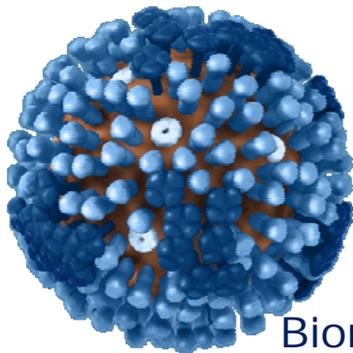
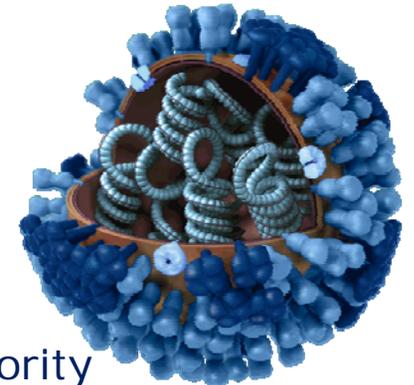




PANDEMIC INFLUENZA OVERVIEW



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BARDA INDUSTRY DAY 2016

Ronald Reagan Building and International Trade Center
Washington, DC • Oct 18-20, 2016



Resilient People. Healthy Communities. A Nation Prepared.

Influenza Morbidity and Mortality

Seasonal Influenza Epidemic in US

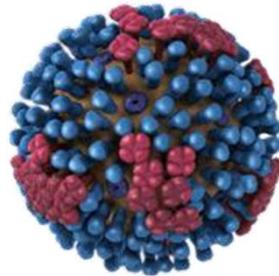
5%-20% of population infected each year

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

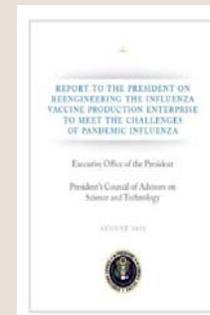
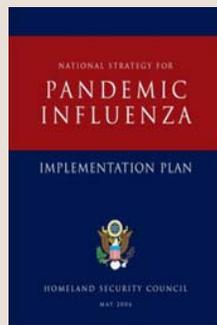
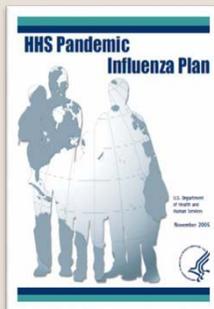
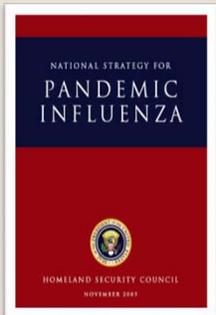
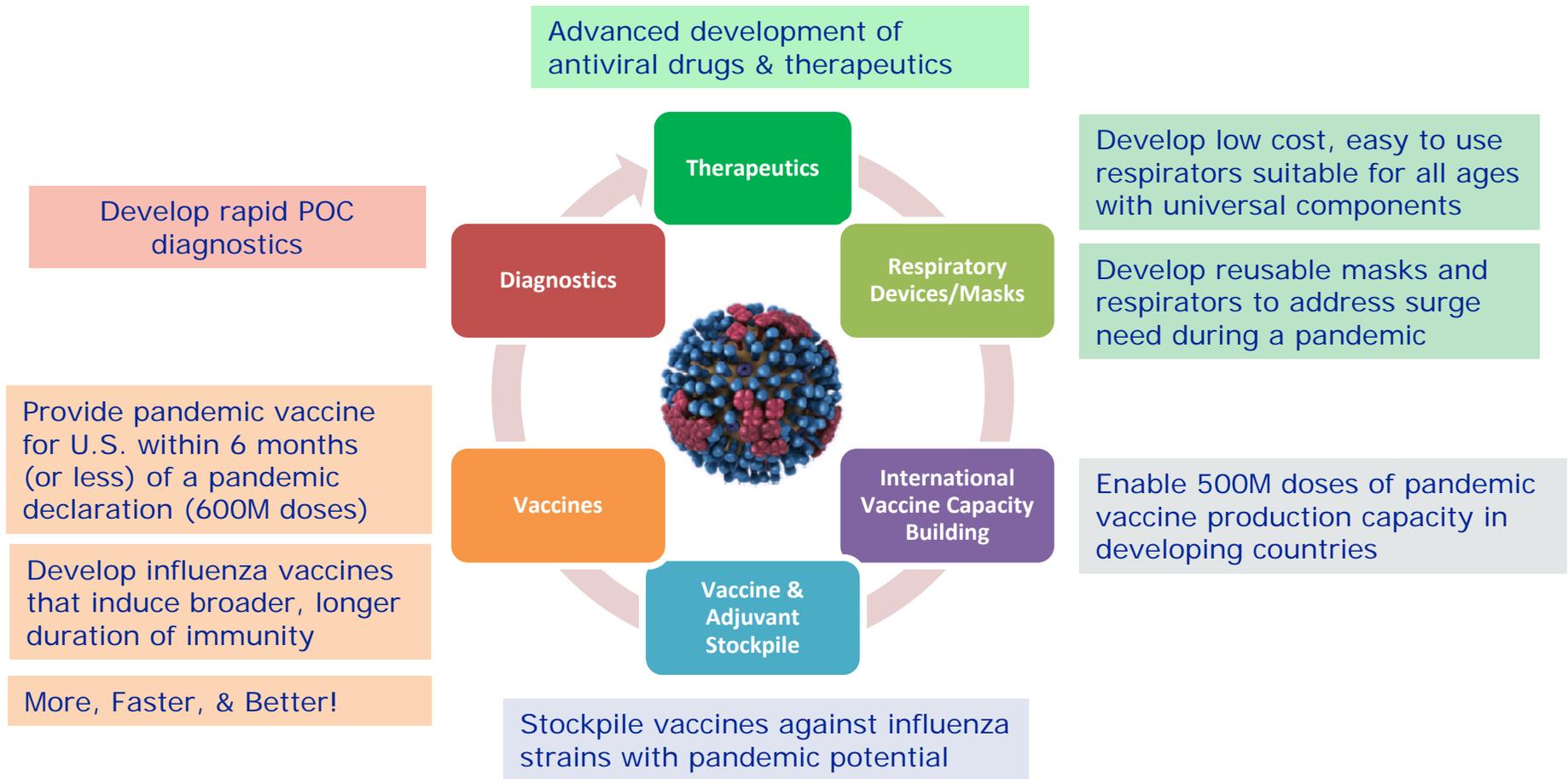
20%-40% infected worldwide

