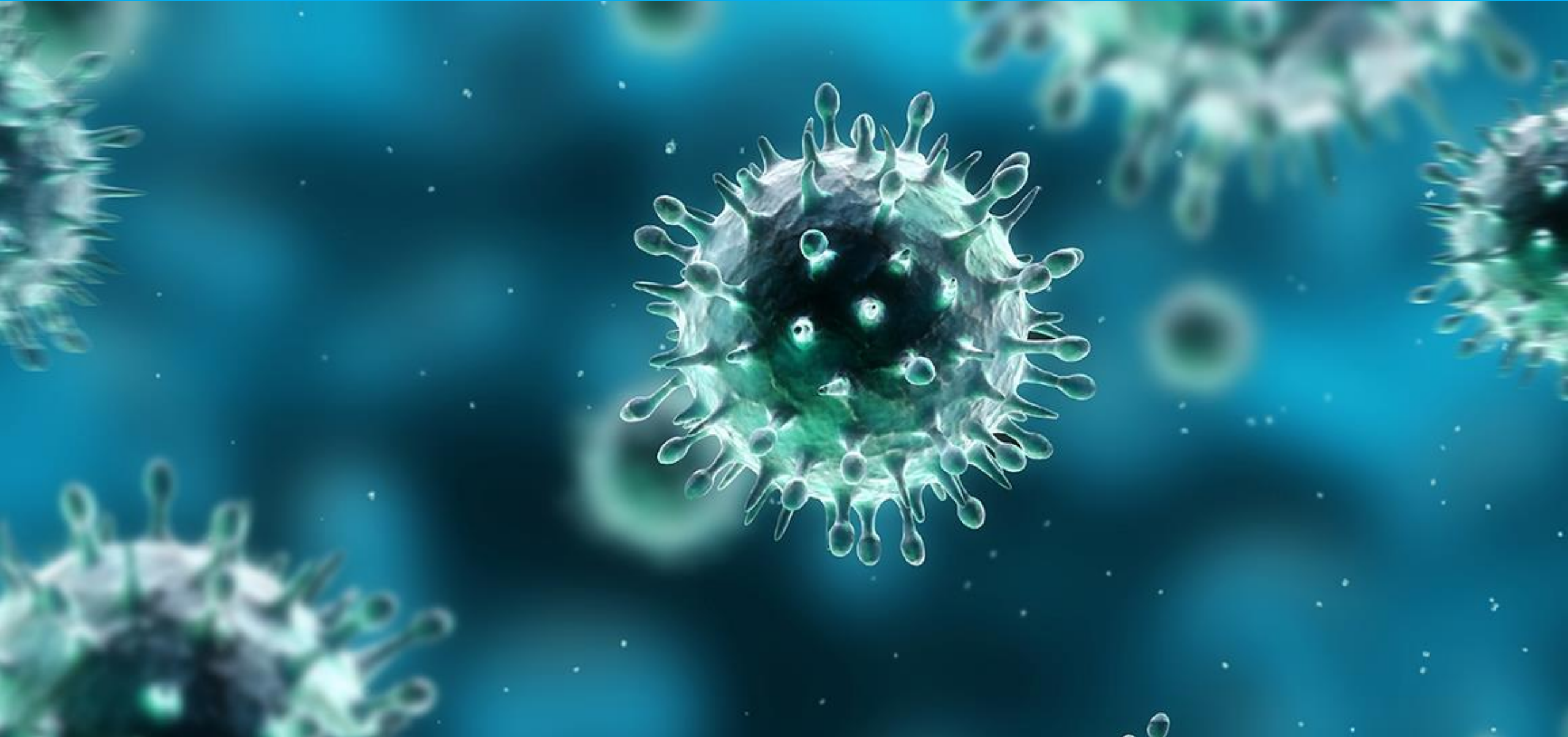
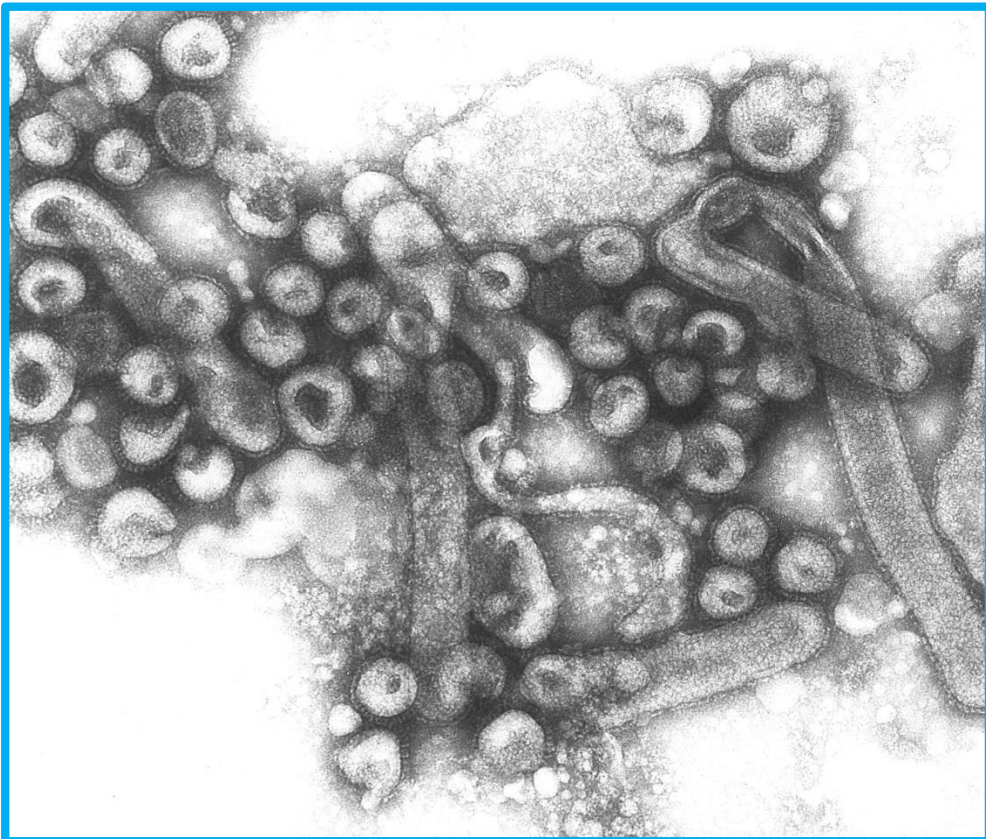


Pandemic Influenza and Vaccine Preparedness





- Emergence of novel influenza virus
 - No immunity in humans
 - Efficient human-to-human transmission
- Pandemic H1N1 2009
- Threat persisting: repeated zoonotic transmission to humans
 - Avian viruses: H5, H7, H9
 - Variant viruses
 - Since 2014: H1N1v, H3N2v, H5N1, H5N6, H7N2, H7N9, H9N2 and H10N8 ...



