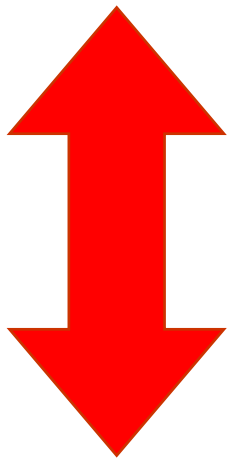
Investments in Innovation:

Seasonal Influenza Preparedness



Pandemic Influenza Preparedness

Bruce Gellin, MD, MPH
Director
National Vaccine Program Office
Department of Health and Human Services

Influenza Means War

“The appalling pandemic of 1918 in the last months of the exhausting conflict of World War I, with massive mobilization of armies and upheaval of civilian populations, has irrevocably linked those two catastrophes.”

“It demonstrated that virulent influenza may be more devastating to human life than war itself ... the onset of another war inevitably recalled the specter of 1918 and the possibility that ... [it] would again result in the epidemiologic conditions which would heighten the severity of influenza to a catastrophic level”

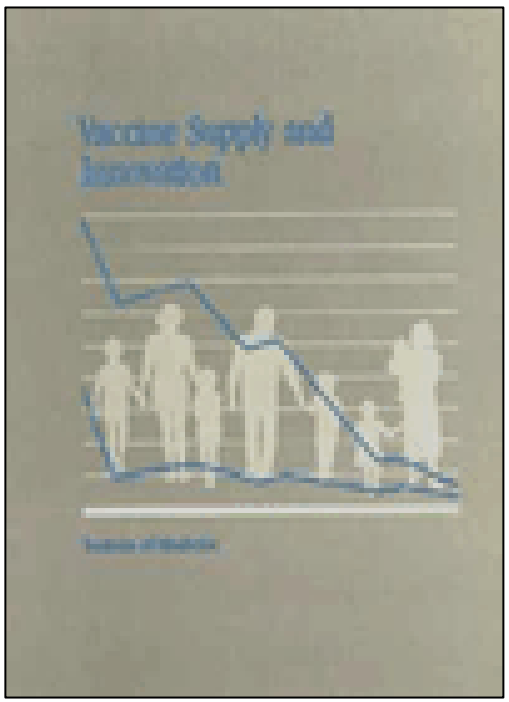
Dr. Thomas Francis Jr,
Chairman, US Influenza Commission (1941)

Influenza Vaccine's WWII Origins

- Improving virus yields from embryonated eggs
- Improving titration accuracy
- Ultracentrifuge and electrophoresis purification
  - Concentrating and purifying the virus on a large scale
- Develop uniform standards for potency and purity
- Field studies to provide the first reliable proof of safety and efficacy.
  - Standardized record systems, observation procedures, and viral and serological tests
  - "It was possible to obtain participation of entire units so that vaccinated persons and controls could be properly designated rather than depending upon the less desirable and unpredictable use of volunteers"

K. Hoyt: Vaccine Innovation: Lessons from World War II (2006)

Vaccine Supply and Innovation



Recent advances in all aspects of biotechnology and particularly gene manipulation offer powerful new approaches to many previously intractable problems. These technologies, combined with a better understanding of the immune process, have opened a new era in vaccine development.

