Session: "Sharing our Recent Experience: Focus on Greatest Risks."

Application of Viral Genetic and Phenotypic Data to Risk Assessment for Pandemic Preparedness

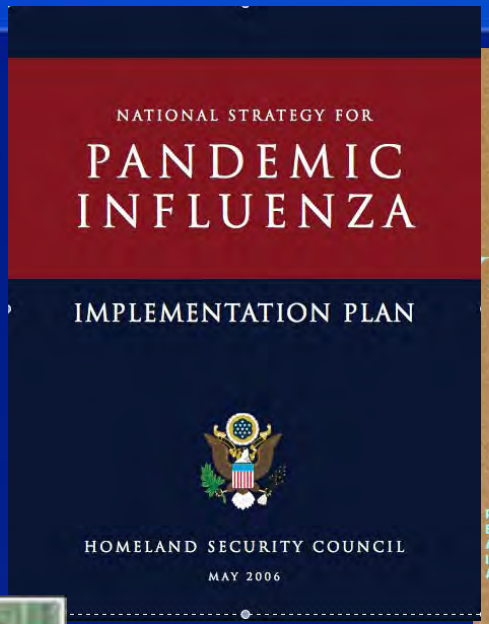
Ruben Donis, Ph.D.

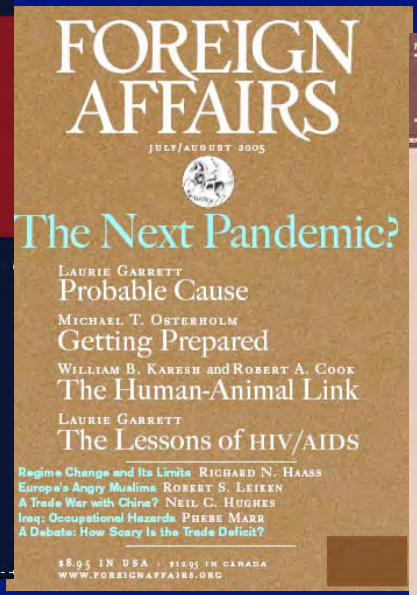
Influenza Division, NCIRD, CDC

"One Flu" Strategic Retreat

Castel Brando in Treviso, Italy, February 1-3, 2011

Pandemic Preparedness Plans: Assumptions



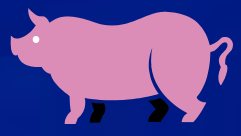


"Those who do not remember *the past* are condemned to repeat it."

George Santayana (1863-1952)

- 1918 H1N1 Pandemic
- 1957 H2N2 Pandemic
- 1968 H3N2 Pandemic
- 1976 Swine flu USA
  -false alarm
- 1977 H1N1 re-entry
- 1997 H5N1 Outbreak




First Detection of 2009 H1N1 in the U.S.

24 April

CDC

MMWR

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Weekly April 24, 2009/ Vol. 58 / No. 15

MWR April 24, 2009

Swine Influenza A (H1N1) Infection in Two Children — Southern California, March–April 2009

On April 21, this report was posted as an MMWR Early Release *on the* MMWR *website* (http://www.cdc.gov/mmwr).

On April 17, 2009, CDC determined that two cases of febrile respiratory illness occurring in children who resided in adjacent counties in southern California were caused by infection with a swine influenza A (H1N1) virus. The viruses from the two