Courtesy of Drs. K.Gopal Murti and Robert Webster
St Jude Children's Research Hospital of Memphis , Tennessee, USA.

- Constantly evolving
 - Multiple species
 - Multiple directions
- Rapid spreading
 - without administrative boundaries



- Surveillance & control measures:
 - Timely
 - Continuous
 - Global

- 1918: “Spanish-flu”



- 3 April 1947 – 3rd Session of Interim Commission
 - Representative from the Netherlands, Dr. C. van den Beek, proposed the establishment of a **World Commission on Influenza**

- Surveillance → preparedness → response: GLOBAL INFLUENZA PROGRAMME

- Milestones:

- 8 July 1948** – WHO Approves the establishment of the **World Influenza Center**

- 15 June 1949** – 2nd WHA **World Influenza Center** development of experimental vaccine

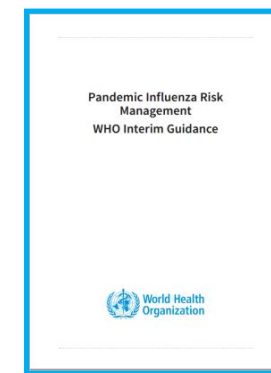
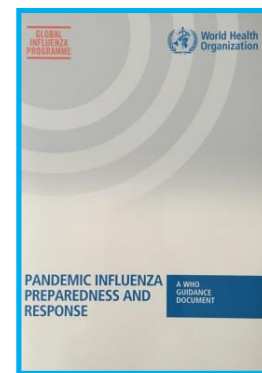
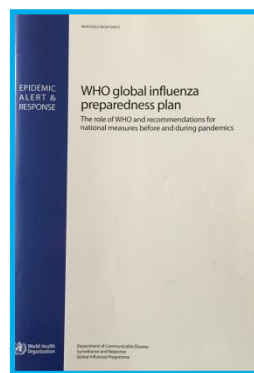
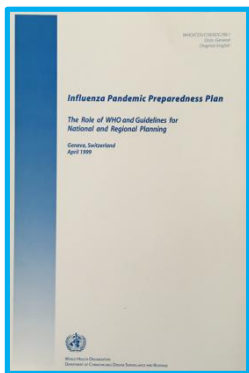
- 21 February 1950** – WHO Executive Board Resolution **EB3.R3**

- Need for information on Influenza available to WHO in Geneva for dissemination

- Sept 1952** – Birth of Global Influenza Surveillance Network (**GISN**)

- Renamed in 2011 → Global Influenza Surveillance and Response System (**GISRS**)





1969

WHA adoption of IHR

1997 1999

H5N1 outbreak in Hong Kong

2002/03

- SARS-CoV outbreak
- Re-emergence of H5N1

2005

WHA adoption of IHR2005



2009

Pandemic H1N1 2009

2011

WHA resolutions:

- Adoption of IHR Review on response to H1N1 2009 pandemic
- Adoption of Pandemic Influenza Preparedness (PIP) Framework

2013



- Rapid containment ✖
- Stockpile H5N1 vaccines
 - Real-time access under SMTA2/PIP Framework
- One-cut response binding to global “Phases” ✖
 - Flexibility
 - Response based on risk assessment
 - Global response critical in certain areas e.g. vaccines
- Post-Ebola: emergency response

Influenza Pandemic Planning

Vaccine

↓ *the*

primary intervention

to reduce influenza mortality and morbidity

■ Seasonal influenza

- **1973** – 1st formal recommendation issued
- **17-18 Feb 1986** – 1st documented WHO annual consultation
- **1998** – start biannual WHO recommendations for northern and southern hemispheres
- **2012** – fourth component formally in WHO recommendation for quadrivalent vaccines.
- **2016** – cell-propagated CVV(Candidate Vaccine Viruses) recommended
- **2016** – *guidance on vaccine formulation recommendation for tropics and subtropics*

■ Pandemic influenza - 2009 H1N1

■ Zoonotic influenza

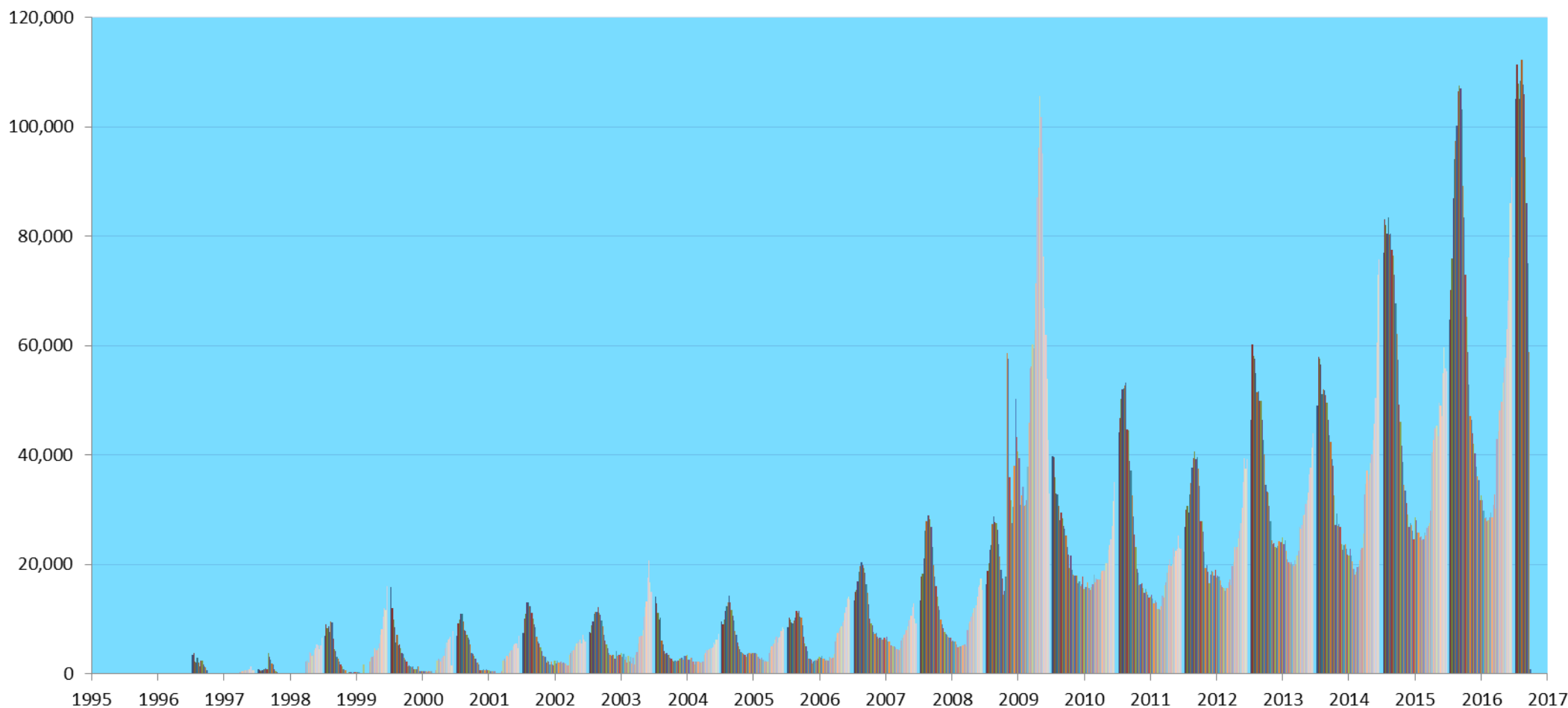
- H5(H1,N6), H7(N7,N9), H9N2, variant viruses