Institute of Medicine 1985

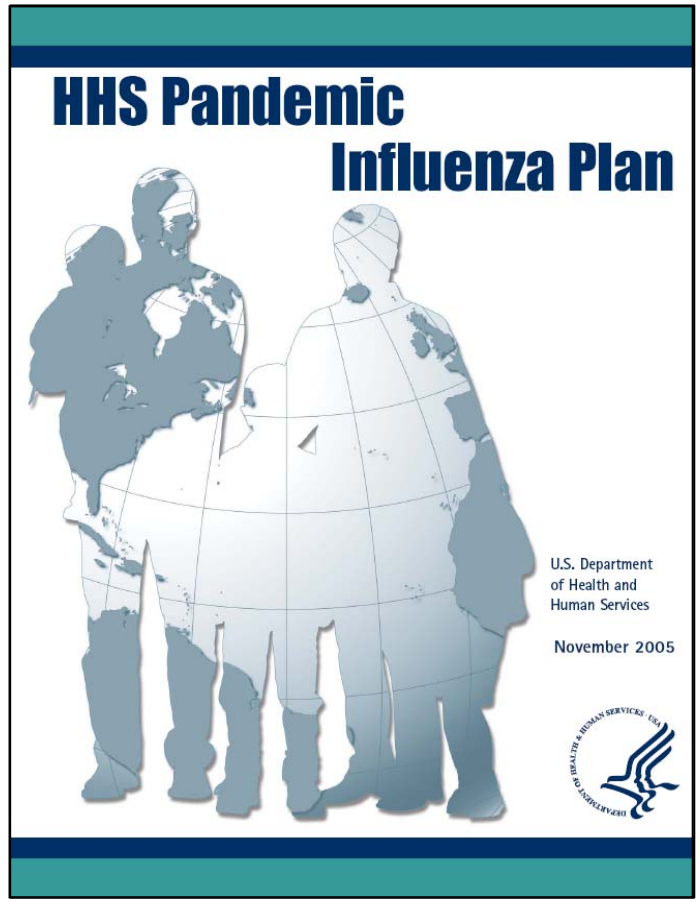
HHS Pandemic Influenza Plan: Vaccine Goals

Vaccine Goal #1:

To establish and maintain a dynamic pre-pandemic influenza vaccine stockpile sufficient for 20 million persons (at 2 doses/person)

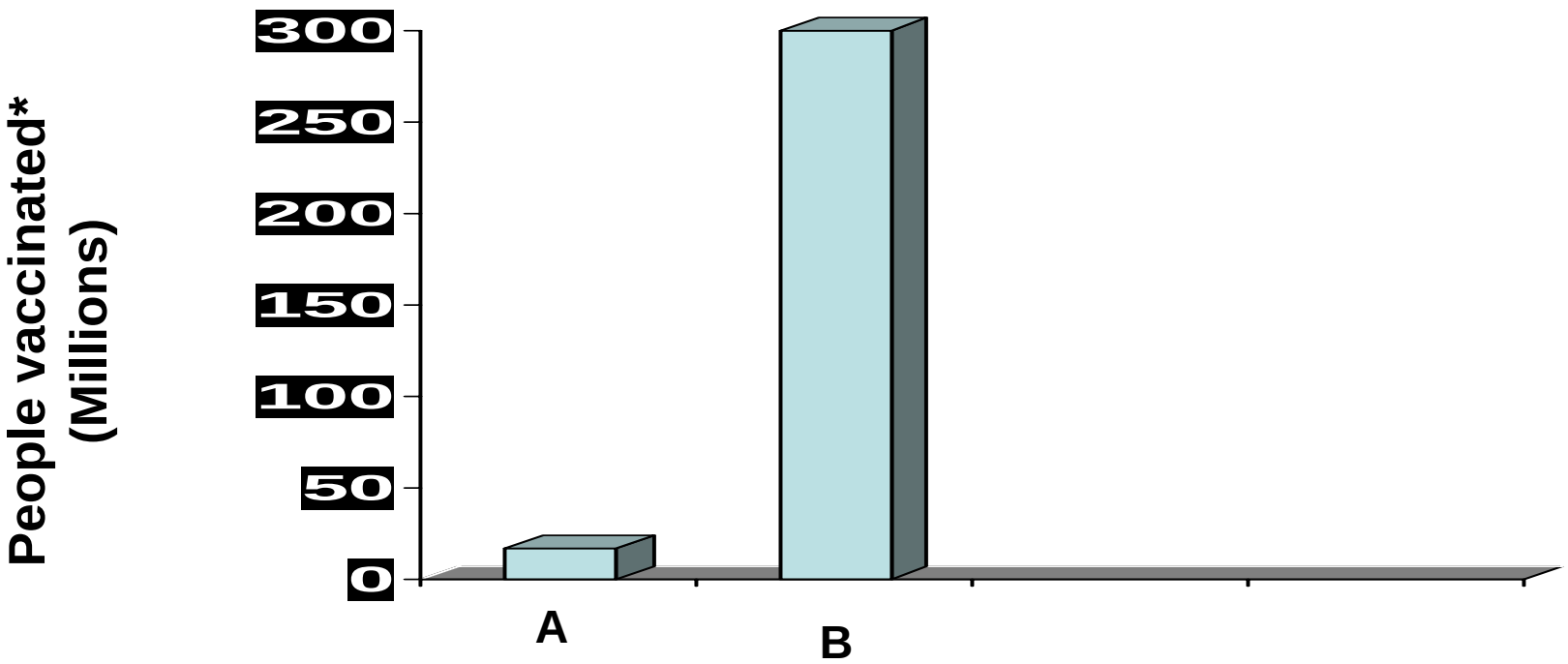
Vaccine Goal #2:

To provide pandemic vaccine to all U.S. citizens within 6 months of a pandemic declaration: 600 million doses pandemic vaccine



HISTORICAL PERSPECTIVE - 2005

Estimated Annual Domestic Production of Pandemic Influenza Vaccine: Capacity, and Need

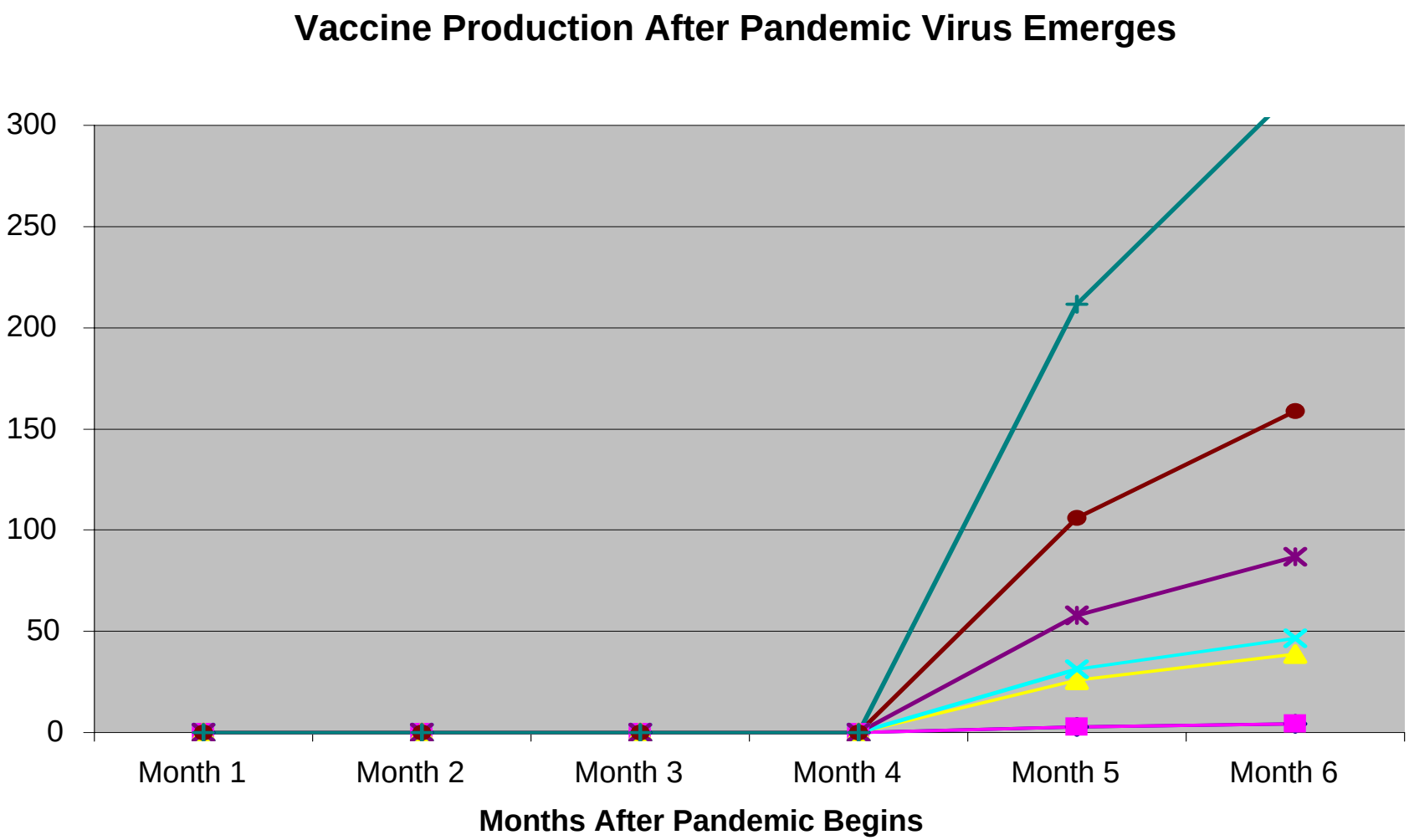


A: Annual domestic capacity - 2005

B: National need

***Assumes 2 doses/person, 90 ug/dose**

