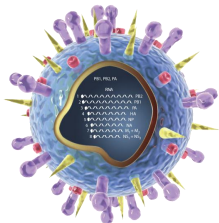




Influenza Vaccine Innovation New Vaccines Approved and on the Way



Rick A. Bright, Ph.D.

Deputy Director, Influenza Division
Biomedical Advanced Research and
Development Authority (BARDA)

**2013 National Adult and Influenza Immunization Summit
May 14 – 16, 2013
Atlanta, GA USA**



The Biomedical Advanced Research and Development Authority

Develop and provide countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases through product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation.



Vaccines



Therapeutics



Diagnostics



Devices



Infrastructure

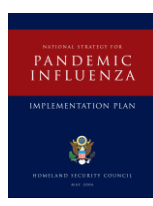
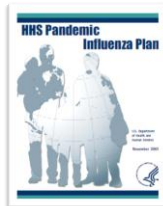
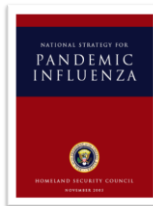
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Requirements



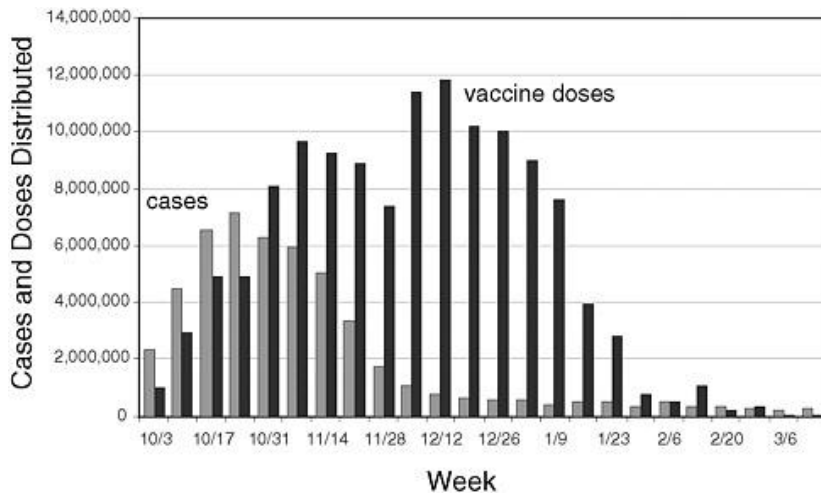
- Requirements addressed by the BARDA Influenza Portfolio are derived from a number of documents that guide the US Government efforts to prepare for pandemics
 - *National Strategy for Pandemic Influenza* (Nov 2005)
 - *HHS Pandemic Influenza Plan* (Nov 2005)
 - *Nation Strategy for Pandemic Influenza Implementation Plan* (May 2006)
 - *Public Health Emergency Medical Countermeasures Review* (Aug 2010)
 - PCAST report on *Reengineering the Influenza Vaccine Production Enterprise* (Aug 2010)