NCBI GenBank

PubMed Entrez BL

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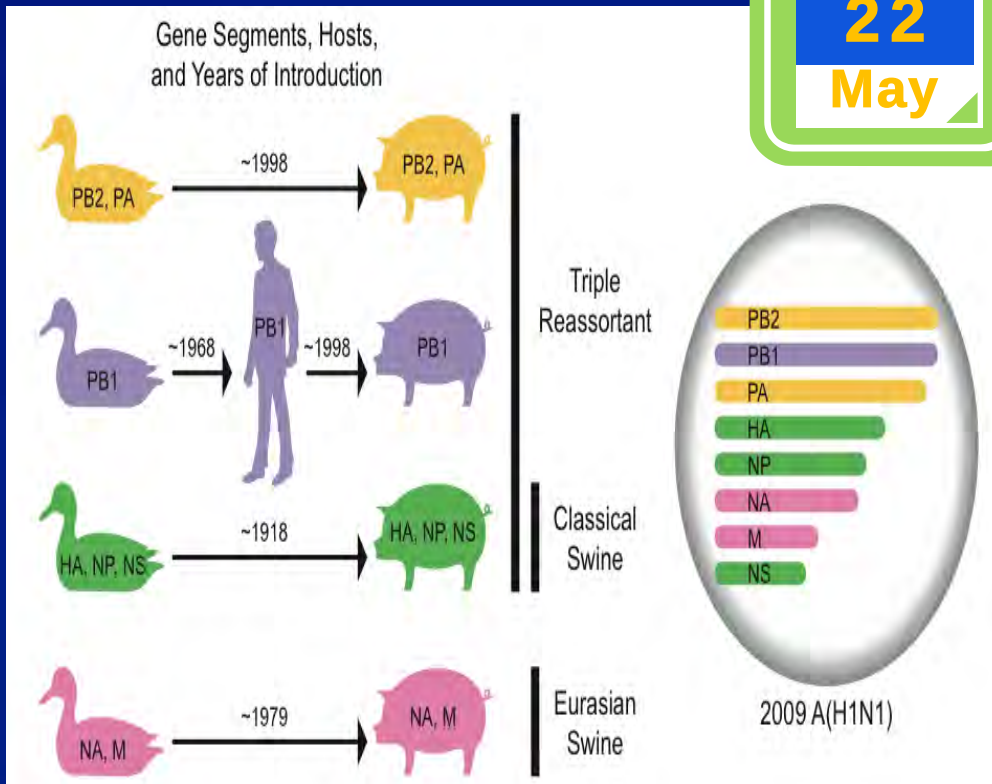
Sciencexpress Report

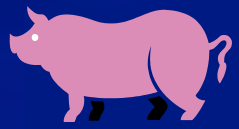
Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans

Rebecca J. Garten*[1], C. Todd Davis*[1], Colin A. Russell[2,3], Bo Shu[1], Stephen Lindstrom[1], Amanda Balish[1], Wendy M. Sessions[1], Xiyan Xu[1], Eugene Skepner[2], Varough Deyde[1], Margaret Okomo-Adhiambo[1], Larisa Gubareva[1], John Barnes[1], Catherine B. Smith[1], Shannon L. Emery[1], Michael J. Hillman[1], Pierre Rivailler[1], James Smagala[1], Miranda de Graaf[2,4], David F. Burke[2], Ron A. M. Fouchier[4], Claudia Pappas[1], Celia M. Alpuche-Aranda[5], Hugo López-Gatell[5], Hiram Olivera[5], Irma López[5], Christopher A. Myers[6], Dennis Faix[6], Patrick J. Blair[6], Cindy Yu[7], Kimberly M. Keene[8], P. David Dotson[9], Sambol[11], Syed H. Abid[12], Kirsten St. George[13], Tammy Bannerman[14], Amanda L. Moore[15], Blevins[17], Gail J. Demmler-Harrison[18], Michele Ginsberg[19], Paula Kriner[20], SteveWaterman[21], Guevara[23], Edward A. Belongia[24], Patricia A. Clark[25], Sara T. Beatrice[26], Ruben Donis[1], Jac[1], B. Bridges[1], Michael Shaw[1], Daniel B. Jernigan[1], Timothy M. Uyeki[1], Derek J. Smith[2,3,4†],

22 May



Other Zoonotic Influenza Infections



- Swine
  - ~ 60 zoonotic H1N1 swine influenza cases reported since 1958
    - Classical swine lineage viruses
    - Eurasian swine lineage viruses
    - "triple reassortant" North American viruses
  - Swine influenza lacked human-to-human transmissibility
- Seals and poultry
  - H7N7 and H7Nx in Europe and North America

Predictions

The Next Influenza Pandemic
Can It Be Predicted?

Jeffery K. Taubenberger, MD, PhD
David M. Morens, MD
Anthony S. Fauci, MD

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(Reprinted) JAMA, May 9, 2007—Vol 297, No. 18

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PLoS PATHOGENS

Opinion

Pandemic Vaccine Preparedness—Have We Left Something Behind?

Ilaria Capua[1]*, Anna Kajaste-Rudnitski[2], Elena Bertoli[1], Elisa Vicenzi[2]

1 Istituto Zooprofilattico Sperimentale delle Venezie, OIE/FAO and National Reference Laboratory for Newcastle Disease and Avian Influenza, OIE Collaborating Centre for Epidemiology, Training and Control of Emerging Avian Diseases, Legnaro, Padova, Italy, **2** Viral Pathogens and Biosafety Unit, Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy

..the assumption that antibodies to human influenza viruses of the H1 and H3 subtypes are cross-reactive towards contemporary avian H1 and H3 viruses of Eurasian lineage is incorrect.