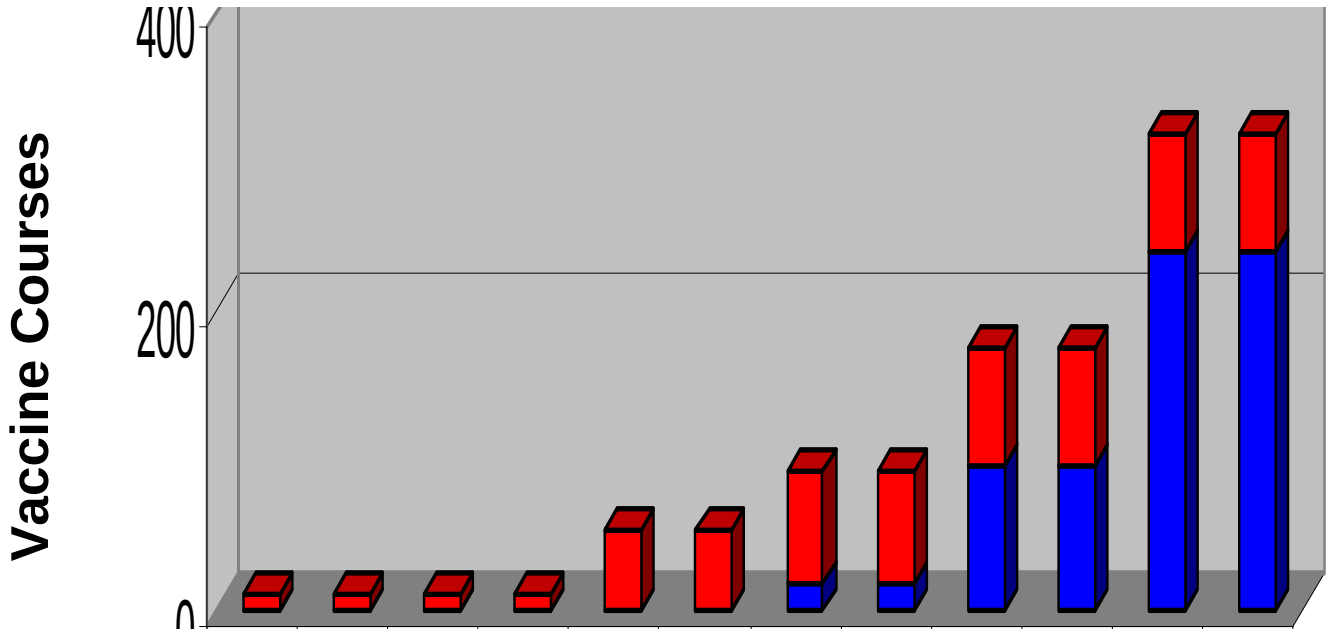
Influenza Vaccine: Surge Capacity



Transforming Technology

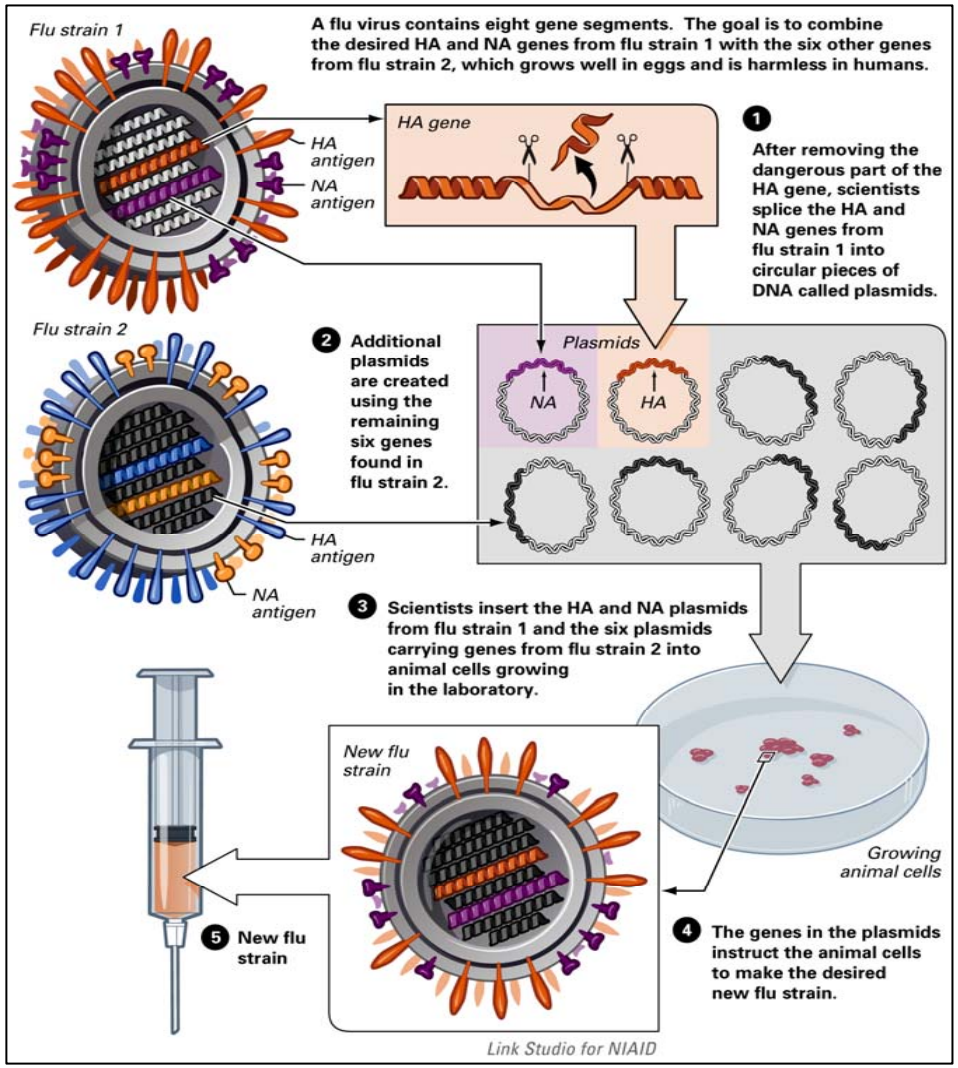
Egg-based production→ Cell-based production