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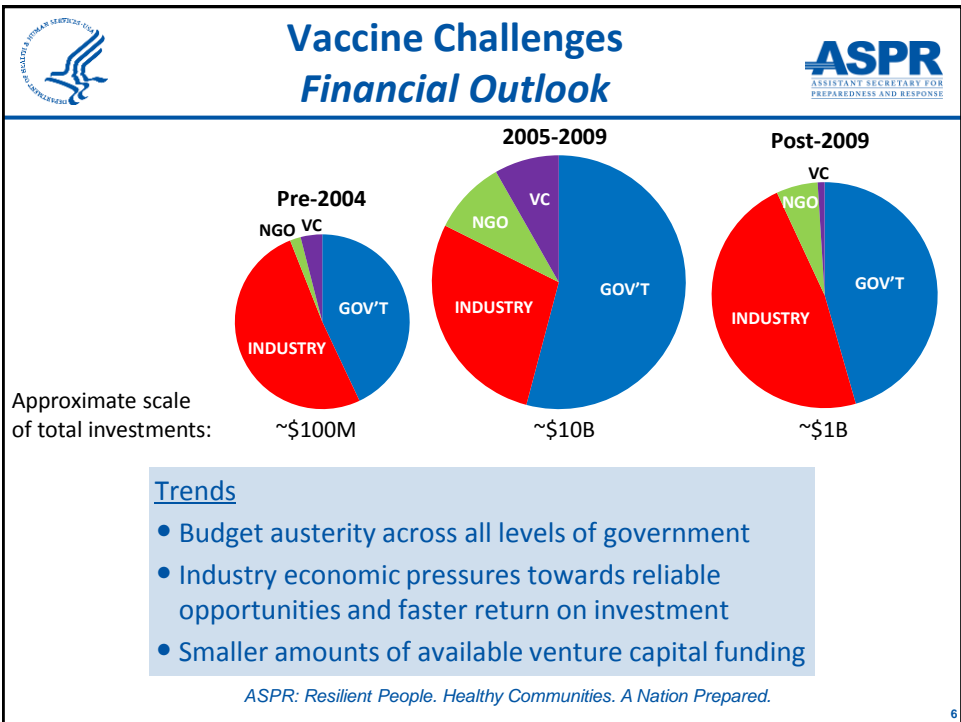
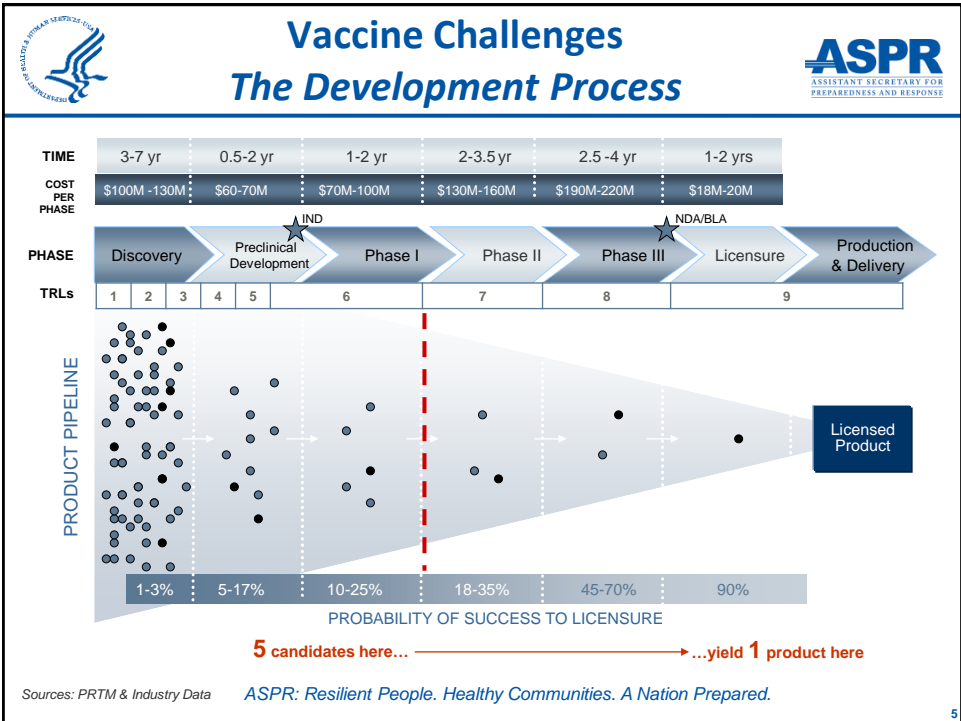


Vaccine Challenges Pandemic Response



National Research Council, "Vaccine Supply," *The 2009 H1N1 Influenza Vaccination Campaign: Summary of a Workshop Series*. Washington, DC: The National Academies Press, 2010.