- > 20000000 specimens tested in GISRS per year since 2015

- > 20

- ~ 10

Number of specimens processed by GISRS as reported to FLUNET



INFORMATION
CONSULTATION
OF INFLUENZA
(FOR 2016)
September

WORLD HEALTH ORGANIZATION
CENTRE FOR
DISEASE PREVENTION
AND CONTROL

Research on Influenza,
London

Global consultation
vaccine for the
2016

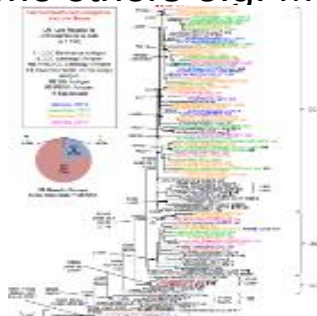
2015

Data → vaccine virus decision

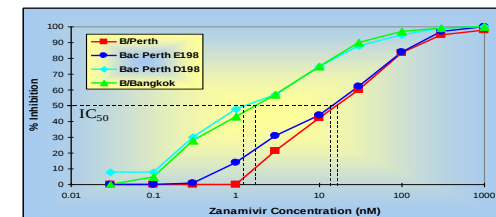
Comparative titres by haemagglutination inhibition assays



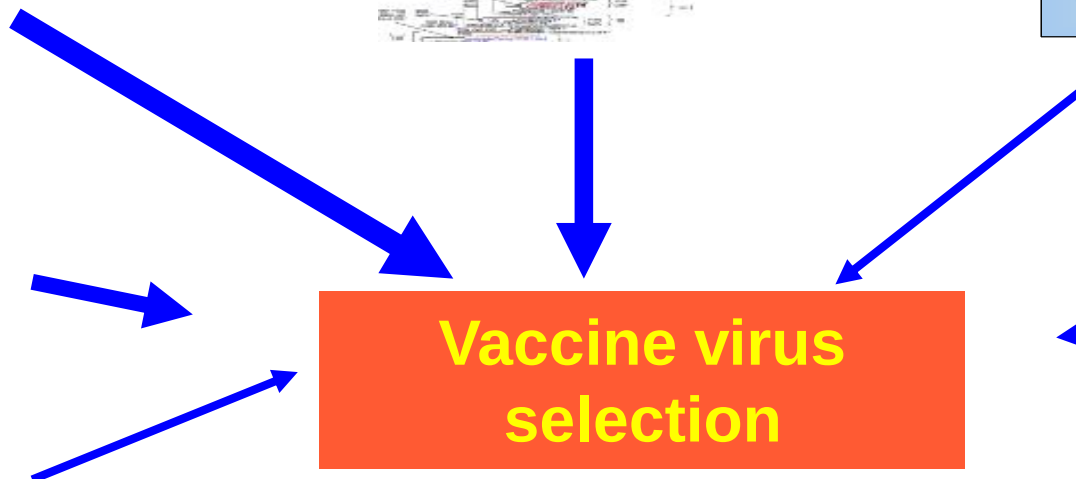
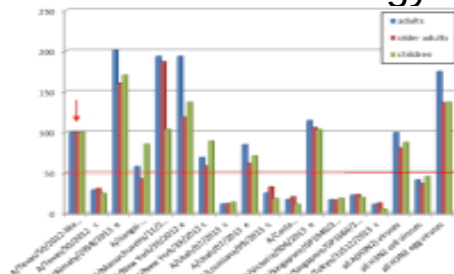
Sequence data
- mainly HA & NA
- Some others e.g. M



Antiviral drug resistance
- Oseltamivir
- Zanamivir
- Other compounds



Human vaccine serology



Other information



Growth in eggs & cells

Other data:

- Epi data, Plaque reduction, Virus neuts, Structural data, VE, virus clade predictive modelling

Revised from Ian Barr slide

Northern hemisphere

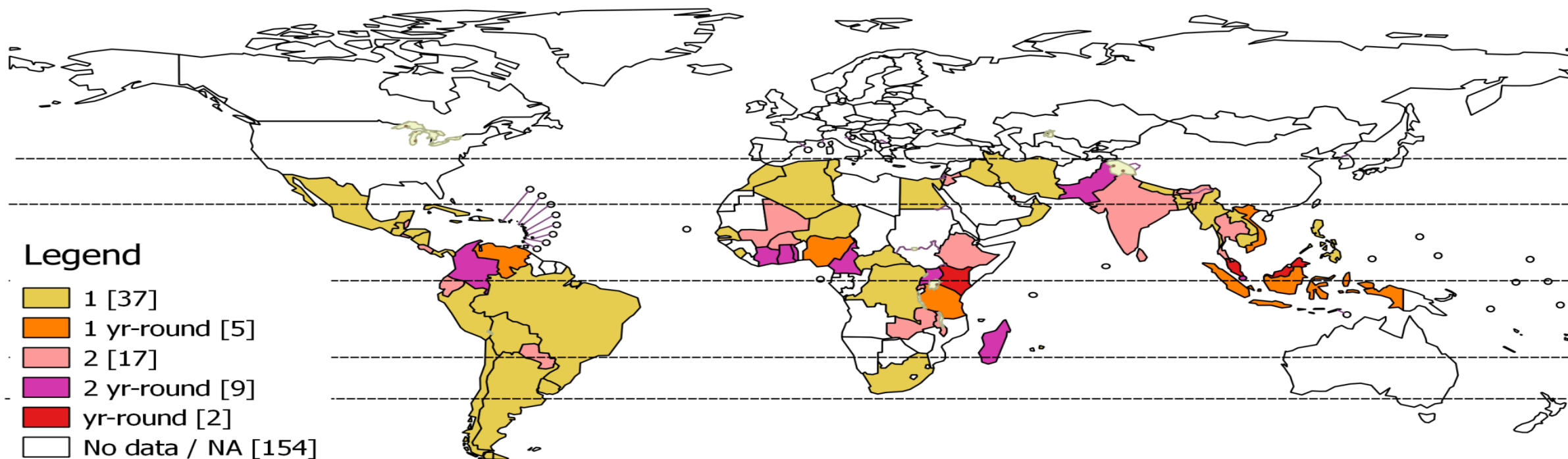
vs.