Current and Projected US Pandemic Influenza Vaccine Capacity

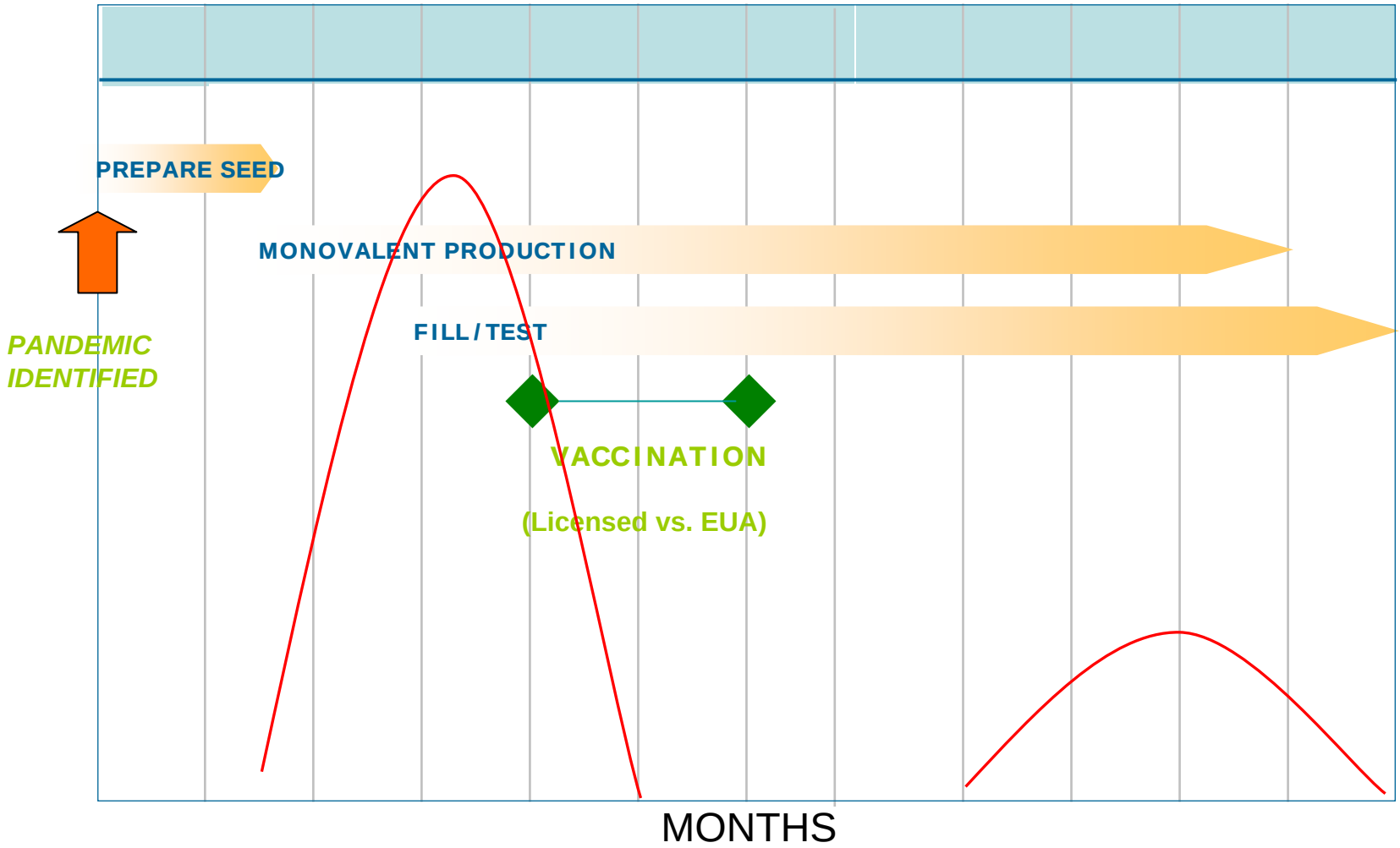


	1H06	2H06	1H07	2H07	1H08	2H08	1H09	2H09	1H10	2H10	1H11	2H11
Egg	8.3	8.3	8.3	8.3	51.6	51.6	77.4	77.4	77.4	77.4	77.4	77.4
Cell	0	0	0	0	0	0	16	16	96	96	240	240

Transforming Technology:
Reverse Genetics



Timing of Pandemic Vaccine Availability



Transforming Technology:
Recombinant Influenza Vaccine

GOAL: Decrease the timeline of vaccine production in response to a newly emerged pandemic influenza strain.