50M deaths worldwide

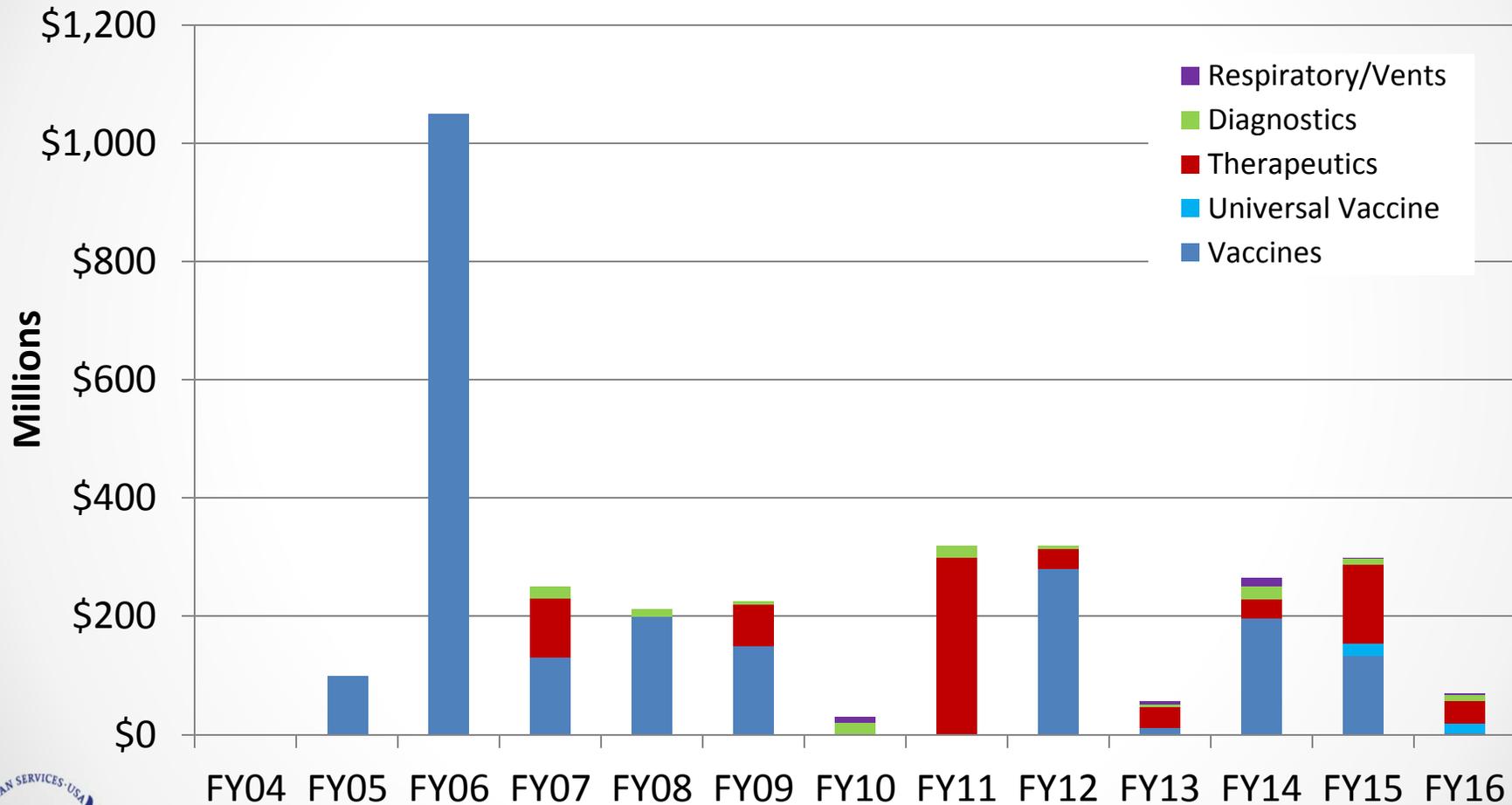
675,000 deaths – US



BARDA Pandemic Influenza Strategy



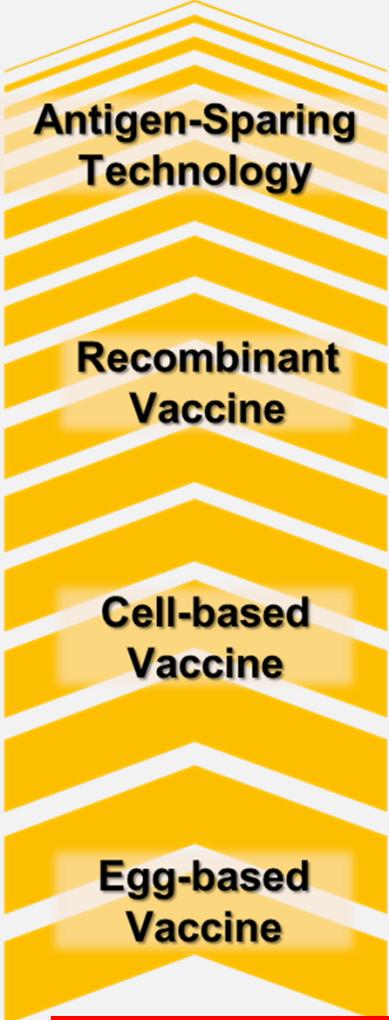
Influenza MCM Program Investments (\$4B)



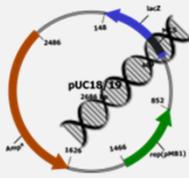
BARDA is Achieving National Pandemic Vaccine Goals

More Effective Vaccines Initiative – FY15

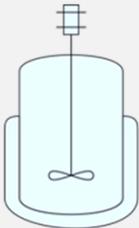
Vaccinate US Population ≤6 mo.