Southern hemisphere



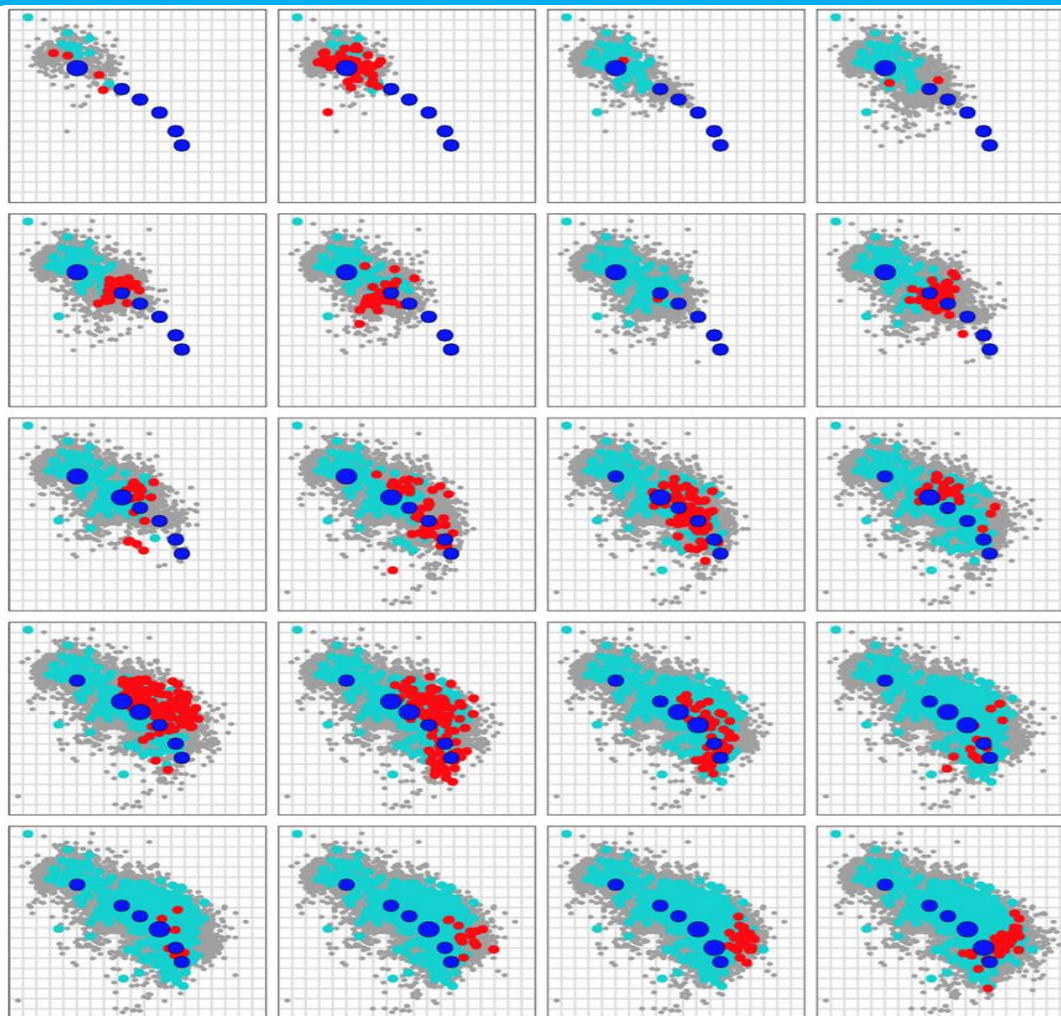
Which formulation
to use in **tropics and subtropics**

Influenza peaks



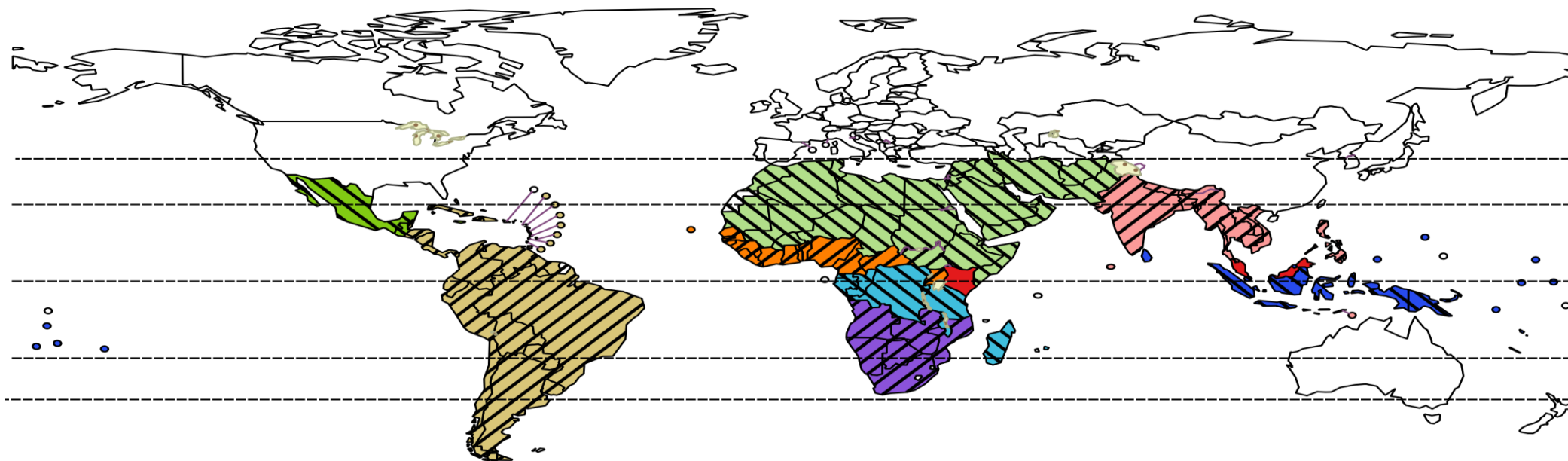
*Summary of seasonality analysis by
CDC, NIVEL, PATH, WHO and published literature*

Antigenic evolution of viruses from tropics



Time series showing the antigenic evolution of human seasonal A/H3N2 viruses isolated from Thailand and from the rest of the world. Red dots indicate viruses isolated in Thailand in particular 3-month period, in subsequent figures red dots become light blue to indicate the antigenic history of the red dots. Grey dots indicate viruses isolated elsewhere in the world and also remain in subsequent figures to show the antigenic history of the grey dots. Time series runs from Q2 2002 to Q4 2006. Blue dots indicate vaccine viruses, which from top to bottom are A/Moscow/10/1999, A/Fujian/411/2002, A/Wellington/1/2004, A/California/7/2004, A/Wisconsin/67/2005, and A/Brisbane/10/2007

