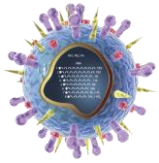
United States Department of
Health & Human Services
Office of the Assistant Secretary for Preparedness and Response

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Update on U.S. Pandemic Influenza Vaccine Development



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Biomedical Advanced Research and Development Authority (BARDA)
Office of the Assistant Secretary for Preparedness & Response

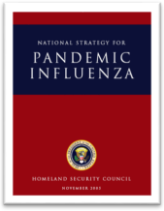
2014 National Adult and Influenza Immunization Summit
May 15, 2014
Atlanta, GA

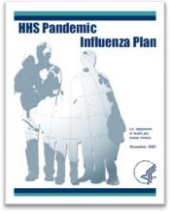
A Nation Unprepared: US Influenza Vaccines in 2004

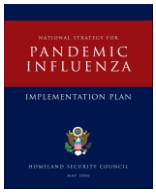
- All licensed seasonal vaccines were egg-based (1940s-1950s technology)
- Vaccine was produced in a six month production window (January-June each year); no capability outside of that window, no egg supply
- Annual immunization was required due to virus drift and limitations of vaccines
  - Vaccine effectiveness estimated at 30-70%
- Shortage of seasonal influenza vaccine in fall 2004 due to production failure at one facility highlighted US vulnerability
- Limited domestic manufacturing capacity to respond to a pandemic, very limited global capacity as well

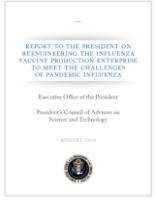
Establishing Pandemic Influenza Vaccine Capabilities: USG Requirements

- The requirements addressed by the BARDA Influenza Portfolio are derived from a number of documents that guide the US Government efforts to prepare for pandemic, include:
  - Establish and maintaining a dynamic pre-pandemic vaccine stockpile
  - Establish manufacturing capacity to produce sufficient pandemic vaccine for the entire U.S. population within 6 months of pandemic declaration
  - Improve, optimize and/or innovate vaccine production technologies
- Goal: More and better influenza vaccine, faster









BARDA's Mission

Enhance national preparedness for CBRN threats, pandemic influenza, and emerging infectious diseases by supporting innovation, developing and acquiring medical countermeasures, and building manufacturing infrastructure.

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BARDA Approach to Making Medical Countermeasures Available

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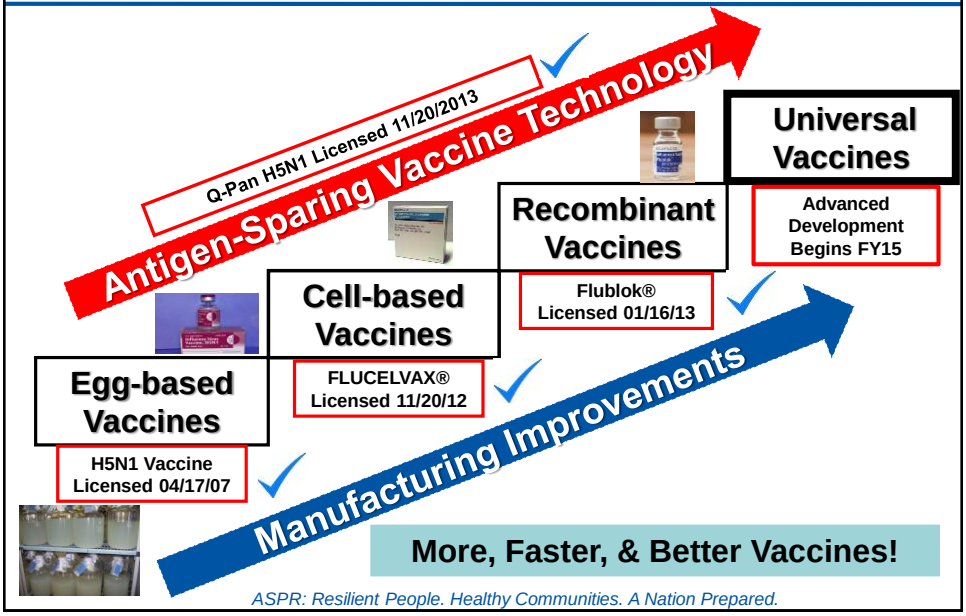
BARDA is Achieving National Pandemic Influenza Vaccine Goals