- The timeline for the availability of egg- and cell-based inactivated pandemic influenza vaccines in the U.S. is estimated at 20-23 weeks post-pandemic onset, which may be towards the end of a first pandemic wave.

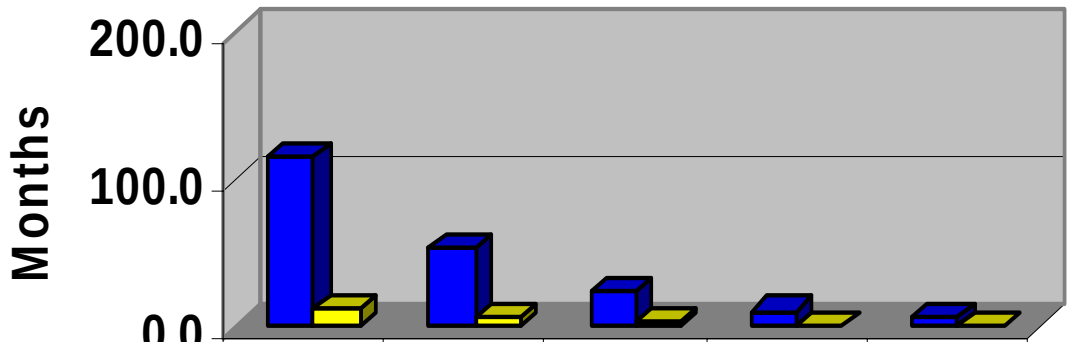
- Recombinant-based influenza vaccines, which may not be dependent on pandemic influenza virus reference strain availability and the production and calibration of potency assay reagents needed for inactivated influenza vaccines, may be available 8 to 12 weeks post-pandemic onset.

HHS Request for Proposal: August 2007

Transforming Technology: Adjuvants

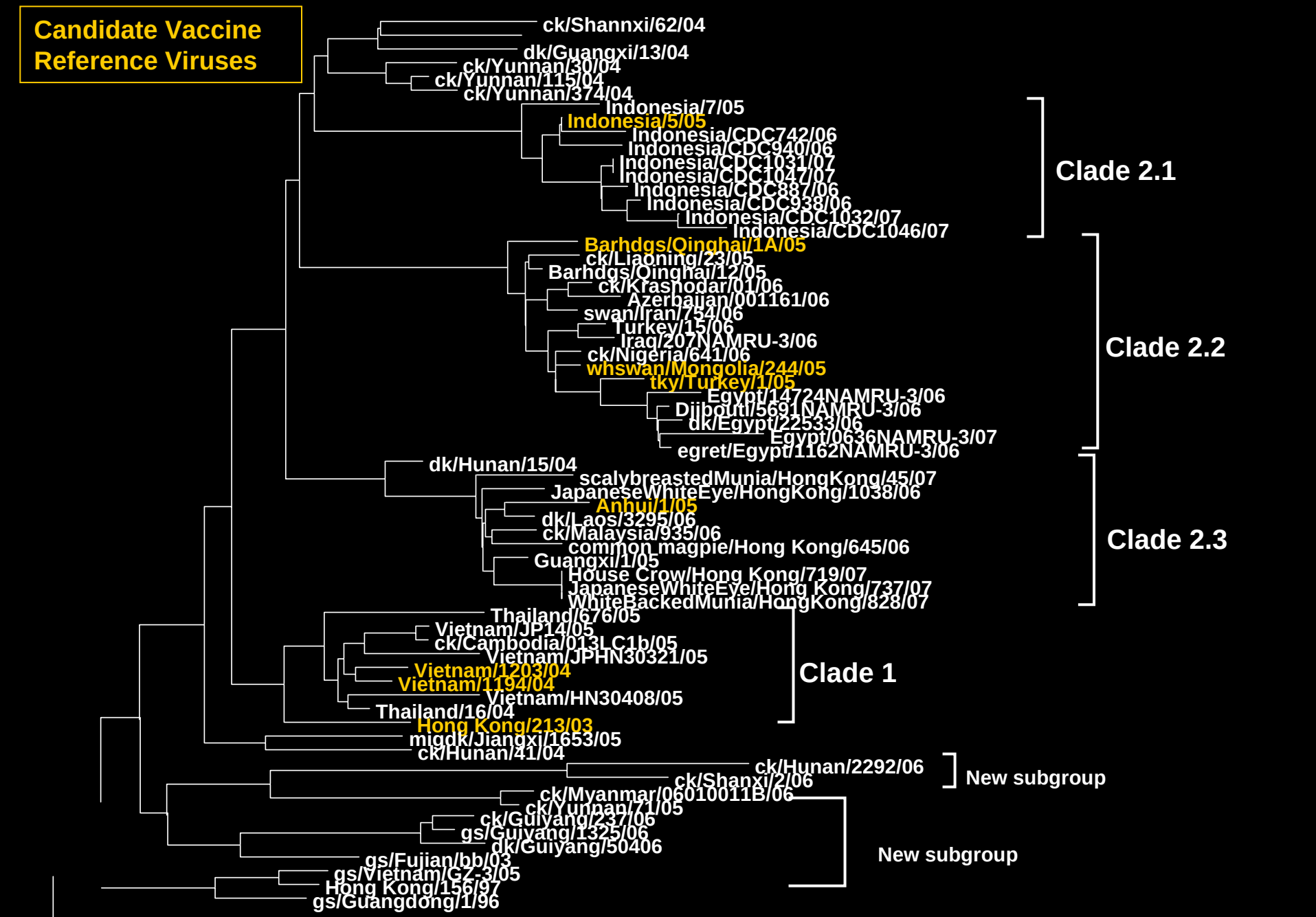
U.S. Pandemic Influenza Vaccine Capacity Forecast

