Influenza Morbidity and Mortality

Seasonal Influenza Epidemic in US
- 5%-20% of population infected each year
- 3,000-49,000 deaths every year
- >200,000 hospitalizations
- $87.1B economic burden every year
- $10.4B medical costs every year

2009-H1N1 Pandemic
- 74 countries affected
- 60.8M infected in U.S.
- 123,000-203,000 deaths worldwide
- 12,469 deaths – US
- 274,304 hospitalizations – US

1918 ‘Spanish’ Pandemic
- All countries affected
- 20%-40% infected worldwide
- 50M deaths worldwide
- 675,000 deaths – US

*Numbers are estimate
BARDA Pandemic Influenza Strategy

- Advanced development of antiviral drugs & therapeutics
- Therapeutics
- Respiratory Devices/Masks
- International Vaccine Capacity Building
- Vaccines
- Diagnostics
- Stockpile vaccines against influenza strains with pandemic potential

Develop rapid POC diagnostics

Provide pandemic vaccine for U.S. within 6 months (or less) of a pandemic declaration (600M doses)

Develop influenza vaccines that induce broader, longer duration of immunity

More, Faster, & Better!

Develop low cost, easy to use respirators suitable for all ages with universal components

Develop reusable masks and respirators to address surge need during a pandemic

Enable 500M doses of pandemic vaccine production capacity in developing countries

Stockpile vaccines against influenza strains with pandemic potential

More, Faster, & Better!
Influenza MCM Program Investments ($4B)
BARDA is Achieving National Pandemic Vaccine Goals

More Effective Vaccines Initiative – FY15

Antigen-Sparing Technology

Recombinant Vaccine

Cell-based Vaccine

Egg-based Vaccine

More, Faster, & Better Vaccines!

Vaccinate US Population ≤ 6 mo.

H5N1 Q-PAN®
Licensed 11/22/13

Flublok®
Licensed 01/16/13

FLUCELVAX®
Licensed 11/20/12

H5N1 Vaccine
Licensed 04/17/07

Manufacturing Improvements
Expanded Domestic Vaccine Manufacturing Surge Capacity

Pandemic influenza vaccine target is two doses for everyone (~600M doses) within 6 months of pandemic onset
Domestic Influenza Vaccine Response Infrastructure

**National Stockpile**

**1st US FDA approved pandemic-ready site for cell-based vaccines & adjuvants**

**sanofi pasteur – Swiftwater, PA**

**Centers for Innovation in Advanced Development and Manufacturing (CIADM)**
Domestic Influenza Vaccine Production Capacity

**Accomplishments**

- Increased egg based vaccine capacity (sanofi)
- Secure, year-round egg supply
- Holly Springs, NC facility (Seqirus)
- Pearl River, NY facility (PSC)
- Domestic adjuvant production
- Three CIADMs for surge capacity
- Fill-Finish network established

**Key Challenges**

- Sustainment of capacity and facilities required for rapid response

**Path Forward**

- Develop preparedness strategy for sustainment to ensure preparedness while achieving best value for USG
- Utilize platform technologies and multi-use capabilities to improve efficiency of production processes
Increased Global Production Capacity of Influenza Vaccines

Licensed/Active Influenza Vaccine Producers
- Romania Cantacuzino Institute
- Kazakhstan RIBSP
- South Korea Green Cross
- China BCHT
- Vietnam IVAC
- Indonesia VABIOTECH
- Thailand GPO

BARDA/WHO Cooperative Agreement/Grantees
- Serbia Torlak Institute
- Mexico Birmex
- Egypt VASERA
- India Serum Institute
- South Africa Biovac
- Brazil Instituto Butantan
- South Africa Biovac

BARDA/WHO Licensed Pandemic Vaccine for Human Use
# National Pre-Pandemic Influenza Stockpile

## Accomplishments
- Achieved stockpile requirements for clades of H5N1 and H7N9 viruses of highest risk
- Pre-EUA approval by FDA
- Established monitoring & evaluation program for stability & usability
- Responded to 2009 H1N1 pandemic & 2013 H7N9 outbreak