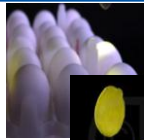
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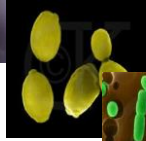


Ideal Attributes of Next-Generation Vaccines

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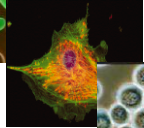
Effective in general and at-risk populations



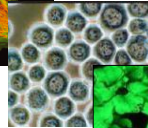
Broadly reactive against multiple strains



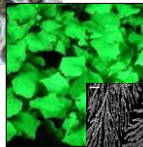
Low cost per dose



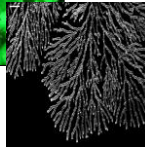
Safe for use in all populations



Rapid, scalable production



Long-lasting immunity



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BARDA's Approach to Vaccine Innovation

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- **More**
 - Maximizing vaccine supply
- **Faster**
 - Minimizing the timeframe from pandemic virus identification to first vaccine dose
- **Better**
 - Driving generational improvements in manufacturability, speed, and effectiveness

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Maximizing Near-Term Technologies



- **Egg-based vaccines**
 - Contracts to ensure year-round egg supply
 - Licensure of first H5N1 vaccine
 - Adjuvanted vaccines
- **Cell-based vaccines**
 - Advanced development of multiple technologies
 - Establish infrastructure for U.S.-based manufacturing
- **International vaccine programs**

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First U.S. Cell-Based Facility Landmark Public-Private Partnership



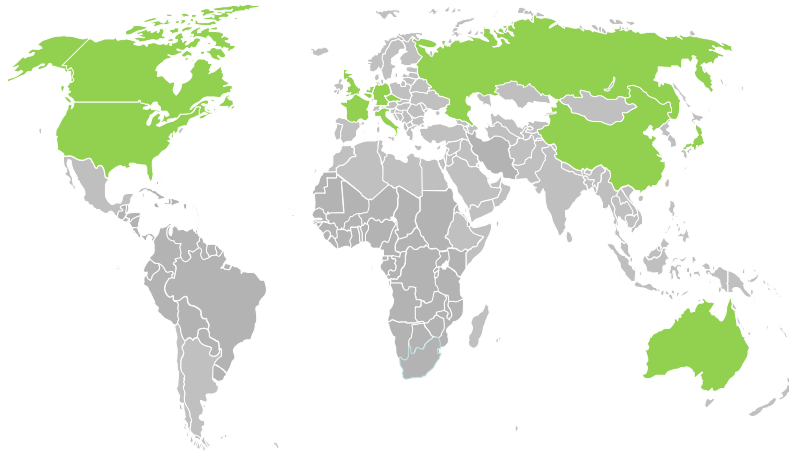
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Global Influenza Vaccine Production circa 2006

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Licensed Influenza Vaccine Producers

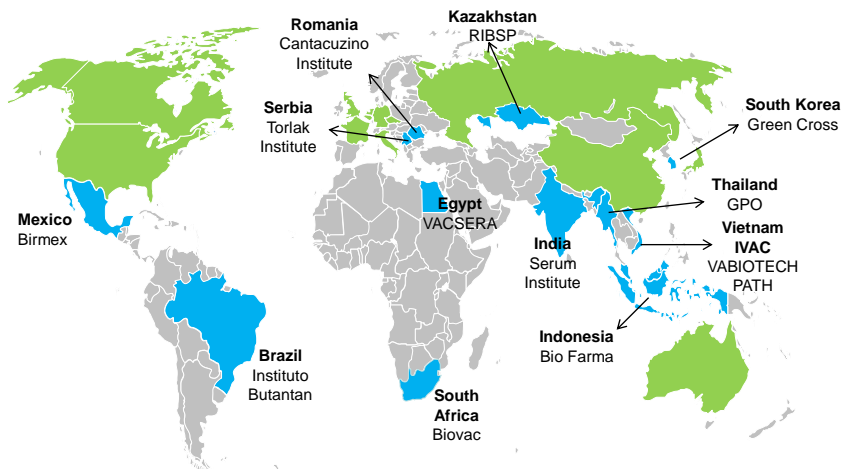
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Global Influenza Vaccine Production circa 2012

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Licensed/Active Influenza Vaccine Producers
 BARDA/WHO Cooperative Agreement Grantees

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BARDA's Approach to Vaccine Innovation

