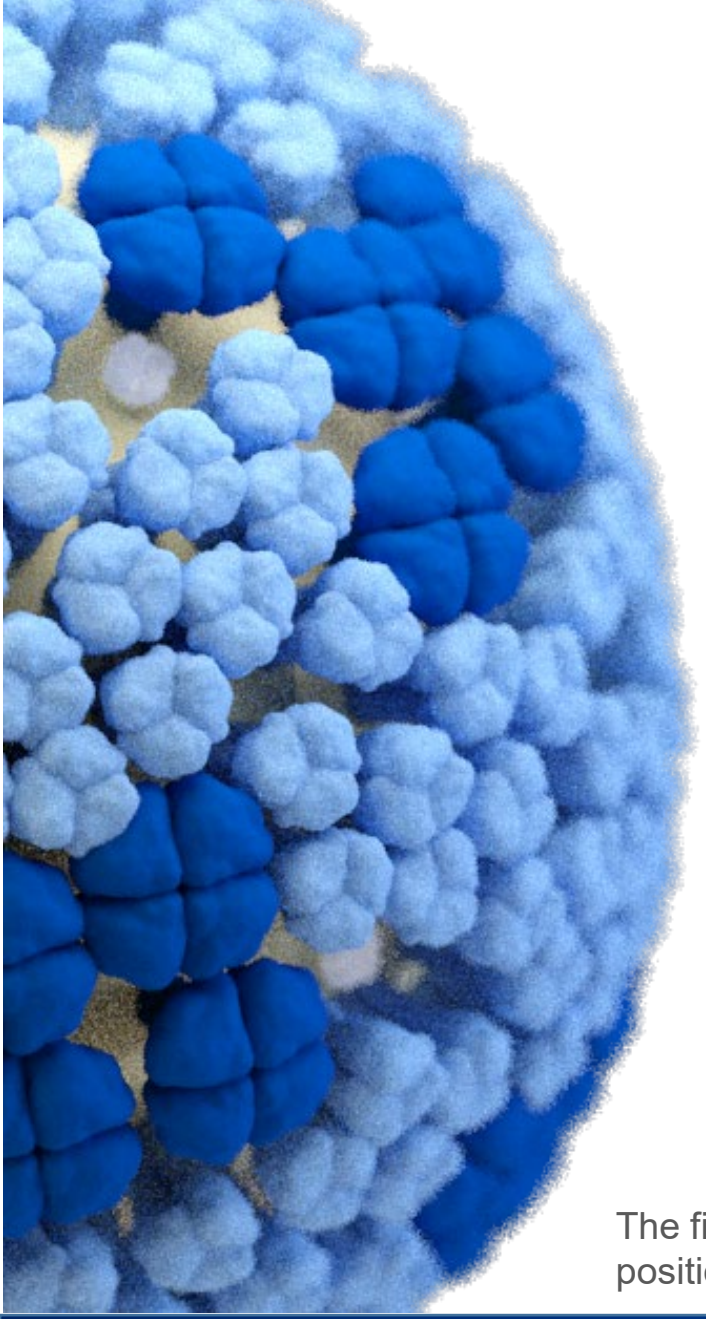


Information For The Vaccine And Related Biological Products Advisory Committee CBER, FDA

Global Influenza Virus Surveillance and Characterization March 12th, 2026

Rebecca Kondor, Ph.D.
Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Atlanta, GA 30333

