

# NIC Data to Global Vaccine Decisions: The Role of CDC in Vaccine Strain Selection

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# Disclaimer

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

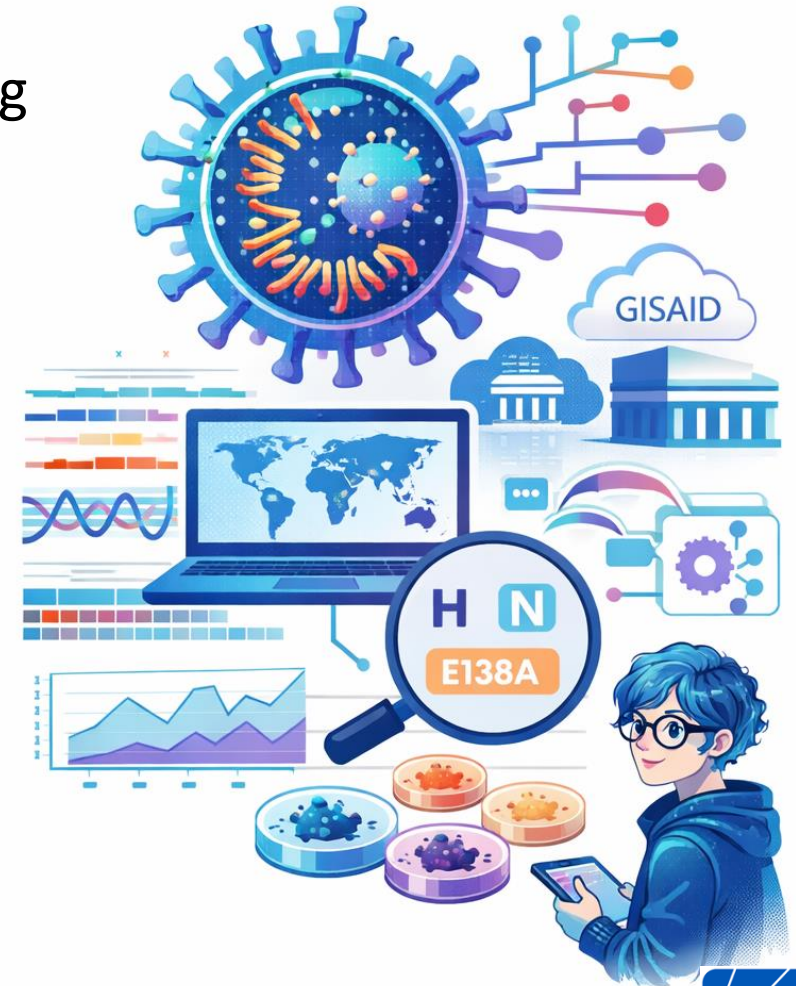
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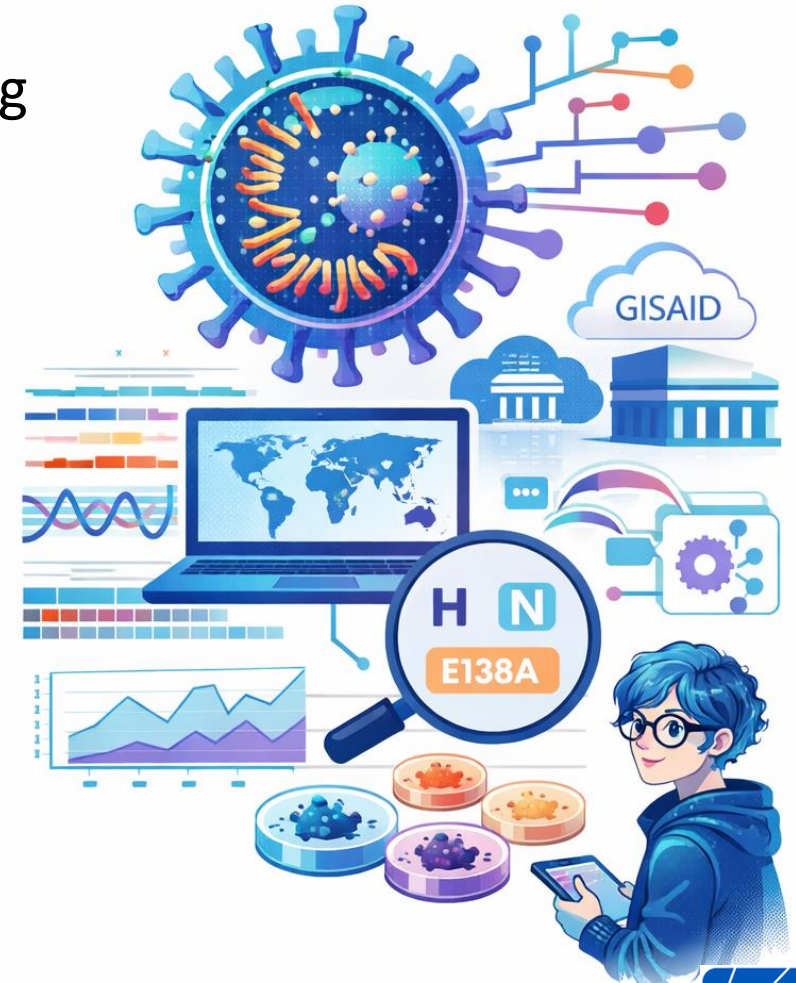
# Training Objectives

- Trainees should be able to
  - **Productionalize** their influenza genomic data processing
  - Submit **timely, high-quality** data to GISAID and NCBI
  - Perform informatic **analyses** (e.g., phylogenetic trees, amino acid mutations) of influenza sequences
  - Generate genomic surveillance **reports** on circulating subtypes and clades



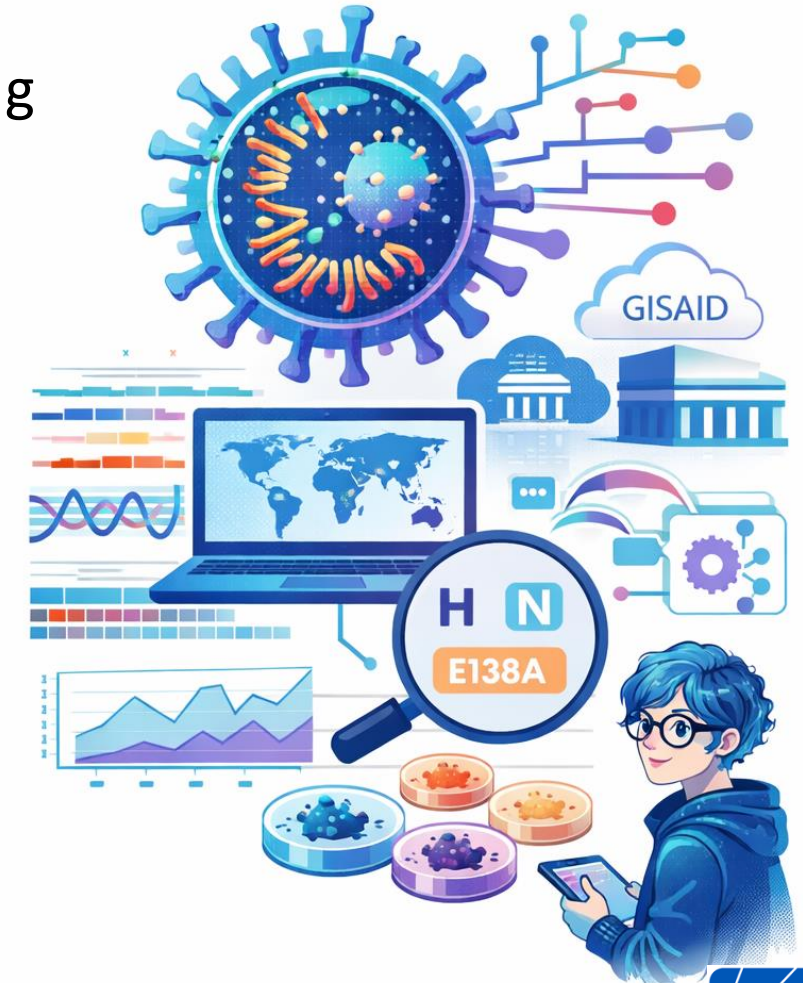
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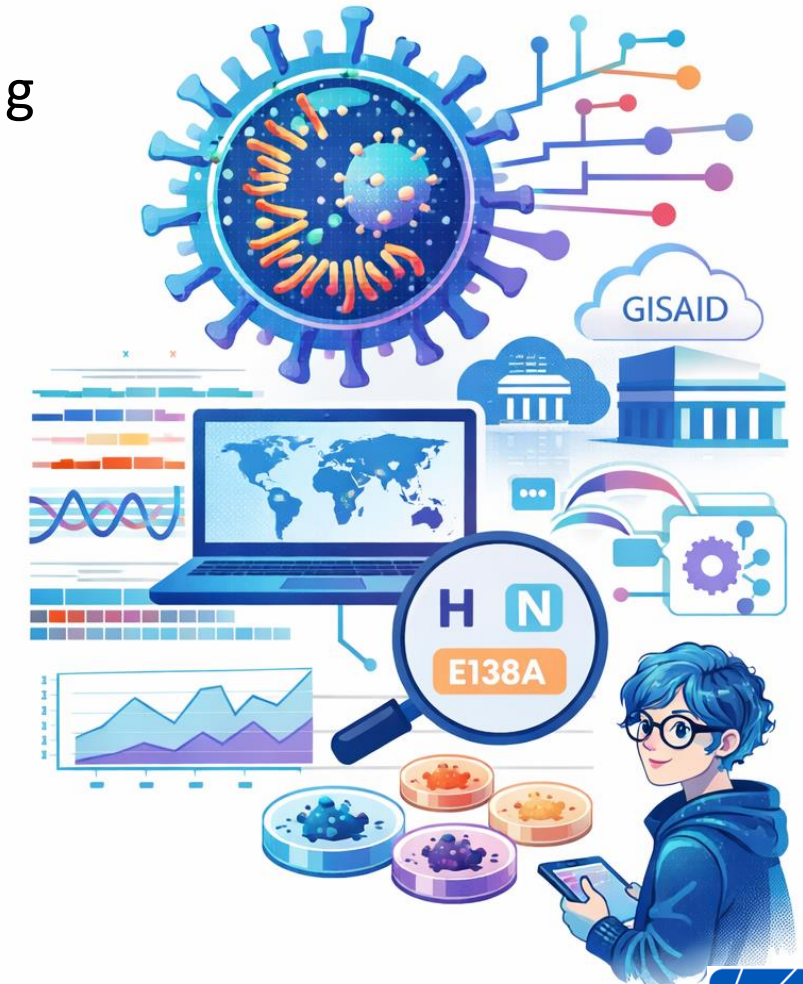
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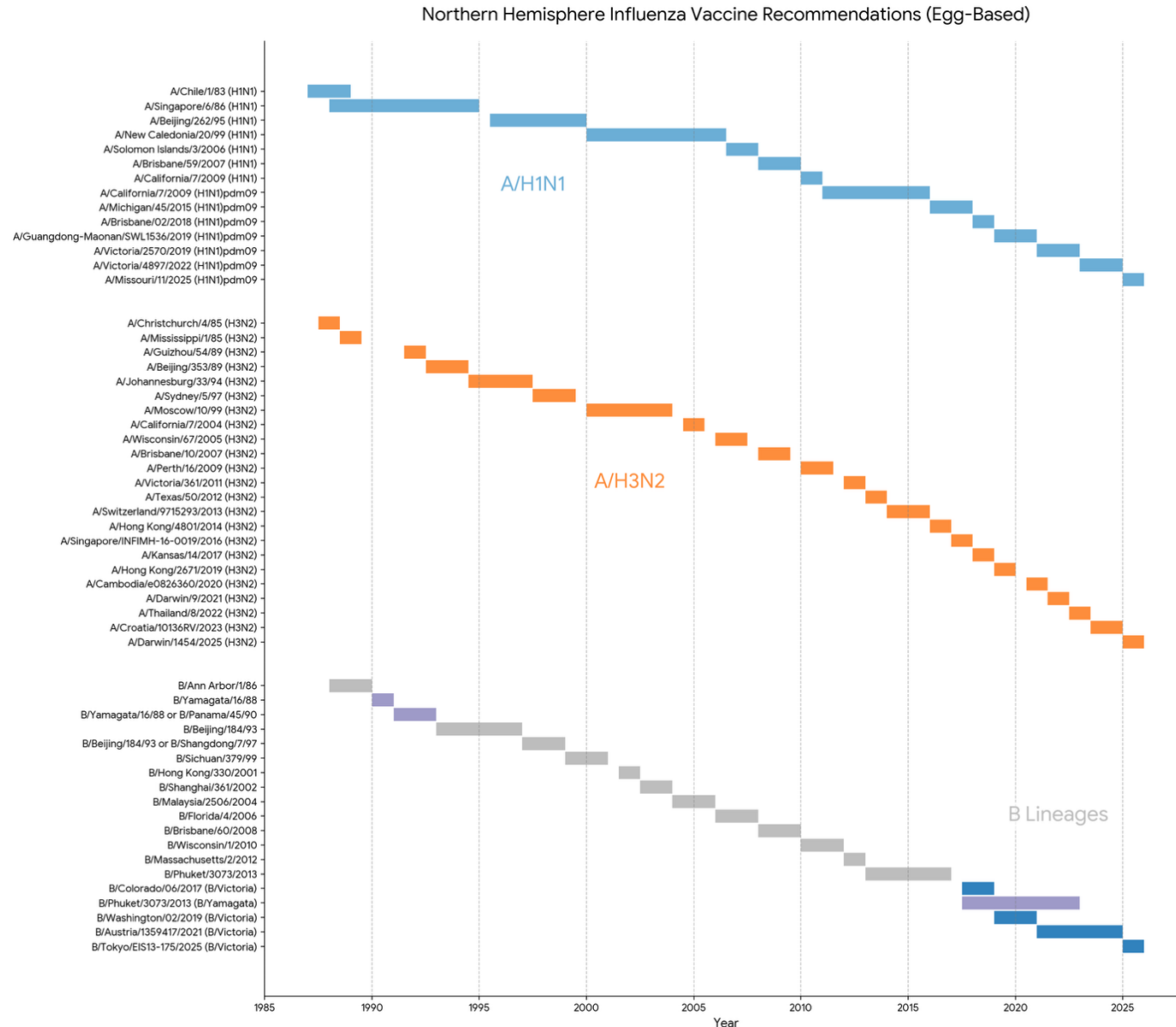