Capua I, et al. 2009. PLoS Pathog 5(6): e1000482.
June 2009 | Volume 5 | Issue 6 | e1000482

Intrasubtype Cross-Protection

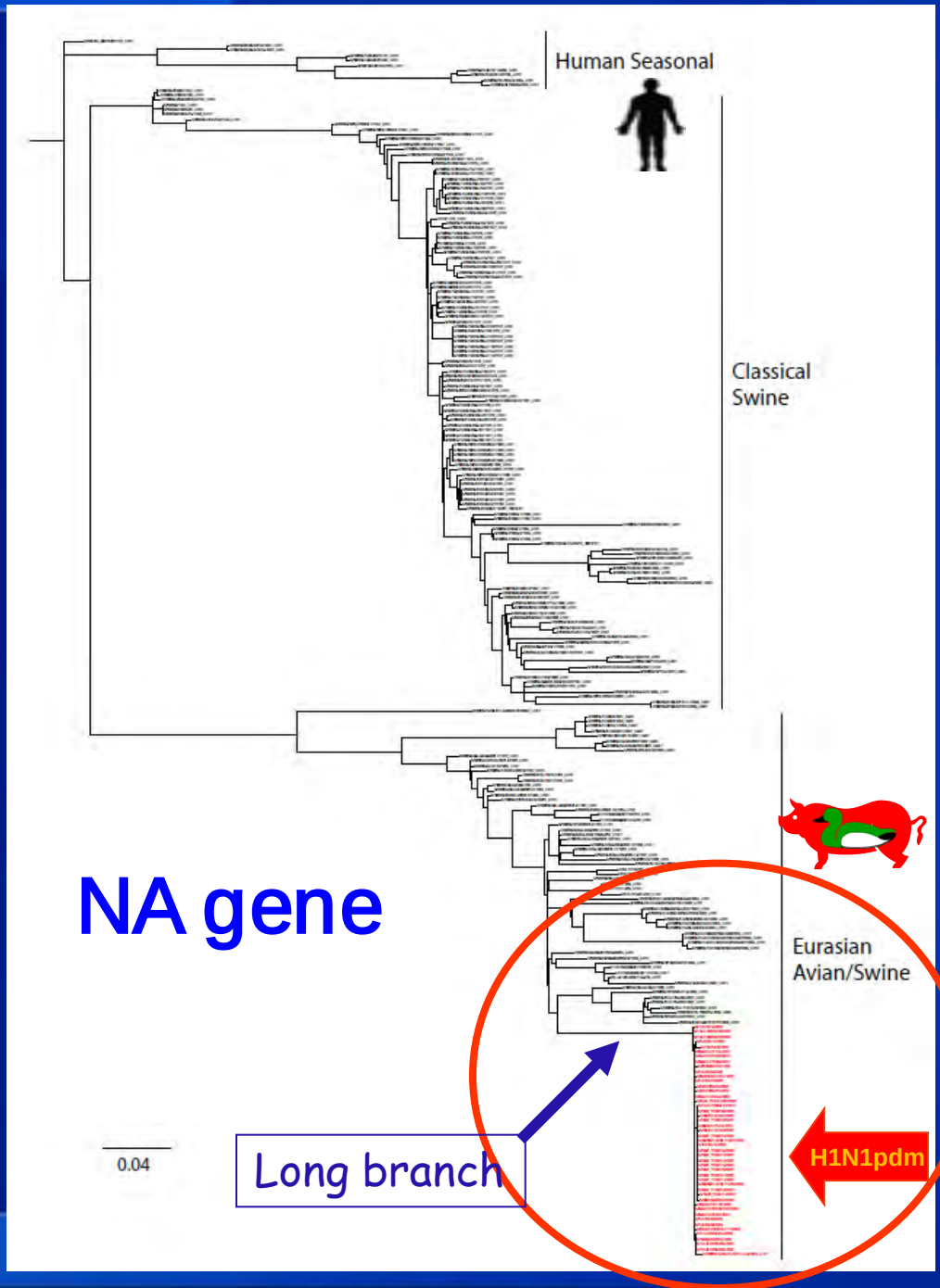
	2009 H1N1	Seasonal H1N1	1935 H1N1	1957 H2N2	Classical Swine H1N1
2009 H1N1	0				
Seasonal H1N1	24	0			
1935 Seasonal H1N1	20	15	0		
H2N2	45	43	41	0	
Classical SwH1N1	1	25	20	46	0