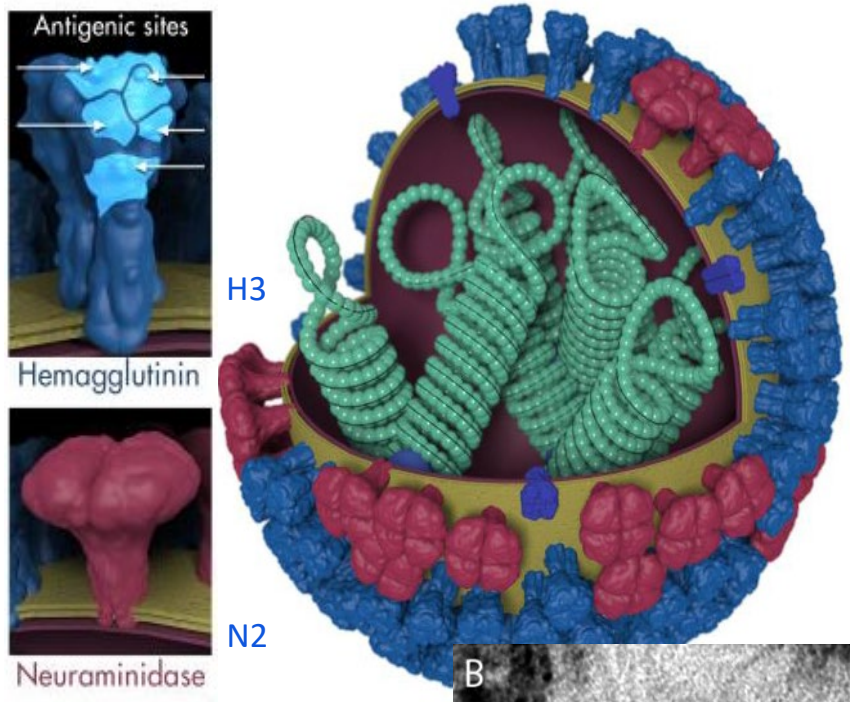
Four Different Influenza Viruses Cause Seasonal Epidemics

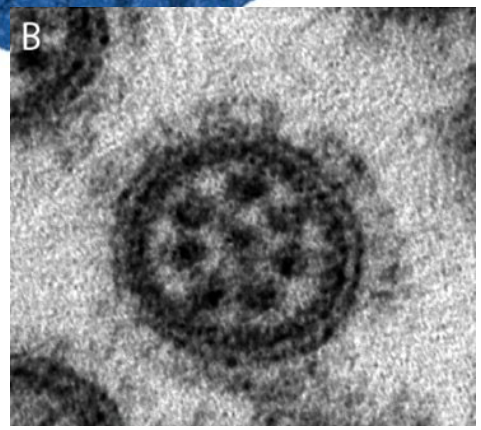
- Co-circulating human influenza viruses
  - Influenza A(H3N2)
  - Influenza A(H1N1)pdm09
  - Influenza B/Victoria
  - *Influenza B/Yamagata*
    - Not detected after March 2020

Alphainfluenzavirus

Betainfluenzavirus

- Major antigens (surface proteins)
  - **Hemagglutinin** – Virus attachment protein
    - Vaccines induce antibodies to block this protein
  - **Neuraminidase** – Important for exit from infected cell
    - Antibodies and antiviral drugs inhibit this protein
- Genomes (~13.5Kb): 8 segments negative sense RNA
  - Enables reassortment during co-infections (2 in -> 256 out)





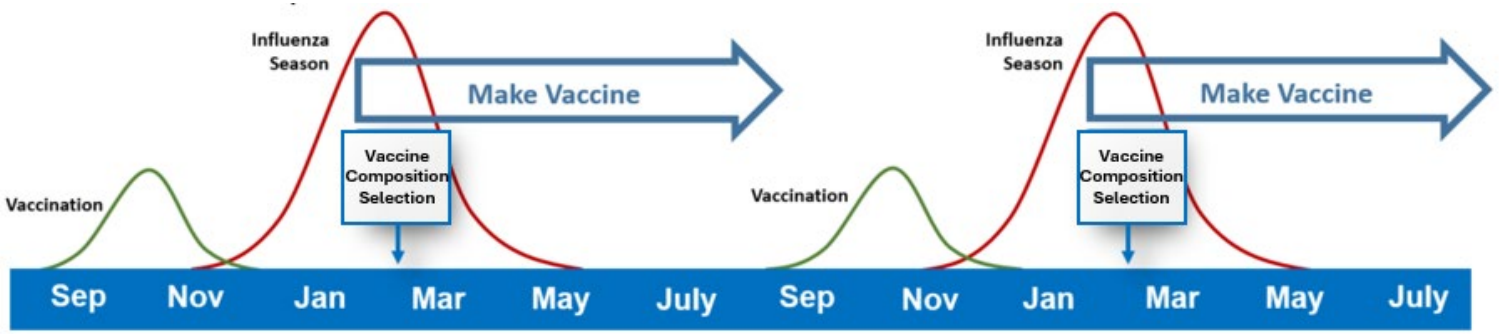
Thin Section EM. T. Noda, et al, Nature 439 (7075):490-492, 2006.