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# Influenza mutates rapidly (drifts) and evades previous host immunity

Vaccine antigen must be updated most years

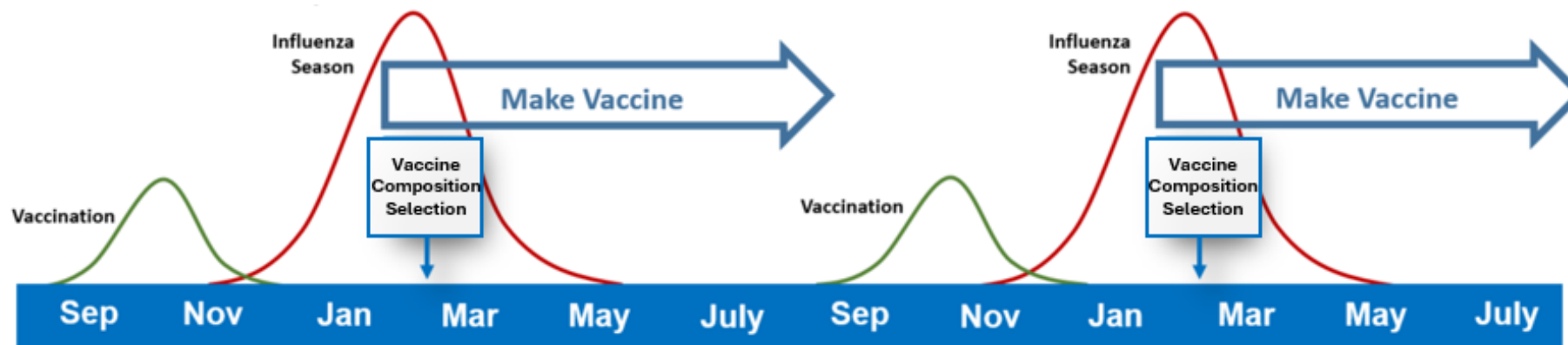


# Vaccine strain is chosen ~8 months before flu season

- WHO convenes technical consultations to recommend viruses for three components:
  - A(H1N1)pdm09, A(H3N2) and B/Victoria lineage
- Two recommendation tracks:
  - ***Egg-based vaccines***
  - ***Cell/recombinant/nucleic acid-based vaccines***
- Prototype names may differ by platform – both represent the best candidate for subtype

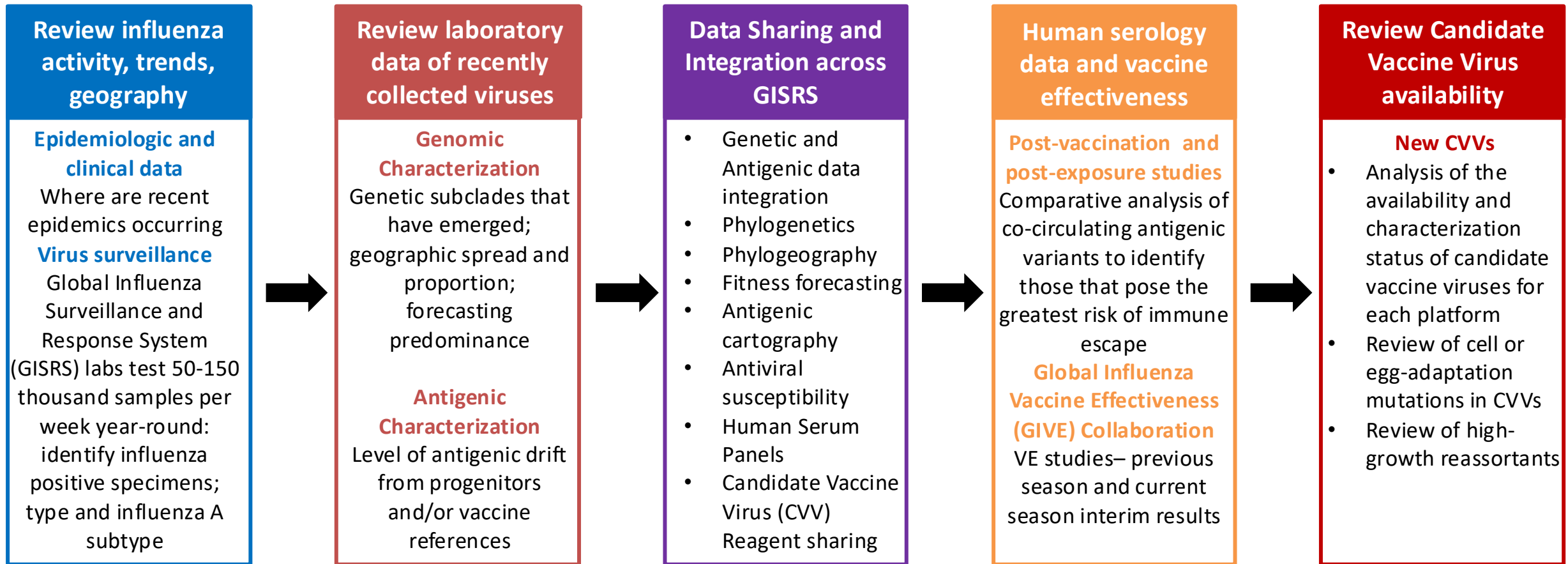
## Timing of Influenza Vaccine Recommendations:

- 6-8 months for the production, regulatory approval and distribution of the manufactured vaccines



# Influenza Vaccine Composition Meeting Decision Process

**Goal** – Identify antigens that elicit immunity against diverse/diverging future viruses



VCM FAQ: [https://cdn.who.int/media/docs/default-source/vcm-northern-hemisphere-recommendation-2026-2027/b.-27-feb-2026-frequently-asked-questions.pdf?sfvrsn=66208818\\_7](https://cdn.who.int/media/docs/default-source/vcm-northern-hemisphere-recommendation-2026-2027/b.-27-feb-2026-frequently-asked-questions.pdf?sfvrsn=66208818_7)

Influenza vaccine strain selection and recent studies on the global migration of seasonal influenza viruses (C.A. Russell, et al., *Science* 26 (4): D31-34, 2008):

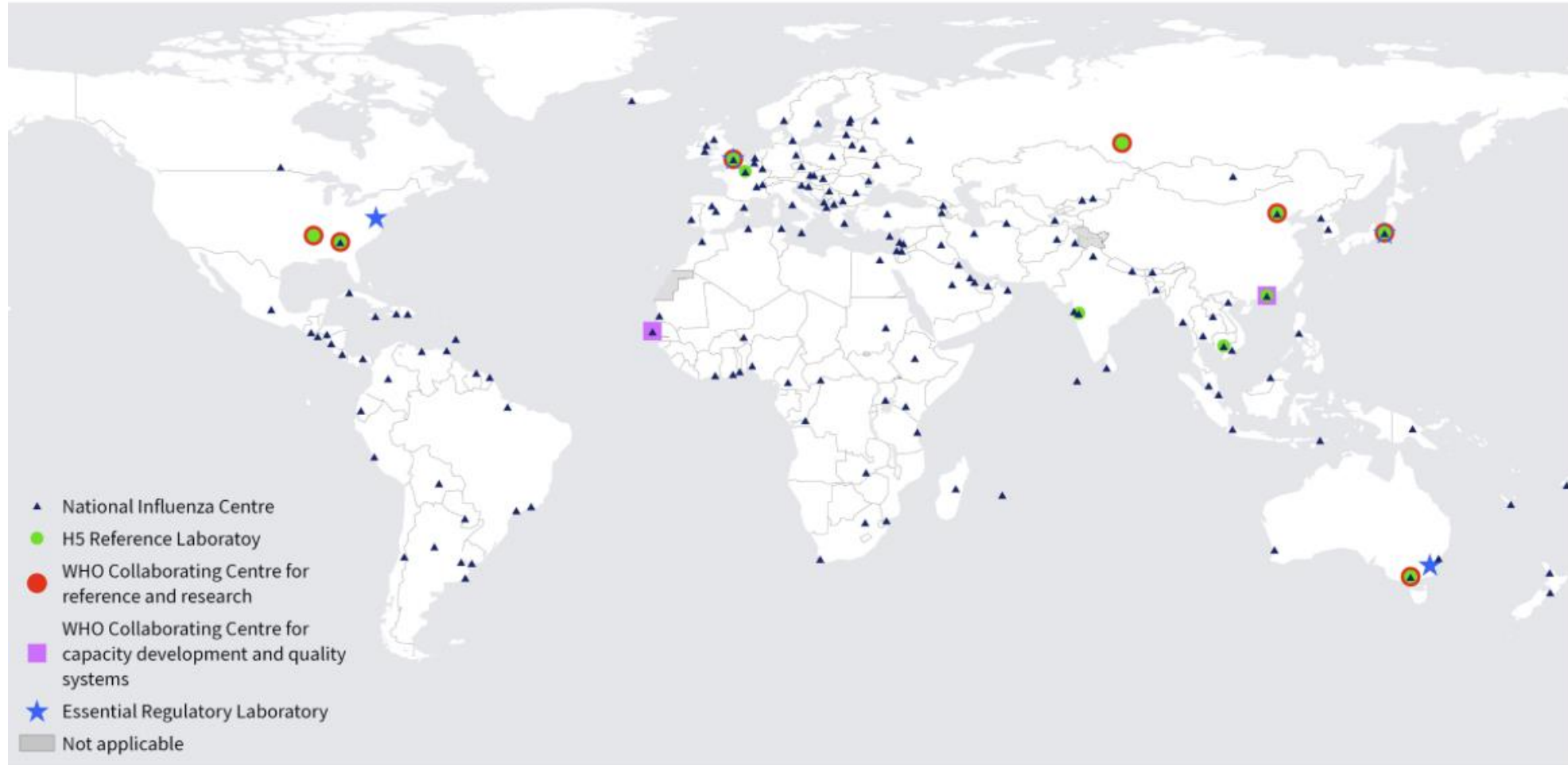
<https://doi.org/10.1016/j.vaccine.2008.07.078>

# It all begins with YOU!



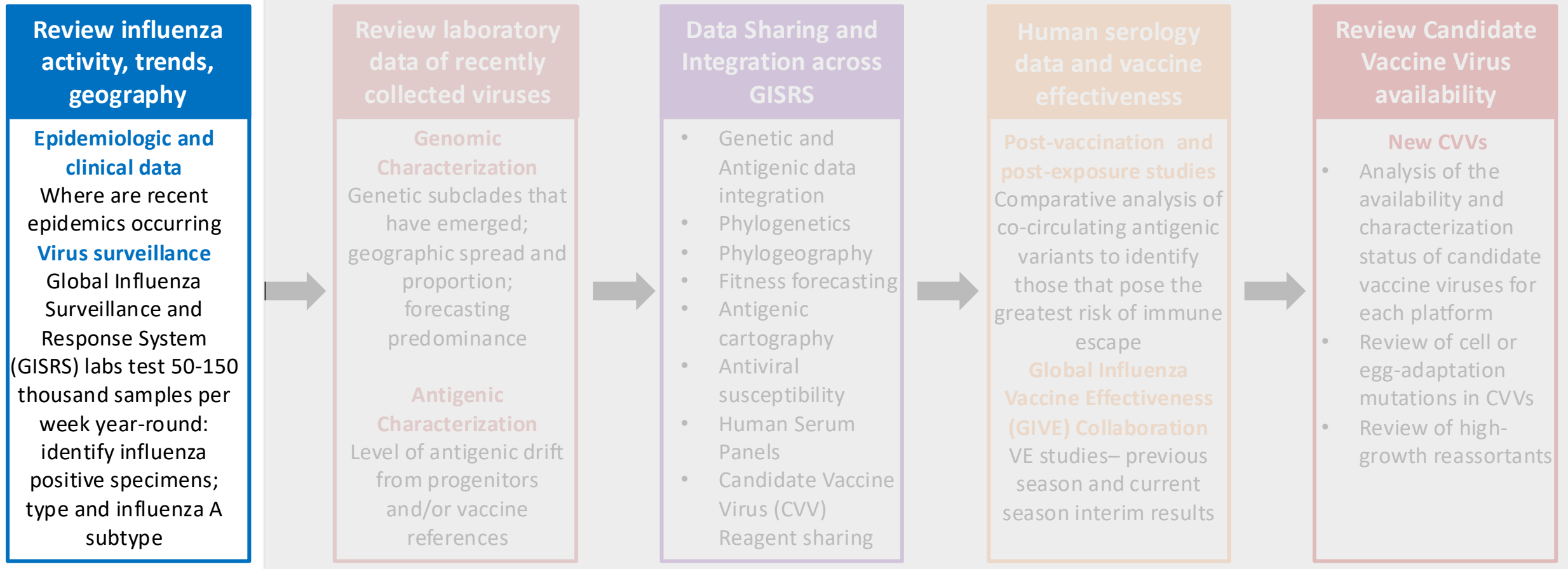
# Global Influenza Surveillance and Response System (GISRS)