U.S. PANDEMIC VACCINE GOAL TIMELINES
(300 M Vaccine Courses)



	2007	2008	2009	2010	2011
Ag Alone (90 ug)	115.4	52.9	23.7	10.4	5.7
Adjuvants	12.8	5.9	2.6	1.2	0.6

Evolution of the H5N1 Hemagglutinin Gene



HHS Prepandemic Vaccine Stockpile

H5N1 Vaccine Strain	Clade	2004	2005	2006	2007	Totals
A/VTN/1203/04	1	0.45	7.05	0.91		8.41
A/Indo/05/05	2.1			6.44	2.25	8.69
A/BHG/QL/1A/05*	2.2				6.42	6.42
A/Anhui/1/05	2.3				2.51	2.51
Totals (90 ug/dose)		0.45 M	7.05 M	7.35 M	11.18 M	26.03 M
Totals w/adjuvants 7.5 ug/dose		5.4 M	84.6 M	88.2 M	134.2 M	312 M

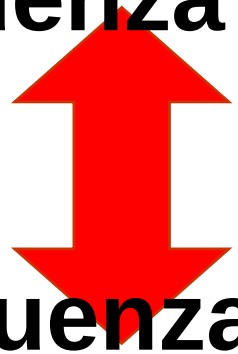
^ doses represented as 90 ug HA/dose antigen alone

HHS Pandemic Vaccine Mix and Match Study

- Strategic Goal: Expand the supply of influenza vaccines available during a pandemic by optimization of antigen content using adjuvants

- Specific Aim: Determine whether stockpiled H5N1 antigens manufactured by one company can be used safety and effectively with adjuvants from other manufacturers during an influenza pandemic under Emergency Use Authorization.

Seasonal Influenza Preparedness



Pandemic Influenza Preparedness

- Enhanced immunogenicity
- Broader Protection
- New delivery platforms
- Different vaccines for different populations
- Shortening vaccine production times
- Improving distribution and vaccine tracking

Decreasing impact of seasonal and pandemic influenza