody>
</table>
U.S. Pan Flu MCM Strategic Goals

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- Between 2004 and 2008 nine contracts were awarded to three contractors (GSK-Novartis-Sanofi Pasteur) for the acquisition of pre-pandemic avian influenza H5N1 vaccine

- The USG acquired 152 million doses @ 15µg/ dose (25.3 M doses @ 90µg/ dose)

- The USG acquired 125 million units of adjuvants for pandemic response in 2008-2009

- Indefinite Delivery Indefinite Quantity (IDIQ) type of contracts were awarded and the manufacturers were requested (if task order issued) to:
  - Manufacture bulk lots of vaccine
  - Store bulk vaccine and perform stability testing
  - Formulate-fill-finish product
  - Modified for the 2009 H1N1 response
## U.S. Pre-Pandemic Vaccine/Adjuvant Stockpile (in Millions)

<table>
<thead>
<tr>
<th>Vaccine Code</th>
<th>90μg/dose</th>
<th>7.5μg/dose</th>
<th>3.75μg/dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/VTN/1203/04 (1)</td>
<td>4.89</td>
<td>58.6</td>
<td>117.2</td>
</tr>
<tr>
<td>A/Indo/05/05 (2.1.3)</td>
<td>8.21</td>
<td>98.5</td>
<td>197</td>
</tr>
<tr>
<td>A/BHG/QL/1A/05 (2.2)</td>
<td>4.23</td>
<td>50.7</td>
<td>101.4</td>
</tr>
<tr>
<td>A/Anhui/1/05 (2.3.4)</td>
<td>1.75</td>
<td>21.0</td>
<td>42</td>
</tr>
<tr>
<td><strong>Total Bulk Vaccine Doses @90μg/dose</strong></td>
<td><strong>19.08</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Bulk Vaccine Doses @7.5μg/dose</strong></td>
<td></td>
<td><strong>228.8</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Total Bulk Vaccine Doses @3.75μg/dose</strong></td>
<td></td>
<td></td>
<td><strong>457.6</strong></td>
</tr>
</tbody>
</table>
Cell-based Influenza Vaccines: BARDA Initiatives

• Robust, flexible, scalable and 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 (each contract)

• Novartis, Baxter, sanofi pasteur, GSK, Solvay, MedImmune

• Two manufacturers have completed Phase 3 clinical studies & are expected to submit BLAs in 2011-2012

• Two manufacturers still in early stage development

• Two manufacturers dropped following down-selection in 2009
Antigen-sparing Vaccine Technologies: BARDA Initiatives

• Adjuvants, immunostimulating molecules, provide dose-sparing effects, cross-strain protection (in animal models) and reactivity in serological assays, and enhanced immune responses to vaccines

• Awarded 3 contracts in 2007 ($133 M) for advanced development of pandemic influenza vaccines with adjuvants towards US-licensure
  – Novartis, GSK, Intercell (formerly IOMAI)
  – One manufacturer is completing Phase 3 clinical studies & is expected to submit BLA in 2011
  – One manufacture 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 adjuvants
    • 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 growth/yield 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-infected 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)
    - Baculovirus infected insect cell expression for production 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
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Current Antiviral Program

• Stockpiles
  – Federal stockpile- Tamiflu®, Relenza®, IV Peramivir®
  – State stockpile-Tamiflu®, Relenza®

• Advanced development
  • BioCryst – i.v. peramivir (NA inhibitor)
    – Initial contract awarded in Jan 2007 for $102.6M for advanced development of peramivir (Additional funds awarded in 2009 and 2011). Total financial support $245M.
    – Planned completion of pivotal Phase 3 clinical trial during 2012-13 Northern Hemisphere influenza season
    – Submission of NDA anticipated in 4Q2013 to support indication approved for treatment of hospitalized patients with influenza
  • Biota – inhaled laninamivir (NA inhibitor)
    – Contract awarded in 2011 for advanced development ($231M)
    – CS8958 (Laninamivir) is a neuraminidase inhibitor in advanced development for treatment of acute, uncomplicated cases of influenza
    – Long duration of action (“one and done” dosing) with a simple to use delivery device, improves compliance
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## Diagnostics Projects