19 March 2026



# Influenza Vaccine Composition Meeting Decision Process

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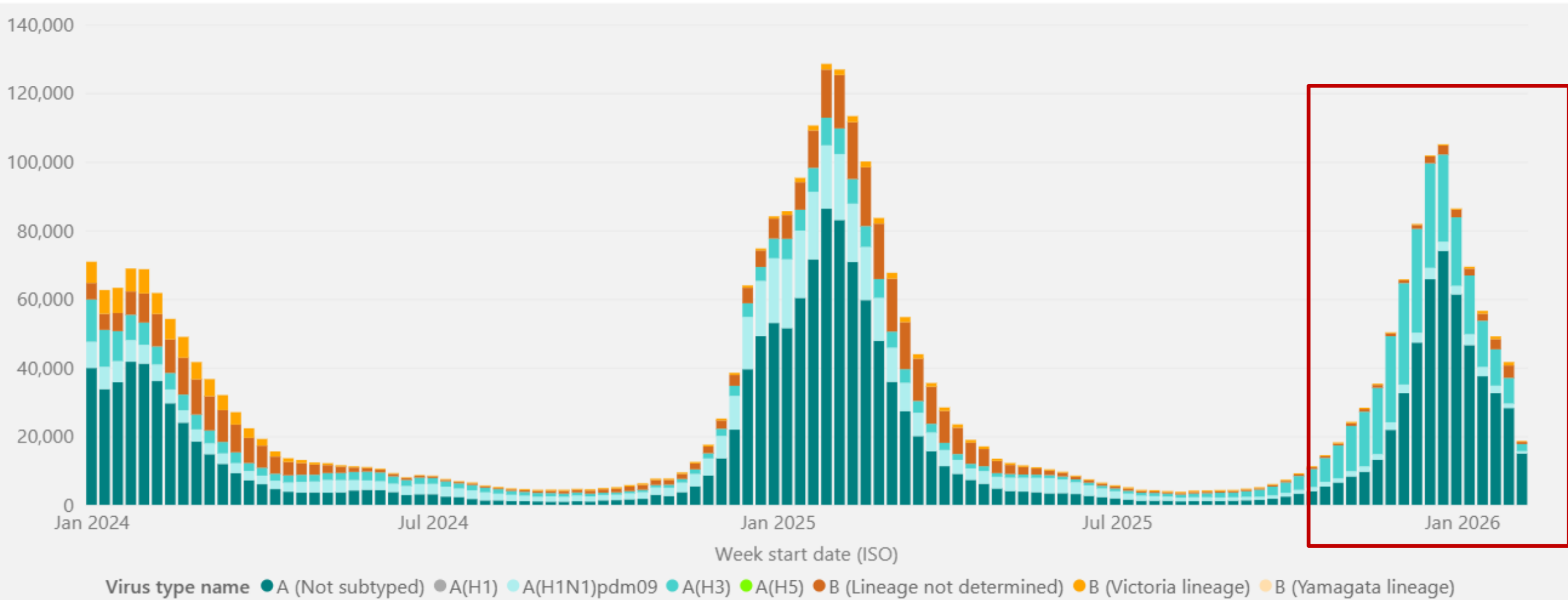
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# Global Circulation of Seasonal Influenza Viruses Since January 2024

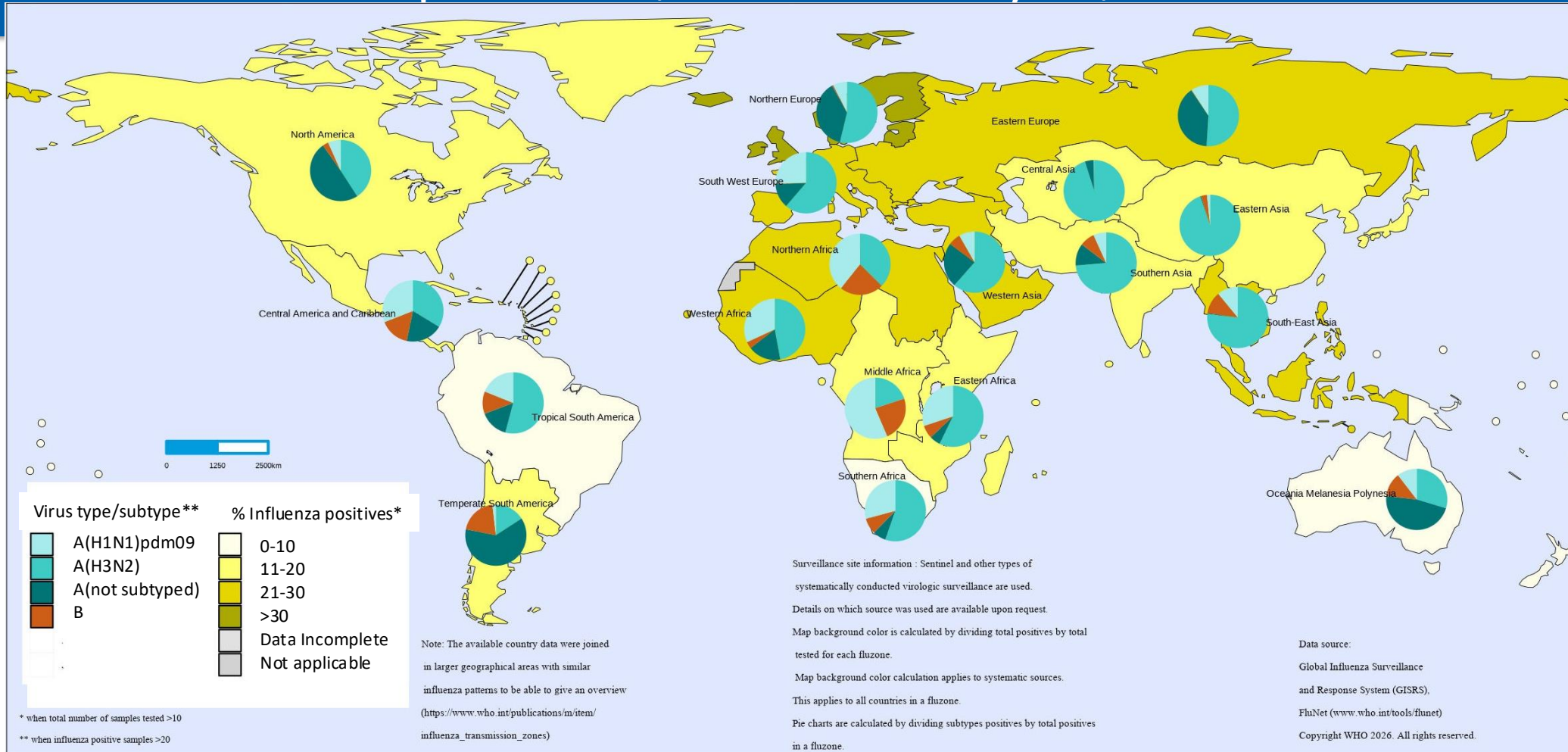


Data reported to FluNet by GISRS National Influenza Centers in 135 member states

VCM Information meeting: <https://www.youtube.com/@who>

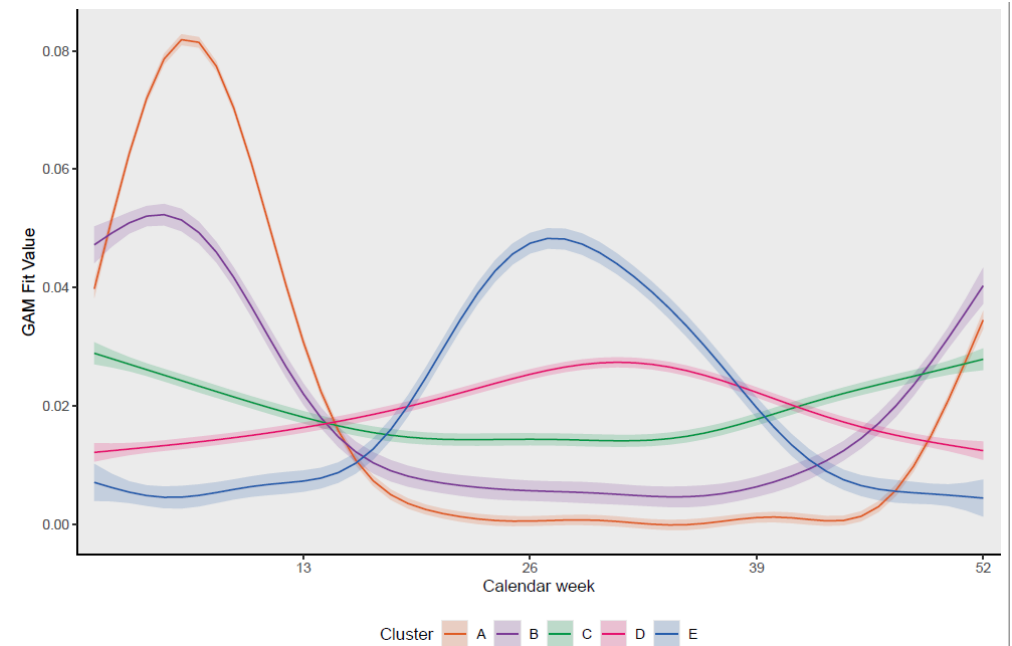
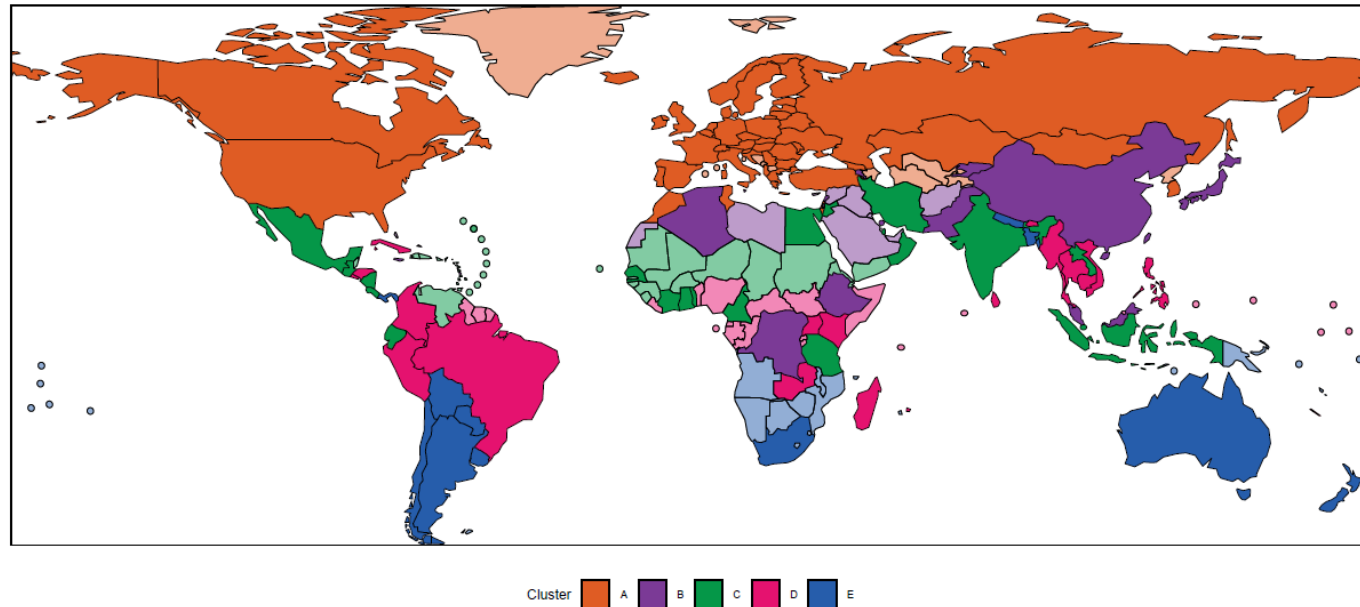
# Influenza activity and global distribution of type/subtype

## September 1, 2025 – January 31, 2026



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

# Your data is leading to more refined definitions of “influenza season”



- A - northern hemisphere pattern - peak influenza activity between October–April and**
- B - northern hemisphere pattern - peak influenza activity between September–March**
- C - tropics -influenza activity between September–March**
- D - southern hemisphere pattern, influenza activity between May–November;  
additional activity in other months**
- E -southern hemisphere pattern, peak influenza activity between May–November**

## Defining Influenza Epidemic Zones through Temporal Clustering of Global Surveillance Data

21 Pages • Posted: 21 Jan 2026

Norman Hassell

Government of the United States of America - Centers for Disease Control and Prevention (CDC)