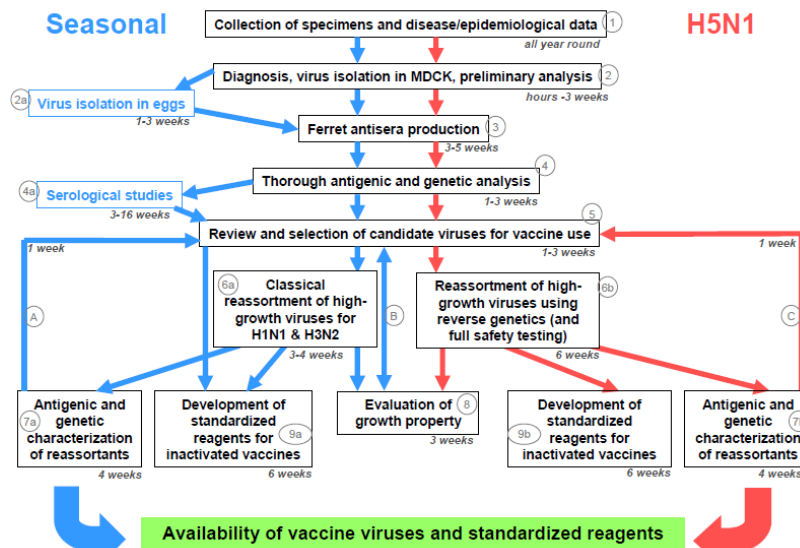


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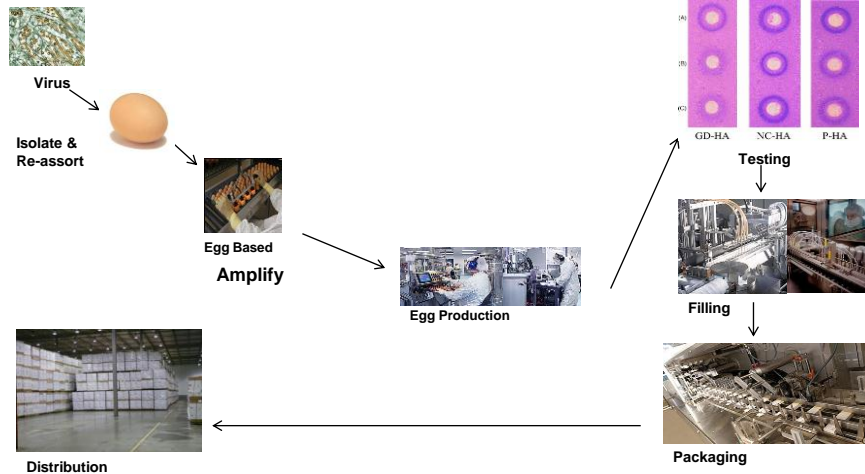
Influenza Vaccine Virus Selection and Development Process



www.who.int/influenza/resources/documents/influenza_vaccine-virus_selection



Traditional Egg-based Vaccine Manufacturing Processes



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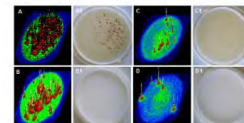
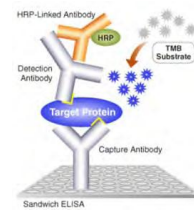


Influenza Vaccine Manufacturing Improvement Initiative



- Novel set of optimized donor viruses
- Faster sterility assays
- Reagent calibration and potency assays