Courtesy: Derek Smith

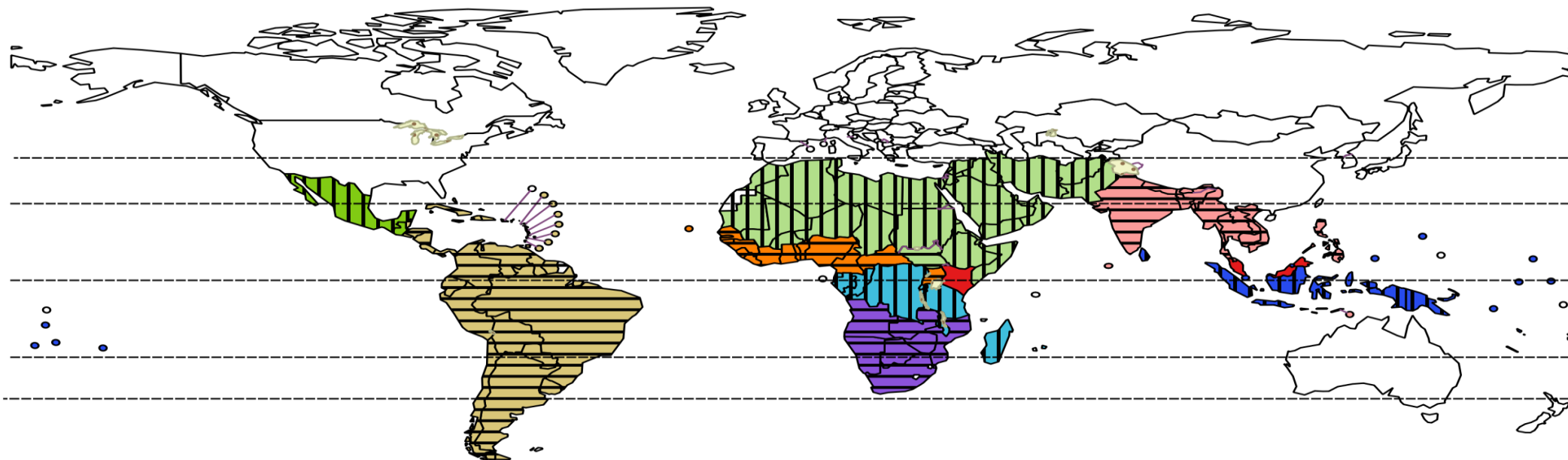


Influenza Vaccination Zones

 North America	 Western Africa	 Tropical Asia
 South America	 Equatorial Africa	 Equatorial Asia
 North Africa & Middle East	 Southern Africa	 Year-round

Vaccine Formulation

 SH
 NH



Influenza Vaccination Zones

 North America	 Western Africa	 Tropical Asia
 South America	 Equatorial Africa	 Equatorial Asia
 North Africa & Middle East	 Southern Africa	 Year-round

Vaccination timing

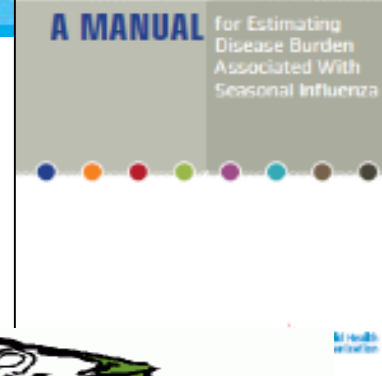
	April
	October

<http://www.who.int/influenza/vaccines/tropics/en/>

Burden of influenza disease

- Provide guidance on how to measure influenza disease burden and associated economic burden
- Use estimates derived from the WHO developed methods as standard and triangulate with estimates derived from other methods
- Map existing knowledge
 - Literature reviews
 - Unpublished data working with networks
 - Hold consultations to identify gaps
- Engage international expertise

- Manual for Estimating Disease Burden Associated With Seasonal Influenza¹
- WHO Manual for estimating the economic burden of seasonal influenza²



1. Available here: http://www.who.int/influenza/resources/publications/manual_burden_of_disease/en/

2. Available here: <http://apps.who.int/iris/bitstream/10665/250085/1/WHO-IVB-16.04-eng.pdf?ua=1>

- Existing knowledge: annual attack rate estimated at 5%–10% in adults and 20%–30% in children. Worldwide, annual epidemics estimated to result in 3 to 5 million cases of severe illness, and 250 000 to 500 000 deaths.¹
- Global **respiratory** mortality studies
 - GBD 2015 Lower respiratory infections death due to influenza
83 100 (55 700-122 100)²
 - **Estimates of respiratory** death per year (As of Feb 2016)