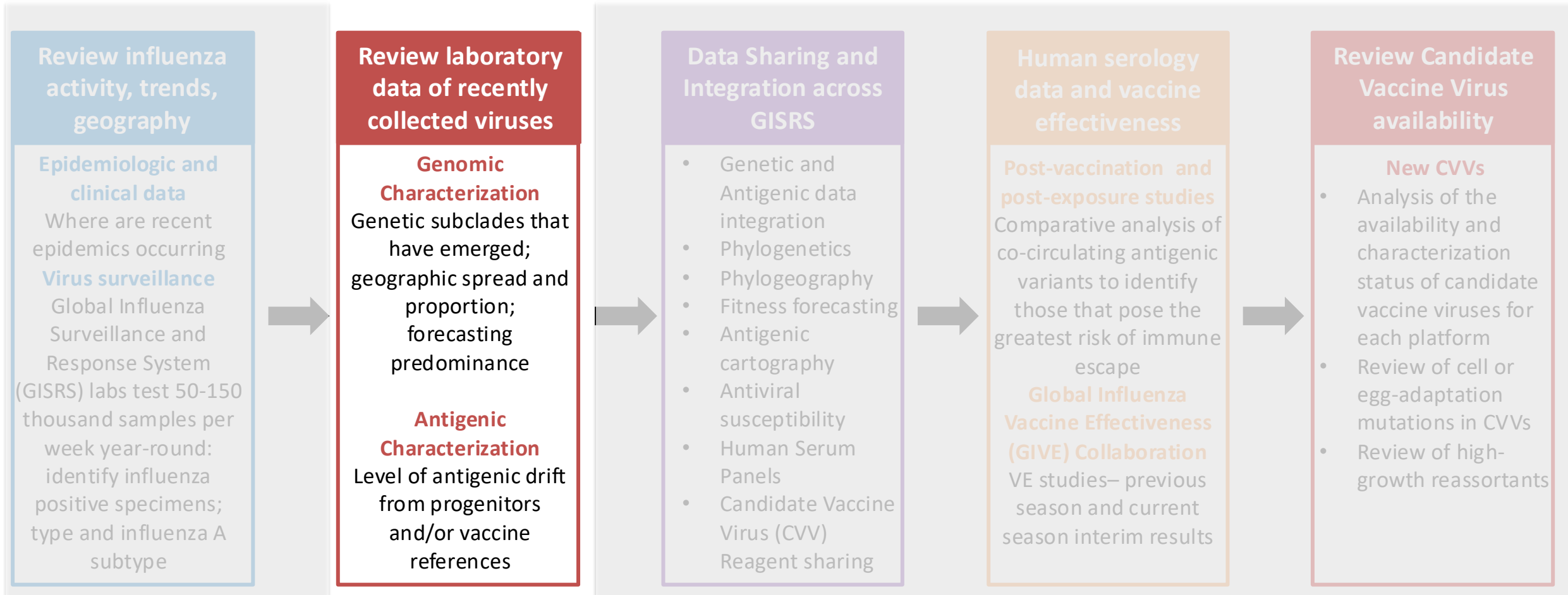
Perrine Marcenac

*affiliation not provided to SSRN*

<https://ssrn.com/abstract=6094038>

# Influenza Vaccine Composition Meeting Decision Process

**Goal** – Identify antigens that elicit immunity against diverse/diverging future viruses

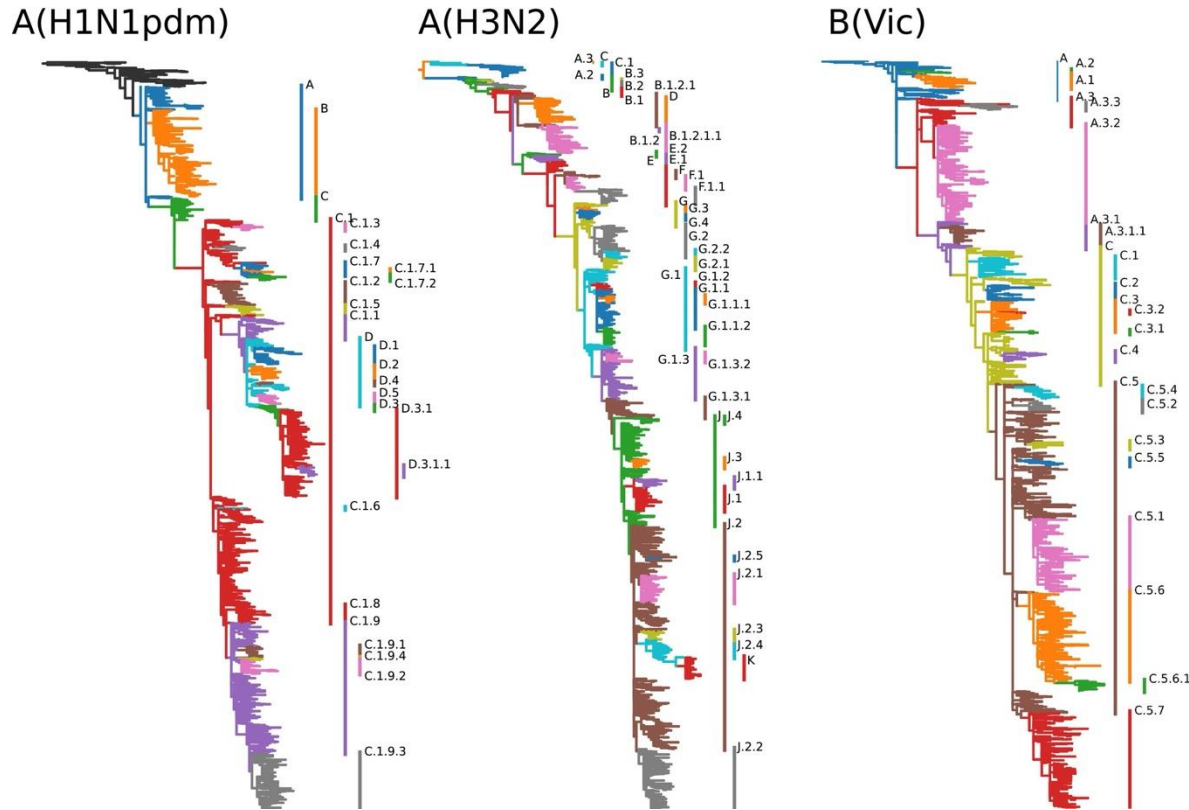


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# Genomic Surveillance: Nomenclature for Hemagglutinin (HA) and Neuramindase (NA)



**Goal: Tracking of relative frequencies of co-circulating subclades**

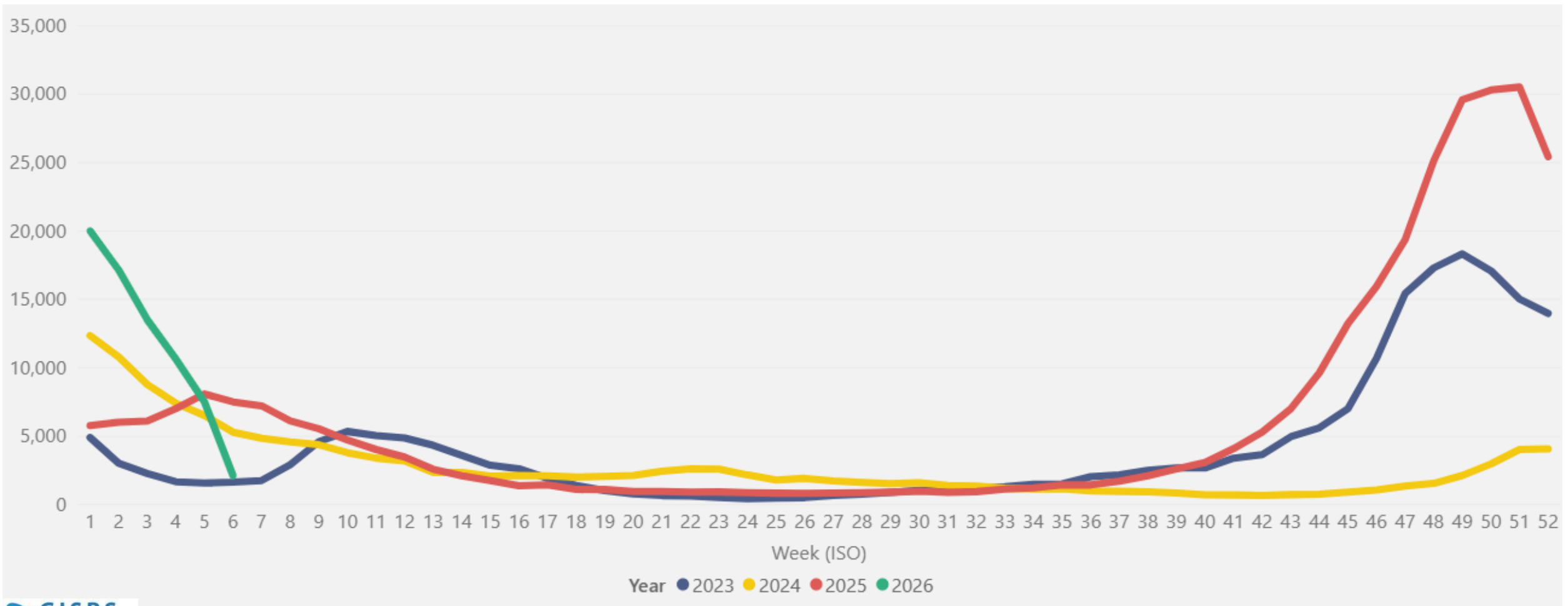
**Criteria for Subclade Definition:**

- **Size and dynamics of the subclade:** Larger, recently expanded groups prioritized
- **Divergence:** More genetic changes since the parent group given higher priority
- **Specific amino acid substitutions:** Significant substitutions that may affect phenotype
- **New subclade and aliases about four times a year – usually after VCM**

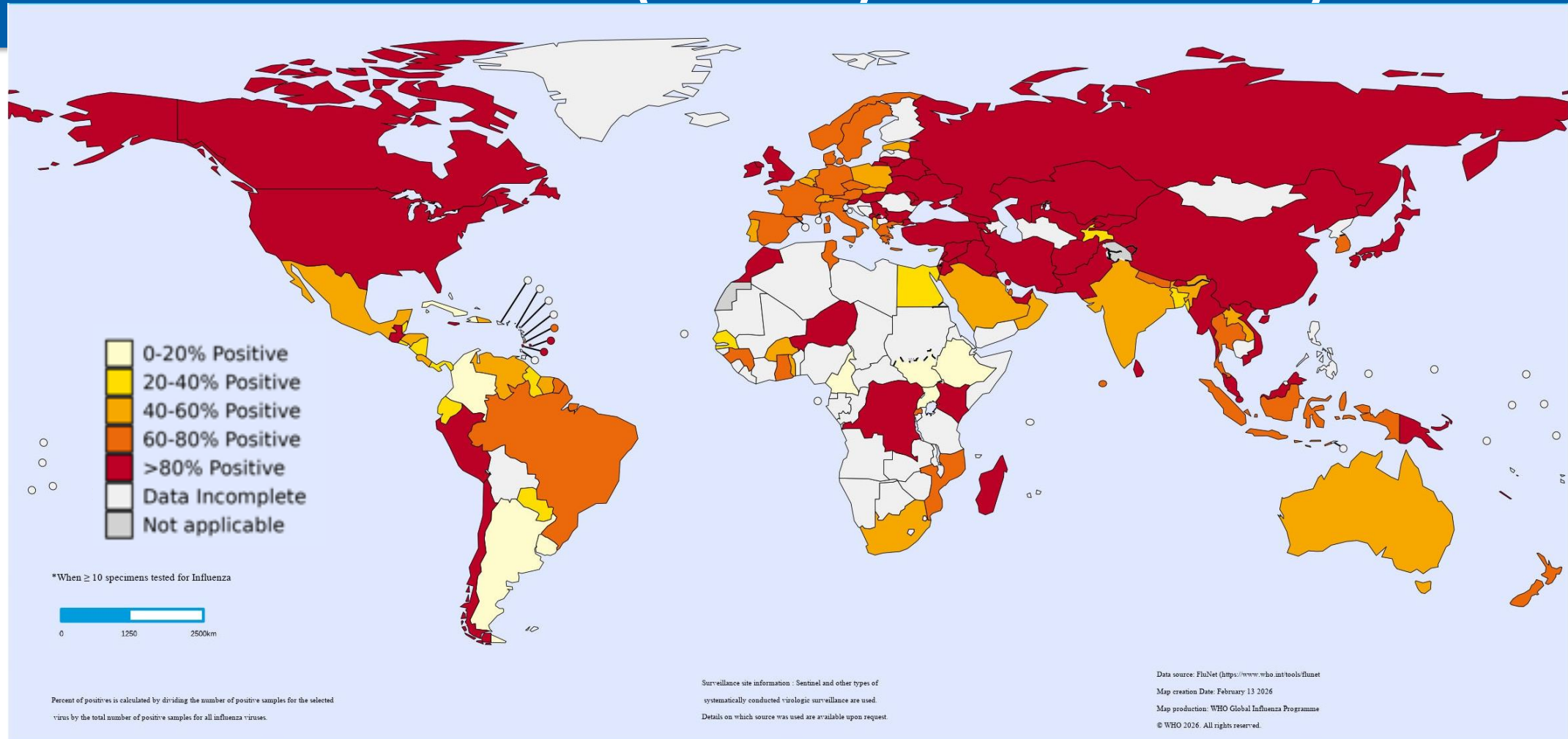
# A(H3N2) Viruses in the 25/26 Northern Hemisphere



# Number of A(H3N2) viruses detected by GISRS



# Influenza A(H3N2) virus activity



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Data source: FluNet, (<https://www.who.int/tools/flunet>),  
Global Influenza Surveillance and Response System (13 February 2026)



VCM Information meeting: <https://www.youtube.com/@who>

# A(H3N2) HA phylogeography

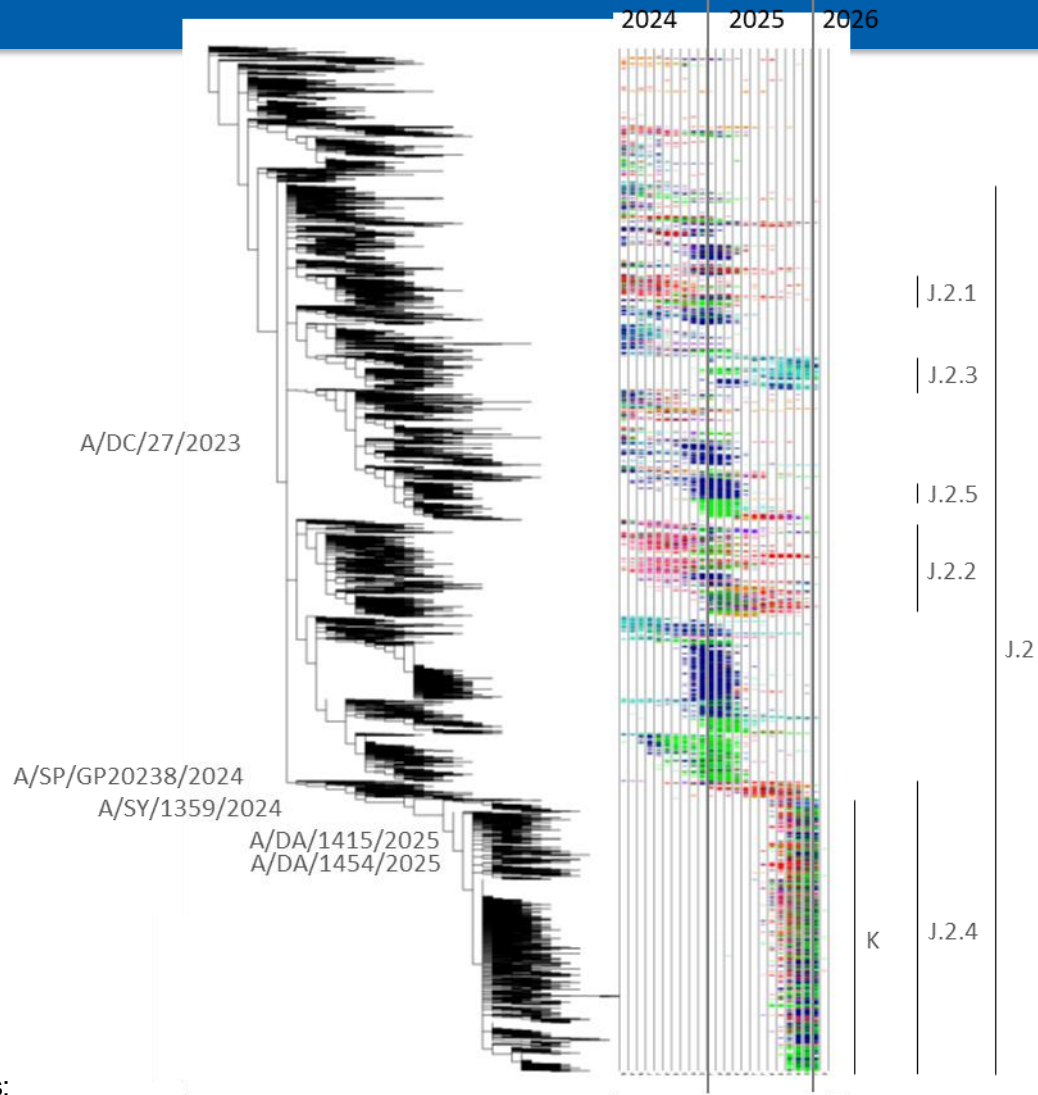
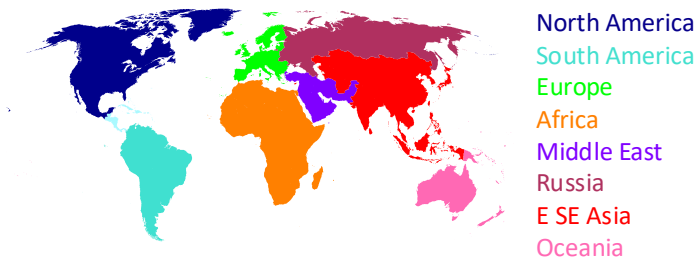


