Influenza Pandemic Risk and Preparedness

John S. Tam
Visiting Professor
The Hong Kong Polytechnic University

Director and Chairman
Asia-Pacific Alliance for the Control of Influenza (APACI)

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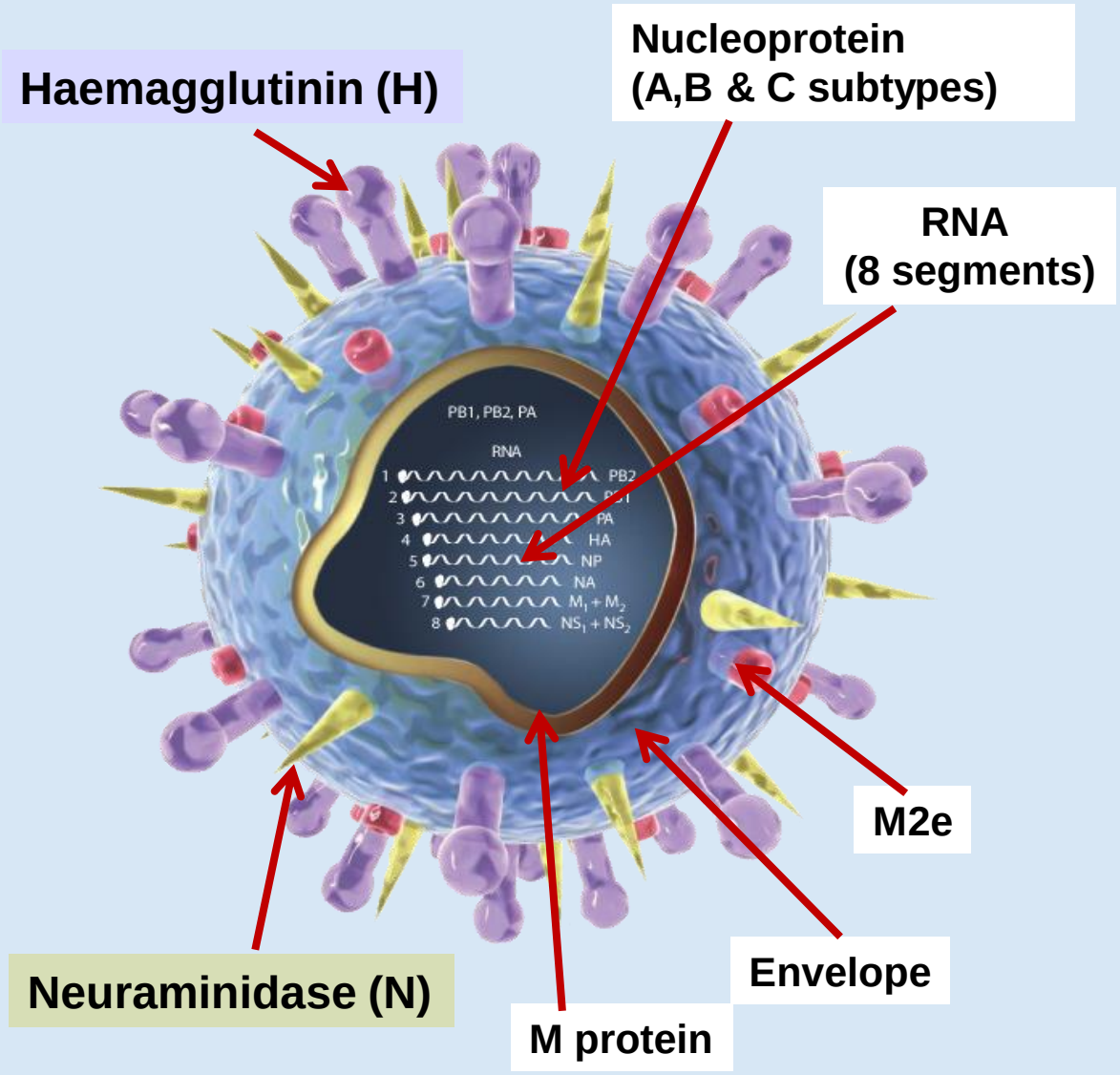
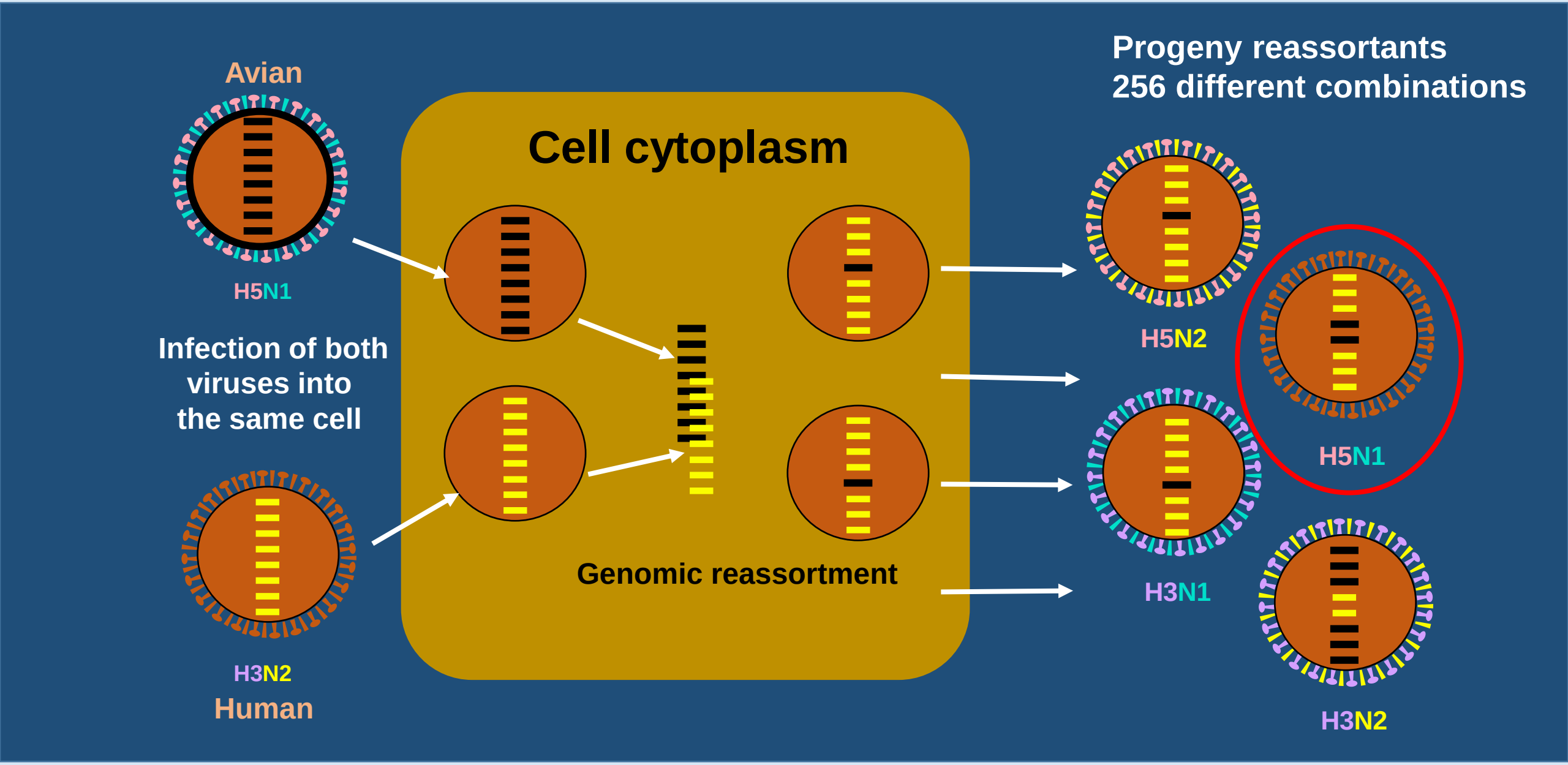
Influenza virus