H5N1 Q-PAN®
Licensed 11/22/13



Flublok®
Licensed 01/16/13



FLUCELVAX®
Licensed 11/20/12



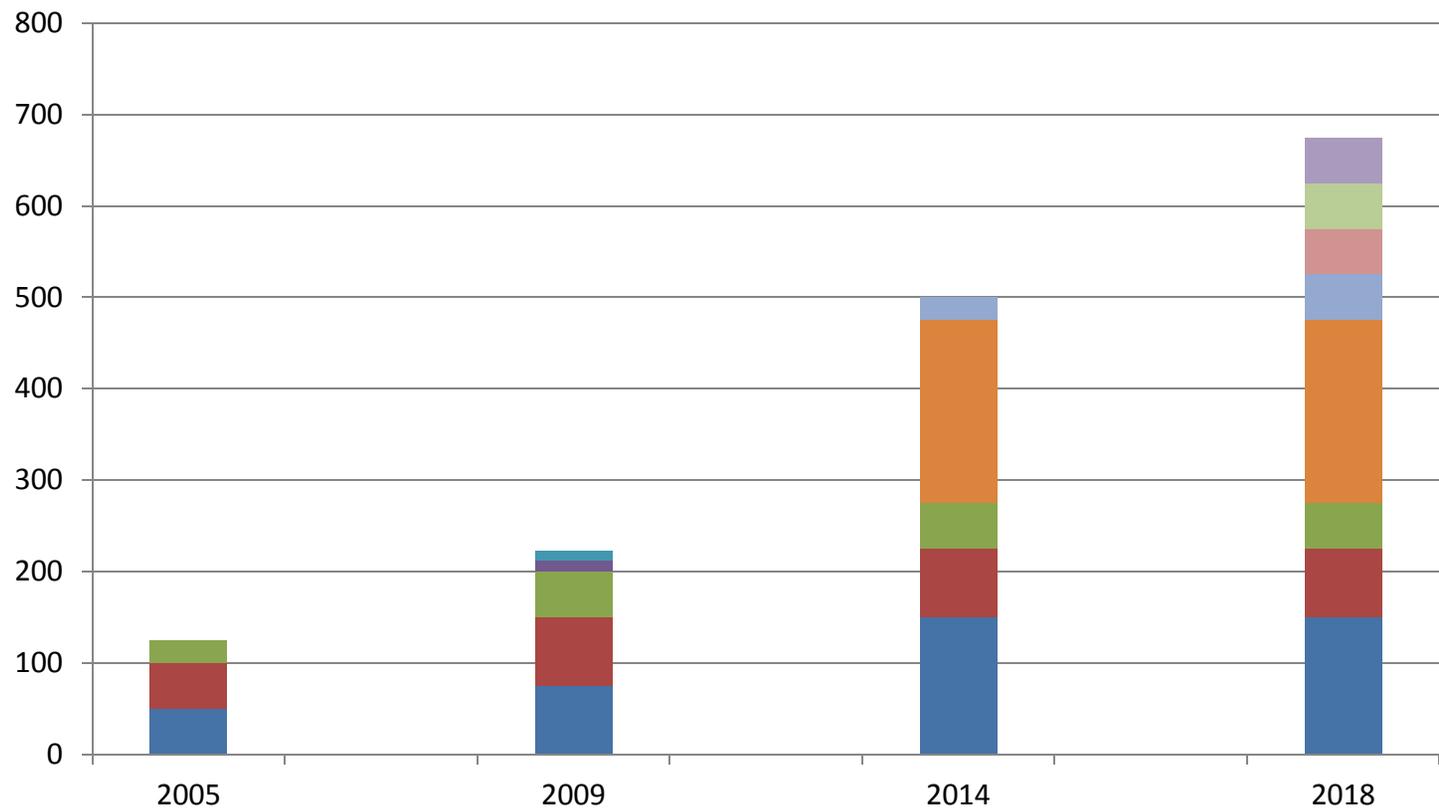
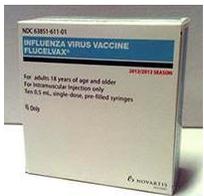
H5N1 Vaccine
Licensed 04/17/07



More, Faster, & Better Vaccines!