Influenza Vaccine Composition Recommendations
Platforms and Timelines

- WHO convenes technical consultations to recommend viruses for each component of influenza vaccines: A(H1N1)pdm09, A(H3N2) and B/Victoria lineage
- Recommendations are divided into ***Egg-based vaccines*** and ***Cell culture-, recombinant protein- or nucleic acid-based vaccines*** encompassing the currently licensed vaccine manufacturing processes and those in clinical development
  - The virus prototype chosen could have a different name between the platforms but both represent the most suitable candidate for the new subclade
- FDA convenes VRBPAC to recommend viruses for US Vaccines

Timing of Influenza Vaccine Recommendations:

- February for the following northern hemisphere influenza season
- September for the following southern hemisphere influenza season
- The recommendation dates are chosen to provide approximately 6-8 months for the production, regulatory approval and distribution of the manufactured vaccines



Influenza Vaccine Composition Meeting Decision Process

Goal – To identify influenza antigen(s) that will elicit immunity against diverse/diverging viruses that will likely co-circulate in the future. Ideal antigens confer breadth of immunity to multiple subclades of viruses and reduce risk(s).

Review influenza activity, trends, geography

Epidemiologic and clinical data

Where are recent epidemics occurring

Virus surveillance

Global Influenza Surveillance and Response System (GISRS) labs test 50-150 thousand samples per week year-round: identify influenza positive specimens; type and influenza A subtype

Review laboratory data of recently collected viruses

Genomic Characterization

Genetic subclades that have emerged; geographic spread and proportion; forecasting predominance

Antigenic Characterization

Level of antigenic drift from progenitors and/or vaccine references

Data Sharing and Integration across GISRS

- Genetic and Antigenic data integration
- Phylogenetics
- Phylogeography
- Fitness forecasting
- Antigenic cartography
- Antiviral susceptibility
- Human Serum Panels
- Candidate Vaccine Virus (CVV) Reagent sharing

Human serology data and vaccine effectiveness

Post-vaccination and post-exposure studies

Comparative analysis of co-circulating antigenic variants to identify those that pose the greatest risk of immune escape

Global Influenza Vaccine Effectiveness (GIVE) Collaboration

VE studies– previous season and current season interim results

Review Candidate Vaccine Virus availability

New CVVs

- Analysis of the availability and characterization status of candidate vaccine viruses for each platform
- Review of cell or egg-adaptation mutations in CVVs
- Review of high-growth reassortants

Global Influenza Vaccine Composition Recommendations for the 2026-2027 Northern Hemisphere

It is recommended that vaccines for use in the 2026-2027 northern hemisphere influenza season contain the following:

Trivalent: Egg-based Vaccines
- **an A/Missouri/11/2025 (H1N1)pdm09-like virus* HA subclade D.3.1;**
- **an A/Darwin/1454/2025 (H3N2)-like virus** HA subclade K; and**
- **a B/Tokyo/EIS13-175/2025** HA subclade C.3.1 (B/Victoria lineage)-like virus.**

