THE QUEST FOR MORE EFFECTIVE INFLUENZA VACCINES

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Resilient People. Healthy Communities. A Nation Prepared.
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

Egg-based Vaccines
- H5N1 Vaccine Licensed 04/17/07

Cell-based Vaccines
- FLUCELVAX® Licensed 11/20/12

Recombinant Vaccines
- Flublok® Licensed 01/16/13

Q-Pan H5N1 Licensed 11/20/2013

More Effective/Universal Vaccines
- Advanced Development Begins FY15

More & Better Vaccines, Sooner!

Manufacturing Improvements
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

-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

<table>
<thead>
<tr>
<th>Property/Vaccine</th>
<th>Desired Primary Characteristics</th>
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<tbody>
<tr>
<td>Breadth of Protection</td>
<td>Protects against antigenically divergent influenza A viruses and viruses from both influenza B virus lineages</td>
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<tr>
<td>Efficacy</td>
<td>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</td>
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<tr>
<td>Duration of Immunity</td>
<td>Protects for two years or more against influenza A subtypes and influenza B lineages</td>
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<tr>
<td>Priming Immunity</td>
<td>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</td>
</tr>
<tr>
<td>Safety</td>
<td>Comparable to licensed vaccines</td>
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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”