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 & adjuvant



2013 ISPE Facility of the Year

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

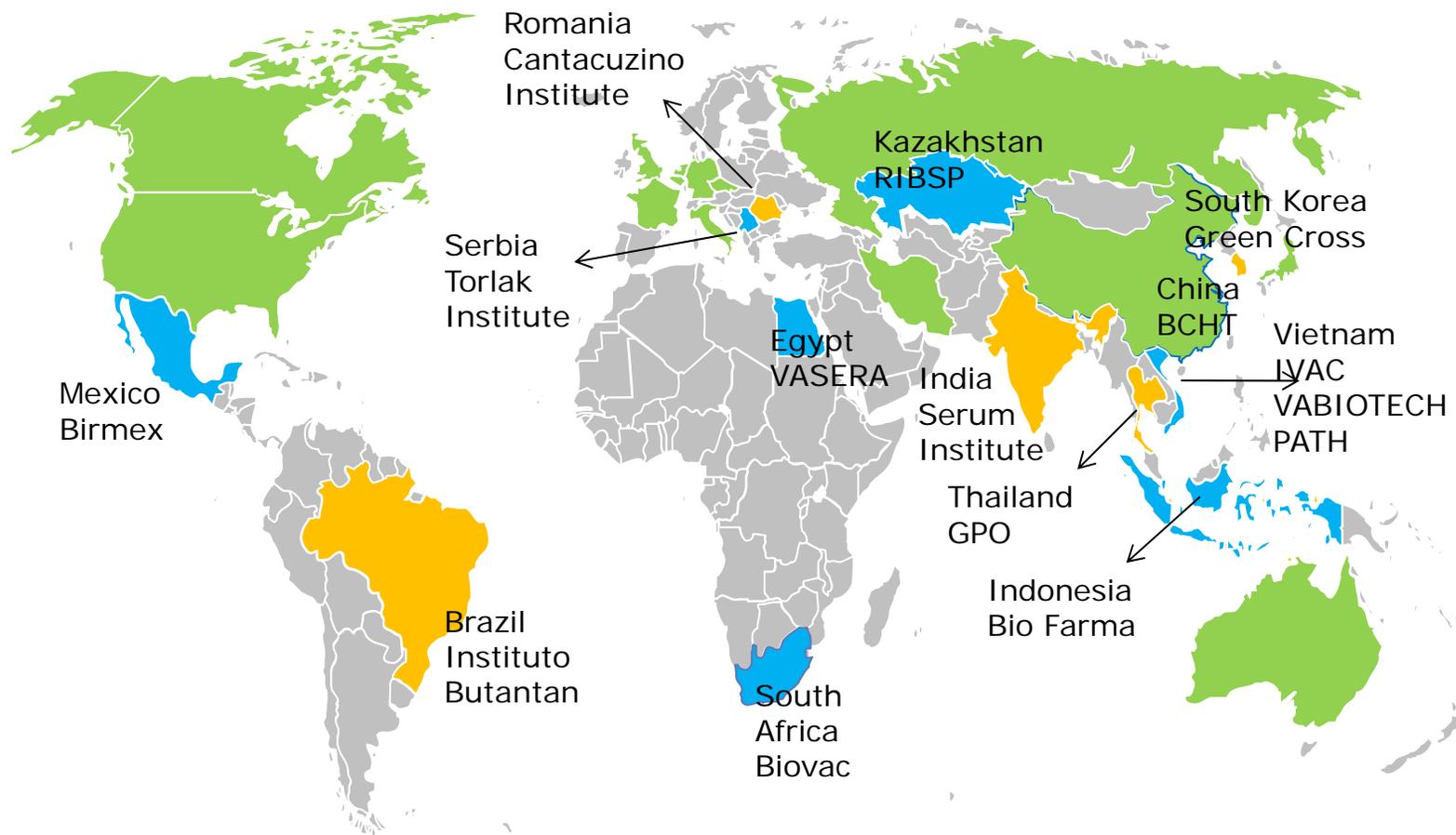
Key Challenges

- 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
- BARDA/WHO Cooperative Agreement/Grantees
- 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