<table>
<thead>
<tr>
<th>Projects</th>
<th>Awards</th>
<th>Contracts / Mechanisms</th>
<th>Objectives</th>
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</thead>
<tbody>
<tr>
<td>Innovative Flu Testing Platform</td>
<td>2010</td>
<td>1</td>
<td>Multi-use, flexible format</td>
</tr>
<tr>
<td>High Throughput Multiplex Testing</td>
<td>2010</td>
<td>1</td>
<td>• Multiple respiratory pathogens, dual effort with CBRN targets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Field deployable</td>
</tr>
<tr>
<td>Manufacturer Support for Flu Test Development</td>
<td>2010</td>
<td>5 contract labs</td>
<td>Studies, validations, reagents for development, and evaluations of influenza tests</td>
</tr>
<tr>
<td>Point of Care</td>
<td>2006</td>
<td>4</td>
<td>• Differentiate novel from seasonal flu in 30 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Accurate results for use in outpatient settings</td>
</tr>
<tr>
<td>Laboratory Influenza Test</td>
<td>2008</td>
<td>2</td>
<td>• Differentiate novel &amp; seasonal influenza viruses</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Less than 3 hr test; 150 specimens/8 h</td>
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## Advanced Development for Next Generation Portable Ventilators: NMI

<table>
<thead>
<tr>
<th>Contract (HHS0100201000060C) Awarded: September 24, 2010</th>
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<tbody>
<tr>
<td><strong>Milestone 1</strong></td>
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<td><strong>Milestone 2</strong></td>
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<td><strong>Milestone 3</strong></td>
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<td><strong>Milestone 4</strong></td>
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<tr>
<td><strong>Milestone 5</strong></td>
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</table>
• A type of government solicitation often used to support research and development activities

• May be used by agencies to fulfill their requirements for scientific study and experimentation directed toward advancing the state-of-the-art or increasing knowledge or understanding rather than focusing on a specific system or hardware solution (FAR Part 35.016)

• The primary basis for selecting proposals for acceptance:
  — Technical merit
  — Alignment with agency priorities
  — Availability of funds
Area of Interest 1: Personal Protective Equipment and Ventilators

**Personal Protective Equipment (Mask & Respirators) and Full-Featured Continuous Ventilators for Influenza Infection and All-Hazards**

1.1 Development and characterization of improved personal protective equipment such as masks or N95 respirators to prevent influenza infections or harmful effects of all-hazards events.

1.2 Development of improved full-featured continuous ventilators
   - support neonate to adult populations
   - be capable of operation by unskilled or minimally trained care providers
   - considerations for ease of stockpiling/maintenance, accommodation and provision of accessories typically used in ventilatory standard of care, low cost per unit, and domestic surge capacity.
# Area of Interest 2: Diagnostics

**Clinical Influenza Test Systems and Diagnostic Tools**

<table>
<thead>
<tr>
<th>2.1</th>
<th>Development of better rapid influenza diagnostic tests</th>
</tr>
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<tbody>
<tr>
<td>2.2</td>
<td>Development of improved respiratory specimen collection materials and methods</td>
</tr>
<tr>
<td>2.3</td>
<td>Development of expanded respiratory pathogen tests on existing test platforms</td>
</tr>
<tr>
<td>2.4</td>
<td>Development of advanced sequence detection methods for identifying novel influenza strains</td>
</tr>
<tr>
<td>2.5</td>
<td>Rapid identification of antiviral resistant influenza strains</td>
</tr>
<tr>
<td>2.6</td>
<td>Rapid identification of influenza immunological response</td>
</tr>
<tr>
<td>2.7</td>
<td>Development and characterization of stable diagnostic reagents or reference material and controls for applications with existing diagnostic test systems on established platforms</td>
</tr>
</tbody>
</table>
Area of Interest 3: Antiviral Therapeutics for Treatment and/or Prophylaxis of Influenza A & B Infections

1.1 Advanced development of antiviral therapeutics at TRL6 or greater with a novel mechanism of action relative to currently approved anti-influenza therapeutics.

1.2 Development of combination therapeutic approaches using influenza antivirals which in combination have achieved at TRL 6 or greater.

1.3 Development of alternative formulations of influenza antivirals for treatment of populations under high risk of influenza-related complications such as pediatric or hospitalized patients. The therapeutic under development must be at TRL6 or greater for its primary indication and formulation to be considered.

1.4 Activities to support identification and validation of surrogate endpoints to predict clinical benefits in patients treated with influenza antiviral therapeutics. Virology and non-virology parameters that reliably predict clinical outcomes in influenza trials that are being conducted to evaluate influenza antivirals at TRL6 or higher are of high interest.
BARDA Influenza BAA Contacts


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