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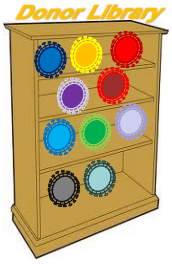
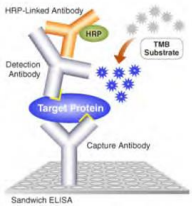
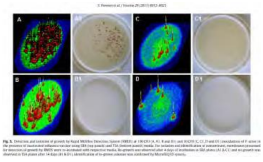
BARDA: Influenza Vaccine Manufacturing Improvement Initiative



6 promising donors to improve vaccine yield



Faster potency reagents, Alternative assays



7 days faster sterility assay

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BARDA: Enhancing Domestic Vaccine Manufacturing Capacity

- **Expanding Existing Capacity by Retrofitting Vaccine Manufacturing Infrastructure**

sanofi pasteur – Swiftwater, PA

- **Changing Flu Vaccine Industry**

Novartis – Holly Springs, NC

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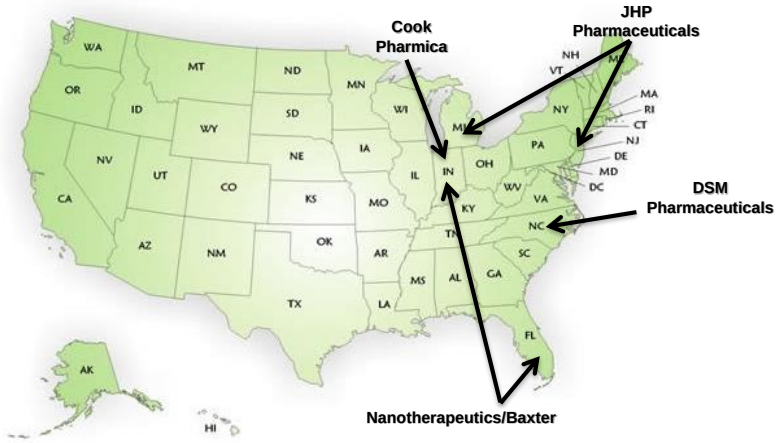
Centers for Innovation in Advanced Development and Manufacturing

Fill Finish Manufacturing Network



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Current Geographical Distribution of Influenza Vaccine Production

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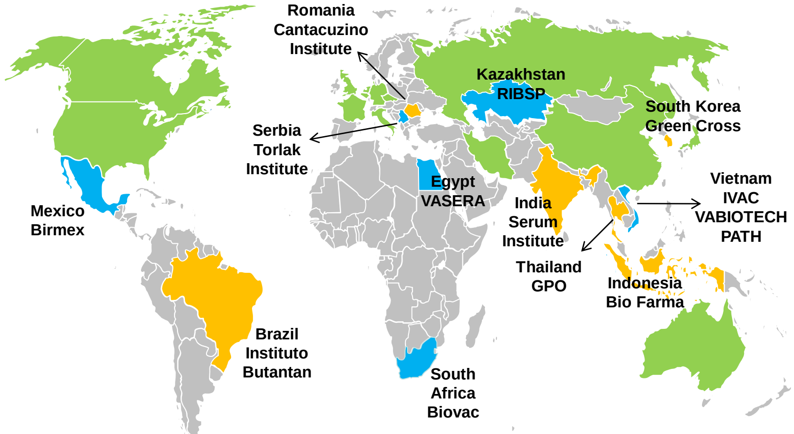

- Licensed/Active Influenza Vaccine Producers
- BARDA/WHO Cooperative Agreement Grantees
- BARDA/WHO Licensed Vaccine for Human Use (as of 2/2014)