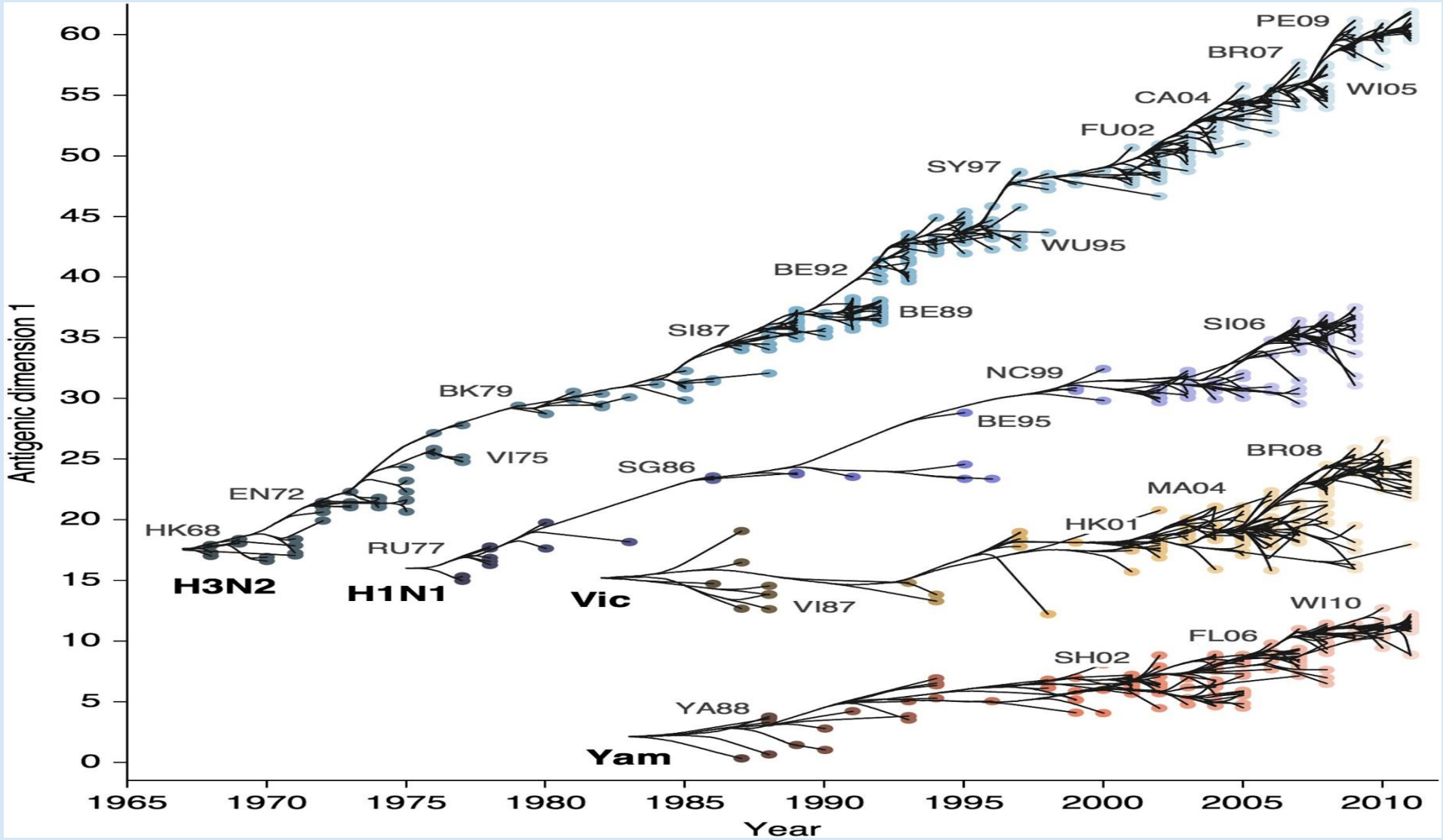
Influenza A	Human	Pig	Horse	Bird	Bat
H types					
H1	✓	✓		✓	
H2	✓	✓		✓	
H3	✓	✓	✓	✓	
H4		✓		✓	
H5	✓	✓		✓	
H6	✓			✓	
H7	✓		✓	✓	
H8				✓	
H9	✓	✓		✓	
H10	✓			✓	
H11-H16				✓	
H17-H18					✓
N types					
N1	✓	✓		✓	
N2	✓	✓		✓	
N3				✓	
N4				✓	
N5				✓	
N6	✓			✓	
N7	✓		✓	✓	
N8	✓		✓	✓	
N9	✓			✓	
N10-N11					✓