## Key Challenges
- Antigen and adjuvants in the stockpile have been stored for up to 10 years
- Stored antigens have variable stability profiles

## Path Forward
- Continue surveillance to monitor for strains of influenza that pose a high risk to humans and add to the stockpile
- Update the current stockpile strategy with a clearly defined pathway to use vaccine and adjuvants that have been stored for long periods
- Assess stockpile vaccine and adjuvant for continual safety and immunogenicity in clinical studies
BRITE Study #1

The BARDA Ready In Times of Emergency “BRITE” study

- Data is being collected regarding the safety and immunogenicity of inactivated monovalent Influenza A/Vietnam (H5N1) virus vaccine, stored for a prolonged period of time, given with and without MF59 adjuvant.
- No serious adverse event related to vaccination was observed. Preliminary immunogenicity results are encouraging and indicate that the vaccine remains safe and immunogenic.

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<td>TOTAL</td>
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Influenza Vaccine Development

Accomplishments

- Expanded age indication of Flucelvax to 4+ & Flublok to 18+ yrs
- Completed IVMI in 2014
- Launched universal flu vaccine program in 2015
- Launched SIVI in 2016
- Q-Pan H5N1 approved - 6mos+ (2016)

Key Challenges

- Effectiveness of current influenza vaccines needs to be improved
- Vulnerability of seasonal vaccines to influenza virus drift
- Recombinant and cell-based vaccines encountering headwinds in the marketplace

Path Forward

- Substantial investment and coordination of effort to develop more effective, next generation influenza vaccines with universal potential
- Coordinate approach to improve seasonal influenza vaccine selection and flexibility in vaccine production cycle
Influenza Therapeutics Program

Accomplishments

✓ Worked with CDC to meet Federal & State antiviral stockpile goals
✓ NDA approved for IV peramivir (2014) for acute, uncomplicated influenza; 1st new influenza drug since 1999
✓ Launched initiative for broad spectrum immunotherapeutics for severely ill, hospitalized patients

Key Challenges

• Lack of relevant clinical endpoint for severely ill, hospitalized influenza patients
• Development of drug resistance
• Limited therapeutic window for existing antiviral drugs

Path Forward

• Evaluate newly identified clinical markers as secondary endpoints in ongoing studies
• Continue support of broad spectrum monoclonal antibodies
• Explore portfolio-based agreements with companies with broad portfolios of influenza therapeutics
Diagnostics & Respiratory Devices

Accomplishments

- Multiple influenza diagnostics received FDA approval, Flu A/B
- Expanded model for rapid dx during ED triage for early treatment
- Supporting rapid mask production
- All Hazards ventilator developed through 2/3 FDA clearance stages

Key Challenges

- Need for rapid, POC diagnostics to guide clinical treatment of influenza
- Need for diagnostic assays for drug resistance
- Cost of stockpiling RPDs
- Sustaining industry interest for low-rapid, portable ventilator

Path Forward

- Advanced development and coordination with CDC/FDA to move diagnostics closer to patient/in-home
- Advanced development of reusable face masks and increased domestic manufacturing capacity for surge production
BARDA Influenza Program Objectives

- **Vaccines**
  - Update and maintain the National Pre-pandemic Influenza Vaccine Stockpile (antigens and adjuvants)
  - Sustain vaccine manufacturing capabilities and infrastructure
  - Continue development of improved influenza vaccines, including those with universal potential
  - HHS Seasonal Influenza Vaccine Improvements Initiative

- **Antivirals / Therapeutics**
  - Continue development of broad spectrum therapeutics with a focus on the severely ill, hospitalized population

- **Diagnostics**
  - Continue development of next-generation sequencing, point-of-care (POC) and home detection influenza diagnostics

- **RPD/Ventilators**
  - Continue development of low cost, portable, all hazards ventilator
  - Reduce cost of preparedness by developing reusable respirators and high-capacity manufacturing capability
Influenza: An Integrated Response

Vaccines

Therapeutics

Diagnostics

Early Detection  ➔  Early Response  ➔  Saving Lives