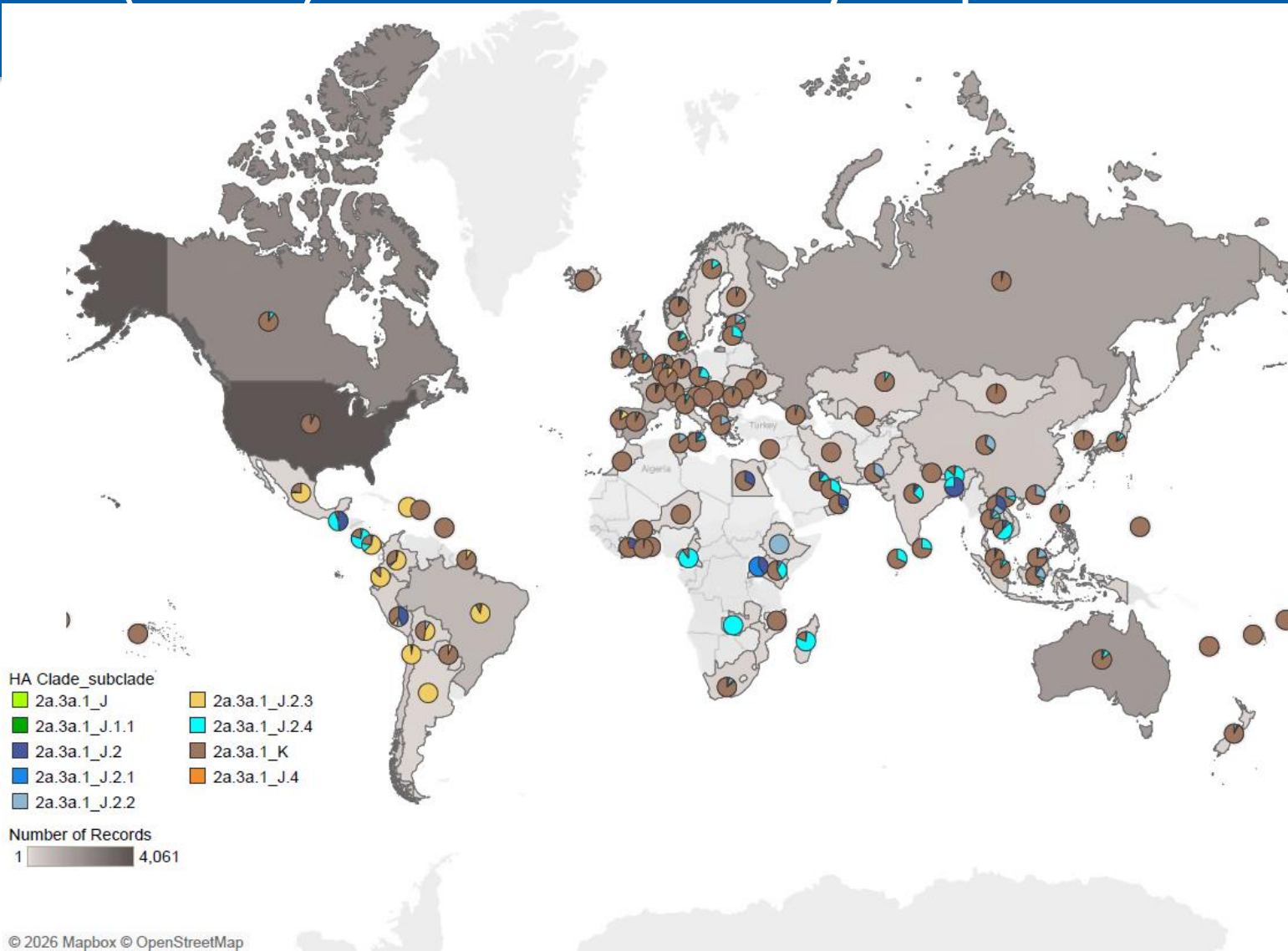
Figure Source: University of Cambridge

Data Source:

HA and NA clade/subclades:  
<https://clades.nextstrain.org/>

VCM Information meeting: <https://www.youtube.com/@who>

# Global A(H3N2) HA clade diversity: Sep 2025 to Jan 2026

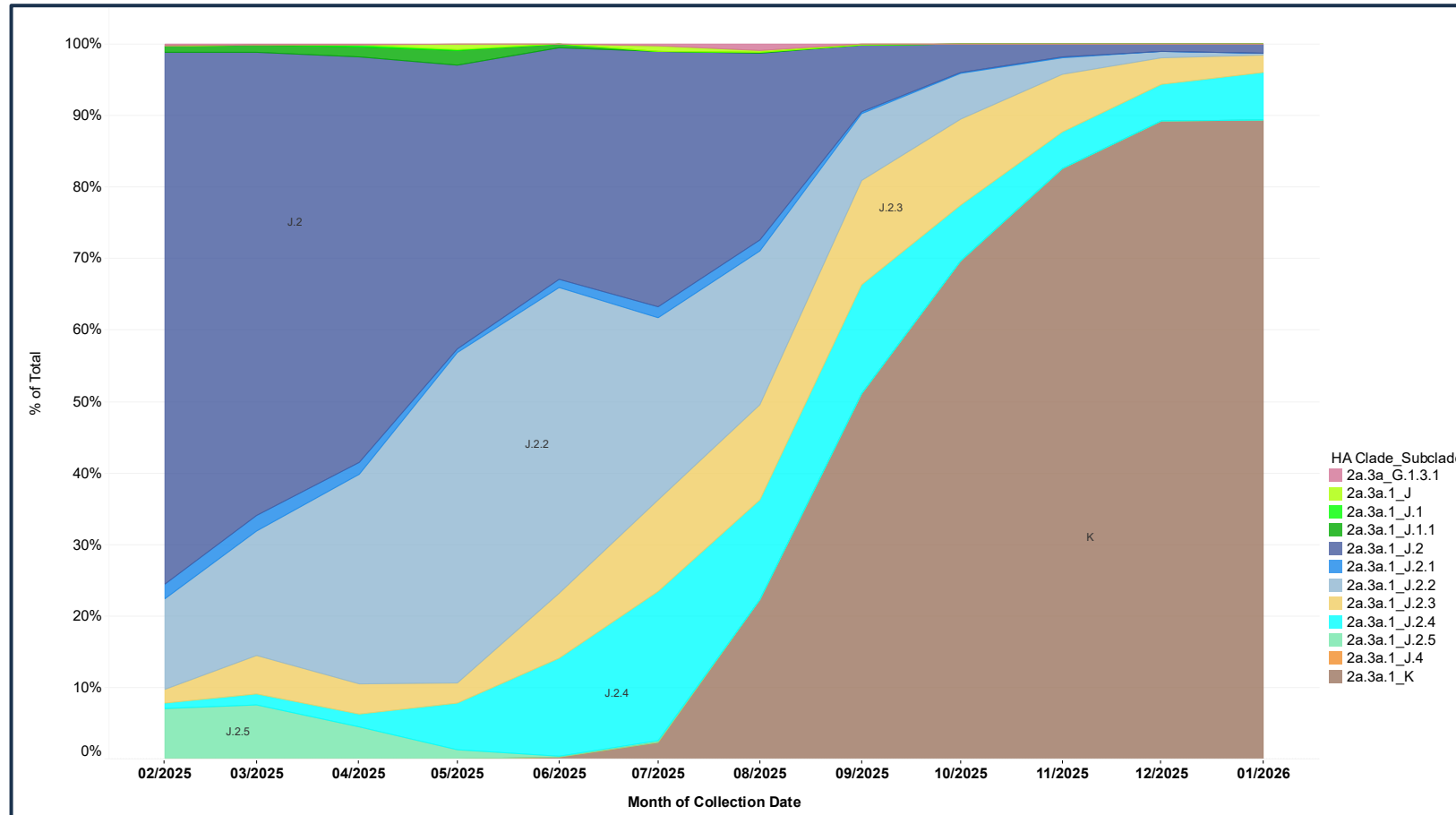



HA and NA clade/subclades:  
<https://clades.nextstrain.org/>

Data Source:

# A(H3N2) Extended Diversity Plot

Global view  
Feb 2025-Jan 2026



Data Source: 

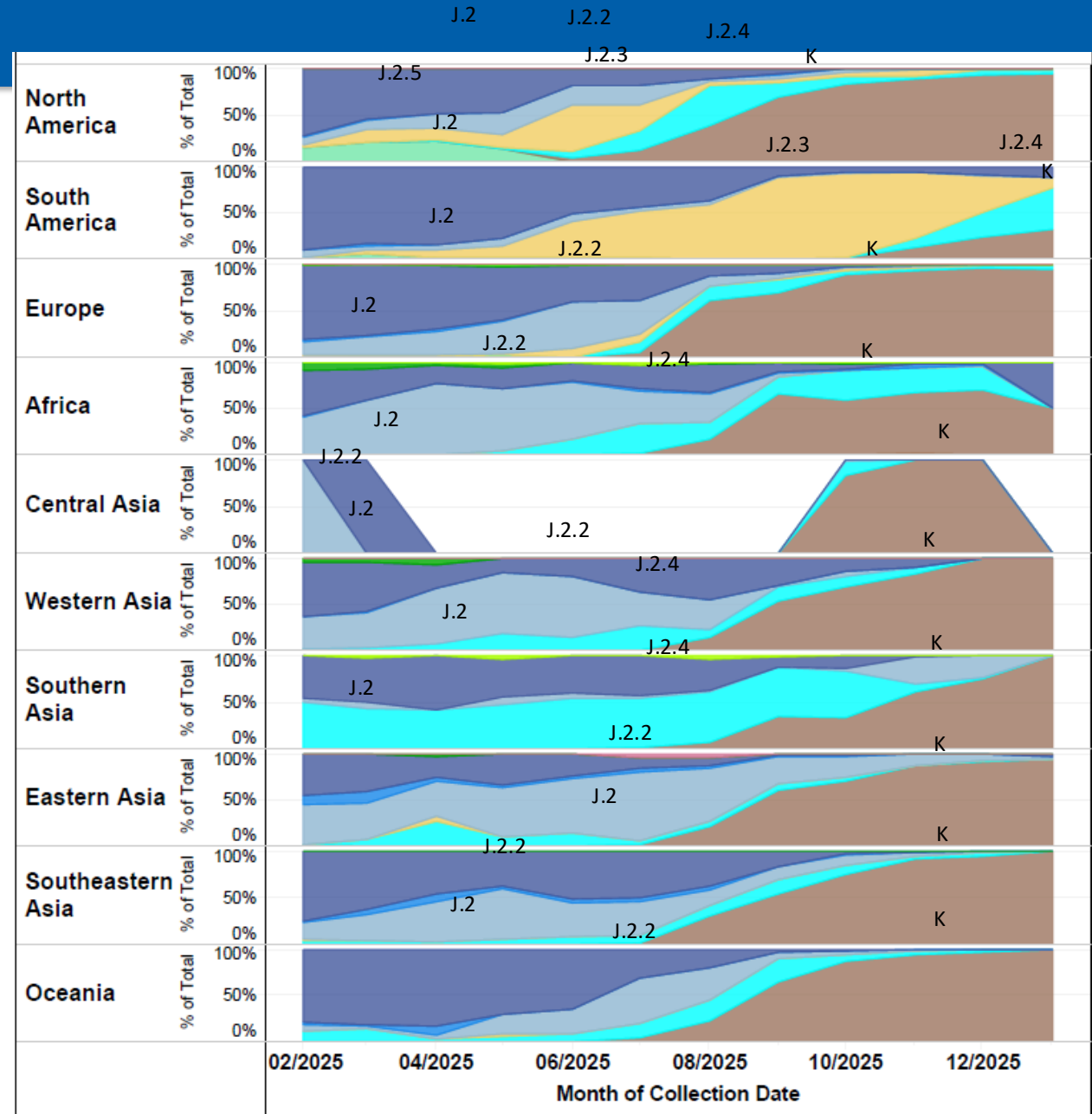
HA and NA clade/subclades:  
<https://clades.nextstrain.org/>


# A(H3N2) Extended Diversity Plot by Geographic Region

February 2025 – February 2026

## HA Clade\_Subclade

- 2a.3a\_G.1.3.1
- 2a.3a.1\_J
- 2a.3a.1\_J.1
- 2a.3a.1\_J.1.1
- 2a.3a.1\_J.2
- 2a.3a.1\_J.2.1
- 2a.3a.1\_J.2.2
- 2a.3a.1\_J.2.3
- 2a.3a.1\_J.2.4
- 2a.3a.1\_J.2.5
- 2a.3a.1\_J.4
- 2a.3a.1\_K