Reassortment of Influenza Virus Genes (antigenic shift)



Antigenic drift of A/H3N2, A/H1N1, B/Vic and B/Yam viruses

Antigenic drift is shown in terms of change of location in the first antigenic dimension through time

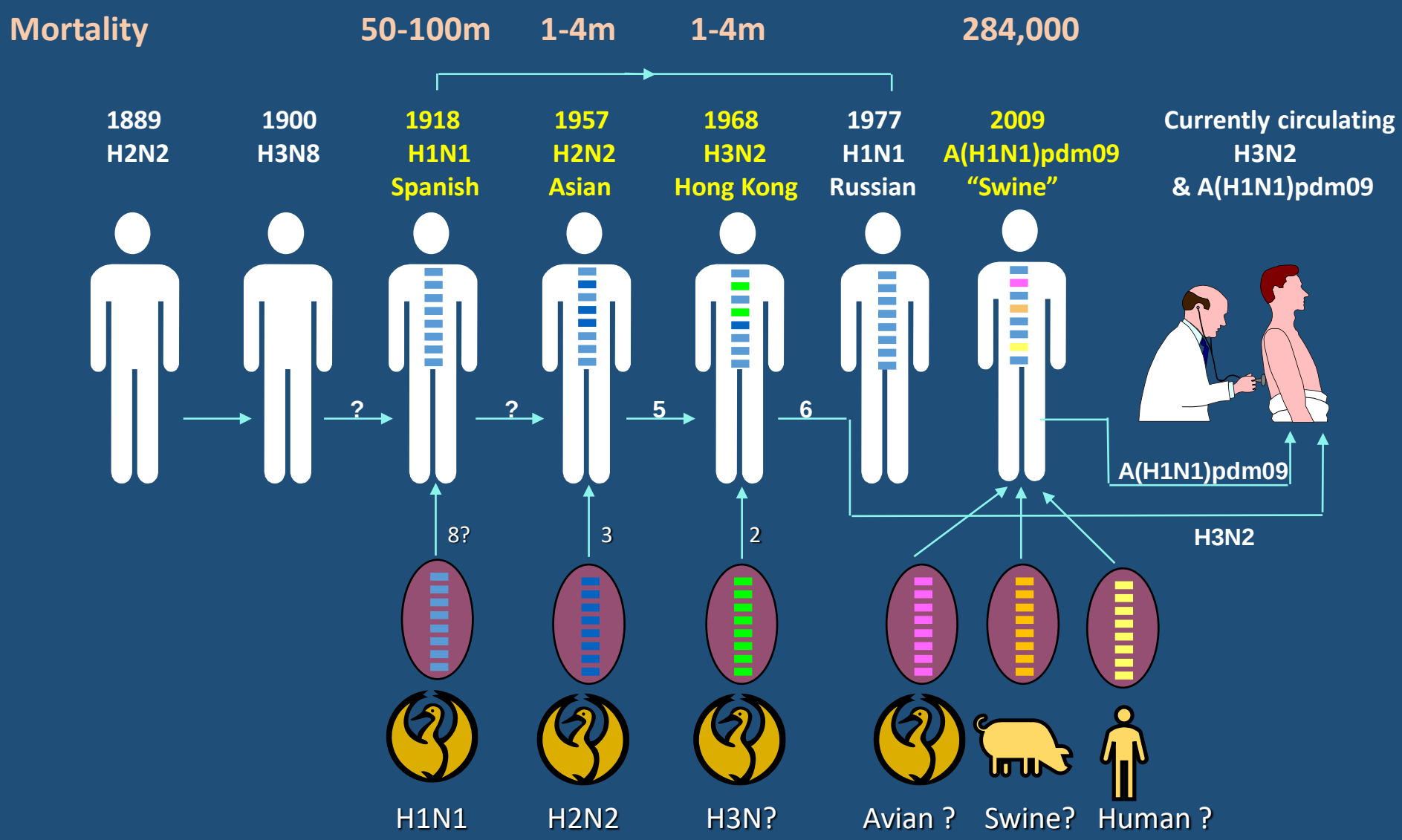


Trevor Bedford et al. eLife Sciences 2014;3:e01914

Consequences of Mutations in Influenza Virus Genes

- Changes in receptor binding characteristics
  - changes viral tropism - avian (α2-3 linkage SA) to human (α2-6 linkage SA)
  - increase risk of non-human subtypes to infect human
  - enhance human-human transmission
- Alteration in pathogenesis
  - aerosol transmission to airborne transmission (H5N1- lab mutation)
  - changes in targeted organs (disease clinical presentations)
- Antigenic changes in neutralizing epitopes on HA protein
  - absence of pre-existing immunity against novel strains
  - escape-mutations leading to vaccine failure
  - reduction of vaccine efficacy
- Antiviral resistance
  - treatment failure in using antiviral drugs