Trivalent: Cell-, recombinant protein- or nucleic acid-based Vaccines
- **an A/Missouri/11/2025 (H1N1)pdm09-like virus* HA subclade D.3.1;**
- **an A/Darwin/1415/2025 (H3N2)-like virus** HA subclade K; and**
- **a B/Pennsylvania/14/2025** HA subclade C.3.1 (B/Victoria lineage)-like virus.**

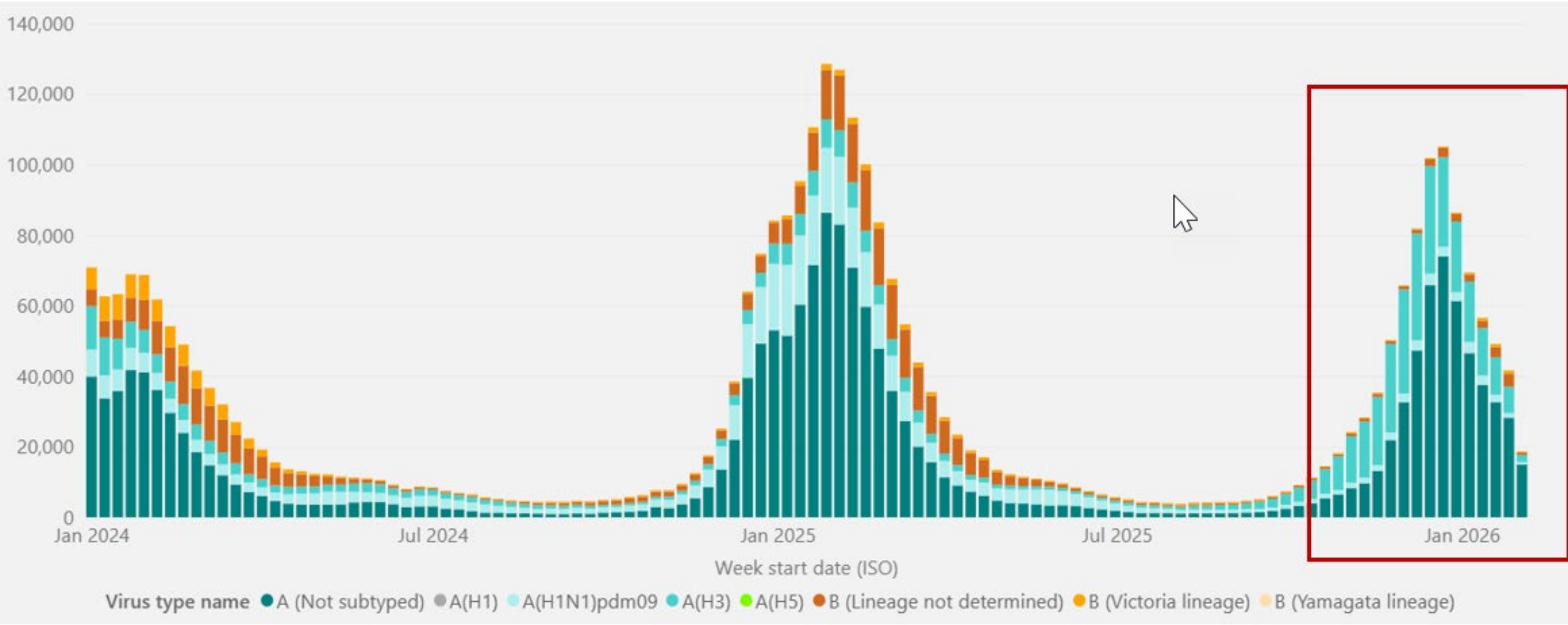
*** Different from what was recommended for the 2025-2026 northern hemisphere season but the same as the 2026 southern hemisphere season**
****Different from what was recommended for the 2026 southern hemisphere and 2025-2026 northern hemisphere seasons**

Recommendation and technical reports available at: https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations