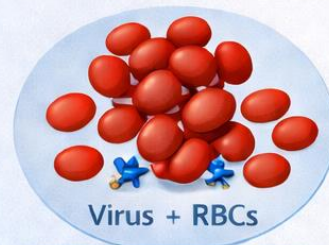
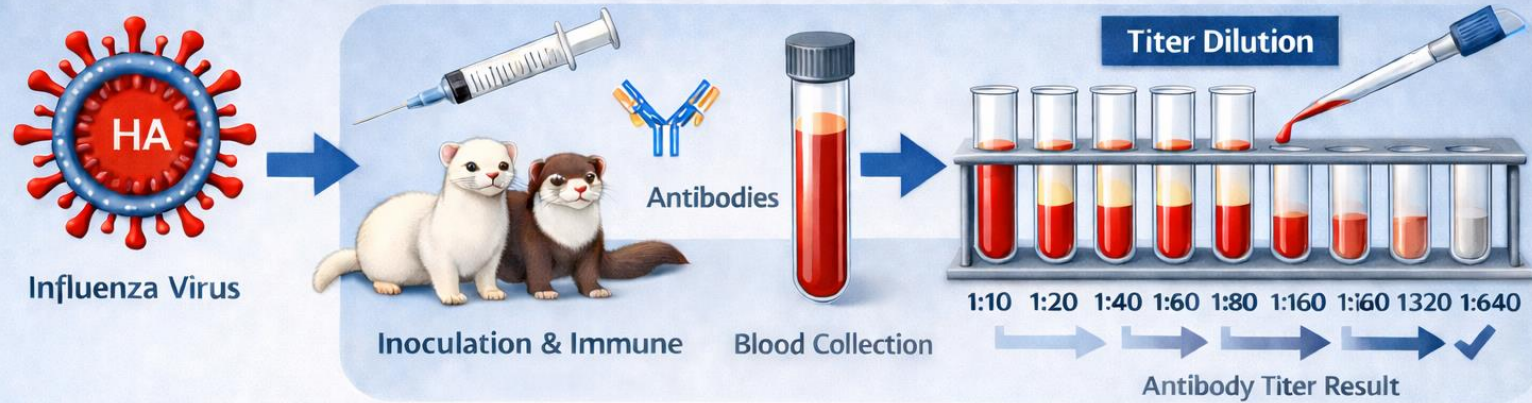


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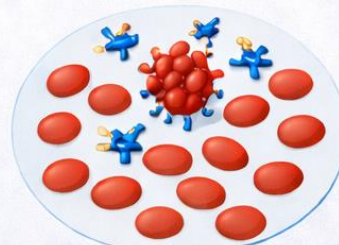
HA and NA clade/subclades:  
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# Influenza phenotyping relies heavily on ferrets and *hemagglutinin inhibition assays*

## Hemagglutination Inhibition (HI) Testing with Ferrets



Agglutination



Inhibition (No Clumping)



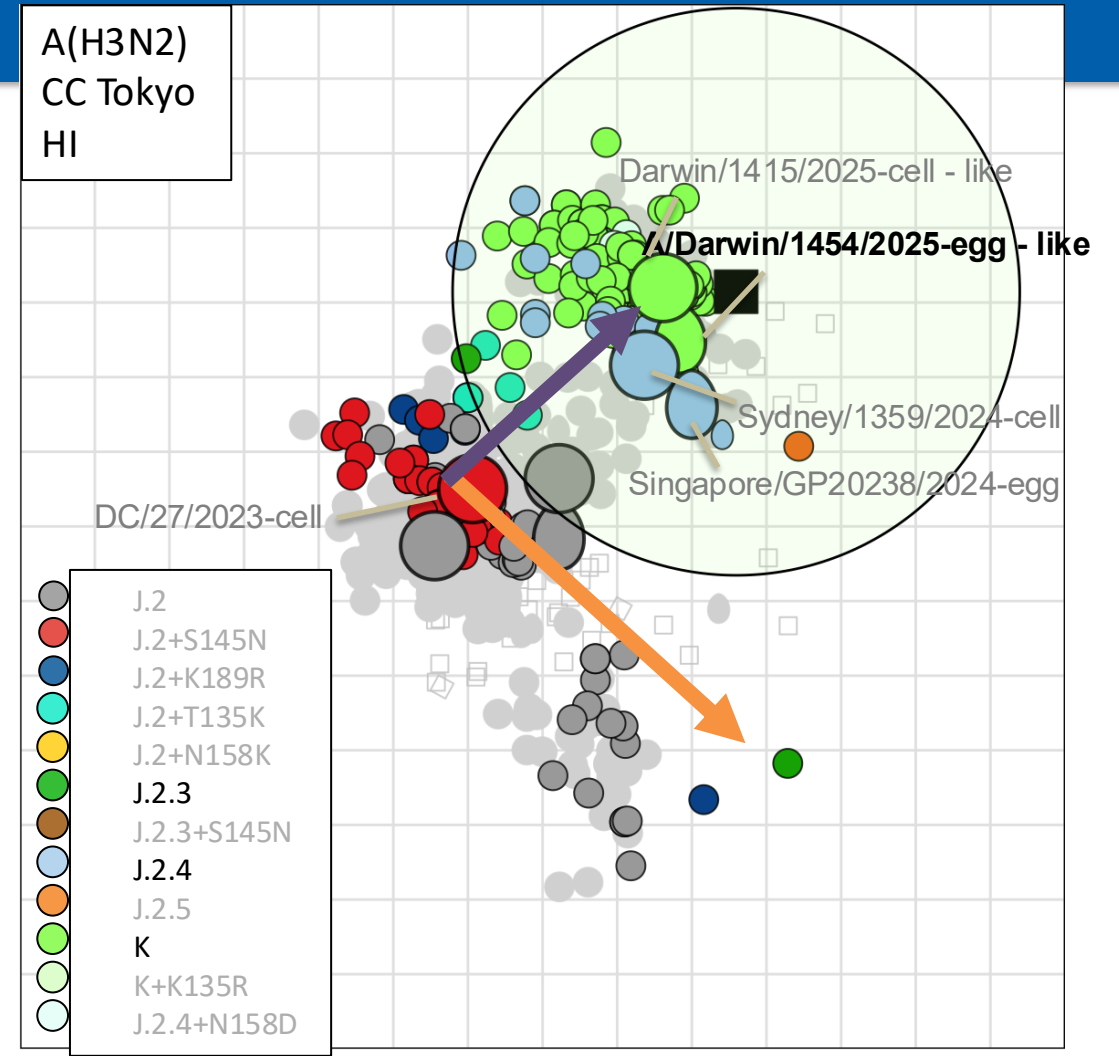
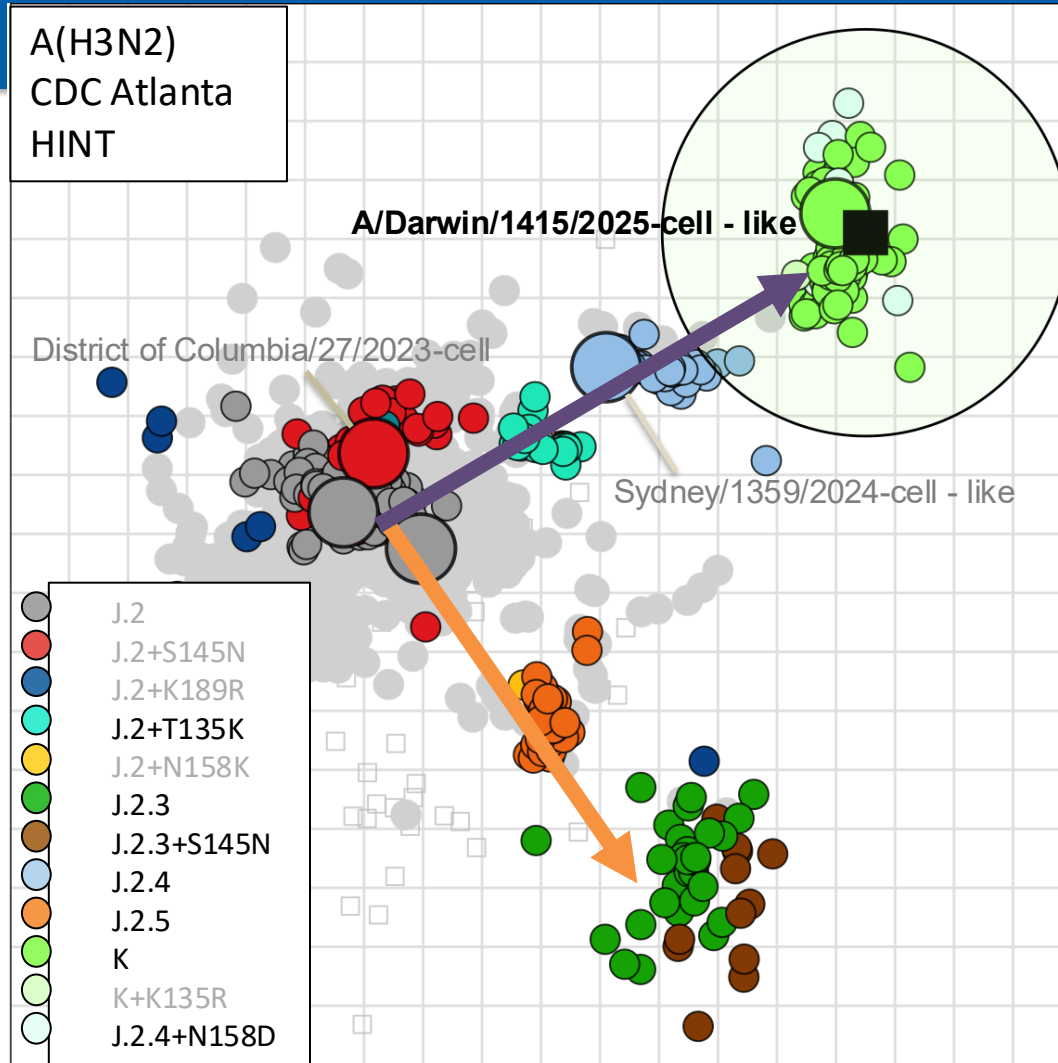
# HI antigenic analysis of A(H3N2) viruses

	HA subclade	Reference Antisera					
		Cell	Cell	Cell	Egg	Cell	Egg
		Cro/10136RV	Neth/10685	Syd/1359	Sing/GP20238	Dar/1415	Dar/1454
		J.2	J.2.3	J.2.4	J.2.4	K	K
<b>Reference virus</b>							
A/Croatia/10136RV/2023	J.2	320	<40	40	40	<40	<40
A/Netherlands/10685/2024	J.2.3	80	640	<40	<40	<40	<40
A/Sydney/1359/2024	J.2.4	160	40	320	2560	640	640
A/Singapore/GP20238/2024	J.2.4	160	160	640	2560	320	320
A/Darwin/1415/2025	K	40	40	160	640	640	640
A/Darwin/1454/2025	K	<40	80	320	1280	1280	640
<b>Test virus</b>							
A/Darwin/2100/2025	J.2.2	320	<40	40	40	<40	<40
A/Singapore/GP14404/2025	J.2.2	320	<40	40	40	<40	<40
A/Victoria/2797/2025	J.2.4	<40	<40	320	640	640	640
A/Sri Lanka/69/2025	J.2.4	80	40	320	2560	640	640
A/Tasmania/1035/2025	K	<40	<40	80	320	320	320
A/Canberra/980/2025	K	<40	<40	80	640	640	320
A/Sri Lanka/111/2025	K	40	<40	160	640	1280	1280
A/Cambodia/IKCM250152/2025	K	<40	<40	160	640	640	320
A/New Caledonia/195/2025	K	<40	<40	80	640	640	640
A/Nepal/S3684/2025	K	<40	<40	80	320	640	640

Source: WHO CC, Australia

VCM Information meeting: <https://www.youtube.com/@who>

# A(H3N2) antigenic cartography



A/Darwin/1415/2025-cell-like serum circle (within 8-fold of homologous titer) A/Darwin/1454/2025-egg-like serum circle (within 8-fold of homologous titer)

Source: University of Cambridge

VCM Information meeting: <https://www.youtube.com/@who>

# Antigenic analysis of A(H3N2) viruses in HI and NT assays

Antisera to northern hemisphere 2025-2026 vaccine virus antigens

WHO CC	A/District of Columbia/27/2023-like Cell 2a.3a.1 (J2) by HI	Low ( $\geq 8$ fold)	WHO CC	A/Croatia/10136RV/2023-Like Egg 2a.3a.1 (J2) by HI	Low ( $\geq 8$ fold)
CDC	19 (9%)	202 (91%)	CDC	8 (4%)	213 (96%)
CNIC	946 (43%)	1231 (57%)	CNIC	520 (24%)	1657 (76%)
FCI	46 (18%)	216 (82%)	FCI	20 (8%)	242 (92%)
NIID	33 (11%)	260 (89%)	NIID	8 (3%)	285 (97%)
VIDRL	124 (9%)	1329 (91%)	VIDRL	47 (3%)	1406 (97%)
<b>Total</b>	<b>1168 (27%)</b>	<b>3238 (73%)</b>	<b>Total</b>	<b>603 (14%)</b>	<b>3803 (86%)</b>

WHO CC	A/District of Columbia/27/2023 -like Cell 2a.3a.1 (J.2) by NT	Low ( $\geq 8$ fold)	WHO CC	A/Croatia/10136RV/2023 -like Egg 2a.3a.1 (J.2) by NT	Low ( $\geq 8$ fold)
CDC	14 (12%)	104 (88%)	FCI	15 (25%)	46 (75%)
FCI	23 (26%)	64 (74%)	<b>Total</b>	<b>15 (25%)</b>	<b>46 (75%)</b>
<b>Total</b>	<b>37 (18%)</b>	<b>168 (82%)</b>			

"Low" represented titers  $\geq 8$ -fold lower than vaccine strain homologous titer

VCM Information meeting: <https://www.youtube.com/@who>

# Antigenic analysis of A(H3N2) viruses in HI and VN assays

Antisera to southern hemisphere 2026 vaccine virus antigens

WHO CC	A/Sydney/1359/2024-like Cell 2a.3a.1 (J.2.4) by HI	Low ( $\geq 8$ fold)	WHO CC	A/Singapore/GP20238/2024-Like Egg 2a.3a.1 (J.2.4) by HI	Low ( $\geq 8$ fold)
CDC	167 (76%)	54 (24%)	CDC	110 (85%)	19 (15%)
CNIC	405 (72%)	154 (28%)	CNIC	368 (22%)	1279 (78%)
FCI	102 (39%)	160 (61%)	FCI	115 (44%)	147 (56%)
NIID	207 (92%)	18 (8%)	NIID	198 (88%)	27 (12%)
VIDRL	1274 (88%)	179 (12%)	VIDRL	1184 (81%)	269 (19%)
<b>Total</b>	<b>2155 (79%)</b>	<b>565 (21%)</b>	<b>Total</b>	<b>1975 (53%)</b>	<b>1741 (47%)</b>

