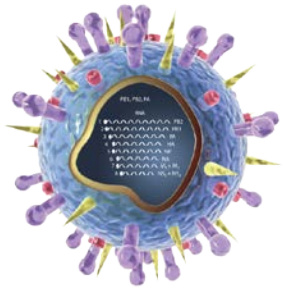
United States Department of
Health & Human Services
Office of the Assistant Secretary for Preparedness and Response

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

U.S. Influenza Vaccine Development and Pandemic Preparedness: Past, Present and Future



Rick Bright, PhD
Acting Director, Influenza Division
Biomedical Advanced Research and Development Authority (BARDA)
Office of the Assistant Secretary for Preparedness & Response

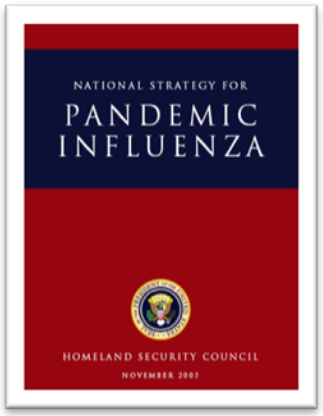
National Vaccine Advisory Committee Meeting
June 10, 2014

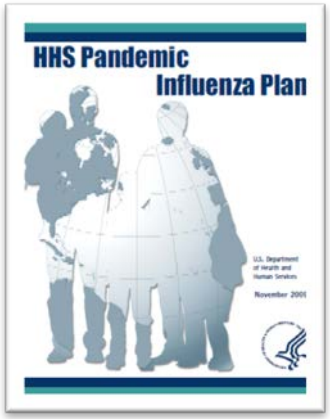
A Nation Unprepared: US Influenza Vaccines in 2004

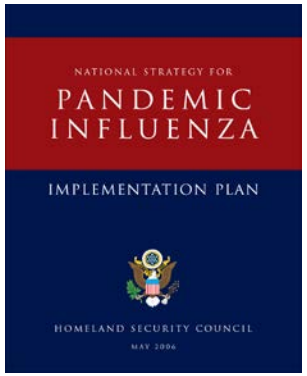
- All licensed seasonal vaccines are egg-based (1940s-1950s technology)
- Vaccine is produced in a six month production window (January-June each year); no production capability outside of that window
- Annual immunization is required
  - Vaccine effectiveness estimated at 50-70% in healthy adults
- Severe 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

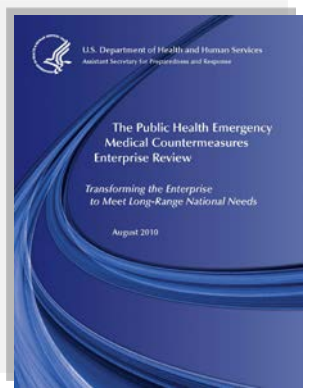
Establishing Pandemic Influenza Vaccine Capabilities: USG Requirements

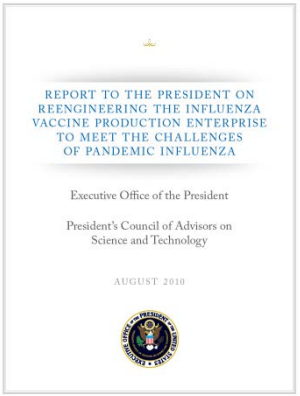
- In 2005, the USG launched an national effort to improve US pandemic preparedness, called for 300+ preparedness actions
- The requirements addressed by the BARDA Influenza Portfolio are derived from a number of documents that guide the US Government efforts to prepare for pandemic, including:
  - Establish and maintaining a dynamic pre-pandemic vaccine stockpile
  - Establish domestic manufacturing capacity to produce sufficient 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











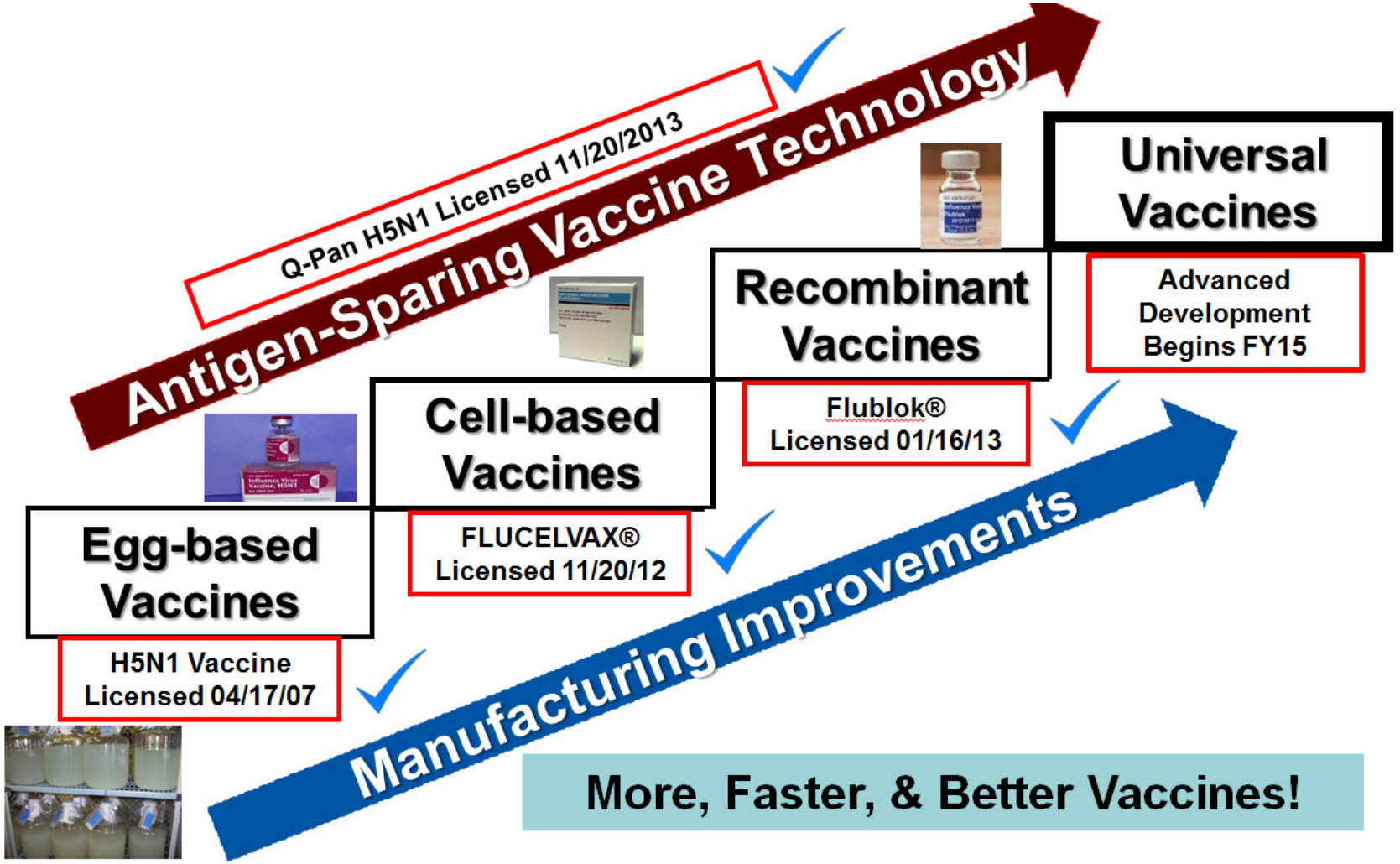
BARDA's Mission

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

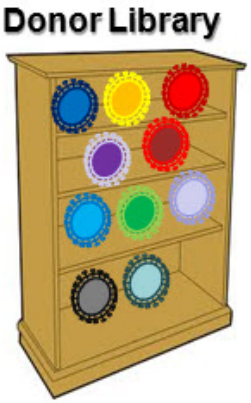
ASPR: Resilient People. Healthy Communities. A Nation Prepared.

