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Building Pandemic Preparedness Through a Sustainable Enterprise for Influenza Vaccines

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Office of the Assistant Secretary for Preparedness and Response

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Building Pandemic Preparedness Through a Sustainable Enterprise for Influenza Vaccines

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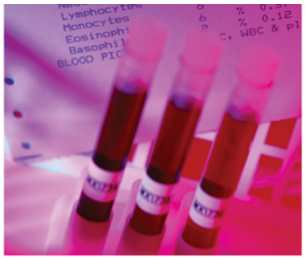
Biomedical Advanced Research and Development Authority

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

BARDA's mission is to ***support development and availability of countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases through advanced product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation.***

Other Countermeasures

Antimicrobials



Diagnostics

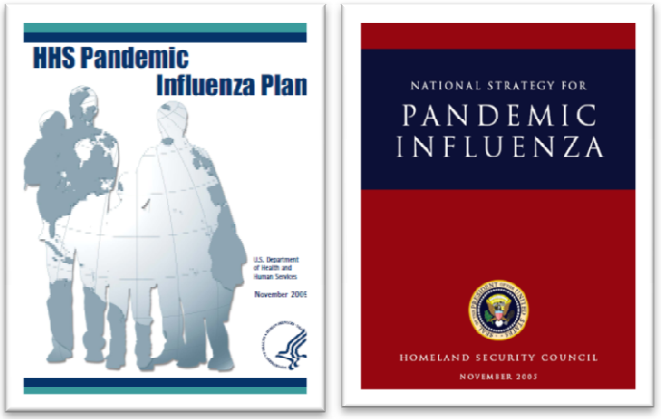
Vaccines

Therapeutics

Influenza Vaccine Goals

- Establish and maintain a dynamic vaccine stockpile against influenza strains with pandemic potential available for up to 20 M persons

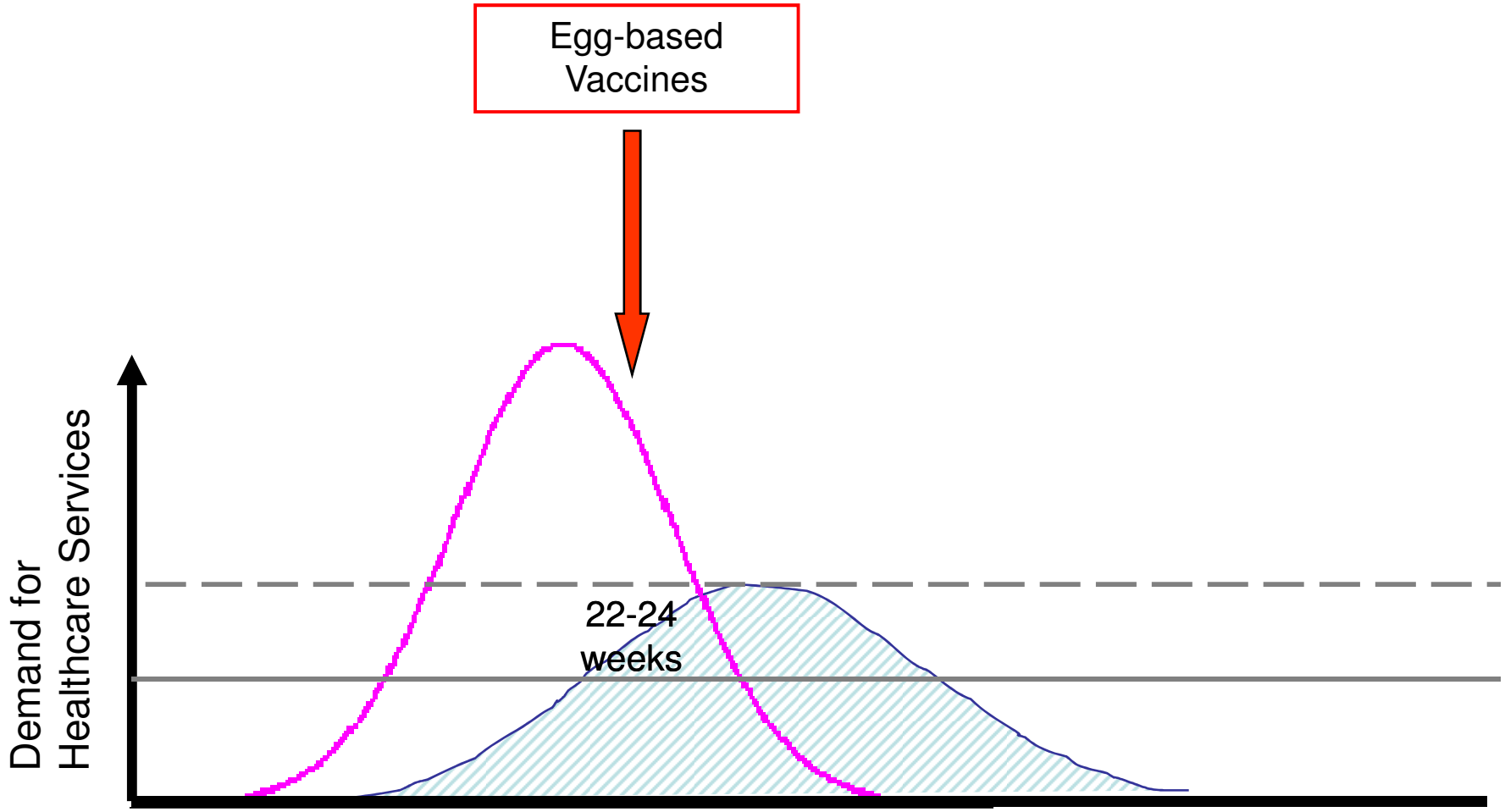
- Provide pandemic vaccine to all U.S. citizens within 6 months of a pandemic declaration (600 M doses)