Pandemic Influenza A Virus Strains



Human infections with avian influenza viruses

Avian viruses

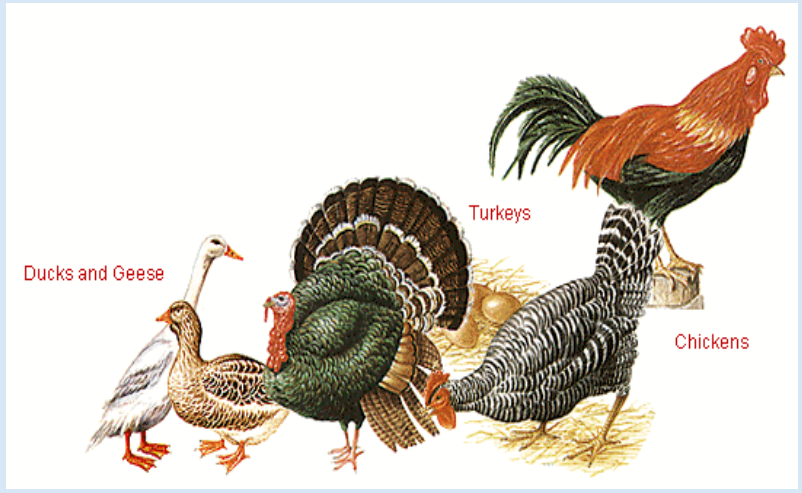
A(H5N1)
A(H7N7)
A(H9N2)
A(H7N2)
A(H10N7)
A(H7N9)
A(H6N1)
A(H10N8)
A(H5N6)

And

….MORE….

Evolution of Novel Influenza Viruses

- cross infection of human & avian influenza in pigs
- leading to reassortment of genes and new strains



Transmission of avian influenza to pigs

New flu virus

Spread by aerosol

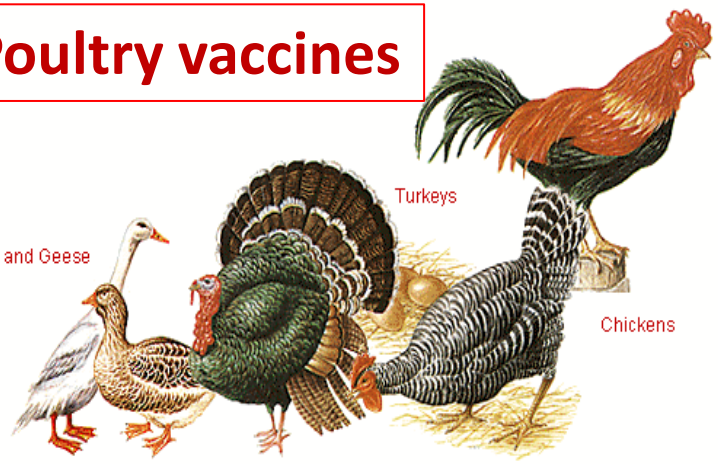
Viral genes reassortment

Transmission of human influenza to pigs

Vaccine Control for Pandemic Influenza

- vaccination of animals – control source
- human vaccination – seasonal and pandemic vaccine to reduce severity and control spread
- **Questions: when? where? who? what? how?**