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Influenza Vaccine Landscape

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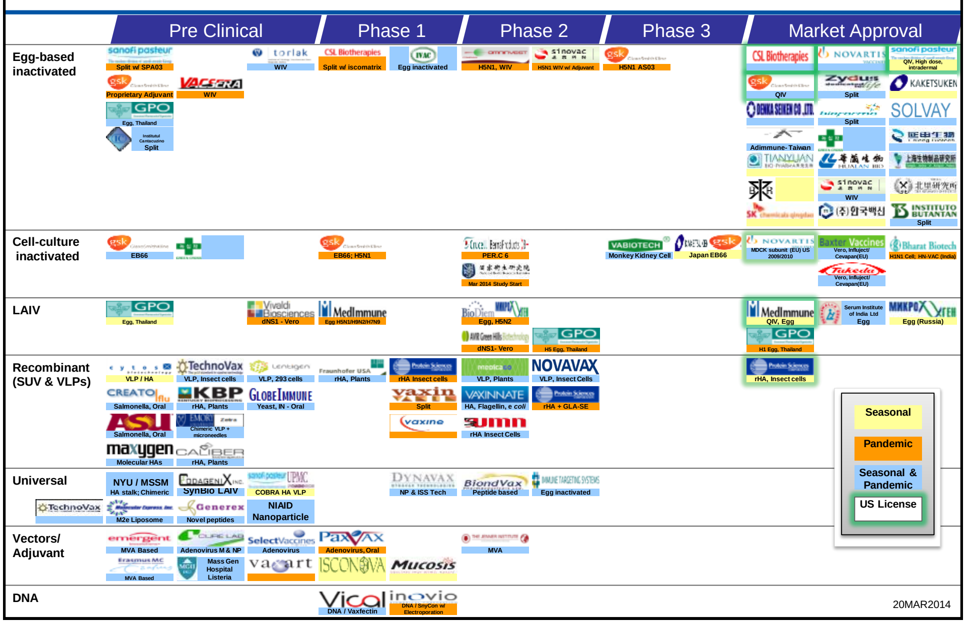
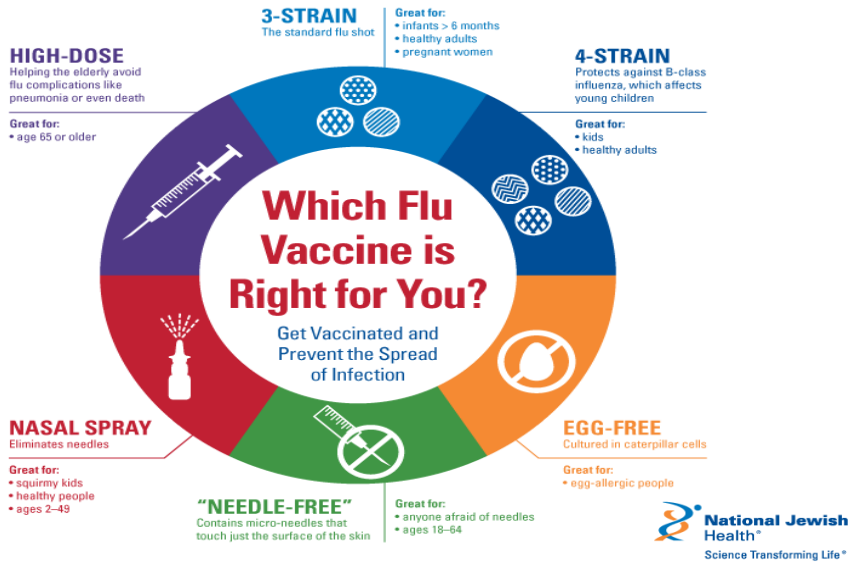


Which Flu Vaccine is Right for You?