National Strategy for Pandemic Influenza (Nov 2005) and ***HHS Pandemic Influenza Plan*** (Nov 2005)

www.pandemicflu.gov

Pre-2003 Pandemic Influenza Vaccine Goal & Strategy



Influenza Vaccine Portfolio

Requirements	Strategies
Infrastructure Building 4 contracts, 7 grants/IAAs	Egg-based Supply Retrofit Existing Mfg Facilities Build New Mfg Facilities Build International Capacity
Stockpiling & Acquisitions 3 contracts (11 contracts)	H5N1 Pre-Pandemic Vaccine (H1N1 vaccines and ancillaries)
Advanced Development 16 contracts	Cell-Based Antigen Sparing Recombinant and Molecular Innovation Vaccine Candidates & Assays

MORE

Build on Existing Egg-based Technology

In the beginning……..

…at BARDA, the egg came first!

Egg-based Technology Investments

- The most attainable goal for near term pandemic preparedness
  - Egg Supply Contract (2004)
    - Established a year round supply of fertilized eggs for influenza vaccine manufacturing
    - Created inventories of other essential supplies (vials, preservative, etc.)
  - Vaccine Stockpile Contracts (2004)
    - 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

BETTER

Newer Influenza Vaccine Technology

Cell-based Influenza Vaccines

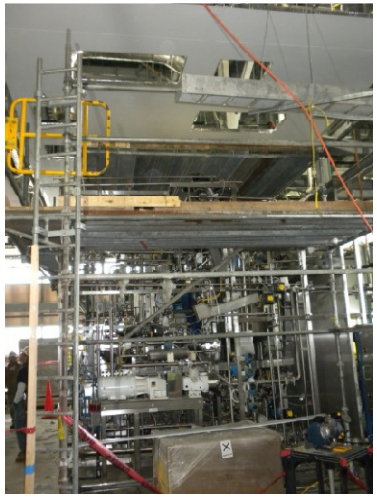
- Provide more robust, flexible, and scalable process for manufacturing influenza vaccines
- Awarded 6 contracts in 2005-06 for advanced development of US licensed cell-based seasonal & pandemic influenza vaccines with commitment for c surge capacity of 150M doses within 6 mos. of pandemic onset
- Novartis, Baxter, sanofi pasteur, GSK, Solvay, MedImmune
  - One manufacturer filed their BLA in October 2012
  - One completed pivotal Phase 3 clinical studies & expected to submit a BLA in 2012-13
  - One manufacturer in early stage development
  - Three programs are no longer active

Antigen-sparing Adjuvant Technologies

- 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

< filled vaccine & adjuvant – Production skid >



- 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

Public Private Partnership Changed U.S. Vaccine Industry

First cell-based influenza vaccine mfg. facility in the U.S. (Novartis):