BARDA Approach to Making Medical Countermeasures Available

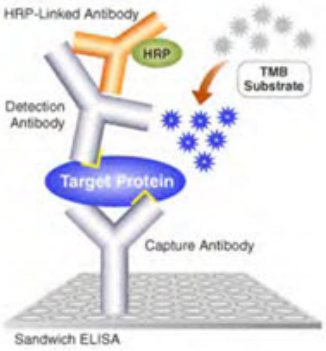
BARDA is Achieving National Pandemic Influenza Vaccine Goals



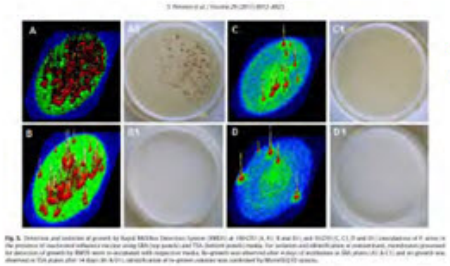
BARDA: Influenza Vaccine Manufacturing Improvement Initiative



6 promising donors to improve vaccine yield



Faster potency reagents



7 days faster sterility assay

BARDA: Enhancing Domestic Vaccine Manufacturing Capacity

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

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

sanofi pasteur – Swiftwater, PA

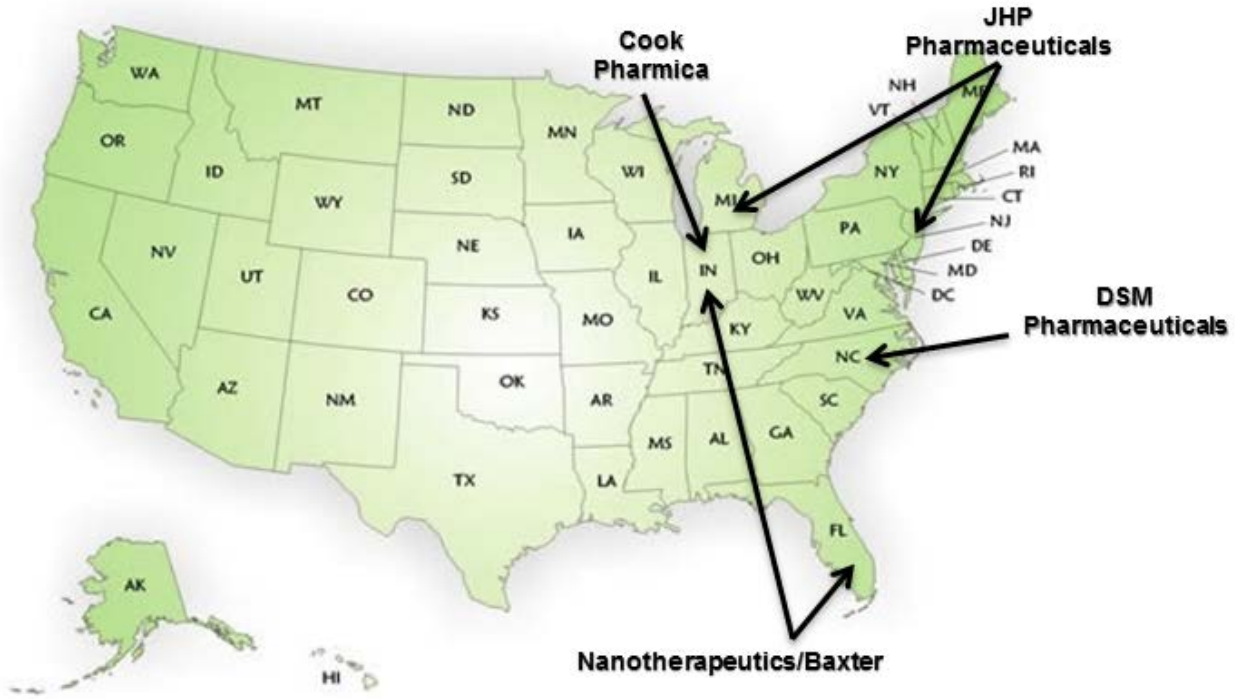
- **Changing Flu Vaccine Industry**

2013 ISPE Facility of the Year

Novartis – Holly Springs, NC

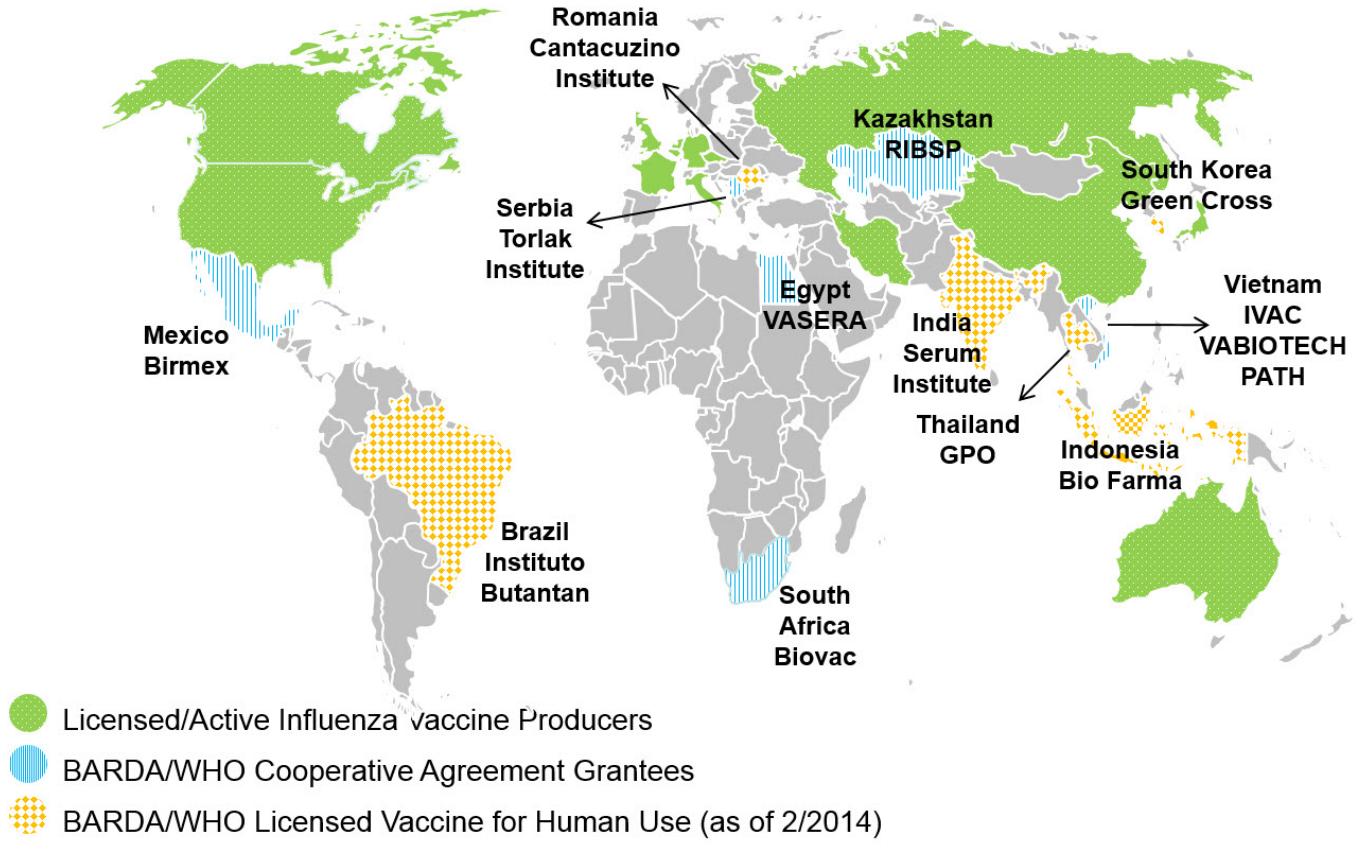
Centers for Innovation in Advanced Development and Manufacturing

Fill Finish Manufacturing Network



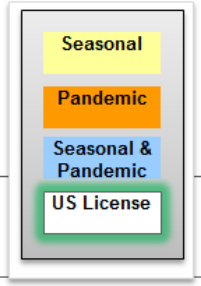
Cook Pharmica (IN)
JHP Pharmaceuticals (MI and NJ)
DSM Pharmaceuticals (NC)
Nanotherapeutics/Baxter (FL and IN)

