

United States Department of

Health & Human Services

**Office of the Assistant Secretary for Preparedness & Response (ASPR)
Biomedical Advanced Research & Development Authority (BARDA)**



Pandemic Influenza Countermeasures Program

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U.S. Pan Flu MCM Strategic Goals



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)

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

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Integrated Portfolio Approach: Pandemic Influenza



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



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Current Pre-pandemic Vaccine Stockpile Contracts



- 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 @ 15 μ g/ dose (25.3 M doses @ 90 μ g/ 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)



	90µg/dose	7.5µg/dose	3.75µg/dose
A/VTN/1203/04 (1)	4.89	58.6	117.2
A/Indo/05/05 (2.1.3)	8.21	98.5	197
A/BHG/QL/1A/05 (2.2)	4.23	50.7	101.4
A/Anhui/1/05 (2.3.4)	1.75	21.0	42
Total Bulk Vaccine Doses @90µg/dose	19.08		
Total Bulk Vaccine Doses @7.5µg/dose		228.8	
Total Bulk Vaccine Doses @3.75µg/dose			457.6



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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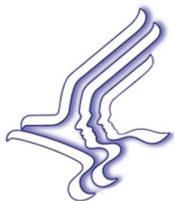
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Diagnostics Projects



Projects	Awards	Contracts / Mechanisms	Objectives
Innovative Flu Testing Platform	2010	1	Multi-use, flexible format
High Throughput Multiplex Testing	2010	1	<ul style="list-style-type: none">• Multiple respiratory pathogens, dual effort with CBRN targets• Field deployable
Manufacturer Support for Flu Test Development	2010	5 contract labs	Studies, validations, reagents for development, and evaluations of influenza tests
Point of Care	2006	4	<ul style="list-style-type: none">• Differentiate novel from seasonal flu in 30 min• Accurate results for use in outpatient settings
Laboratory Influenza Test	2008	2	<ul style="list-style-type: none">• Differentiate novel & seasonal influenza viruses• Less than 3 hr test; 150 specimens/8 h



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Advanced Development for Next Generation Portable Ventilators: NMI



Contract (HHS0100201000060C) Awarded: September 24, 2010



Milestone 1	July 2011	Product Development, Milestone & Regulatory Master Plan
		Prototype Delivery
Milestone 2		Complete performance (bench and usability) testing
		Final Technical Specifications
		Manufacturing Plan
		Well-defined Regulatory Plan
Milestone 3		Finalize Independent Evaluation Testing
		Analysis of Manufacturing Ramp-up Capacity
		All 510(k)s Submitted
Milestone 4		Manufacturing Release
		Final Device Testing
Milestone 5	September 2013	Final Report
		Completed FDA Pre-market Clearance



BARDA Influenza BAA



- **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

- 2.1 Development of better rapid influenza diagnostic tests**
- 2.2 Development of improved respiratory specimen collection materials and methods**
- 2.3 Development of expanded respiratory pathogen tests on existing test platforms**
- 2.4 Development of advanced sequence detection methods for identifying novel influenza strains**
- 2.5 Rapid identification of antiviral resistant influenza strains**
- 2.6 Rapid identification of influenza immunological response**
- 2.7 Development and characterization of stable diagnostic reagents or reference material and controls for applications with existing diagnostic test systems on established platforms**



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



<https://www.fbo.gov/spg/HHS/OOS/OASPHEP/BAA-11-100-SOL-00021/listing.html>

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