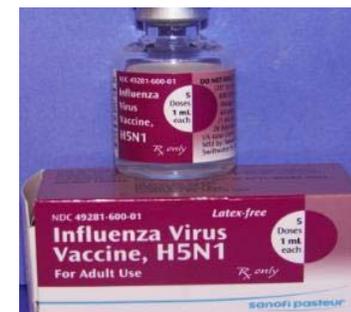
- Antigen and adjuvants in the stockpile have been stored for up to 10 years
- Stored antigens have variable stability profiles

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.

| Study Groups | No. of Subjects | A/Vietnam (H5N1) (mfr year / filled year) | Adjuvant mfd in 2009 | Adjuvant mfd in 2013 |
|--------------|-----------------|---|----------------------|----------------------|
| 1 | 70 | 7.5 µg HA (2005 / 2015) | X | |
| 2 | 70 | 15 µg HA (2005 / 2015) | X | |
| 3 | 70 | 7.5 µg HA (2005 / 2015) | | X |
| 4 | 70 | 15 µg HA (2005 / 2015) | | X |
| 5 | 70 | 90 µg HA (2005 / 2015) | | |
| 6 | 70 | 90 µg HA (2004 / 2006) | | |
| TOTAL | 420 | | | |





Influenza Vaccine Development



Accomplishments

- ✓ Licensed egg- (2007), cell- (2012), adjuvanted (2013) & recombinant- (2013) vaccines
- ✓ 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

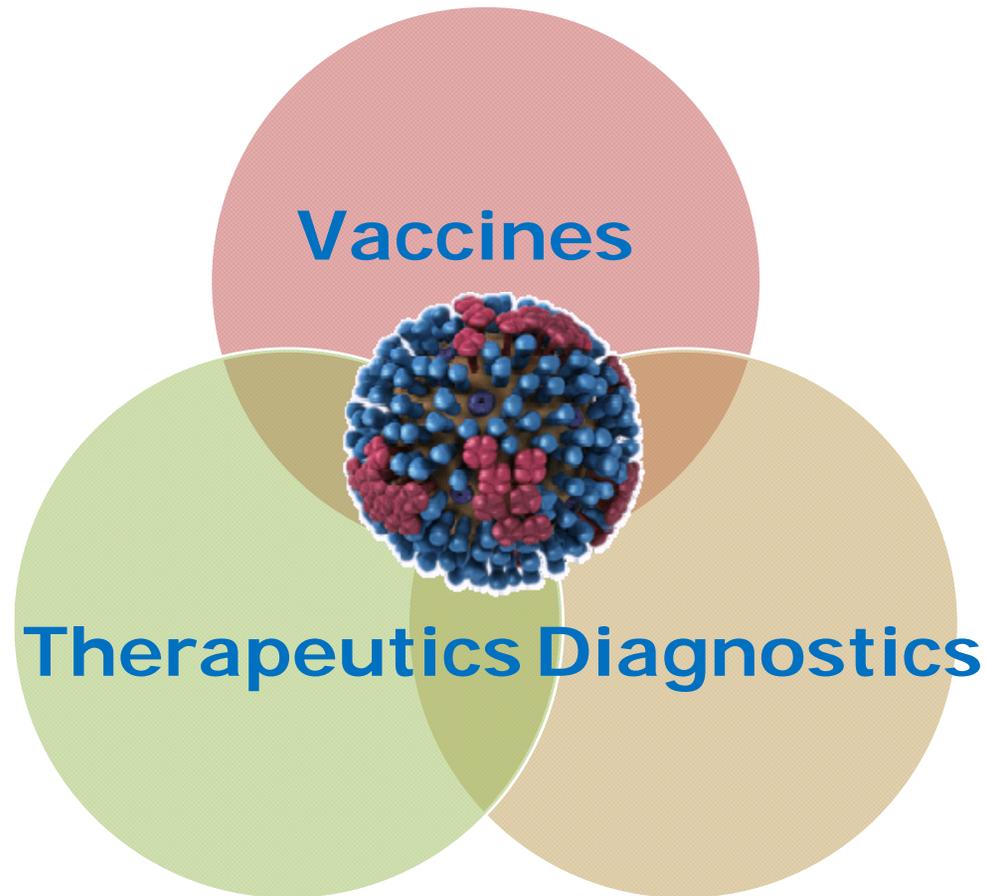


BARDA Influenza Program Objectives

- **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



Early Detection → Early Response → Saving Lives