Current Geographical Distribution of Influenza Vaccine Production

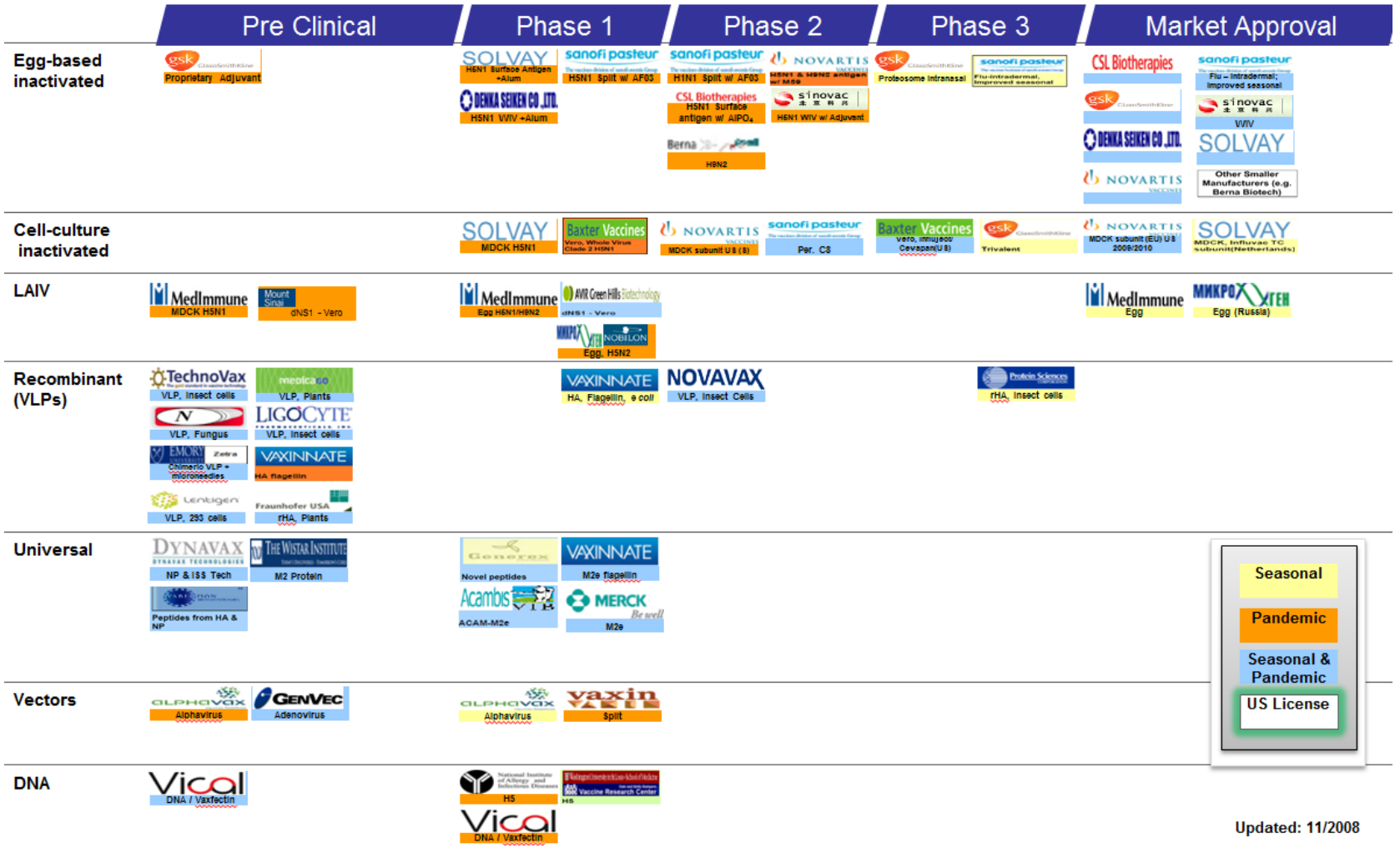


Influenza Vaccine Landscape

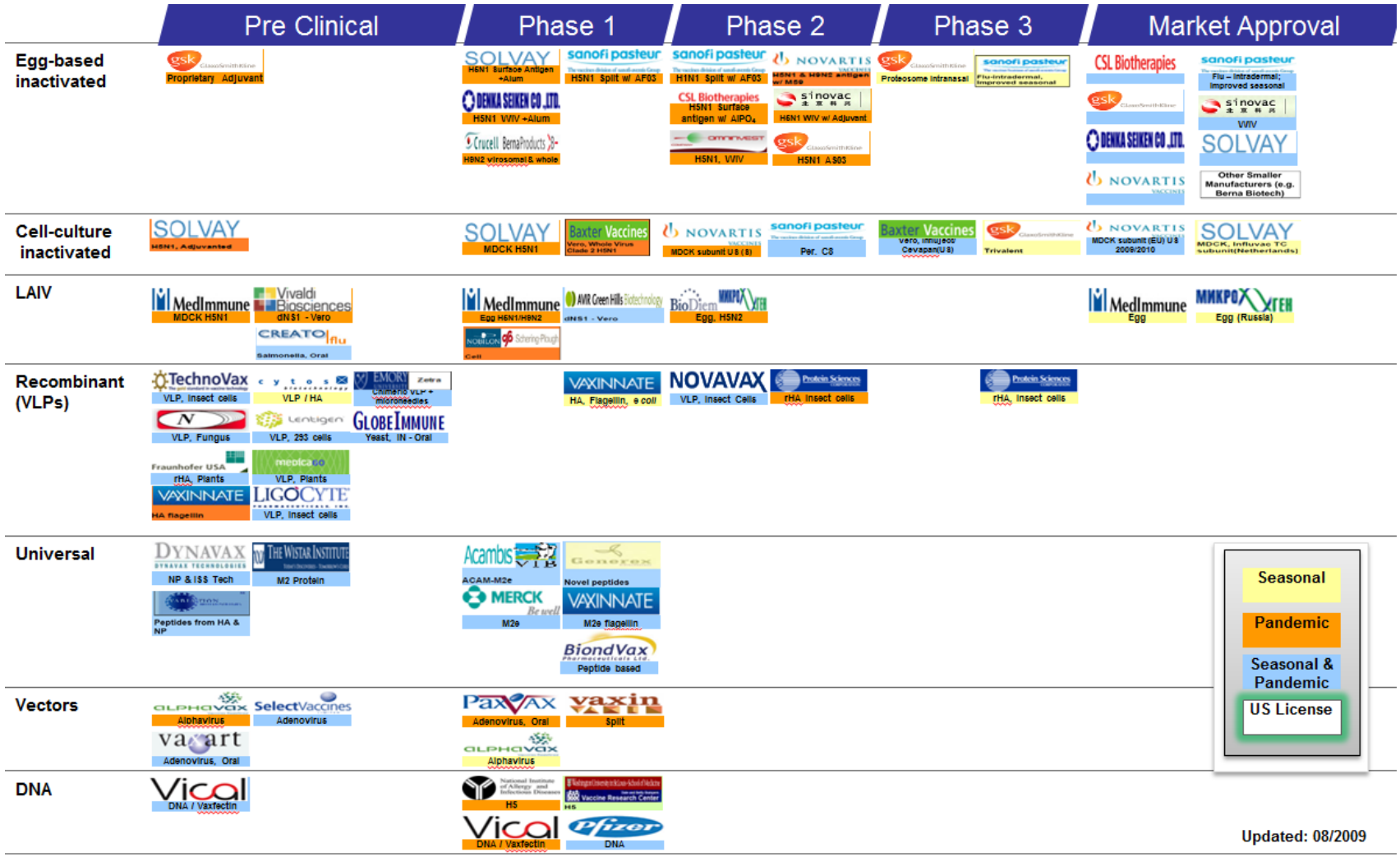
	Pre Clinical	Phase 1	Phase 2	Phase 3	Market Approval
Egg-based inactivated					
Cell-culture inactivated					
LAIV					
Recombinant (VLPs)					
Universal					
Vectors					
DNA					