Donor Library



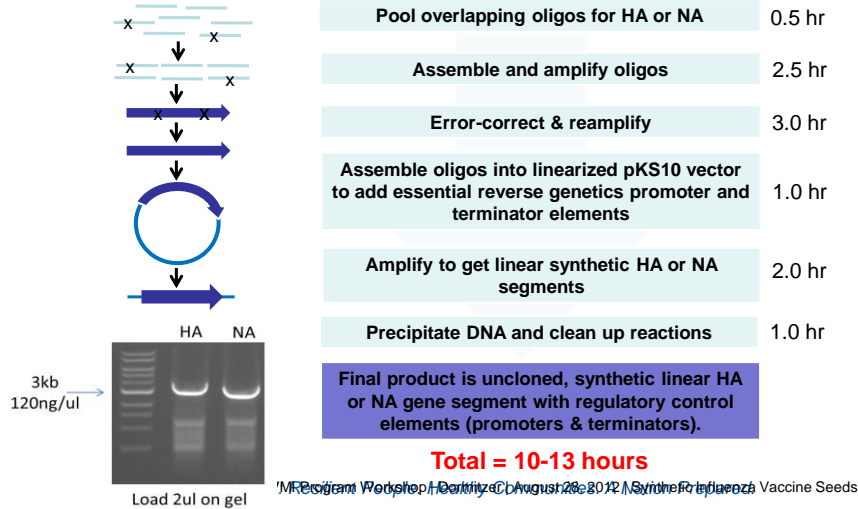
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Synthetic Biology Vaccine Seed Production

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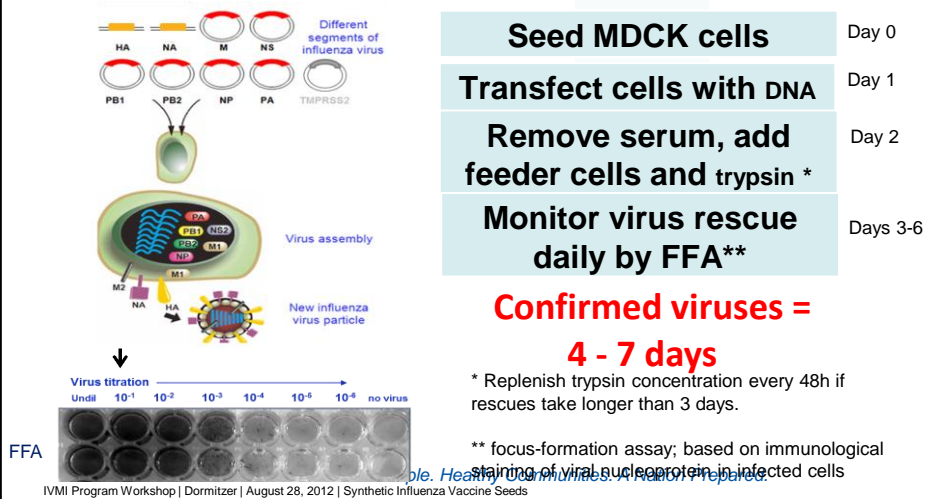
Rapid synthesis process to assemble oligos
into flu HA and NA segments in <1 day



Synthetic Biology Vaccine Seed Production

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Robust process to rescue influenza virus
using synthetic gene segments
in vaccine-approved MDCK cells





BARDA's Approach to Vaccine Innovation



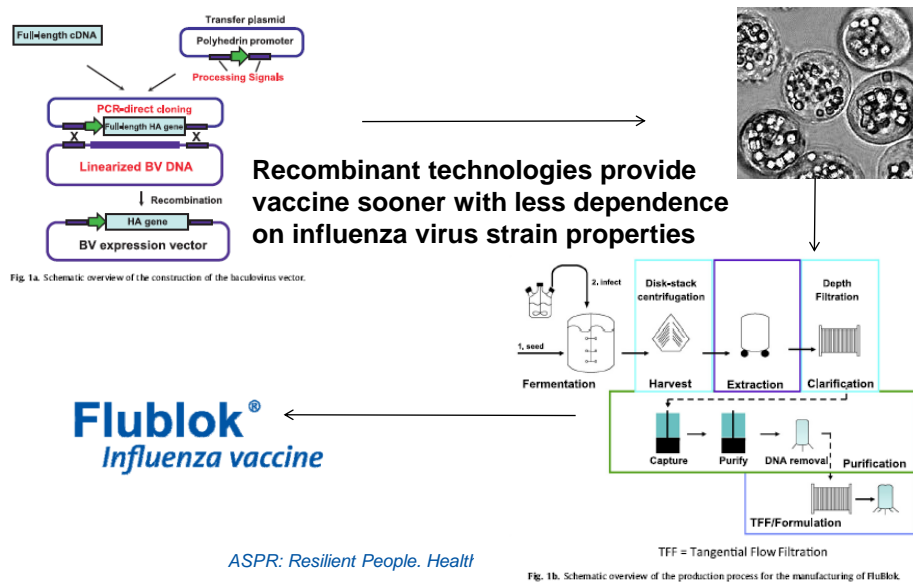
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Recombinant Vaccine Production