Poultry vaccines



New flu virus

Pandemic vaccines

Viral genes reassortment

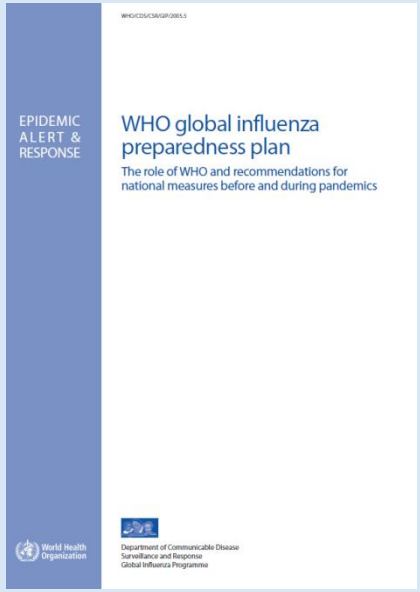
Animal vaccines

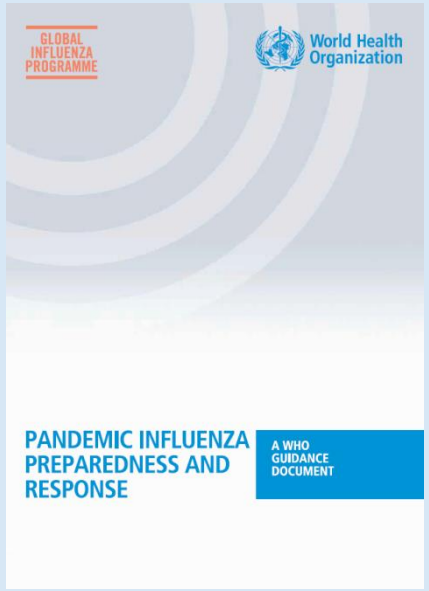
Seasonal vaccines

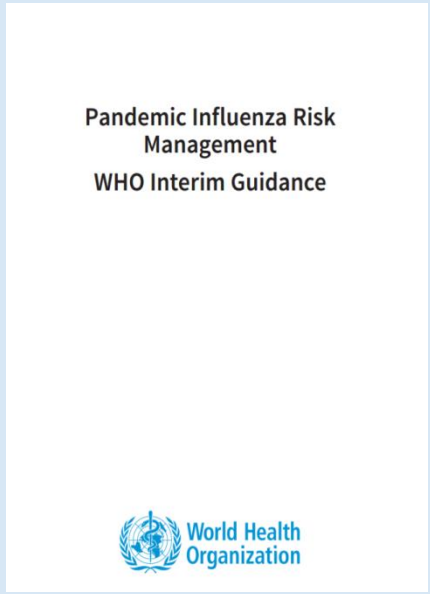
Vaccine Control for Pandemic Influenza – when? where? how?

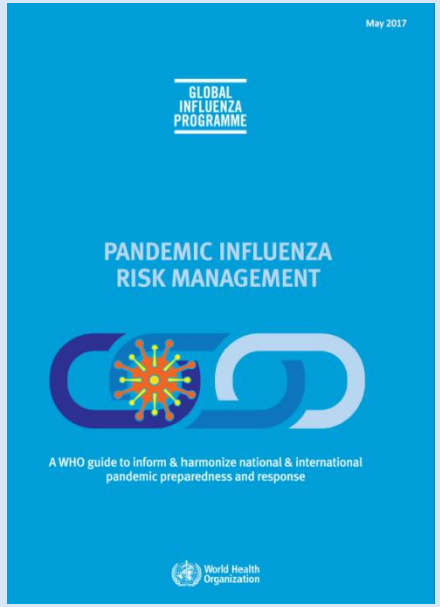
WHO Pandemic Influenza Risk and Impact Management

Evolution of WHO Guidelines
Pandemic Influenza Risk Management (PIRM), 2017





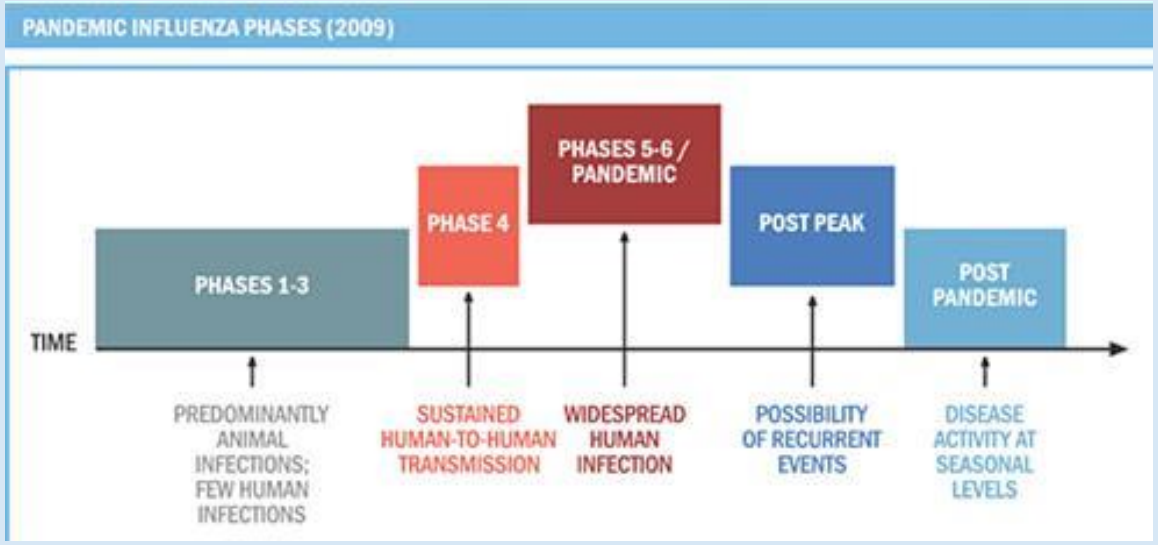




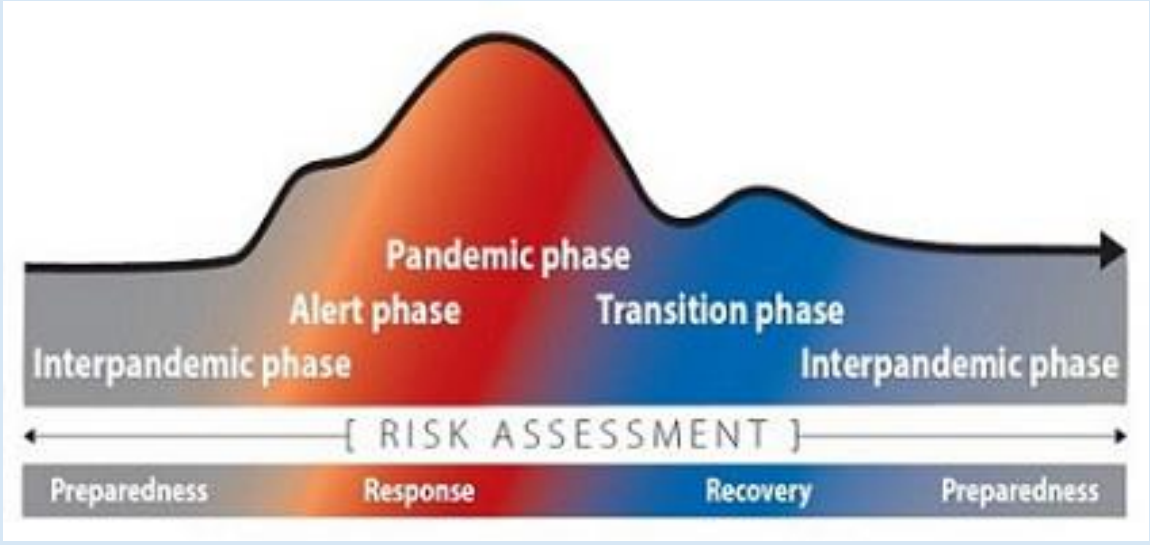
http://www.who.int/influenza/preparedness/pandemic/influenza_risk_management_update2017/en/