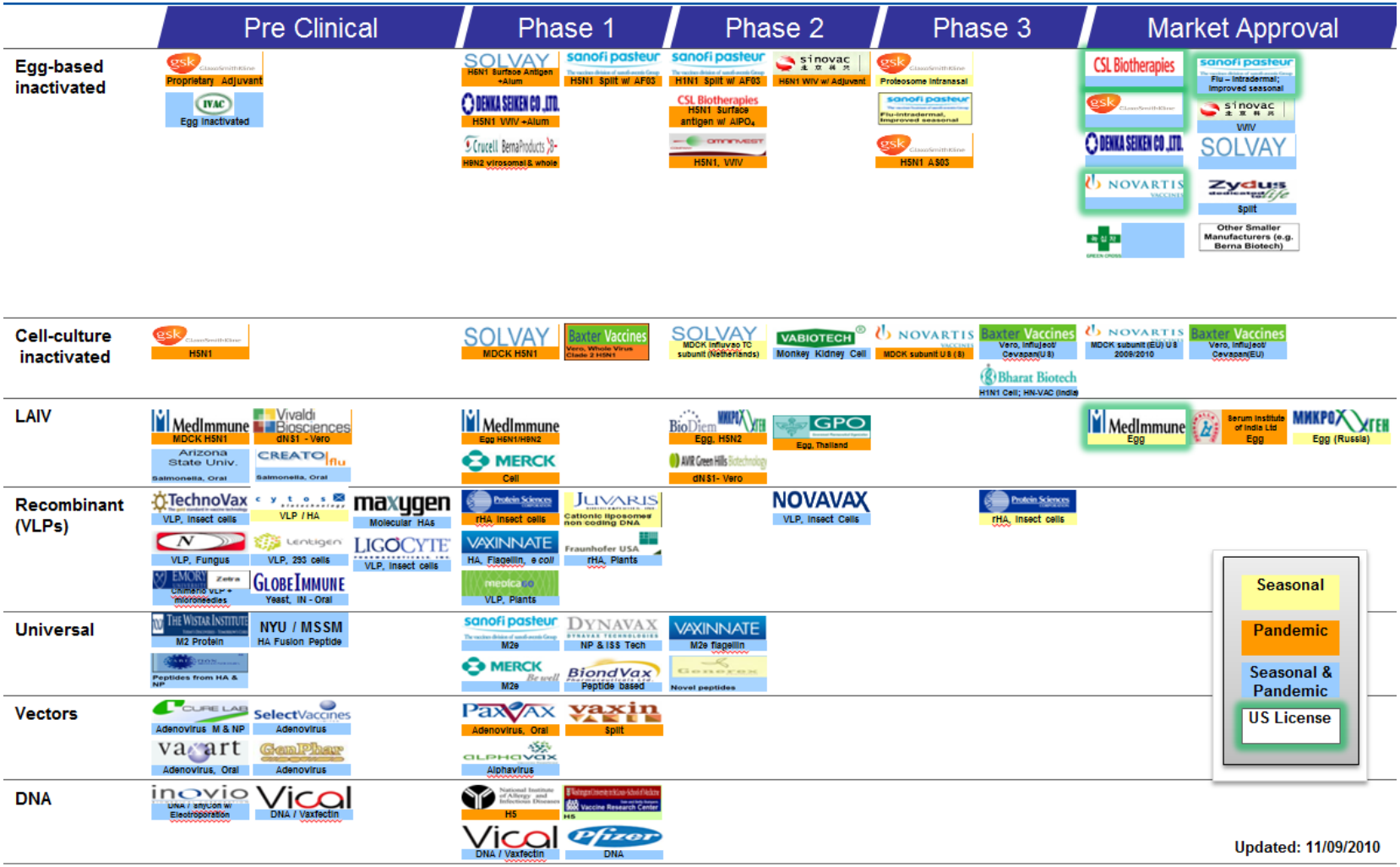
2008 Influenza Vaccine Landscape



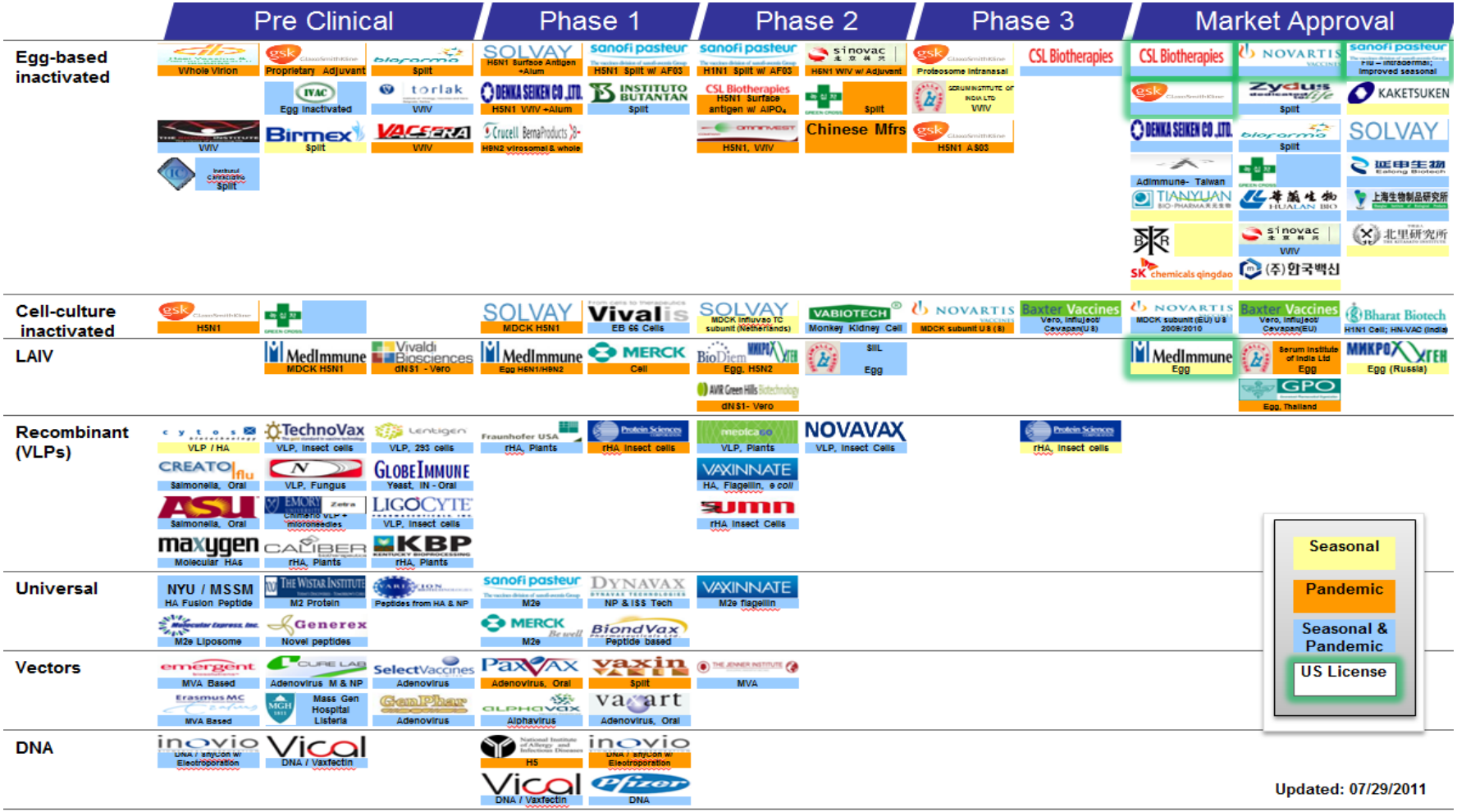
2009 Influenza Vaccine Landscape



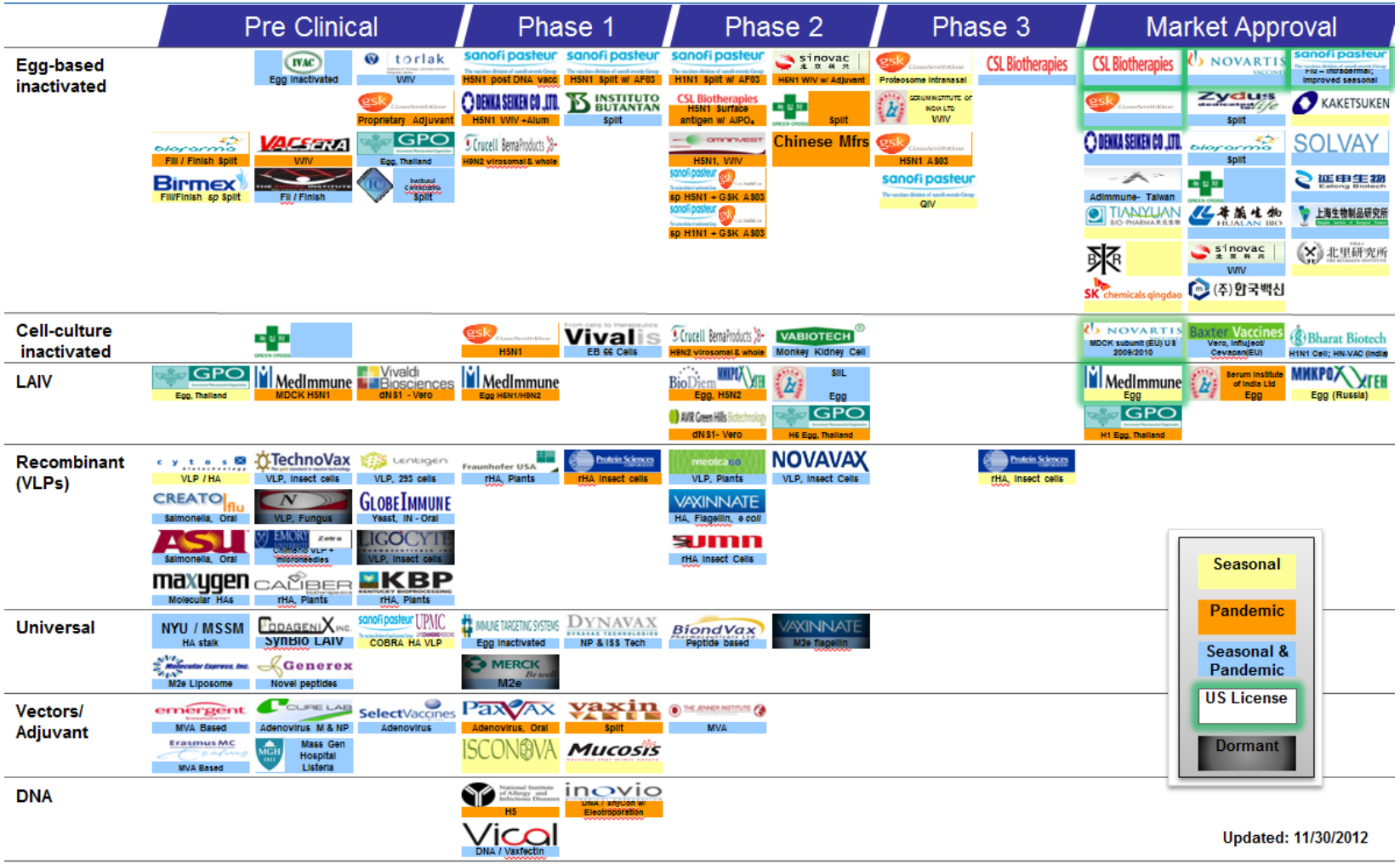
2010 Influenza Vaccine Landscape



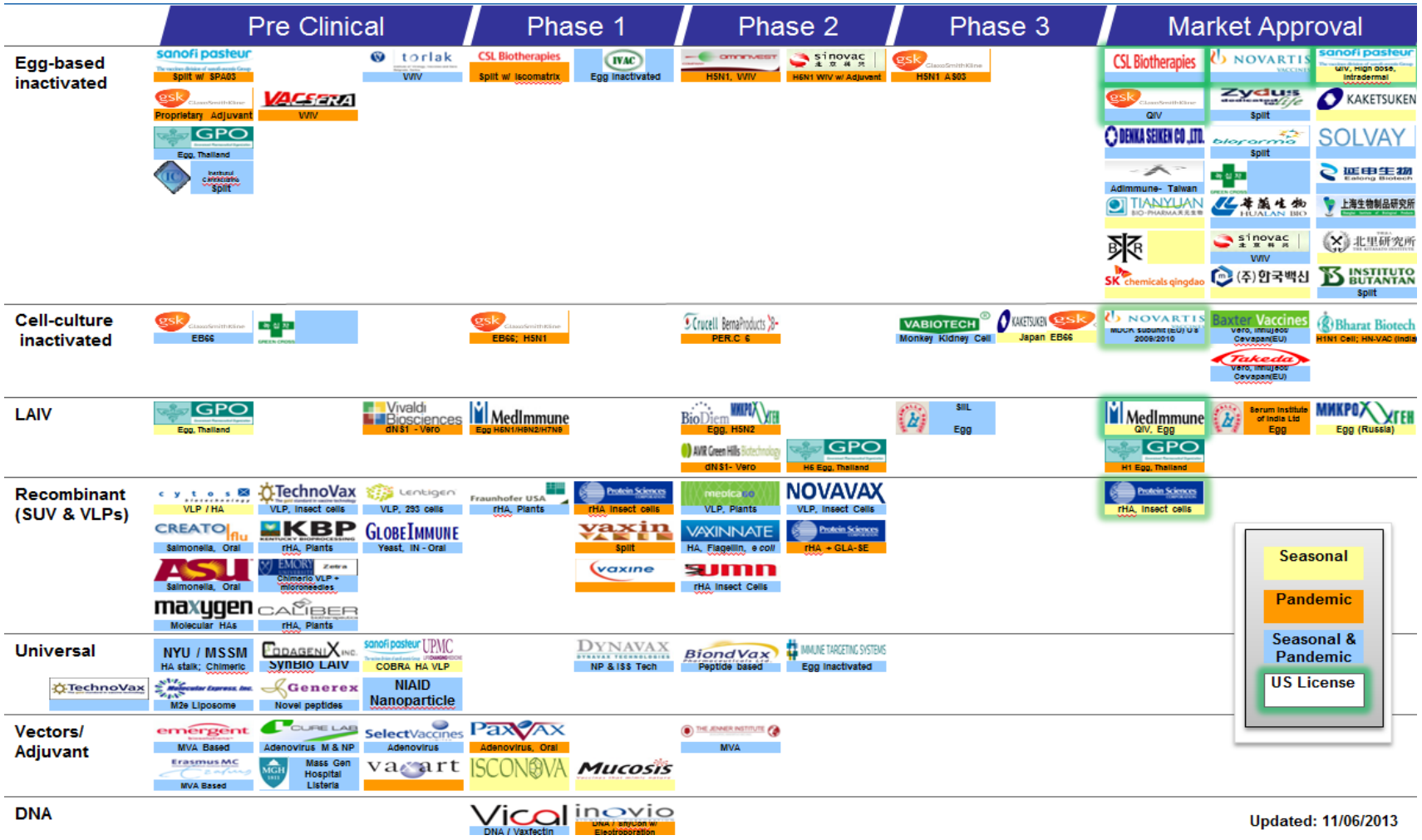
2011 Influenza Vaccine Landscape



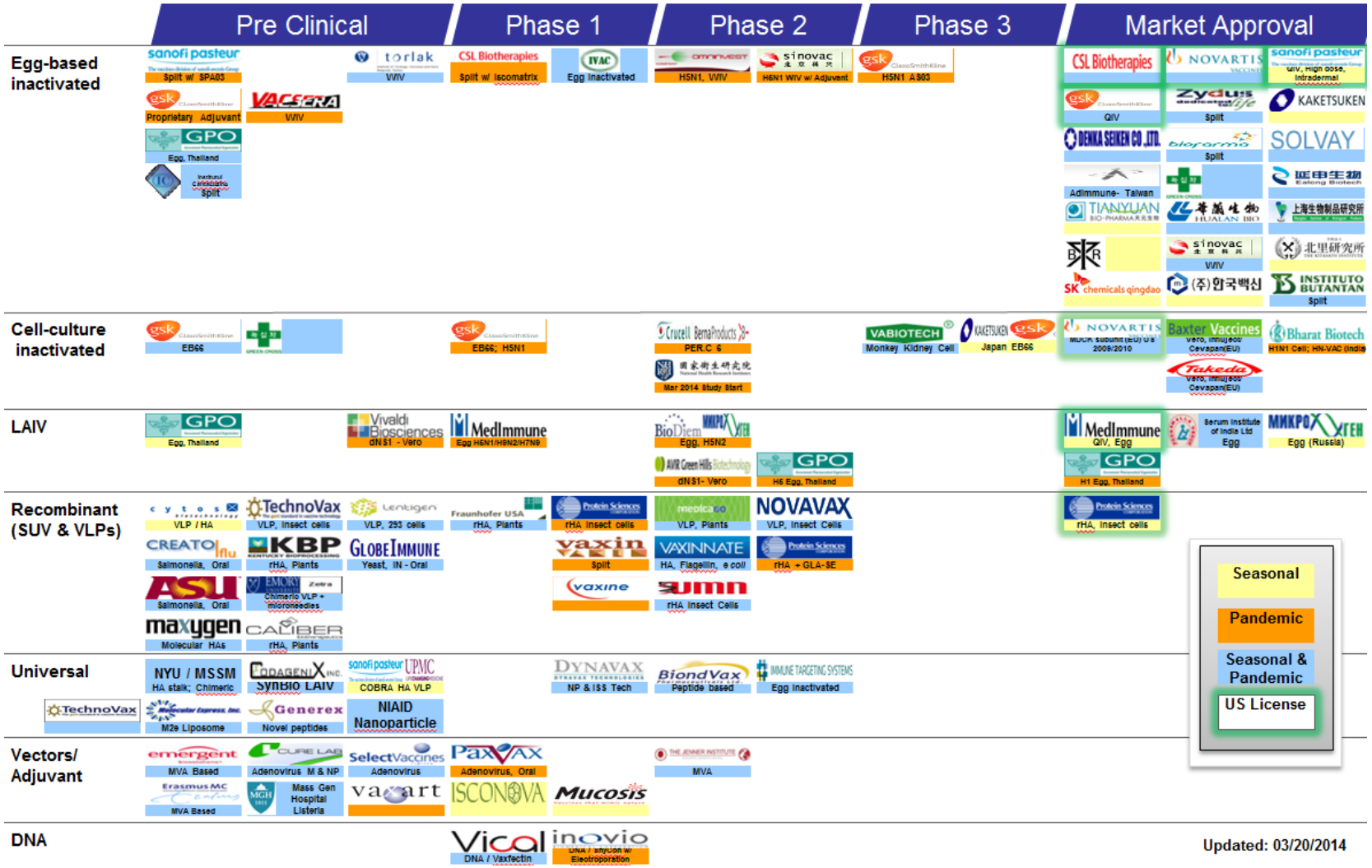