Amino acid divergence between H1 and H2 is 40–46%
Divergence between human and swine H1 is ~25%
Divergence between seasonal human H1 up to 15%

Gaps in Surveillance

Lesson #1

- No recent ancestors known
- ~9-17 years evolving without detection
- Escaped virologic surveillance



Vaccine Preparedness

APRIL | MAY | JUNE | JULY | AUG | SEPT | OCT

Week 2 4 6 8 10 12 14 16 18 20 22 24 26 28

Prepare high growth reassortant

Working seed

Prepare monovalent pilot lot

Production monovalent vaccine

Potency testing

FDA release

Formulate & Fill

Distribution

25 APRIL

26 MAY

5 OCTOBER

World Health Organization

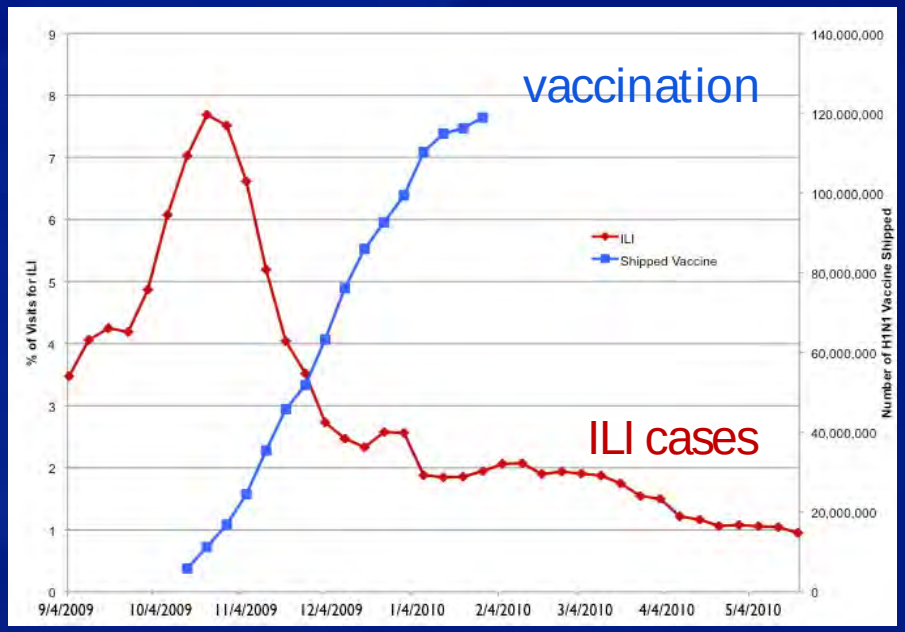
Availability of a candidate reassortant vaccine virus for the novel influenza A (H1N1) vaccine development