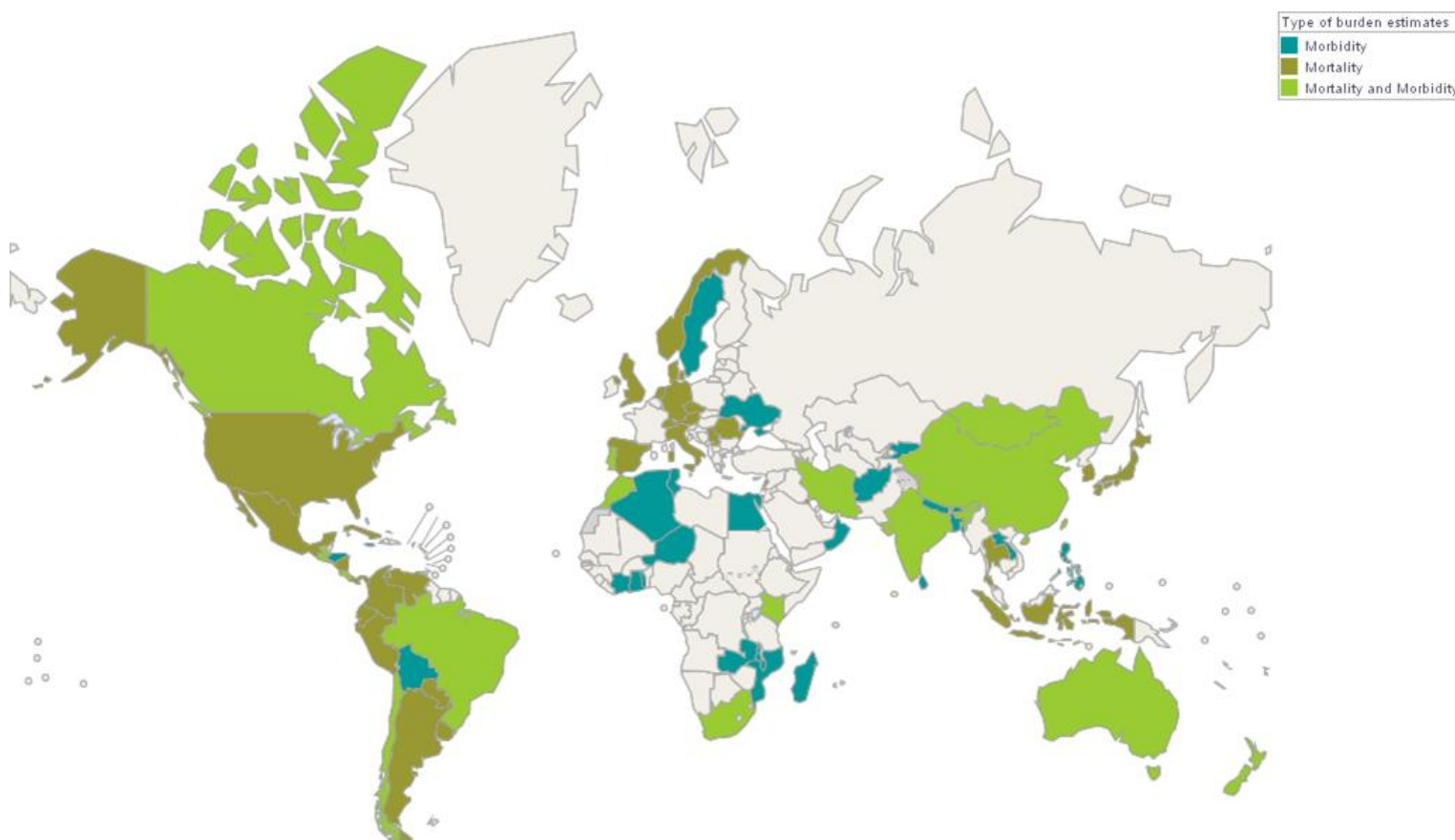
CDC Global	269 731 – 617 897 (or 3.8 – 8.7/100 000)
GLAMORII	226 000 – 427 000 (or 3.1 – 5.8/100 000)
- Influenza is associated with 10% of **respiratory** hospitalizations in children³

1. WHO fact sheet seasonal influenza March 2014 <http://www.who.int/mediacentre/factsheets/fs211/en/>

2. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015 Wang, Haidong et al. The Lancet , Volume 388 , Issue 10053 , 1459 - 1544

3. Lafond KE, Nair H, Rasooly MH, Valente F, Booy R, Rahman M, et al. (2016) Global Role and Burden of Influenza in Pediatric Respiratory Hospitalizations, 1982–2012: A Systematic Analysis. PLoS Med 13(3): e1001977. doi: 10.1371/journal.pmed.1001977pmid:27011229

- Reaching out to countries with influenza associated hospitalization estimates
→ seeking agreement to participate
- Using expert panel to advise on extrapolation model



■ ***By the end of 2017***

- A global influenza-associated respiratory hospitalization and mortality estimate
- Representative country estimates on influenza hospitalization burden
- A tool to estimate influenza economic burden and country estimates

■ ***Post- 2017***

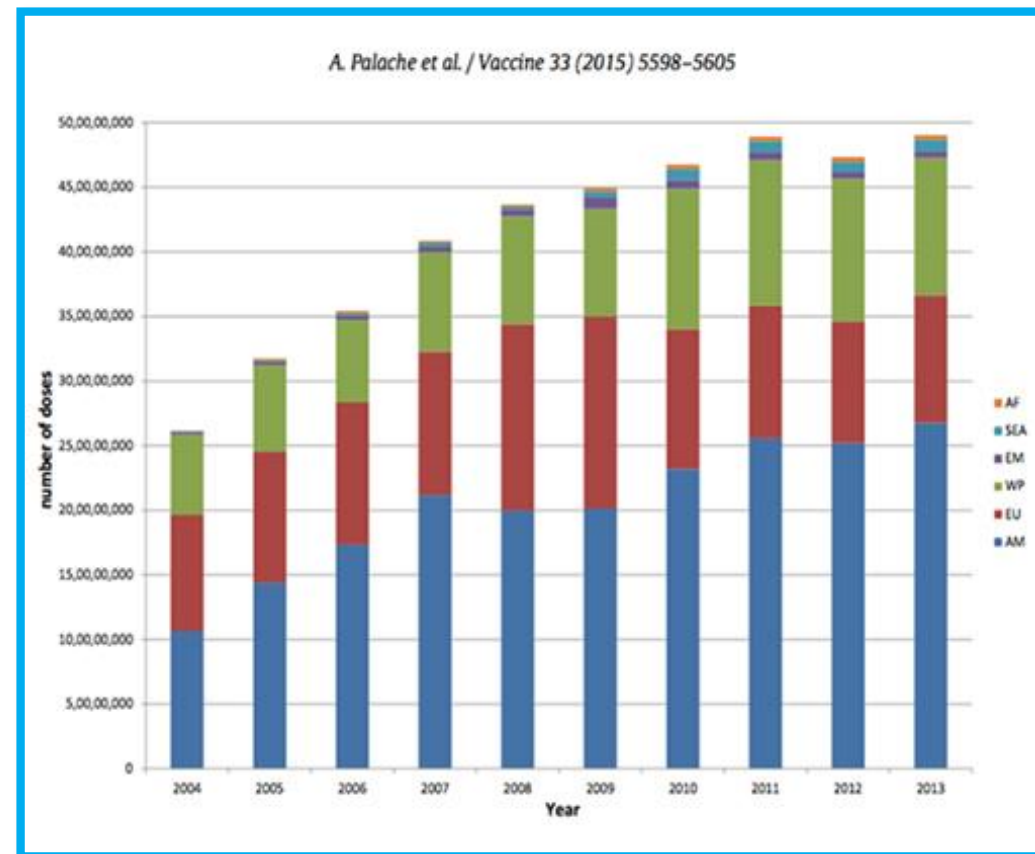
- A mechanism to generate annual global BoD
- Application of BoD to public health policies
 - in particular seasonal influenza vaccine introduction (combined with cost-effective studies)
- Estimate whole spectrum of the burden (cardiovascular, outpatients)
- Methodology development to support country estimates

■ **Directions: *draw data closer* to policies**

Pandemic vaccine response

- **Determination of a PHEIC:** The responsibility of determining a PHEIC lies with the WHO Director-General under Article 12 of the IHR (2005). The determination of a PHEIC leads to the communication of temporary recommendations.
- **Declaration of a pandemic:** During the period of spread of human influenza caused by a new subtype, based on risk assessment and appropriate to the situation, the WHO Director-General may make a declaration of a pandemic.

