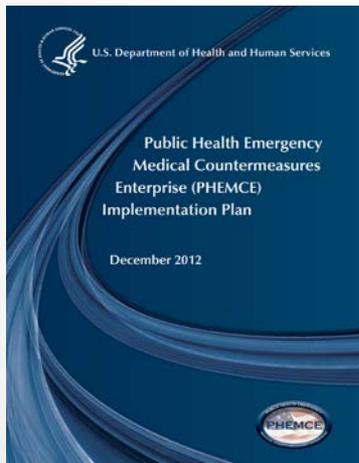
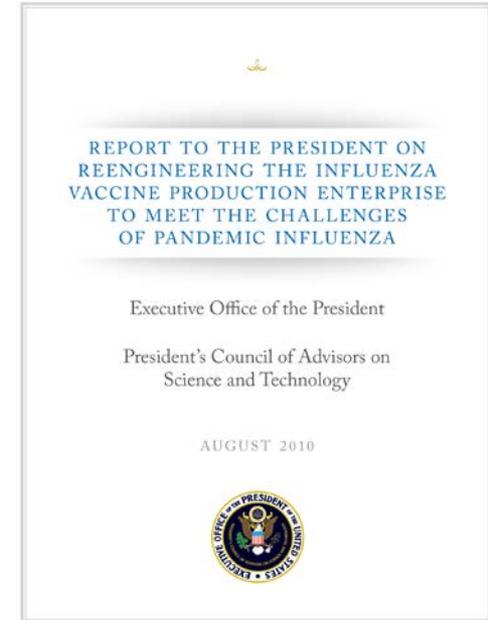


Recognized Need for Improved or Universal Influenza Vaccines

2010 PCAST Report “Because a universal vaccine would completely change the outlook on protecting the population against influenza virus infections, the Federal Government should support and encourage efforts to design a universal vaccine through various mechanisms.”



2012 PHEMCE Implementation Plan programmatic priority “Develop a novel antigen or “universal” flu vaccine that will eliminate the need for annual modifications to the influenza vaccine or annual boosters”



BARDA is Achieving National Pandemic Influenza Vaccine Goals

Q-Pan H5N1 Licensed 11/20/2013 ✓

Antigen-Sparing Vaccine Technology

More Effective/Universal Vaccines



Recombinant Vaccines

Advanced Development Begins FY15



Cell-based Vaccines

Flublok® Licensed 01/16/13 ✓



Egg-based Vaccines

FLUCELVAX® Licensed 11/20/12 ✓

H5N1 Vaccine Licensed 04/17/07 ✓

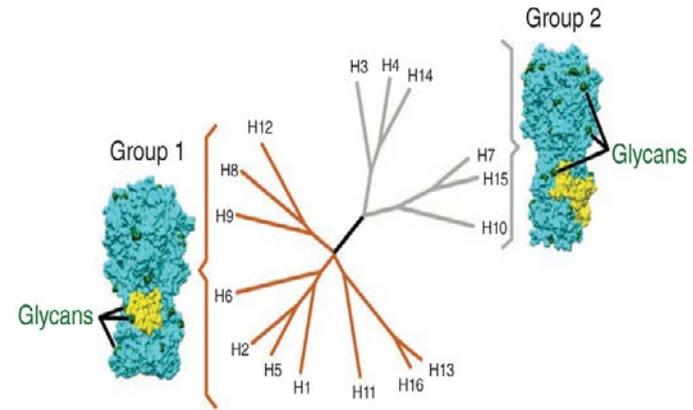
Manufacturing Improvements



More & Better Vaccines, Sooner!

What is a More Effective/Universal Influenza Vaccine?

- A vaccine that provides safe, **more effective** and **long-lasting** immunity against a **broad** spectrum of divergent influenza viruses in all ages and people in high risk groups



Non-structural proteins. Conserved
Potential targets for T cell immunity

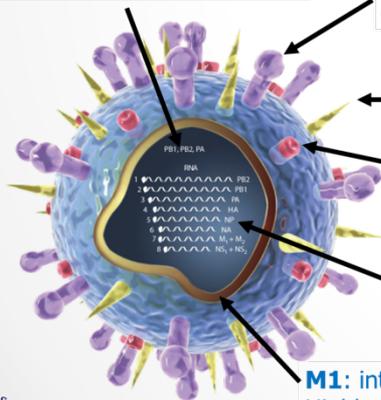
HA: surface, highly variable
immunodominant head,
conserved stem