WHO CC	A/Sydney/1359/2024-like Cell 2a.3a.1 (J.2.4) by VN	Low ( $\geq 8$ fold)	WHO CC	A/Singapore/GP20238/2024-Like Egg 2a.3a.1 (J.2.4) by VN	Low ( $\geq 8$ fold)
CDC	96 (81%)	22 (19%)	FCI	11 (13%)	76 (87%)
FCI	73 (84%)	14 (16%)	<b>Total</b>	<b>11 (13%)</b>	<b>76 (87%)</b>
<b>Total</b>	<b>169 (82%)</b>	<b>36 (18%)</b>			

“Low” represented titers  $\geq 8$ -fold lower than vaccine strain homologous titer

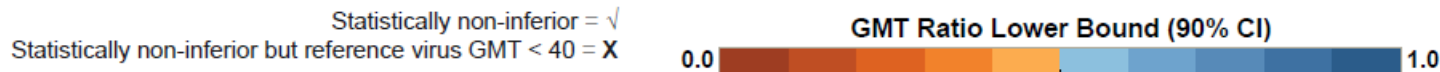
VCM Information meeting: <https://www.youtube.com/@who>

# Human post-vaccination serum analysis of A(H3N2) viruses (CDC data)

				J.2	J.2.3	J.2.4	K	J.2.5
				-	+N145S +N158K +K189R	+T135K (CHO-) +N145S +K189R	+T135K (CHO-) +N145S +N158D +I160K +K189R	+N158K
				*DC/27	AK/08	MS/37	WI/114	KY/29
				SIAT	SIAT	SIAT	SIAT	SIAT
A/DISTRICT OF COLUMBIA/27/2023 SIAT [REF]	Pediatric (6-35M)	USA	ccIIIV3 (cell)	139	50	88	61	√
	Pediatric (3-8Y)	USA	ccIIIV3 (cell)	437	197	√	279	288
	Adult (18-49Y)	USA	ccIIIV3 (cell)	279	174	√	169	√
			RIV3 (recombinant)	1413	√	√	780	√
	Elderly (≥65Y)	USA	HD-IIIV3 (egg)	166	77	√	102	√

Geometric Mean Titer (GMT) ratios between reference and test antigens are calculated with 90% (CI) confidence intervals for each cohort and panel location. Unadjusted model results are shown. If the CI lower bound is greater than 50%, it is statistically non-inferior (95% confidence level); otherwise, it is *possibly* inferior. Heat map cells are colored using the GMT ratio lower bound. Blue indicates statistical non-inferiority and orange denotes *possible* inferiority. Numbers shown are post-vaccination GMTs for the unadjusted model. They are shown for *reference antigens*\* and possibly inferior test antigens. Marks, √ or X, denote statistically significant non-inferiority when the reference virus GMT is ≥40 or <40, respectively.

Strains abbreviated: A/ALASKA/08/2025 (AK/08); A/DISTRICT OF COLUMBIA/27/2023 (DC/27); A/KENTUCKY/29/2024 (KY/29); A/MISSISSIPPI/37/2025 (MS/37); A/WISCONSIN/114/2025 (WI/114).



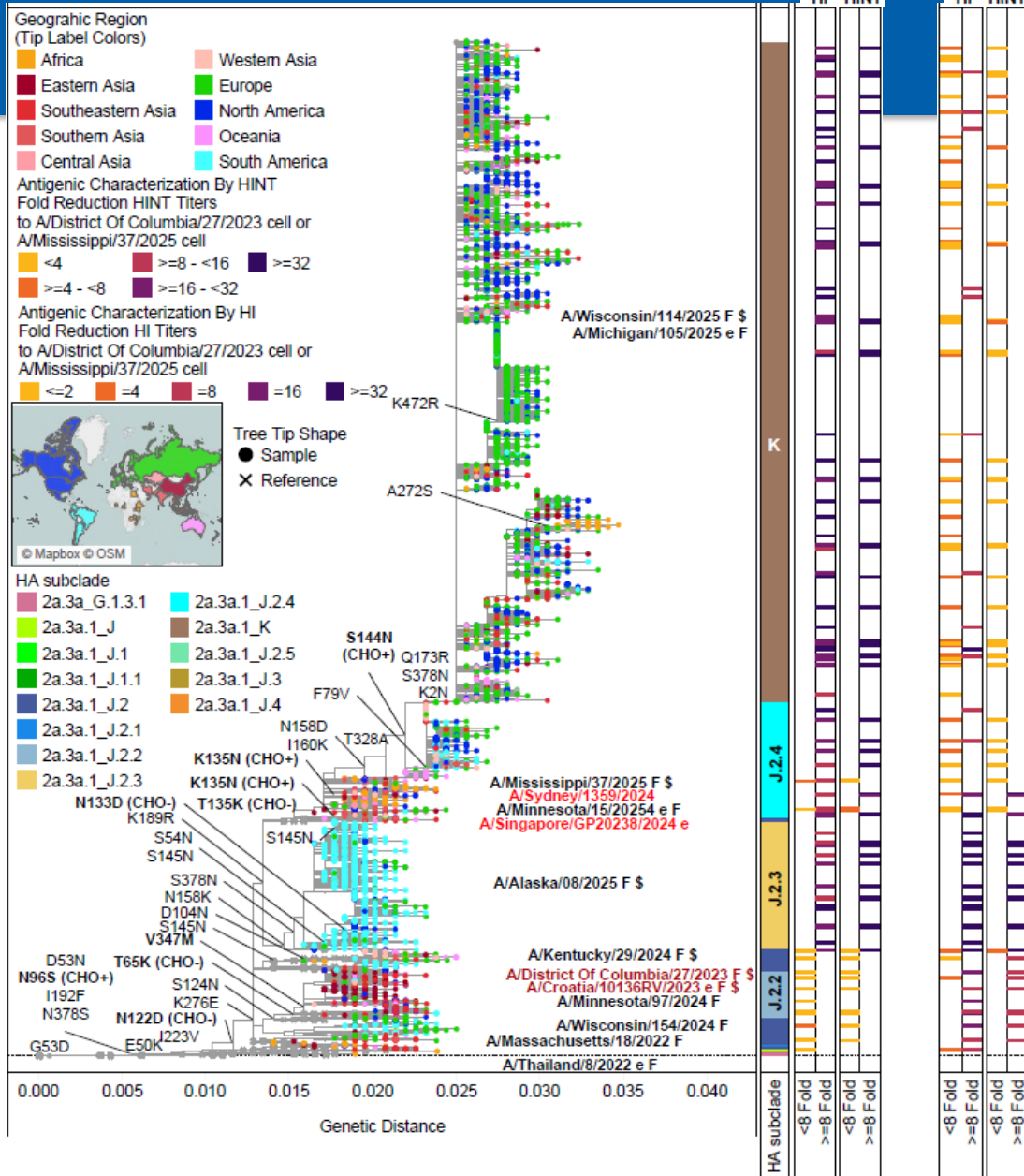
# A(H3N2) Integrated Genotype and Phenotype Analysis

Antigenic Characterization By HINT  
 Fold Reduction HINT Titers  
 to A/District Of Columbia/27/2023 cell or  
 A/Mississippi/37/2025 cell

<4    >=8 - <16    >=32  
 >=4 - <8    >=16 - <32

Antigenic Characterization By HI  
 Fold Reduction HI Titers  
 to A/District Of Columbia/27/2023 cell or  
 A/Mississippi/37/2025 cell

<=2    =4    =8    =16    >=32



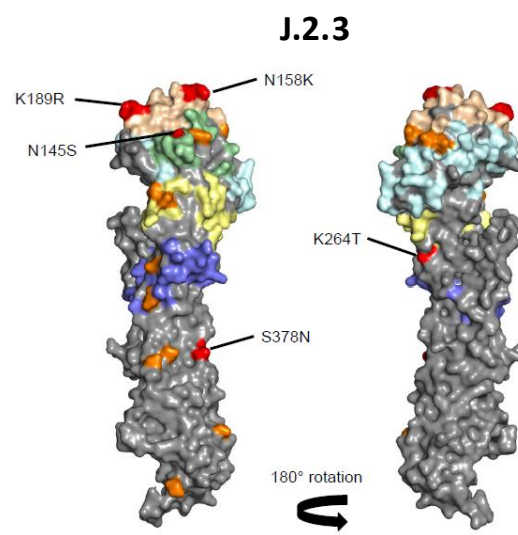
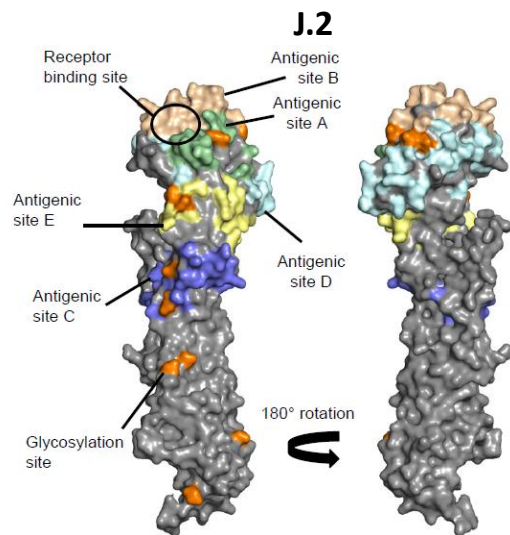
Data Source:

HA and NA clade/subclades:  
<https://clades.nextstrain.org/>

# A(H3N2) Circulating Subclades

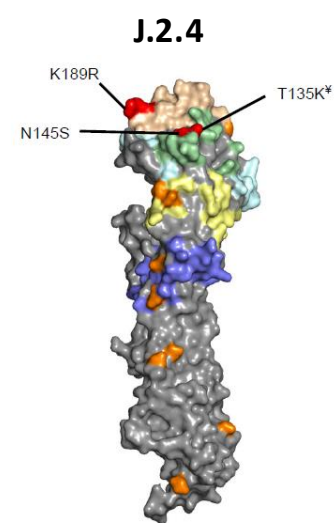
- Multiple subclades with additional HA substitutions co-circulated
- Ferret antisera to A/District of Columbia/27/2023 (J.2) viruses show reduced to poor reactivity with viruses from HA subclades J.2.3, J.2.4 and K
- Ferret antisera to A/Sydney/3549/2024-like (J.2.4) viruses show reduced to poor reactivity with viruses from HA subclades J.2.3 but recognised most J.2.4 viruses and many subclade K viruses well

**A/District of Columbia/27/2023  
2025SH and 2025-26NH Vaccine**



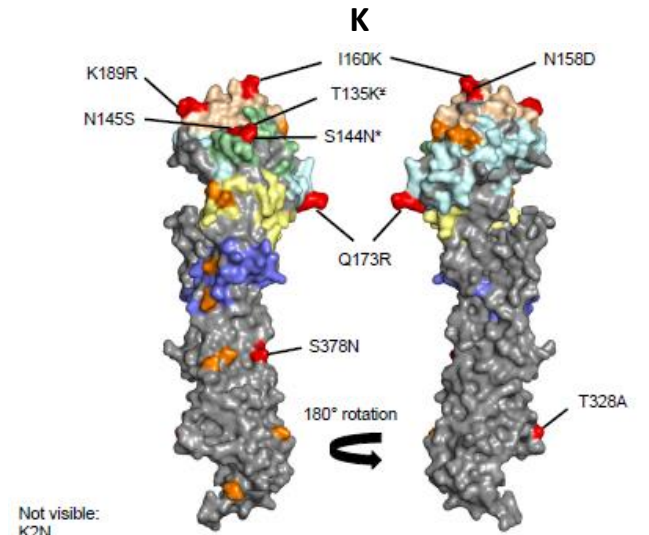
Emerged Fall 2024

**A/Sydney/3549/2024  
2026 SH Vaccine**



Emerged Summer 2024

**A/Darwin/1415/2025  
2026-27NH Vaccine**



Emerged Summer 2025

# Influenza A(H3N2): antiviral susceptibility

## Neuraminidase inhibitors

- Of 4,458 influenza A(H3N2) viruses examined by genetic and/or phenotypic analyses, two viruses showed evidence of reduced susceptibility to NAIs; both had an NA E119V substitution.

## Endonuclease inhibitors

- Of 4,828 A(H3N2) viruses examined by genetic and/or phenotypic analyses, nine viruses showed evidence of reduced susceptibility to the endonuclease inhibitor baloxavir marboxil:
  - 3 had a PA I38T substitution
  - 3 had a PA I38I/T substitution
  - 2 had a PA I38I/M substitution
  - 1 had a PA E199E/G substitution

# Influenza A(H3N2) summary (1)

## Phylogenetics of A(H3N2) HA genes

- The vast majority of viruses belonged to one of the J.2 subclades, expressing HA N122D and K276E substitutions.
- HA genes have diversified with many subclades
  - J.2.2 (characterized by S124N),
  - J.2.3 (characterized by N158K, K189R and S378N),
  - J.2.4 (characterized by T135K [a potential loss of an N-glycosylation site] and K189R)
  - K (formerly designated as J.2.4.1; characterized by K2N, S144N [a potential addition of an N-glycosylation site], N158D, I160K, Q173R, T328A and S378N).
- During this reporting period, subclade K viruses were detected in all regions and predominated in many countries.
- There was still circulation of other J.2 subclades, notably J.2 or J.2.3 in South America, J.2.2 or J.2.4 in Africa and Asia.

