BARDA International and Domestic Capacity Building Activities

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January 15, 2013
Why do we need to prepare for pandemics?

1918: “Spanish Flu”
A(H1N1)
20-100 m deaths
~500,000 in US

1957: “Asian Flu”
A(H2N2)
1-4 m deaths
60-80,000 in US

1968: “Hong Kong Flu”
A(H3N2)
1-4 m deaths
~30,000 in US

1976 Swine Flu – The “No-Show Pandemic”

“2009 H1N1 Pandemic”

Credit: US National Museum of Health and Medicine

Requirements are Set

- The requirements addressed by the BARDA Influenza Portfolio are derived from a number of documents that guide the US Government efforts to prepare for pandemics
  - *National Strategy for Pandemic Influenza* (Nov 2005)
  - *HHS Pandemic Influenza Plan* (Nov 2005)
  - *Nation Strategy for Pandemic Influenza Implementation Plan* (May 2006)
  - PCAST report on *Reengineering the Influenza Vaccine Production Enterprise* (Aug 2010)
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 - Achieved
  – 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 - Achieved
  – Goal #2: Provide influenza antiviral drug stockpiles for strategic limited containment at onset of pandemic (6 M treatment courses) - Achieved

• 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
Vaccine Strategy – leverage seasonal vaccine business

Building on existing egg-based technology – MORE
Modernize the influenza manufacturing process – BETTER
Use new technology approaches to manufacture influenza vaccine - FASTER
Egg-based Technology Investments

• The most attainable goal for near term pandemic preparedness
  • Established a year round supply of fertilized eggs for influenza vaccine manufacturing
  • Created inventories of other essential supplies (vials, preservative, etc.)
  • Contracts to produce vaccine for pre-pandemic stockpile and in the event of a pandemic (2009)
  • Manufacturing base gains experience producing pandemic virus vaccine at commercial scale
  — Facility Retrofit Contracts (2007)
  • Expanded domestic facilities for inactivated and live-attenuated influenza vaccine production
Cell-based Influenza Vaccines

• Provide more robust, flexible, and scalable process for manufacturing influenza vaccines

• Awarded 6 contracts in 2005-06 for advanced development of US licensed cell-based seasonal & pandemic influenza vaccines ($1.2B) with commitment for domestic surge capacity of 150M doses within 6 mos. of pandemic onset

• Novartis, Baxter, sanofi pasteur, GSK, Solvay, MedImmune
  – Novartis vaccine was licensed for 18+ in November 2012
  – One completed pivotal Phase 3 clinical studies & expected to submit a BLA in 2013
  – One manufacturer in early stage development
  – Three programs are no longer active
First cell-based influenza vaccine mfg. facility in the U.S. (Novartis):

**Dedicated as Pandemic Ready in December 2011**

**Antigen Sparing Technology**

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

- ASPR/BARDA awarded 3 contracts in 2007 ($133 M) for advanced development of US-licensed pandemic influenza vaccines with adjuvants
  - Novartis, GSK, Intercell (formerly IOMAI)
  - One manufacturer (GSK) has completed Phase 3 clinical studies & submitted a BLA in February 2012
  - One manufacturer has completed Phase 2 clinical studies
  - One contract is no longer active
Recombinant & Molecular Vaccine Technologies

• Recombinant & molecular technologies may provide vaccine sooner with less dependence on influenza virus strain properties

• BARDA awarded contracts in 2009 & 2011 for advanced development of US-licensed recombinant-based seasonal & pandemic influenza vaccines with commitment for domestic manufacturing surge capacity of 50 M doses in 6 months of pandemic onset & initial lot release in 12 weeks

• Protein Sciences, Novavax, & VaxInnate
  — One manufacturer completed Phase 3 clinical trials & BLA submitted
  — Two manufacturers in Phase 2 clinical studies
• Build or Retrofit Manufacturing Facilities
  ─ Newly constructed or retrofitted existing facilities in the U.S. will utilize state-of-the-art flexible manufacturing approaches for platform vaccine and biopharmaceutical product technologies

• Provide ADM Core Services for CBRN/Influenza MCMs
  ─ Upstream & downstream process development, optimization, scale up, and validation
  ─ Manufacturing process validation
  ─ Product formulation chemistry
  ─ Lot release & clinical testing assay development, optimization, and validation
  ─ Quality systems (Control & Assurance – GMP & GLP compliance)
  ─ Regulatory affairs (IND, EUA, BLA, NDA submissions & strategy)
  ─ Clinical investigational lot manufacturing (pilot scale)
  ─ Commercial scale manufacturing
  ─ Program management

• Workforce Development Training Program

• Provide Emergency Flexible Vaccine Manufacturing for Pan Flu & Other Threats
  ─ Pandemic influenza vaccine manufacturing capacity should be at least 50 million doses
High return on Investment: $59M USG --> $538M leveraged locally

- 14 grantees in 13 countries
- 200 scientists trained in advanced biomanufacturing skills
  - Improvements realized in process development and quality systems
- 8 manufacturers have initiated human clinical trials
  - In 2012, India, Bangladesh, Vietnam, Thailand, Russia
- 6 countries have licensed influenza vaccine
  - In 2012, 1st cGMP licensed vaccine at Butantan (Brazil), WHO Prequalification (India)
- 2 countries have adjuvant production capability
  - In 2012, completed production transfer, prepared for tox and future clinical trials
Thank You for Your Attention

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