NA: surface,
variable, slower drift

M2: surface, fairly conserved.
Possible Ab-mediated protection

NP: internal highly conserved.
Induces CMI

M1: internal
Highly conserved
Induces CMI



- **Prime** for emergence of a pandemic influenza virus
- Improve vaccine effectiveness
- Reduce the need for annual vaccination



More Effective/Universal Influenza Vaccine: Target Product Profile

Property/Vaccine	Desired Primary Characteristics
Breadth of Protection	<i>Protects against antigenically divergent influenza A viruses and viruses from both influenza B virus lineages</i>
Efficacy	<i>Shows 20% or greater efficacy above a licensed influenza vaccine comparator as measured by clinical endpoints or surrogate endpoints (e.g. seroprotection or seroconversion rates) predicative of clinical benefit</i>
Duration of Immunity	<i>Protects for two years or more against influenza A subtypes and influenza B lineages</i>
Priming Immunity	<i>Primes for baseline immunity such that a single dose of pandemic influenza vaccine will boost immune response to protective levels against the pandemic influenza virus</i>
Safety	<i>Comparable to licensed vaccines</i>



Path to Partnership



BARDA Guidance to Developers

- Vaccine candidate means the vaccine **intended for clinical development**
- Supporting data for the vaccine intended for clinical development must be provided
 - Evidence that supports only the follow is not acceptable
 - the 1st generation of a 2nd generation vaccine
 - Components of a combination vaccine
 - Platform technology for an unrelated vaccine
- Incremental approaches may be considered with appropriate supportive data



BARDA's Core Service Assistance Programs



- Generate data to support existing animal models or establish new ones
- Develop MCM studies to support advancement of candidate products in the regulatory pathway for licensure
- Evaluate candidate products as MCMs through Proof of Concept studies

- Provide comprehensive, Phase 1 – IV clinical study services to evaluate safety, dosage, PK/PD, and efficacy of MCM candidates

Overview Information

- Title: Broad Agency Announcement for the Advanced Development of Medical Countermeasures for Pandemic Influenza
- BAA-16-100-SOL-00002 (FBO.GOV)
- Purpose: Identify innovative and promising technologies for advanced development of medical countermeasures for influenza and other emerging infectious diseases.
- Submission interim deadlines:
 - Round 1: 30-Jan-2016
 - Round 2: 30-Apr-2016
 - Round 3: 30-Jul-2016
 - Round 4: 30-Oct-2016
 - Round 5: 30-Jan-2017
 - Round 6: 30-Apr-2017
 - Round 7: 30-Jul-2017
 - Round 8: 30-Oct-2017



Area of Interest #5: Influenza Vaccines

- Technical Point of Contact: Armen Donabedian;
Armen.Donabedian@hhs.gov
- Priorities:
 - Vaccines that induce long-lasting and broad (heterotypic and/or heterosubtypic) immunity in all populations compared to currently licensed influenza vaccines.
 - Vaccines that induce broad immunity so as to prime the population against newly emerging influenza viruses or other respiratory viruses of pandemic potential



Data Expectations

- Pre-clinical and clinical studies supporting the ability of your candidate vaccine to elicit cross-reactive immune responses against antigenically diverse influenza A viruses
- Demonstration of rapid onset under “Priming Immunity” will be evaluated favorably
- Pre-clinical and/or clinical data regarding the duration of the immune response raised by your vaccine candidate



Data Expectations

- Data that demonstrate statistically-relevant improvements in immunogenicity/efficacy as compared to existing licensed vaccines
- Communications with the FDA on regulatory pathway for your vaccine candidate
- Information on all immunological assays used to evaluate immune responses in clinical trials. Included, where assays were done, qualification/validation state of the assay, and all data that may be used to correlate specific immune responses with clinical benefit



Improved/Universal Influenza Vaccine – Needs for Success

- New public/private partnership and a different way of thinking
 - It takes a Program
 - Combinations of technologies that will result in the development of vaccines that stimulate broadened, long lasting antibody, cellular and mucosal responses to influenza viruses that meet the universal TPP
 - New ways to design, evaluate and regulate these vaccines
 - New vaccine approaches and targets
 - Alternate potency/release assays will be needed
 - Ferrets as the pathogenicity model
 - Humans as immunological model
 - Assess markers of immunological response
 - that could ultimately lead to a correlate of protection
 - Financial commitment
 - High development costs



Ultimate Goal

“An Influenza Vaccine for Life”