2012 Influenza Vaccine Landscape



2013 Influenza Vaccine Landscape



2014 Influenza Vaccine Landscape



Which Flu Vaccine is Right for You?

Which Flu Vaccine is Right for You?
Get Vaccinated and Prevent the Spread of Infection

HIGH-DOSE - Helping the elder avoid flue complications like pneumonia or even death
Greater for:
- **age 65 or older**

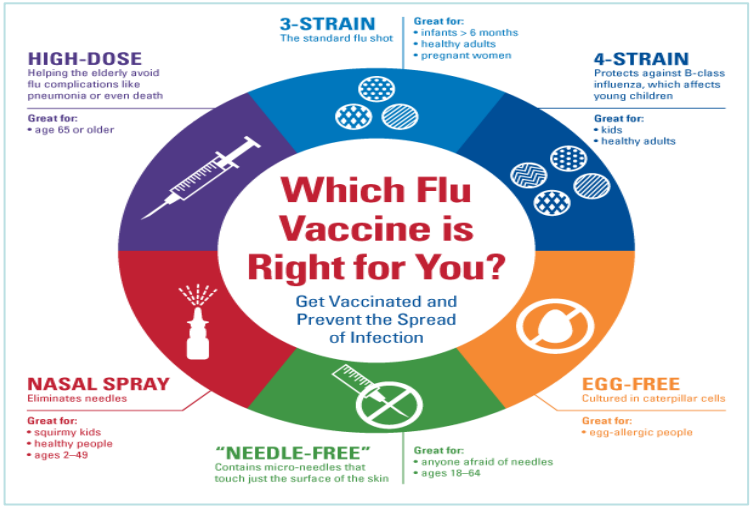
NASAL SPAY – Eliminates needles
Great for:
- **squirmy kids**
- **healthy people**
- **age 2-49**

“NEEDLE-FREE” - Contains micro-needles that touch just the surface of the skin
Great for:
- **anyone afraid of needles**
- **age 18-64**