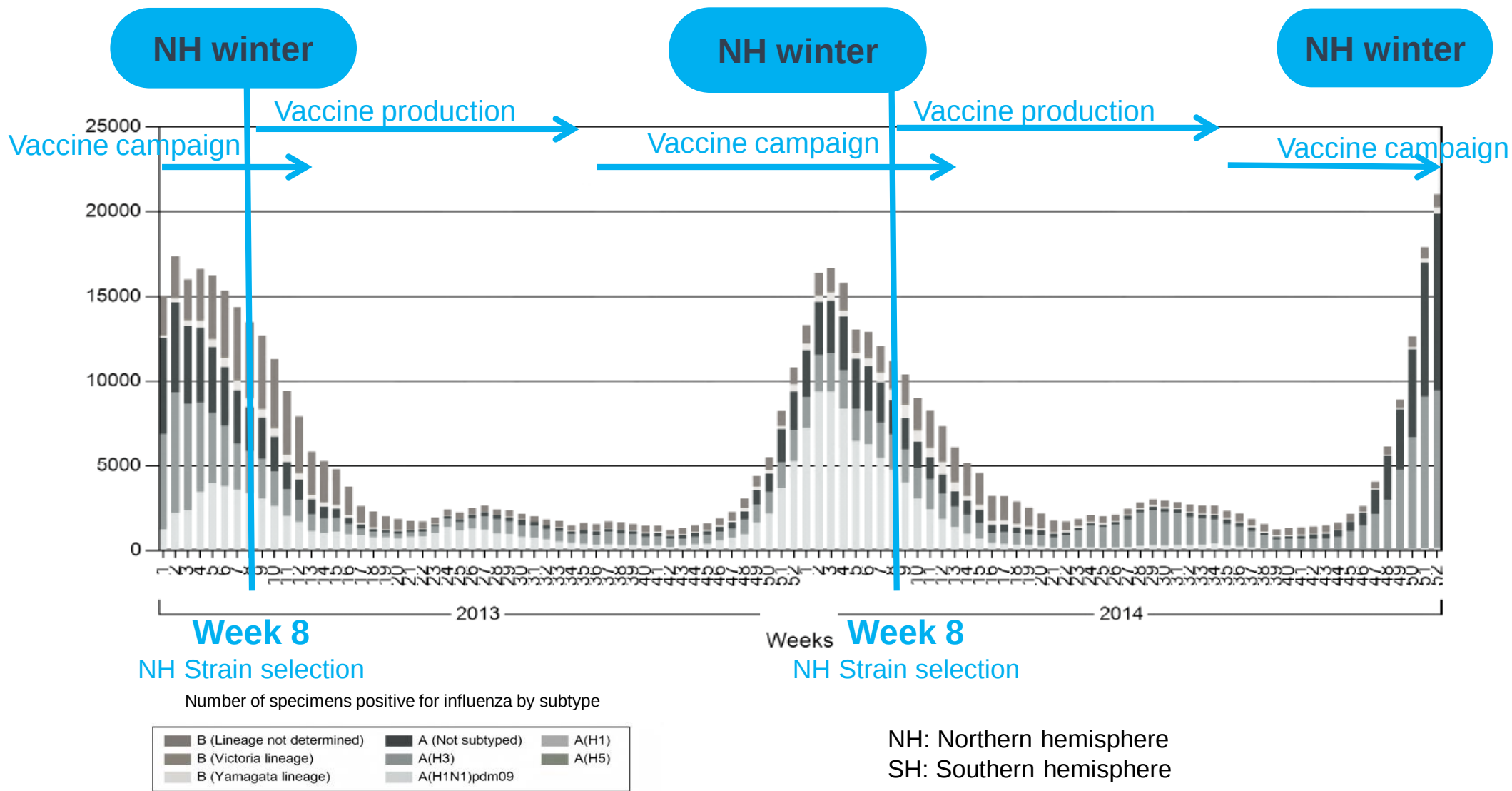
- Vaccine response
 - Estimates of burden of influenza disease
 - → Seasonal influenza vaccine use
 - SMTA2/PIP
 - Concluded with 8 vaccine manufacturers
 - Donate 7.5% - 10%
 - Reserve 1% - 7.5%
 - “Switch” from seasonal to pandemic vaccine production



- Vaccine capacity building
 - Global Action Plan for influenza vaccines (GAP)
 - Approved vaccines through GAP
 - 6 pandemic (2 PQ'd) India, Korea, Romania, Thailand
 - 3 seasonal (1 PQ'd) Brazil, India, Indonesia
 - Predicted capacity in developing countries through GAP

