Influenza Priorities Update

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The Problem: Influenza Causes Widespread Morbidity and Mortality

- 5%-20% infected every year
- 3,000-49,000 deaths every year
- >200,000 hospitalizations every year
- $87.1B economic burden every year
- $10.4B medical costs every year

Seasonal Influenza Epidemic in US

2009-2010 H1N1 Pandemic
- 74 countries affected
- 123,000-203,000 deaths worldwide
- 60.8M infected in US
- 12,469 deaths in US
- 274,304 hospitalizations in US

1918 ‘Spanish’ Pandemic
- 20%-40% infected worldwide
- 12,469 deaths in US
- 50M deaths worldwide
- 675,000 deaths in US

*Numbers are estimate
The Problem: Influenza Viruses Constantly Evolve
The Problem: Response Capabilities Insufficient to Address the Threat

- No National Strategy for influenza pandemic preparedness
- No pre-pandemic vaccine or antiviral stockpile – federal or state
- Less diverse landscape for MCM development
- Limited domestic manufacturing capability for pandemic response
- Limited partnerships between USG & industry for MCM development
- Global lack of vaccine supply for a pandemic response
- Candidate pandemic influenza vaccines were poorly immunogenic
- All US licensed seasonal vaccines were egg-based (1940s-1950s technology)
  - No cell-based and no recombinant-based influenza vaccine licensed
  - No adjuvanted pandemic vaccines licensed
Need for **More** Vaccine and **Faster** Response
Strategic Guidance

BARDA Influenza Division: Goals & Approaches to 2014

**Bar 1:**
- **Goal:** Provide pandemic vaccine to all U.S. within 6 months (or less) of a pandemic declaration (600 M doses)

**Bar 2:**
- **Goal:** Enable 500 M doses of pandemic vaccine production capacity in developing countries

**Bar 3:**
- **Goal:** Stockpile vaccines against influenza strains with pandemic potential for 20 M person critical workforce

**Bar 4:**
- **Goal:** Stockpile of influenza antiviral drugs
- **Goal 2:** Advanced development of new antiviral drugs

**Bar 5:**
- **Goal:** Advanced development of rapid diagnostics and low-cost, easy to use ventilators

**Bar 6:**
- **Goal:** International vaccine capacity building
Accomplishments: More Vaccines

**Egg-based Vaccines**

H5N1 Vaccine
Licensed 04/17/2007

sanofi pasteur – Swiftwater, PA

**1st US FDA approved pandemic-ready site for cell-based Vaccines**

Centers for Innovation in Advanced Development and Manufacturing (CIADM)

Accomplishment: Expanded Domestic Vaccine Manufacturing Surge Capacity

Pandemic influenza vaccine target is two doses for everyone (~ 600 M doses) within 4 months of pandemic onset
BarDA/WHO Cooperative Agreement Grantees

- Mexico: Birmex
- Brazil: Instituto Butantan
- South Africa: Biovac
- Egypt: VASERA
- India: Serum Institute
- Vietnam: IVAC, VABIOTECH, PATH
- South Korea: Green Cross
- Serbia: Torlak Institute
- Romania: Cantacuzino Institute

Accomplishment: More International Vaccine Manufacturing Capacity
Accomplishment: **Faster Response Capability**

**Recombinant-based Influenza Vaccine:**

*Flublok®*

Protein Sciences
Licensed 01/16/2013

**Influenza Vaccine Manufacturing Improvement Initiative**

**Fill Finish Manufacturing Network**

**Centers for Innovation in Advanced Development and Manufacturing (CIADM)**

Pandemic Vaccine Stockpile: Better Prepared

- Program established in 2005
  - With adjuvant, the stockpiled H5N1 vaccines can potentially provide 200-400M doses
- Modified in 2012 to be more flexible to allow staged response
  - Incorporation of additional risk assessment tools to inform stockpiling decisions/actions
- New RFP planned for FY2015
Pandemic Vaccine Stockpile: Faster Response

- **2005 H5N1 outbreak in SE Asia**
  - Established stockpile and met stockpile goals
  - Implemented innovative Mix and Match program

- **2009 H1N1 Pandemic**
  - 186 M doses of H1N1 vaccine were filled by the manufacturers
  - 120 M doses of bulk adjuvants (AS03 & MF59) purchased as a contingency

- **2012 H3N2v outbreak in the US**
  - Clinical lots were made and clinical trials conducted

- **2013 H7N9 outbreak in China**
  - Clinical lots were made and clinical trials conducted
  - Stockpiled bulk antigen
Challenge: **Better Protection**

**Universal Influenza Vaccine**

- Identify broadly reactive epitopes (HA Stalk, M2 extracellular, NP)
- Multi-epitope vaccines
- Vector delivered vaccine
- Target occluded sites
- Exploit existing vaccines

**Vaccine Design**

- Broaden B cell epitope recognition
- Th1 vs Th2 responses
- Humoral vs Cell-mediated

**Adjuvants**

**Administration**

- Location: Intranasal, intradermal or intramuscular
- Timing: Prime/boost
- Regimen

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Source: NIAID [http://tinyurl.com/69n9lap](http://tinyurl.com/69n9lap)
Accomplishment: More Antiviral Drugs

• Collaborated with CDC and State and local partners to establish antiviral stockpiles
• IV peramivir: 1st Emergency Use Authorization (EUA) issued for unapproved drug
  — Used to treat hospitalized patients during 2009 H1N1 pandemic

Peramivir
BioCryst
NDA filed in 2013
• New influenza therapeutics are needed to address:
  • Severely ill, hospitalized patients
  • Pediatric population
  • Novel mechanism of action
    • Wider therapeutic treatment window
    • Threat of resistance
  • Broad spectrum activity for influenza and emerging diseases
  • Potential for combination therapy
FY 2015 New Initiatives

• **Universal Influenza Vaccine**
  • Broad spectrum, long duration immunity
  • RFP planned for early FY 2015

• **New Influenza Therapeutics**
  • Novel Mechanism of Action
  • Targeted to pediatric and severely ill, hospitalized populations
  • RFP planned for early FY 2015

• **National Pre-pandemic Influenza Vaccine Stockpile**
  • RFP planned for mid FY 2015
Watch this space:

Website: http://www.phe.gov/about/barda

Broad Agency Announcement (BAA)
https://www.medicalcountermeasures.gov/newsroom/2013/now-open-broad-agency-announcements.aspx

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