27 May 2009

IDCDC-RG15

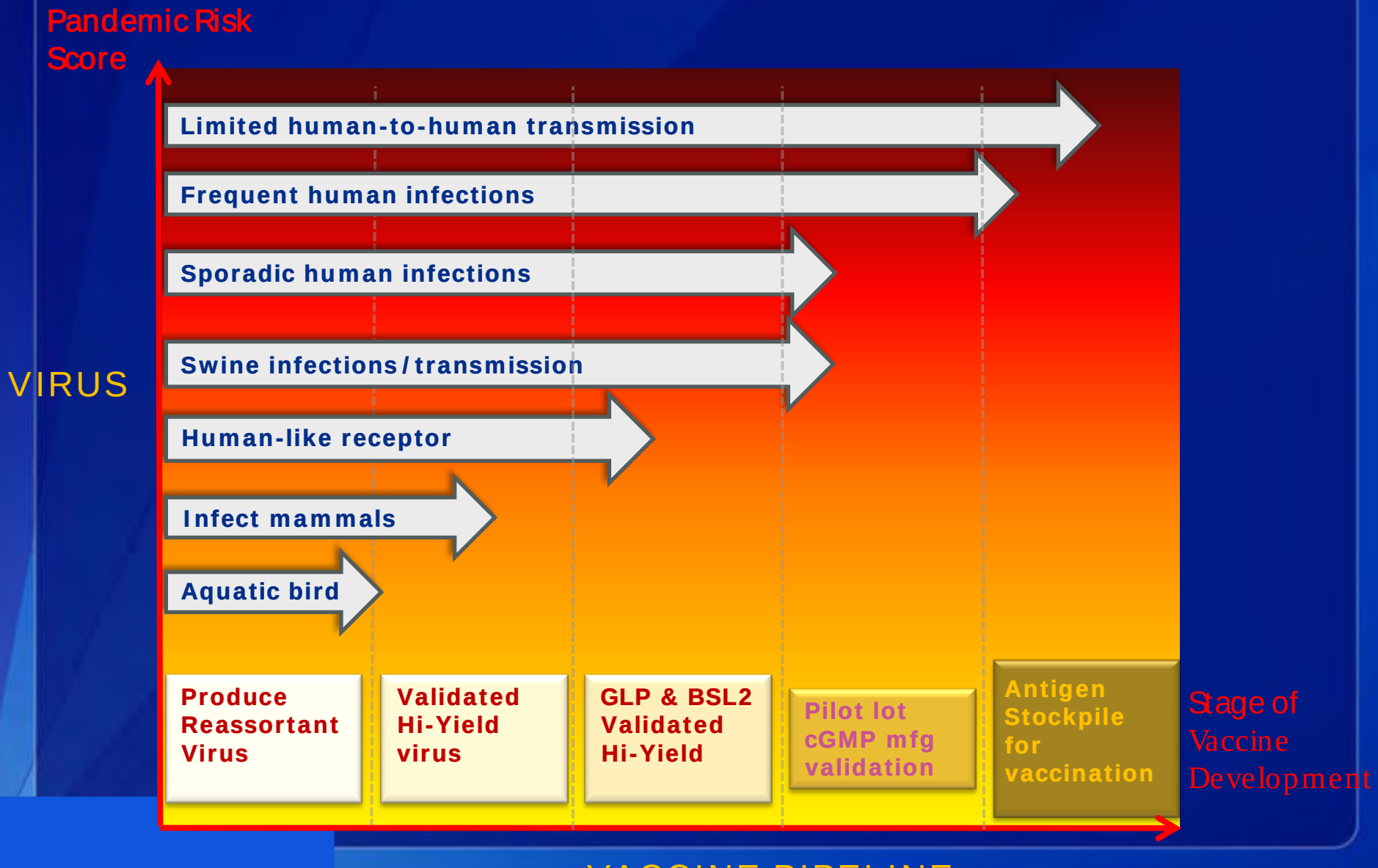
A candidate reassortant vaccine virus (IDCDC-RG15) has been developed, using reverse genetics technology, from an A/Texas/5/2009 (H1N1)v virus, by the WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza in the Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA.