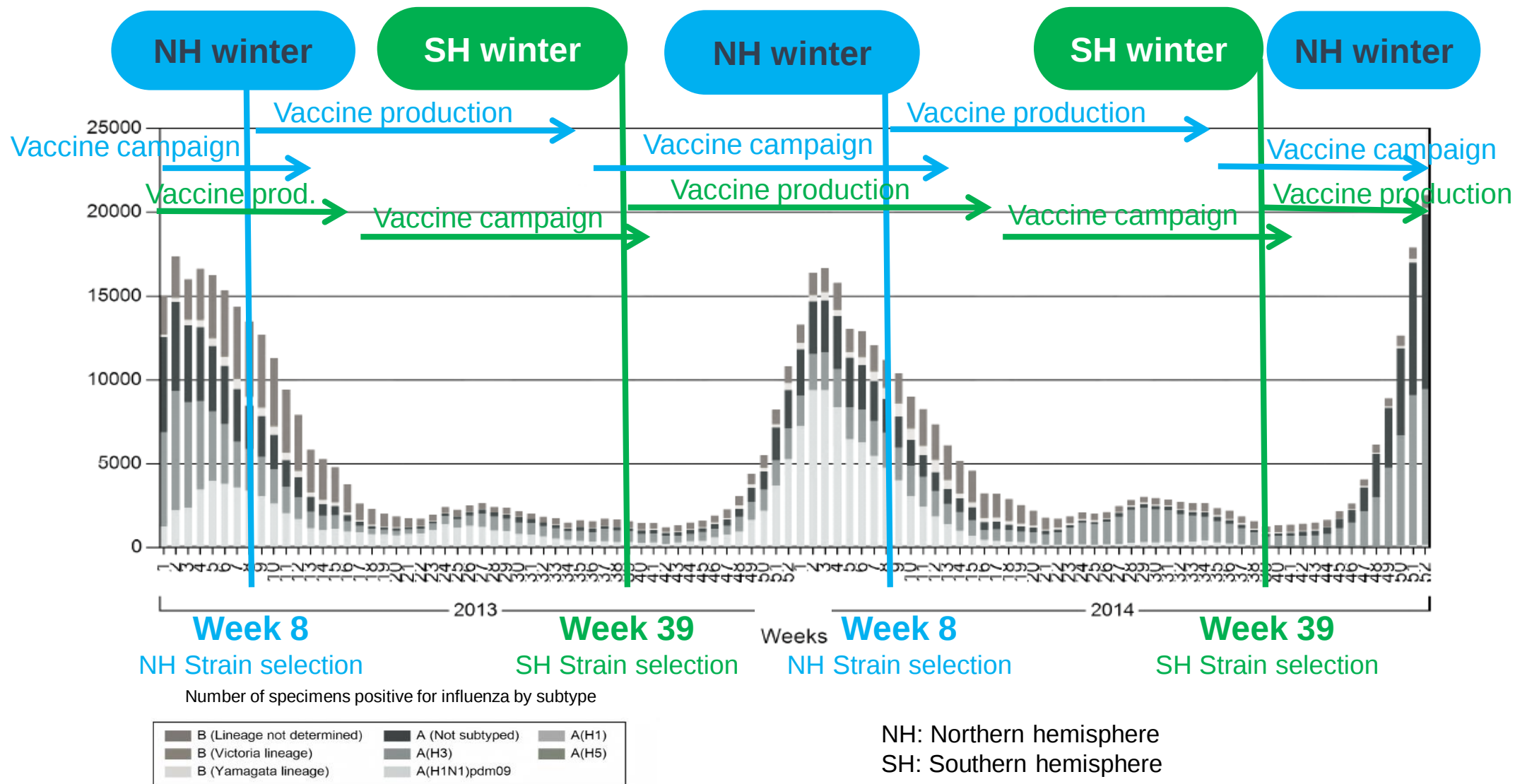


	2006	2015	2016/17	2018/19
■ Reg				
■ Dep	0	338	600	>1.100



Data source: FluNet (www.who.int/flu-net), GISRS

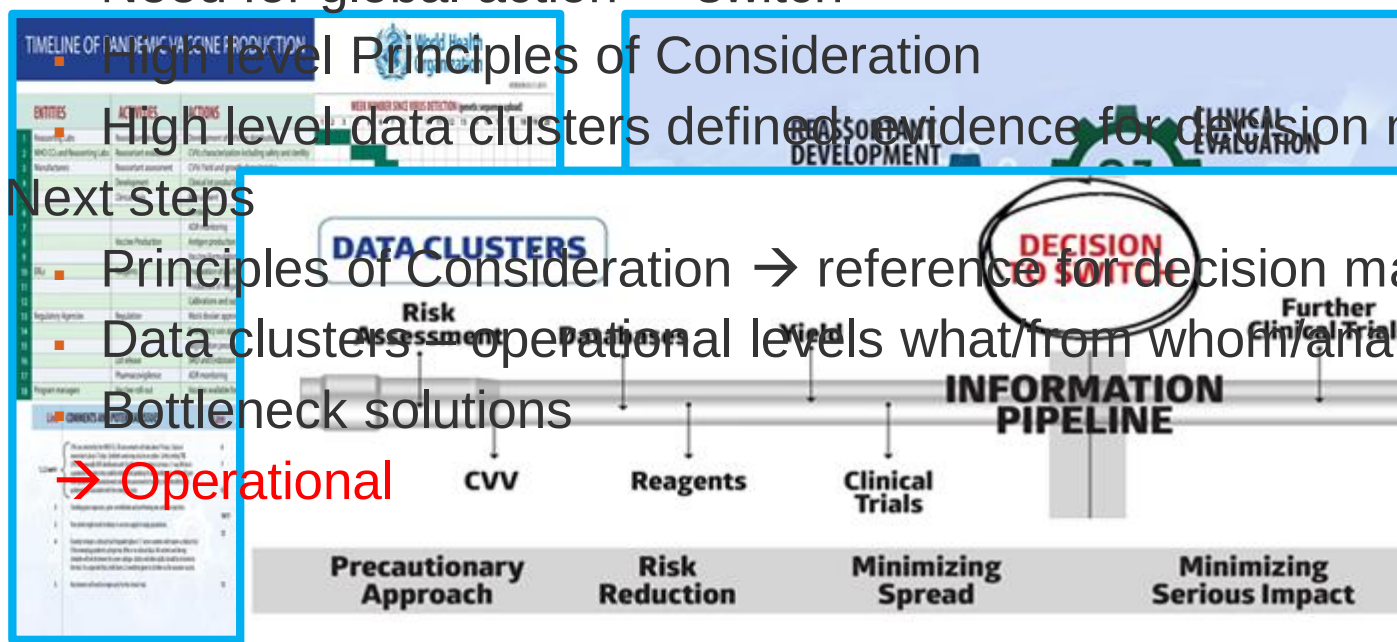
Cycle of vaccine strain selection, production and campaign



Data source: FluNet (www.who.int/fluNet), GISRS

■ Vaccine response

- “Switch” from seasonal to pandemic vaccine production (ongoing; 2 WHO informal consultations)
- Achieved:
 - Clarity of the complexity
 - Better understanding of response (who, when, how)
 - Need for global action – “switch”

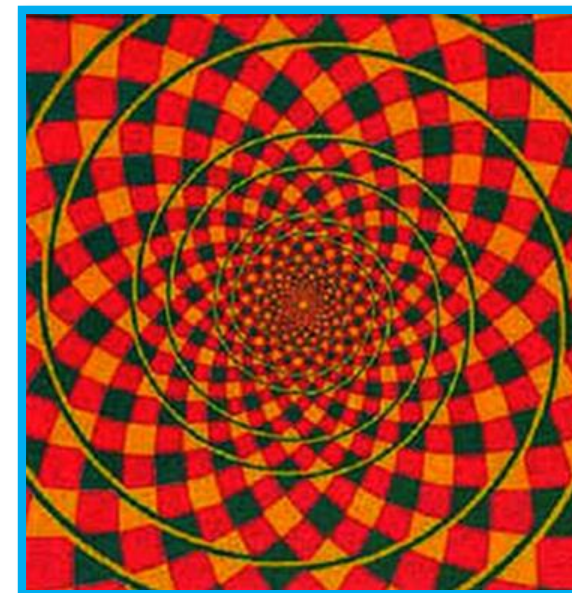


■ From the viruses

- Further evolving and spreading of zoonotic viruses
 - Multi-subtypes, multi-clades, more countries/regions

■ From the world

- Competing priorities
 - Long-term (?) investment vs. short-term needs
- Dynamics of the world
 - Pandemic, epidemic, endemic; emergency, outbreak
- “Flu fatigue”



- Influenza – only known will-be-a-pandemic so far
 - At unknown time, might be very soon
 - Better planning → more life saving
- World's influenza pandemic preparedness better ... **BUT** ...
- Shared responsibility
 - Global coordination key - WHO commitment

Urgency – time is running out

Act now!



- GISRS - Global Influenza Surveillance and Response System
 - WHO Collaborating Centres, National Influenza Centres
- GIP - Global Influenza Programme
- Julia Fitzner, Siddhi Hiver

Thank you

Merci

Gracias

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谢谢

благодаря