EGG-FREE – Cultured in caterpillar cell
Great for:
- **egg allergic people**

4-STRAIN – Protect against B-class influenza, which affect young children
Great for:
- **Kids**
- **healthy adults**

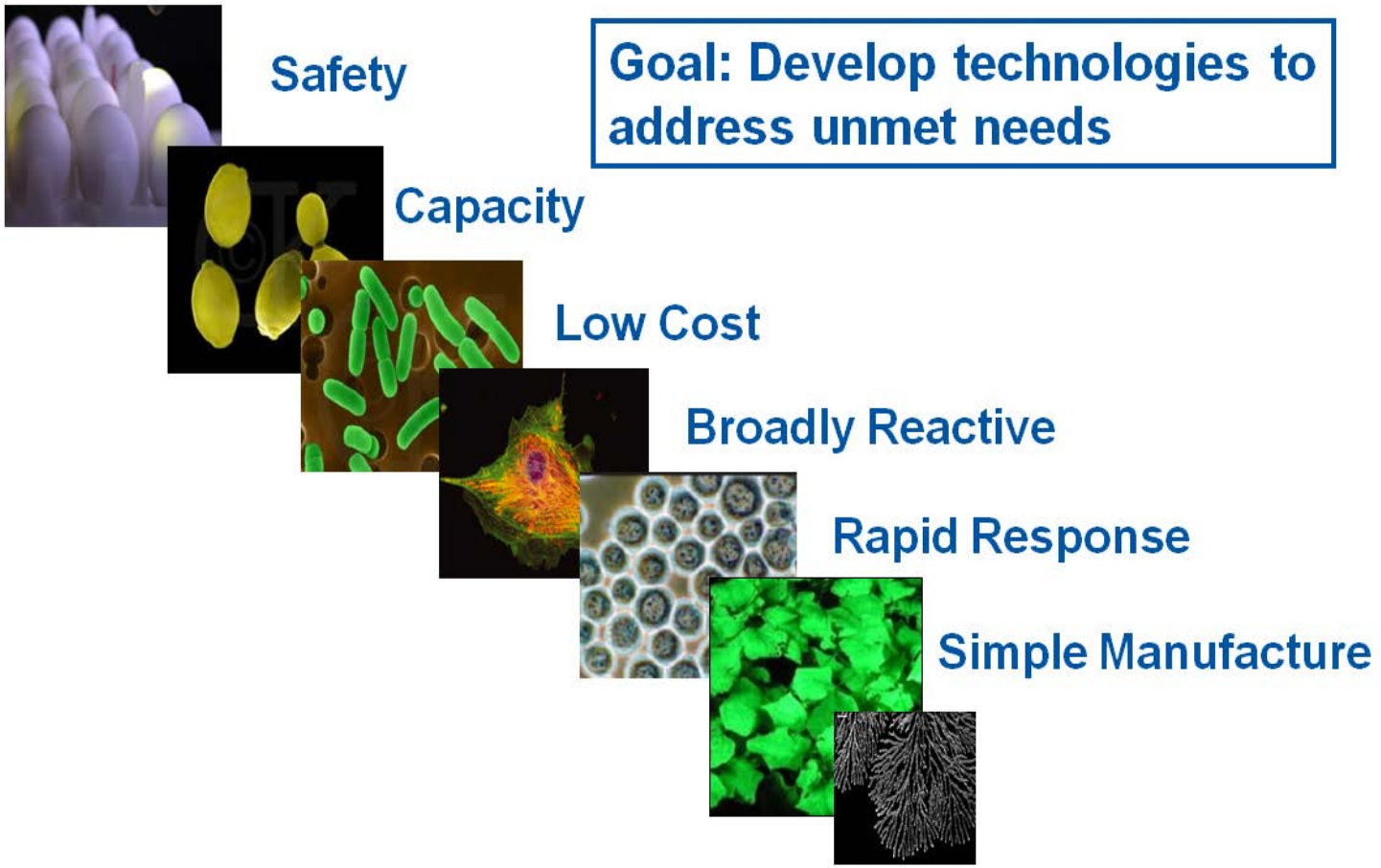
3-STRAIN – The standard flu shot
Great for:
- **infants > 6 month**
- **healthy adults**
- **pregnant women**