2009 H1N1 Pandemic Vaccine

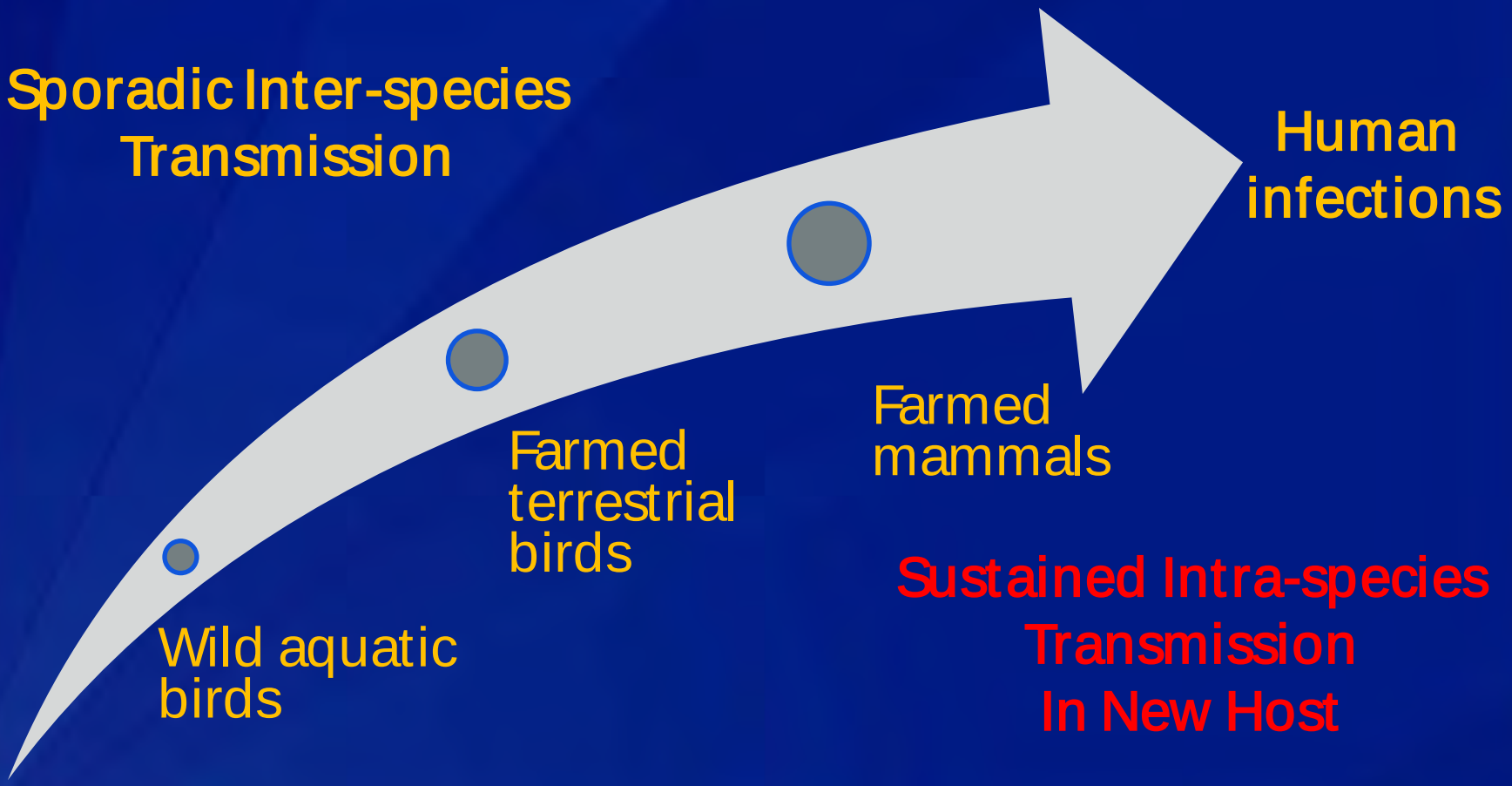


- Pandemic vaccines not available before the second wave of 2009 H1N1
- HHS Influenza Manufacturing Improvement Project

Coupling Vaccine Development to Pandemic Risk

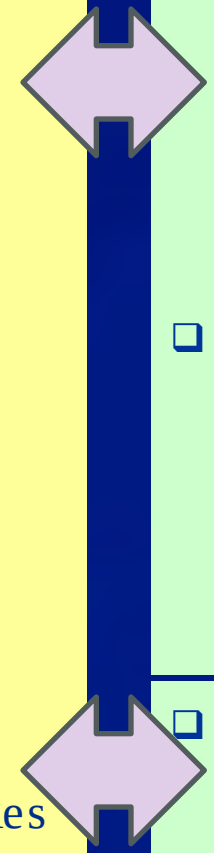


Transmission and Host Adaptation



Assess pandemic potential of viruses

- Virus Properties (organismal)
  - Human infections
    - Severity of human infections
  - Horizontal transmission in other mammals
    - Hierarchy (swine, Carnivores, marine)
    - Natural or experimental
  - Sporadic infection in mammals
  - Terrestrial poultry
  - Exclusively aquatic bird viruses
- Virus Properties (cell/molecular)
  - HA cleavability
  - Human-like receptor binding properties



- Human Host Population
  - Immune status
  - Age structure
  - Social, cultural, economic
- Animal Host Population
  - Immune status
  - Population structure
  - Management

- Environment
  - Animal-human interface
  - Weather
  - Ecosystem

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- Todd Davis
- Pierre Rivailler
- James Stevens
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- Cathy Smith
- John Barnes
- Becky Garten
- Sasha Lipatov
- Michael Shaw
- Joe Bresee
- Jacqueline Katz
- Alexander Klimov
- Ann Moen
- Tim Uyeki
- Dan Jernigan
- Joe Miller
- Nancy Cox
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- MVVB, VSDB, IPB,
- Influenza Division

Beyond CDC

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- Tung Nguyen, NCVD, Vietnam
- Ilaria Capua, Padova, Italy
- Gavin Smith, Singapore
- Malik Peiris, HK SAR
- Wilina Lim, HK SAR
- Ervin Fodor, U Cambridge
- Richard Webby, S Jude CRH
- Daniel Perez, UMD
- Kanta Subbarao, NIH
- Armen Donabedian, BARDA
- Michael Perdue, BARDA

PERSPECTIVE

FOREVER UNPREPARED — THE PREDICTABLE UNPREDICTABILITY OF PATHOGENS

Forever Unprepared — The Predictable Unpredictability of Pathogens

Kent A. Sepkowitz, M.D.