# Influenza A(H3N2) summary (2)

## Antigenic characteristics of A(H3N2) viruses

- Post-infection ferret antisera raised against cell culture-propagated A/District of Columbia/27/2023-like and egg-propagated A/Croatia/10136RV/2023-like (clade 2a.3a.1, subclade J.2) viruses, representing the A(H3N2) component for the NH 2025-2026 influenza vaccines, showed poor recognition with recently circulating subclade J.2.3 (e.g., A/Netherlands/10685/2024), J.2.4 (e.g., A/Sydney/1359/2024) and K (e.g., A/Darwin/1415/2025) viruses.
- Ferret antisera raised against reference viruses from J.2.3 subclades showed good recognition of viruses expressing HA from J.2.3, but poor recognition of other subclades.
- Post-infection ferret antisera raised against cell culture-propagated A/Sydney/1359/2024-like and egg-propagated A/Singapore/GP20238/2024-like J.2.4 viruses, representing SH 2026 influenza vaccines, recognised most J.2.4 viruses and many subclade K viruses well.
- However, subclade K viruses and J.2.4 viruses with HA substitutions F79V, S144N (addition of a potential N-glycosylation site), N158D, I160K, T328A were better recognised by post-infection ferret antisera raised against cell culture-propagated A/Darwin/1415/2025-like and egg-propagated A/Darwin/1454/2025-like (subclade K) viruses.

VCM Information meeting: <https://www.youtube.com/@who>

# Influenza A(H3N2) summary (3)

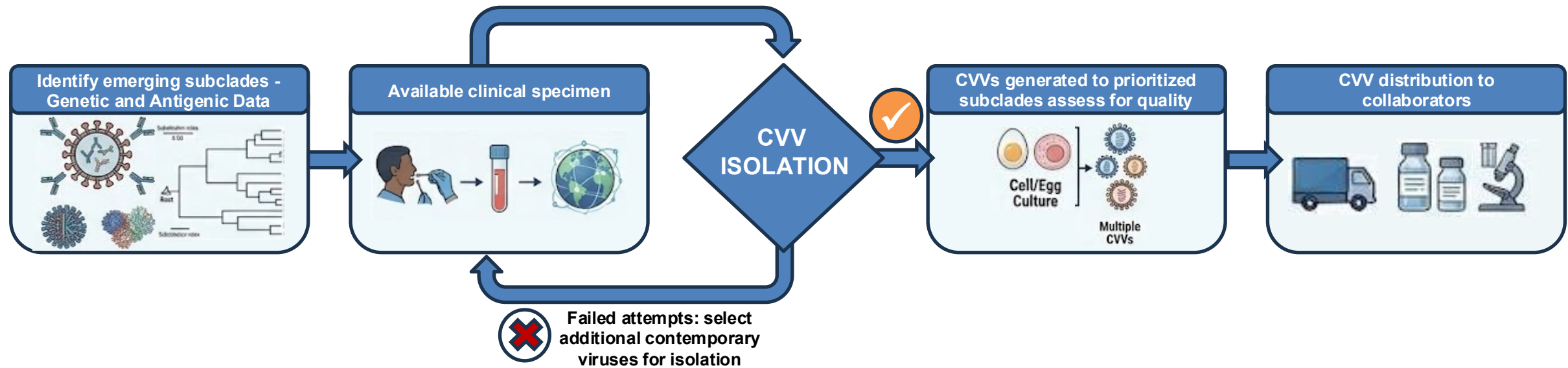
## Human serology studies

- Human serology studies were conducted using the serum panels by HI and virus neutralization (VN) assays with recent circulating A(H3N2) viruses with HA genes from subclades J.2, J.2.2, J.2.3, J.2.4, J.2.5 and K.
- When compared to titers against cell-propagated A/District of Columbia/27/2023-like vaccine reference viruses, post-vaccination HI GMTs or VN GMTs against many of the recent viruses in all subclades tested were significantly reduced in many serum panels.

**The data supported recommending a cell-propagated A/Darwin/1415/2025 (H3N2)-like (K) virus and an egg-propagated A/Darwin/1454/2025 (H3N2)-like (K) virus as the A(H3N2) vaccine antigens for the 2026-2027 northern hemisphere.**

# The analysis process *never* stops!

**Goal** – To create CVVs of emerging subclades for cell-based and egg-based vaccines ahead of Vaccine Consultation Meetings



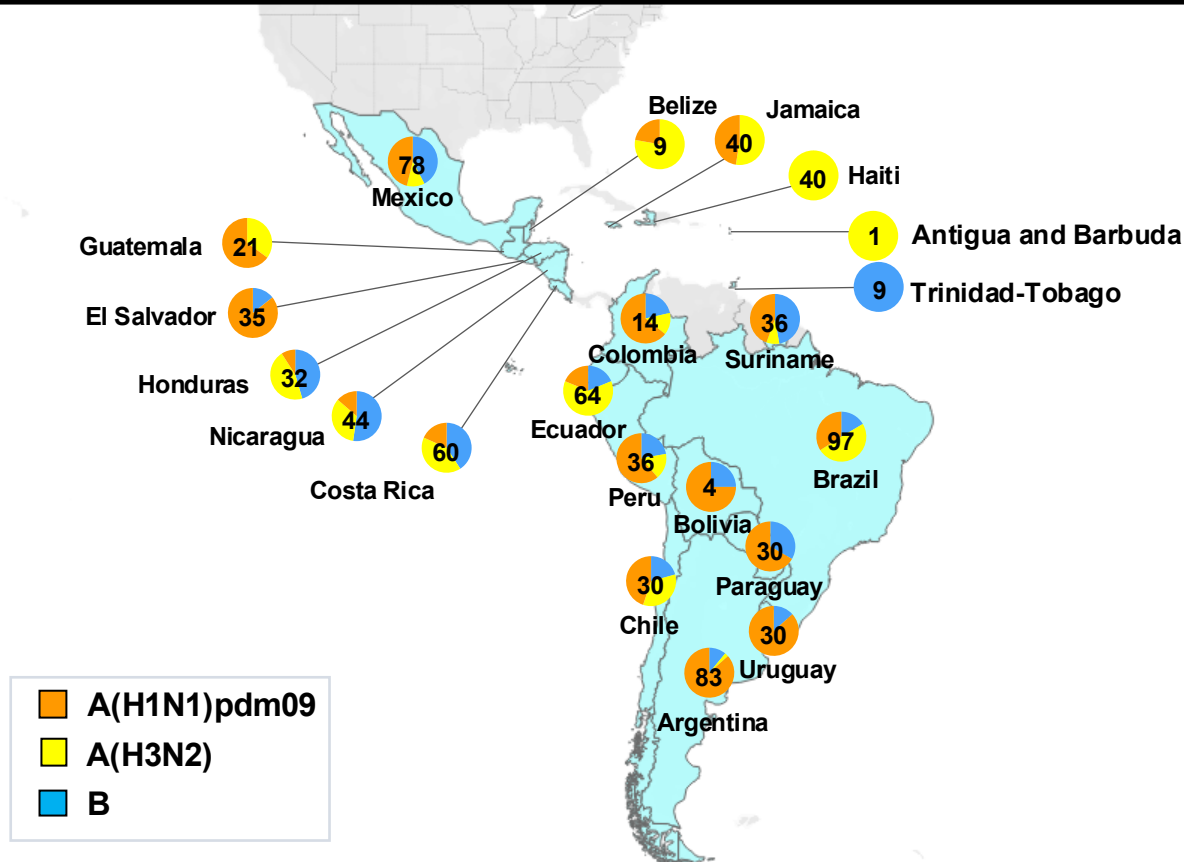
## Prioritization Process

- New CVVs are created as needed for each type/subtype
- Epidemiologic and Virologic surveillance data drives prioritization

# Specimens Received at CDC

February 1, 2025 to present

Thank you for submitting influenza virus positive specimens to WHO CC at CDC. Your contributions ensure the best possible representation of circulating viruses to inform the recommendations for the composition of seasonal influenza vaccines and to analyze antiviral susceptibility.



**CDC International Sender Reports**  
January 2026 – for shipments received through September 20, 2025

April 2026 – for shipments received since October 1, 2025

# Seasonal Influenza Specimen Shipping Guidelines for CDC

**CDC can support up to 4 shipments a year:**

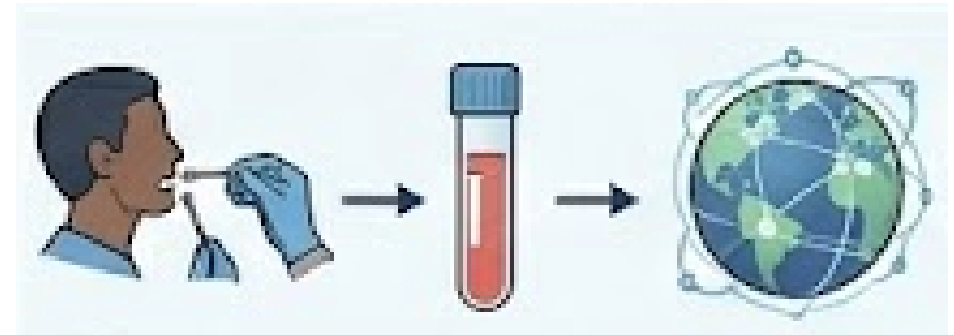
Please contact [InfluenzaVirusSurveillance@cdc.gov](mailto:InfluenzaVirusSurveillance@cdc.gov) to initiate shipments.

## **Recommended timing of shipments:**

- 1) One shipment ensuring *receipt* of the shipments at CDC **by December 31, 2025** (coincides with February VCM).
- 2) One shipment ensuring *receipt* at CDC between **April and June 2026**.
- 3) One shipment ensuring *receipt* at CDC **by August 1, 2026** (coincides with September VCM).
- 4) One shipment ensuring *receipt* at CDC between **October and November 2026**.

## **Ideal specimens:**

- Influenza positive and SARS-CoV-2 negative original clinical specimens
- CT values < 28 for either InfA or InfB
- 0.5 mL volume
- 30 recently collected (<6 weeks)
  - 10 A(H1N1)pdm09
  - 10 A(H3N2)
  - 10 B/Victoria



**Reminder** – if you have **Influenza A Unsubtypeables** --- immediately contact [flusupport@cdc.gov](mailto:flusupport@cdc.gov) to assist

# Thank you!

## CDC Influenza Division

## CDC Traveler's Genomic Surveillance

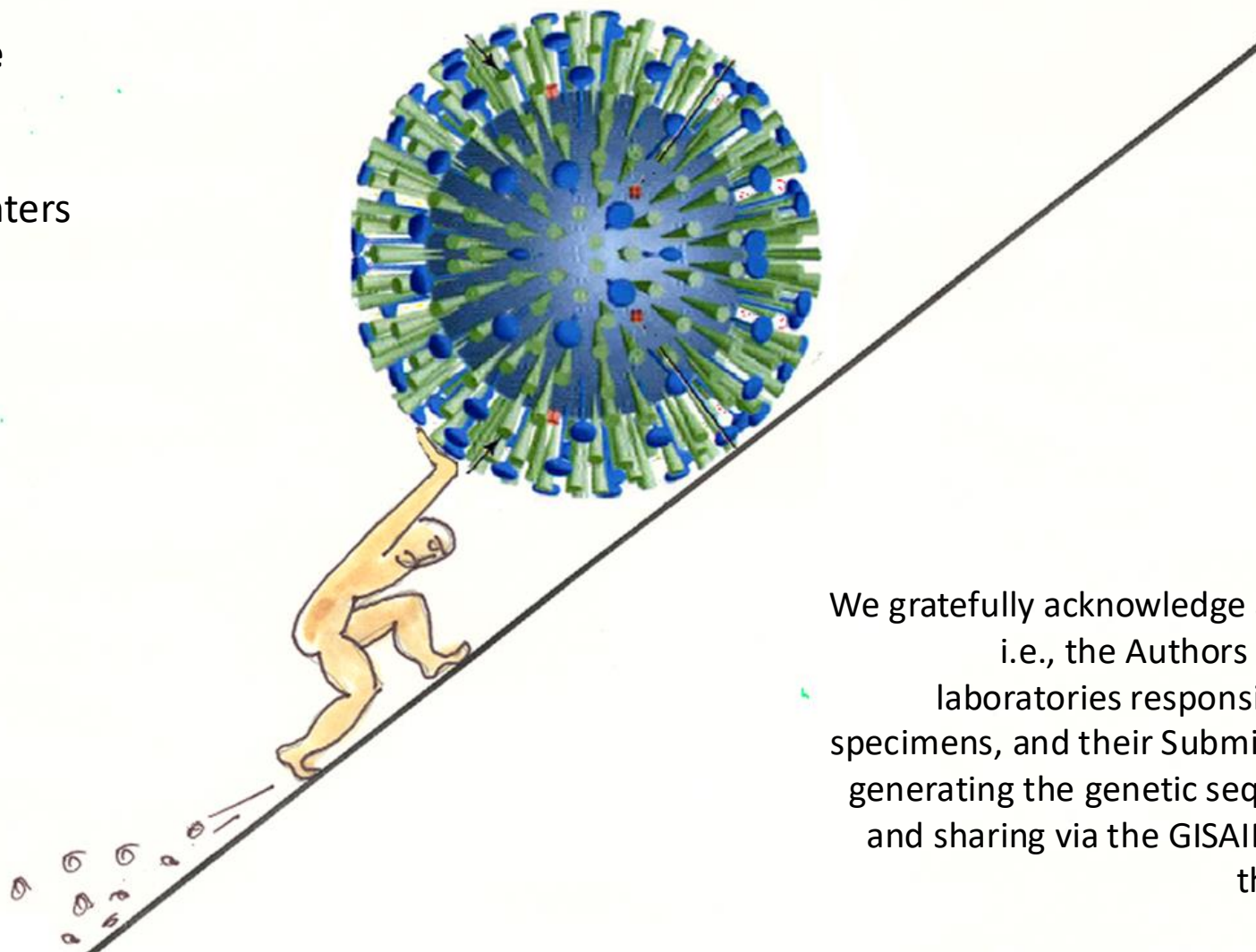
## US Public Health Laboratories

- National Influenza Reference Centers
- APHL



## Global Influenza Surveillance and Response System

- National Influenza Centers
- WHO CCs/ERL
- WHO H5 Ref Labs
- University of Cambridge
- NextStrain
- Previr



We gratefully acknowledge all data contributors, i.e., the Authors and their Originating laboratories responsible for obtaining the specimens, and their Submitting laboratories for generating the genetic sequence and metadata and sharing via the GISAID Initiative, on which this research is based.