Highlights of 2017 WHO PIRM Framework:
the Risk-based and Integrated Approaches

- Promote all-hazards approach to **Emergency Risk Management for Health**
- Strengthen **whole of government** and **whole of society** approach to risk management
- Emphasize **risk-based approaches** with high-level guidance on **risk and severity** assessment
- **Uncouple global phases from national actions**
  - Introducing flexibility in countries for planning and response
- Incorporate **new developments** e.g. PIP Framework

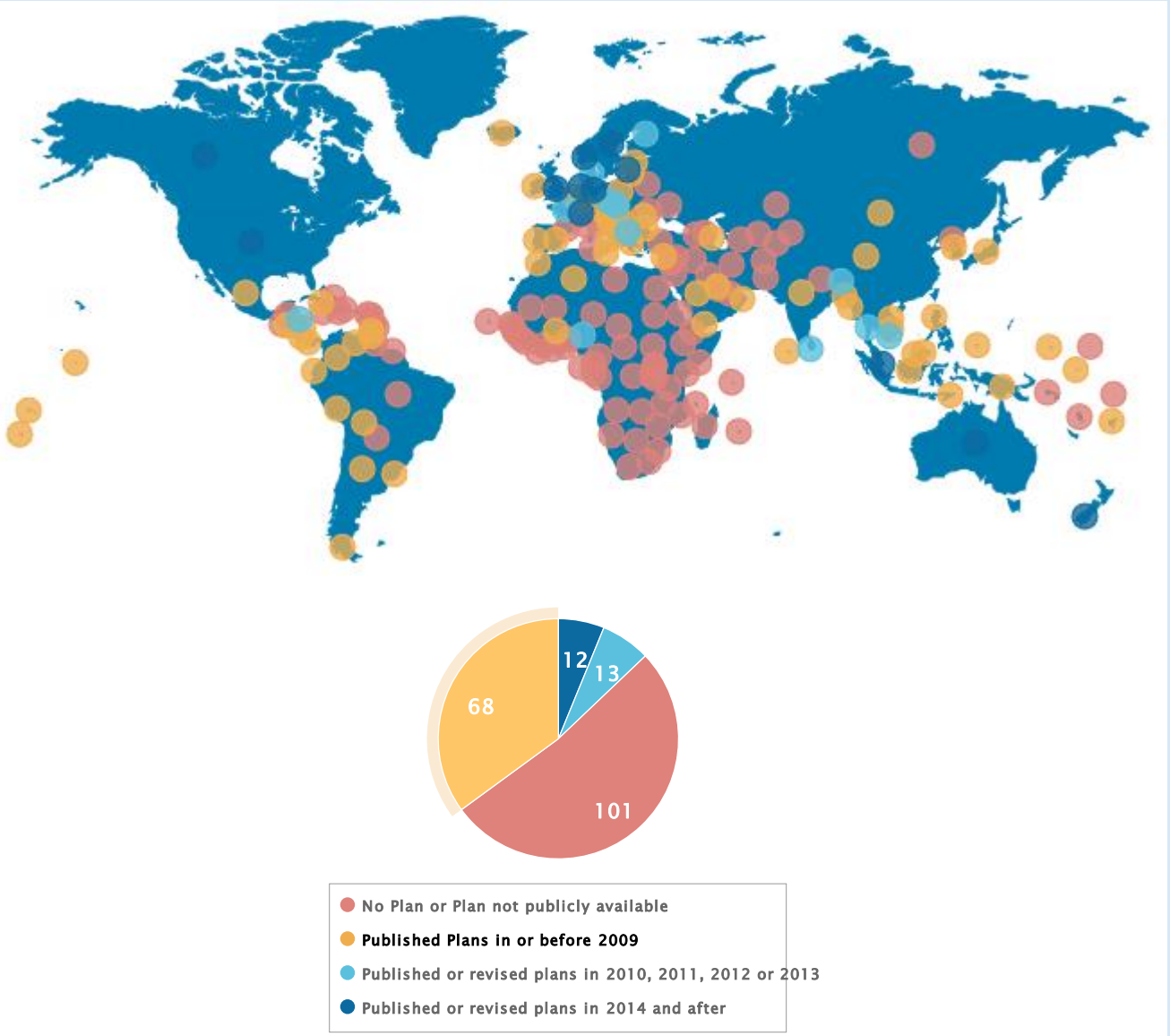


Pandemic Influenza Preparedness and Response 2004