Dedicated as Pandemic Ready in December 2011

FASTER

Technology Innovation for Influenza Vaccines

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

Centers for Innovation in Advanced Development and Manufacturing

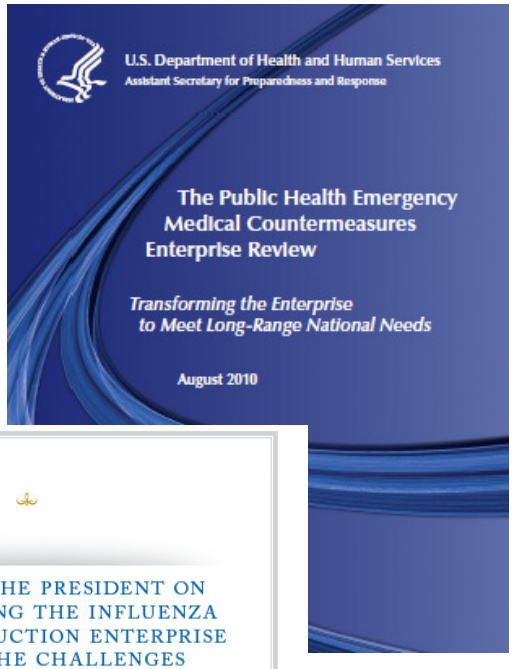
- Build or Retrofit Manufacturing Facilities
  - Newly constructed or retrofitted existing facilities in the U.S. will utilize state-of-the art flexible manufacturing approaches for platform vaccine and biopharmaceutical product technologies
- Provide ADM Core Services for CBRN\ID MCMs
  - Upstream & 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

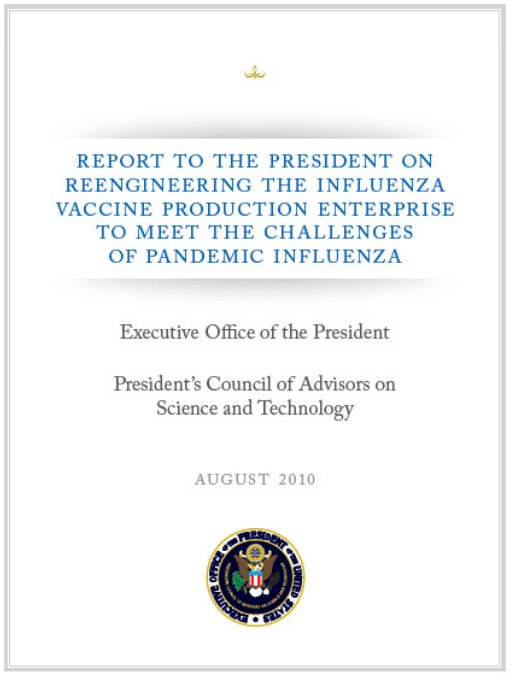
– Pandemic influenza vaccine manufacturing capacity should be at least 50 million doses