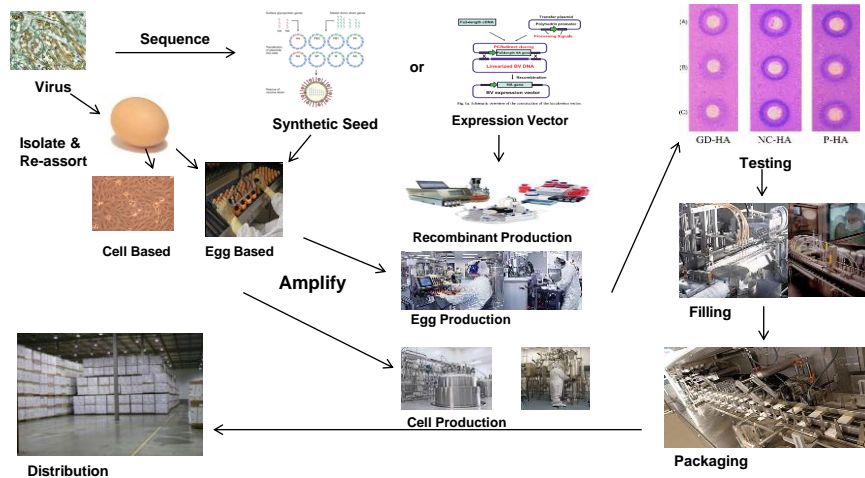


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New Vaccine Production Paradigm

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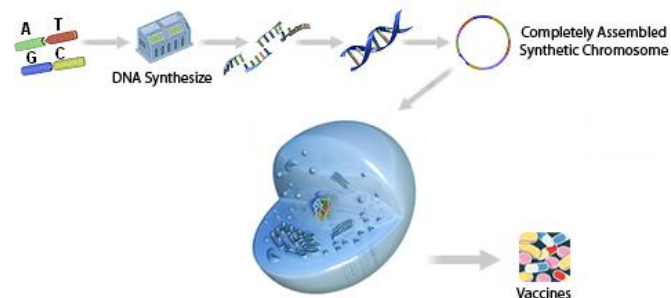
23



Other Novel Approaches

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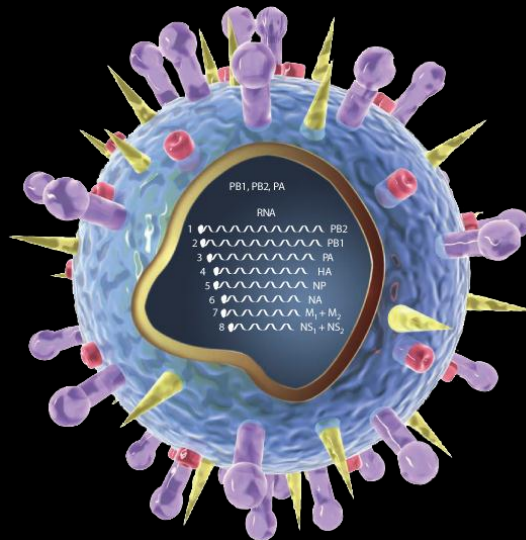
- DNA vaccines
- Live-viral vectors (adenovirus, modified vaccinia)
- Other expression systems (*E. coli*, *Neurospora*)
- Synthetic vaccinology – from sequence to vaccine