Candidate vaccine viruses & publications

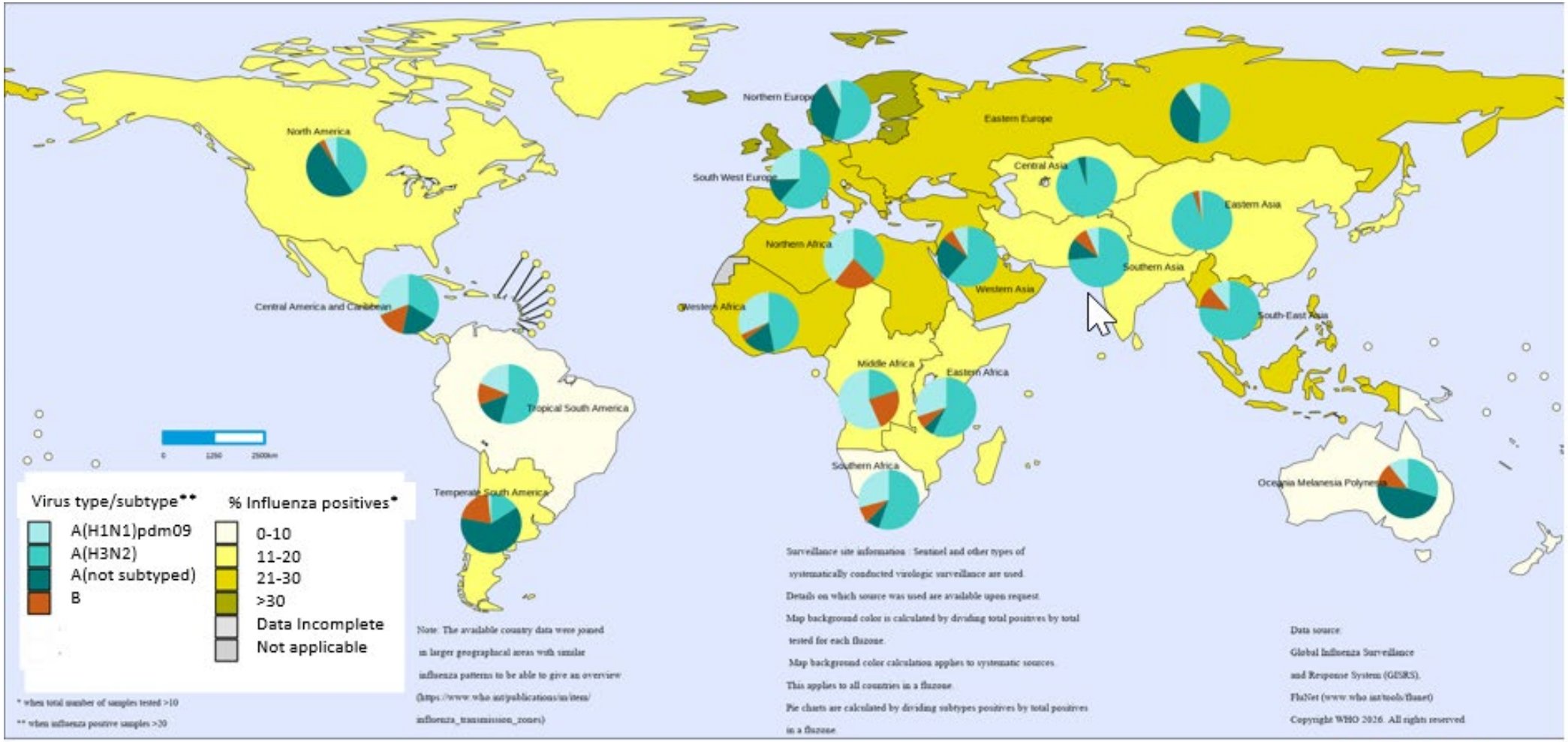
- The recommended candidate viruses for vaccine development and production for NH 2026-2027 and FAQ;
  - https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations
- Candidate vaccine viruses and reagents
  - https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/candidate-vaccine-viruses
- Guidance to tropical and subtropical countries: which formulation (northern hemisphere vs. southern hemisphere) and when to start vaccination:
  - https://www.who.int/teams/global-influenza-programme/vaccines/vaccine-in-tropics-and-subtropics
- Zoonotic influenza summary reports and candidate vaccine viruses on H5/H7/H9 and variant influenza vaccine viruses:
  - https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations
  - https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/zoonotic-influenza-viruses-and-candidate-vaccine-viruses