BARDA Core Services

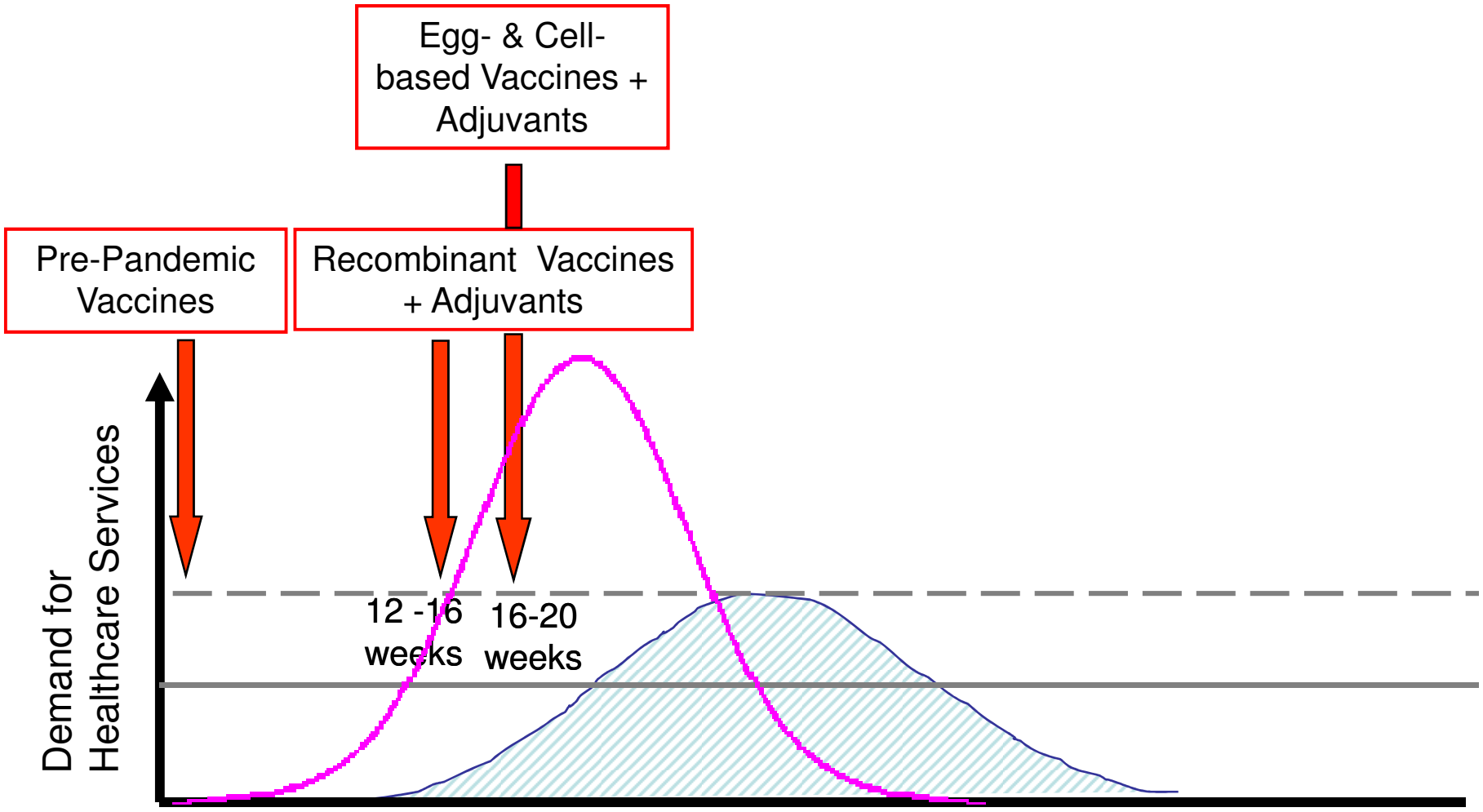
Selected PCAST and MCER Recommendations

- **Interagency Initiatives: (BARDA, CDC, FDA, NIH) + Industry**
  - **Establish HHS interagency program with industry to optimize influenza virus vaccine strains for production yield**
  - **Develop faster potency & sterility assays**





Pandemic Influenza Vaccine Gap Closure Goals - 2012



Summary

BARDA has used a staged approach to build a sustainable influenza vaccine enterprise for pandemic preparedness by investing in technologies that produce:

MORE vaccine
BETTER vaccine
FASTER vaccine

"Hot off the press" or "This just tweeted" in 2012

- **Quadrivalent Seasonal Influenza Vaccines**
  - 29 Feb 2012: MedImmune FluMist Quadrivalent influenza vaccine licensed by the FDA for active immunization of individuals 2 through 49 years of age (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm294057.htm)
  - 01 Mar 2012: Novavax announces ongoing enrollment of Ph2 trial for quadrivalent seasonal influenza virus-like particle vaccine (http://www.novavax.com/download/releases/Novavax%20Launches%20Phase%202%20Seasonal%20Flu%20Study.pdf)
  - 05 Mar 2012: GSK submitted US and EU regulatory applications for a quadrivalent influenza vaccine (http://www.gsk.com/media/pressreleases/2012/2012-pressrelease-963574.htm)
- **Pre-pandemic Vaccines**
  - 02 Mar 2012: Baxter receives marketing authorization in EU for Vepacel pre-pandemic influenza vaccine – first approved Vero cell vaccine
  - 05 Mar 2012: GSK submitted US and EU regulatory applications for a H5N1 influenza vaccine (http://www.gsk.com/media/pressreleases/2012/2012-pressrelease-963574.htm)
  - Mar 2012: Novavax starts two Phase 1 clinical studies with adjuvanted H5N1 influenza virus-like particle vaccine (http://www.novavax.com/go.cfm?do=Press.List&Year=2012)
- **Universal Influenza Vaccines**
  - 31 Jan 2012: Inovio shows cross-strain immune responses in animals generated by SynCon® consensus sequence DNA vaccine
  - 23 Feb 2012: Biondvax Phase IIa with elderly volunteers. Created immune response alone and improved immune response when used as a booster.

Thank You for Your Attention

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