Pandemic Influenza Risk Management 2017

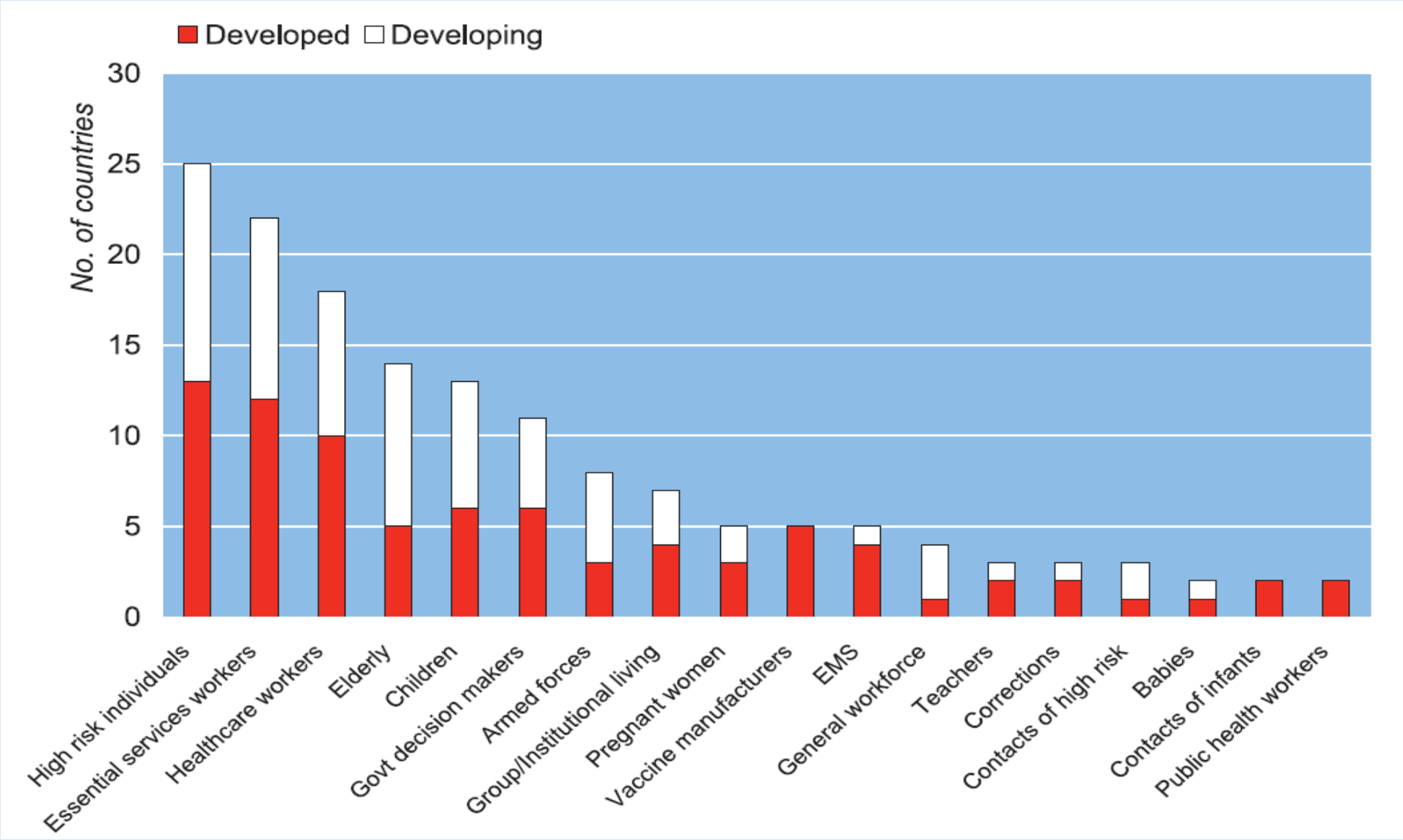
Review of National Pandemic Influenza Preparedness Plans



- 101 of 194 (52%) Member States either have not yet developed a plan or plans are not yet publicly available
- Of the 93 Member States with a publicly available plan:
  - only 25 (27%) updated their plans since 2009 pandemic
  - only 12 (13%) updated their plans since WHO published the new interim guidance on pandemic preparedness in 2013

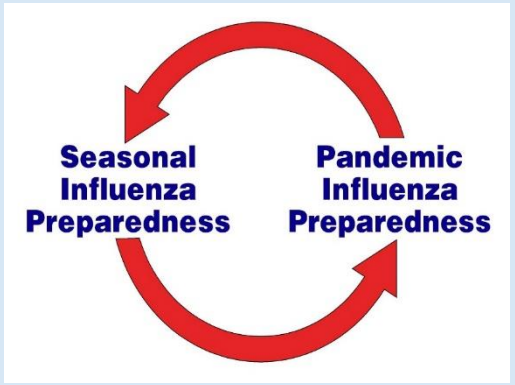
https://extranet.who.int/spp/influenza

Vaccine Control for Pandemic Influenza – who?