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The Influenza Crystal Ball



Adapted from: Paul Lewis, MD
Oregon State Public Health



Universal Influenza Vaccine

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- Many definitions for a universal influenza vaccine
 - A single influenza vaccine that would provide “protection” against any given subtype of influenza A and/or B
 - Could be used for several influenza seasons before reformulation
 - Reduce annual “guesswork” for strain selection
 - Reduce production costs (thus vaccine costs/year round production)
 - Reduce vaccine “mismatches”
 - Reduce the potential for vaccine shortages
 - Increase the global supply of vaccine
- Could be stockpiled for epidemics/pandemics
- Surge capacity
 - Rapid scale-up, reduce production bottlenecks

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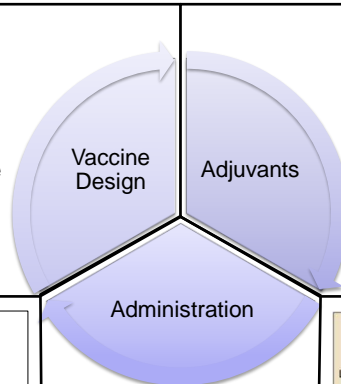
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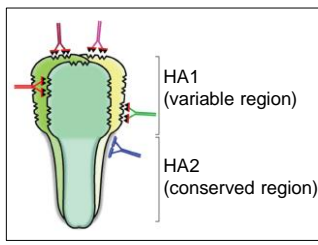
Universal Vaccine Strategies Leveraging Old and New Discoveries

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

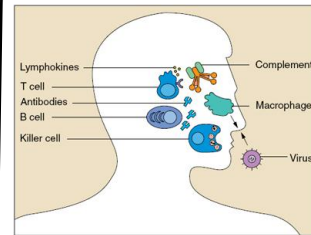


- Broaden B cell epitope recognition
- Th1 vs Th2 responses
- Humoral vs Cell-mediated



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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Developmental Challenges for Universal Vaccines



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- No universal definition or target product profile
- Regulatory science will need to evolve with the technical science development
 - Protective immune responses may be to something other than the HA protein (non-HAI)
 - New surrogates of immunity may need to be identified
 - Alternate potency/release assays will be needed
- Large scale efficacy trials or other “creative” clinical development approaches may be required
- Funding is limited
 - Most candidates are in preclinical development stage

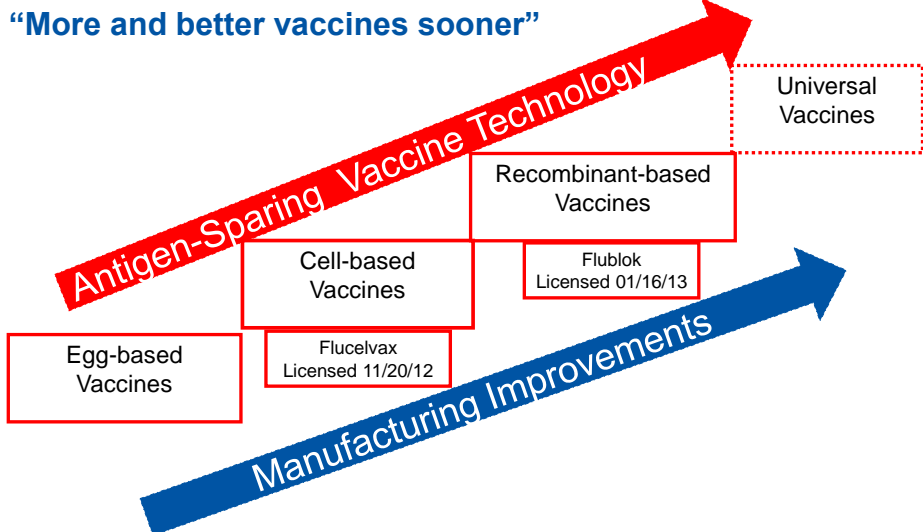
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National Pandemic Influenza Vaccine Development Strategy: Multi-Step & Integrated Approach



“More and better vaccines sooner”



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Final Thoughts

- The landscape of new influenza vaccine development is active and rapidly evolving
- Significant technical challenges for innovative technologies
- Continued scientific discoveries provide greater opportunities for innovation
- Post-pandemic fatigue and economic challenges affect all partners
- Leveraging government, nonprofit and industry collaborations will be essential to continued public health success

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