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Influenza Vaccine Challenges: Limitations of Current Vaccines

- Vulnerable to antigenic drifts and shifts
  - Antibodies target highly variable regions of HA and NA
  - Single site mutations can reduce efficacy
- Provide minimal cross-protection within subtypes or against other subtypes of influenza
- Short duration of immunity, particularly in at-risk populations (e.g., pediatric, geriatric)
- Vaccine efficacy is modest
- Requires viral isolate for production
- Avian influenza strains will likely require adjuvant

There is a need for new, improved influenza vaccines

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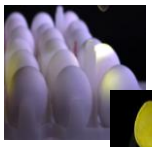
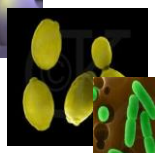
Where Do We Go From Here?

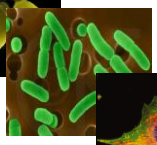
Goal: Develop more effective influenza vaccines that provide a long duration of protection against a broad range of influenza viruses



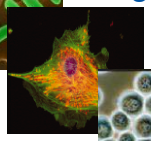
Safe for all ages



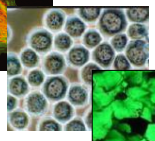
Effective



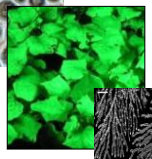
Long lasting immunity



Broadly Reactive



Rapid Response



Simple Manufacture

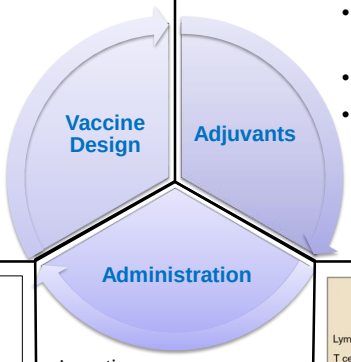
Universal?

Universal Influenza Vaccines

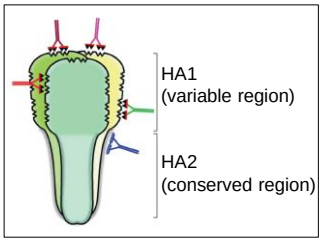
- **What is a "universal vaccine"?**
  - Idealized vaccine: single vaccine for any influenza A subtype
  - A vaccine that provides safe, effective and long-lasting immunity against a broad spectrum of influenza viruses
- **Could be used for several seasons**
  - Simplify the vaccine strain selection process
  - Simplify the influenza vaccination process
  - Reduce vaccine mismatches
  - Reduce potential for vaccine shortages
  - Increase global supply of vaccine
- **Potentially reduce vulnerability to novel influenza viruses**
  - **Population would be "primed" for newly emerging viruses**

Universal Vaccine Strategies Leveraging Old and New Discoveries

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

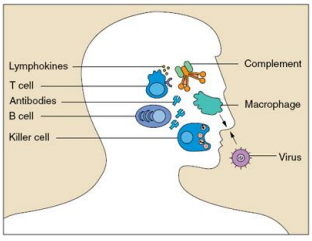


- Broaden B cell epitope recognition
- Th1 vs Th2 responses
- Humoral vs Cell-mediated



R. Rappuoli, *F1000 Medicine Reports* 3 (2011): 16.

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



Source: NIAID http://tinyurl.com/69n9lap

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Closing Thoughts

- In 2005, the US was in a very vulnerable position to be able to respond to seasonal or pandemic outbreaks of influenza
- The USG, through BARDA, NIH, FDA and CDC, has taken bold and significant steps to address these vulnerabilities, particularly in areas of innovation for new technologies in the areas of vaccines, therapeutics and diagnostics for influenza
- There has never been a greater global capacity to respond to a pandemic outbreak of influenza, nor a greater global capacity to produce influenza vaccines
- There has never been a greater variety of influenza vaccines available to address population variation than there are today
- The landscape of new influenza vaccine development is active and rapidly evolving – 94+ products/candidates; continued scientific discoveries will provide greater opportunities for innovation
- While the field of influenza vaccine types appear to be moving towards a variety of niche vaccines in the near term, it is apparent from the landscape that the ultimate aim is to develop a single, more effective influenza vaccine that could be used by all populations

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