National Jewish Health®
Science Transforming Life®

ASPR: Resilient People. Healthy Communities. A Nation Prepared.

Need for New High Performance Platform Technologies



Goal: Develop technologies to address unmet needs

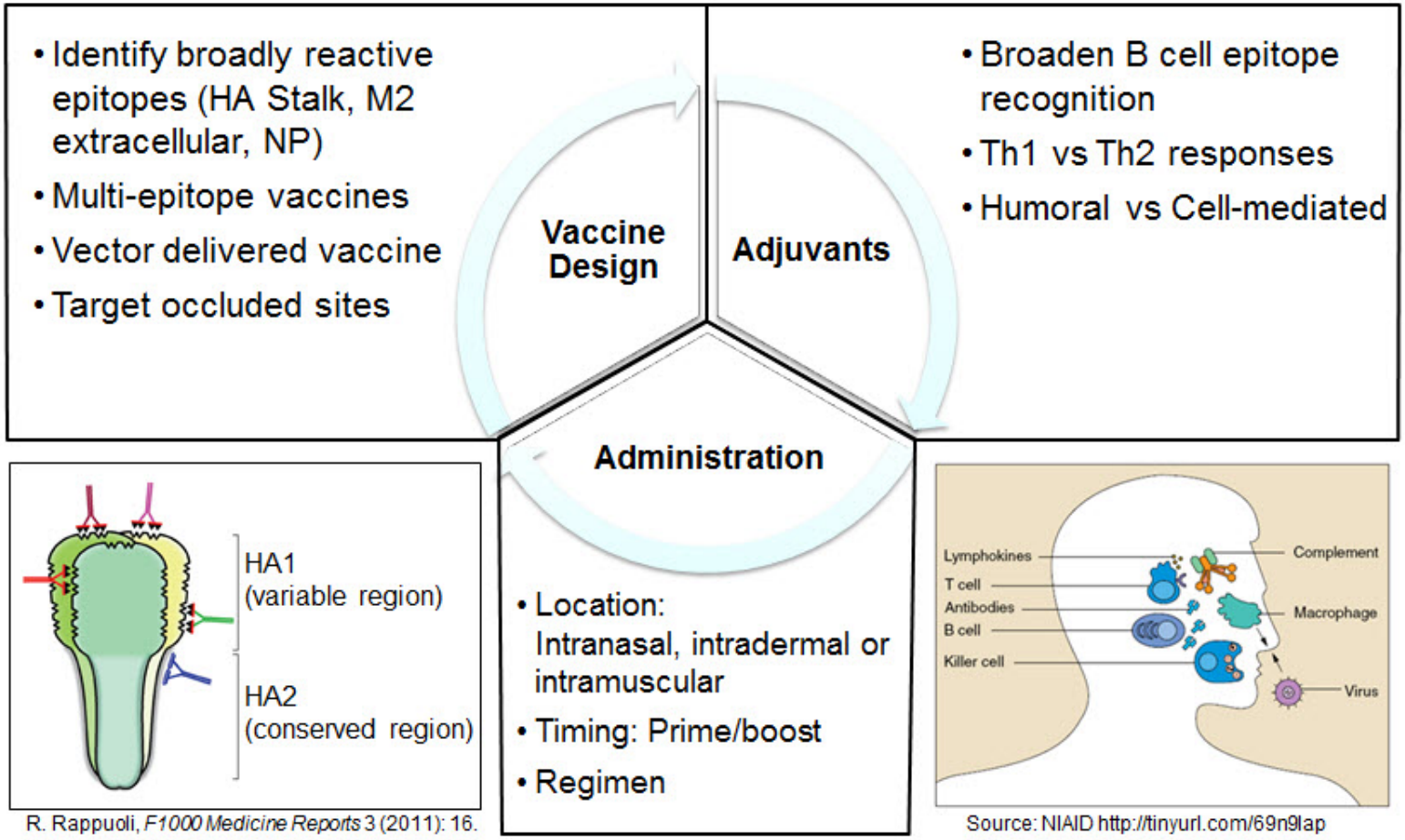
Universal Influenza Vaccines

- **What is a "universal vaccine"?**
  - Idealized vaccine: single vaccine for any influenza A subtype
- **Could be used for several seasons**
  - Remove annual 'guesswork' for strain selection
  - Reduce production costs
  - Eliminate vaccine mismatches
  - Reduce potential for vaccine shortages
  - Increase global supply of vaccine
- **Stockpile of vaccine for epi/pandemics**
- **Year round production**

Universal Influenza Vaccine Target Characteristics

- **Vaccine Target: All influenza A subtypes**
  - Nasal > intramuscular > intradermal administration
  - Low antigen dose - safe and effective
- **Duration of response**
  - Single dose: annually < biannually < decennially
- **Target morbidity or mortality as endpoint of efficacy?**
  - Reduction in spread of disease
- **Population targeted**
  - < 6mo – 85+ years of age
- **Storage conditions**
  - Room temperature

Universal Vaccine Strategies Leveraging Old and New Discoveries



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

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

R. Rappuoli, *F1000 Medicine Reports* 3 (2011): 16. Source: NIAID http://tinyurl.com/69n9lap

Closing Thoughts

- There has never been a greater variety of influenza vaccines available to address population variety than there are today
- The landscape of new influenza vaccine development is active and rapidly evolving – 94+ products/candidates
- Technical and regulatory challenges exist for innovative technologies
- Continued scientific discoveries 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 vaccine that could be used by all populations

Rick Bright, PhD
Acting Director
Influenza Division
BARDA
U.S. Department of Health and Human Services

Rick.Bright@HHS.GOV