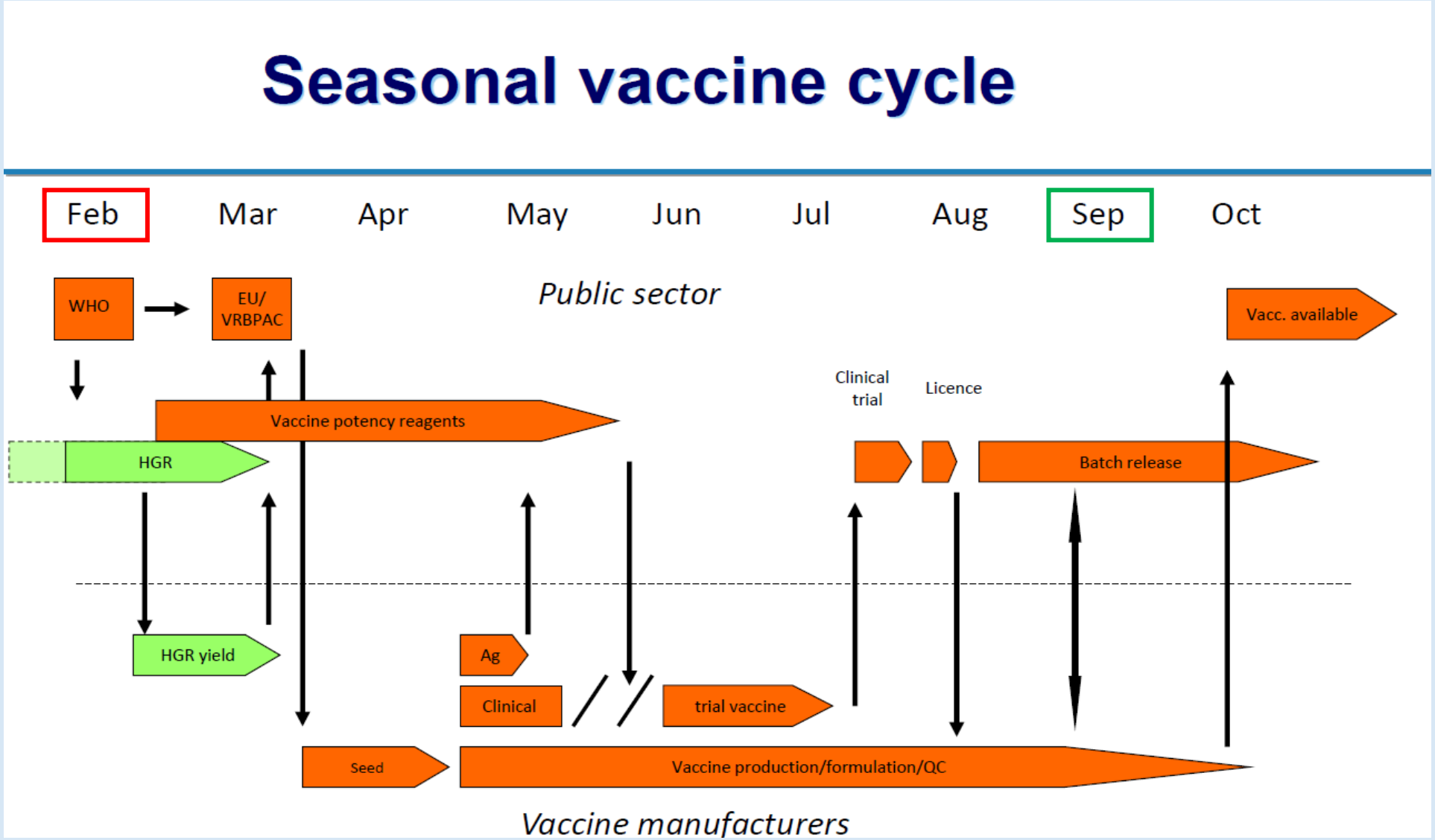
Vaccine Control for Pandemic Influenza – what?

Vaccine and Immunization Research



- Influenza vaccine is unique among other vaccines:
  - Include all ages and recommendations for specific groups
  - Seasonal applications (Northern vs. Southern)
  - Repeated annual vaccination
- Prediction of variant viruses for vaccine production:
  - Requires an extensive global surveillance system
  - Tight manufacturing schedule
  - Unable to match new viruses within the manufacturing cycle
- Vaccine performance
  - Effectiveness varies from year to year and for different groups
  - Vaccine viruses may not correspond to circulation viruses
- Manufacturing capacity unable to match timing and volume required for PANDEMIC control

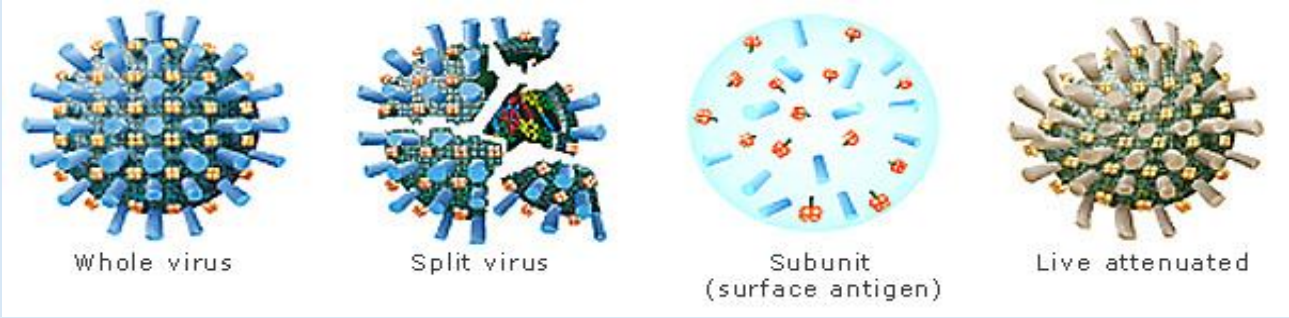
Influenza vaccines production



http://asvac2015.com/wp-content/uploads/2015/06/4.-PS03_Zhang_GISRS_VVS_20150611.pdf

Technology for Influenza Vaccine Production

- Egg-derived inactivated split
- Egg-derived inactivated whole virion
- Cell-culture derived inactivated virus (split or whole)
- Egg-derived Live Attenuated Influenza Vaccine (LAIV)
- Adjuvanted inactivated split
  - MF59, ASO-3 etc.
- Recombinant antigen production (VLP etc.)
  - Baculovirus, plant-based production, *E. coli*, cell culture,..



Overall Challenges for Universal Vaccine Development

- Safety
- New carriers, vectors, fusion proteins, substrates, adjuvants
- Scalability
- Formulation and potency determination
  - Standardizing and stabilizing the protein
  - Each new substrate may require new, specialized release assays
- Complicated/uncertain regulatory pathways
- Funding

New vaccine development is a time-consuming and expensive process

Thank you.
Questions? Comments?