Global Circulation of Seasonal Influenza Viruses Since 2024



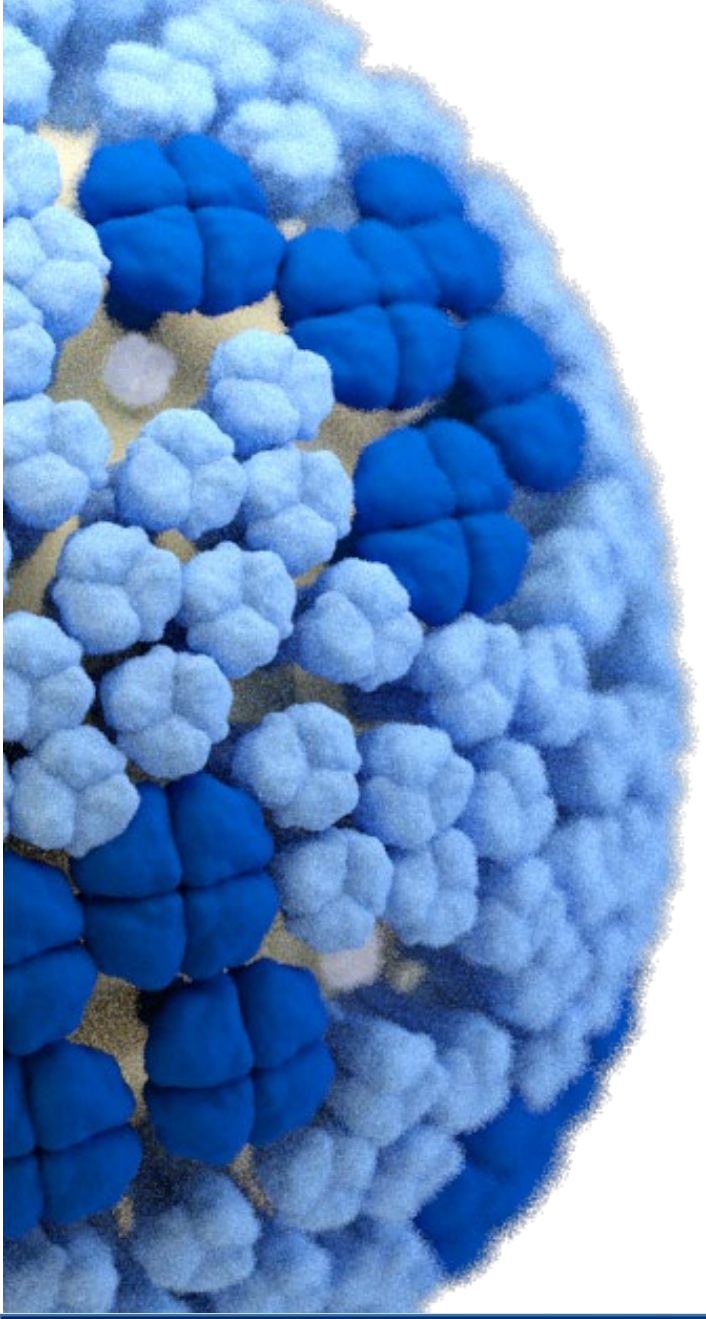
VCM Information meeting: https://www.youtube.com/@who

Influenza activity and global distribution of type/subtype
September 2025 – January 2026



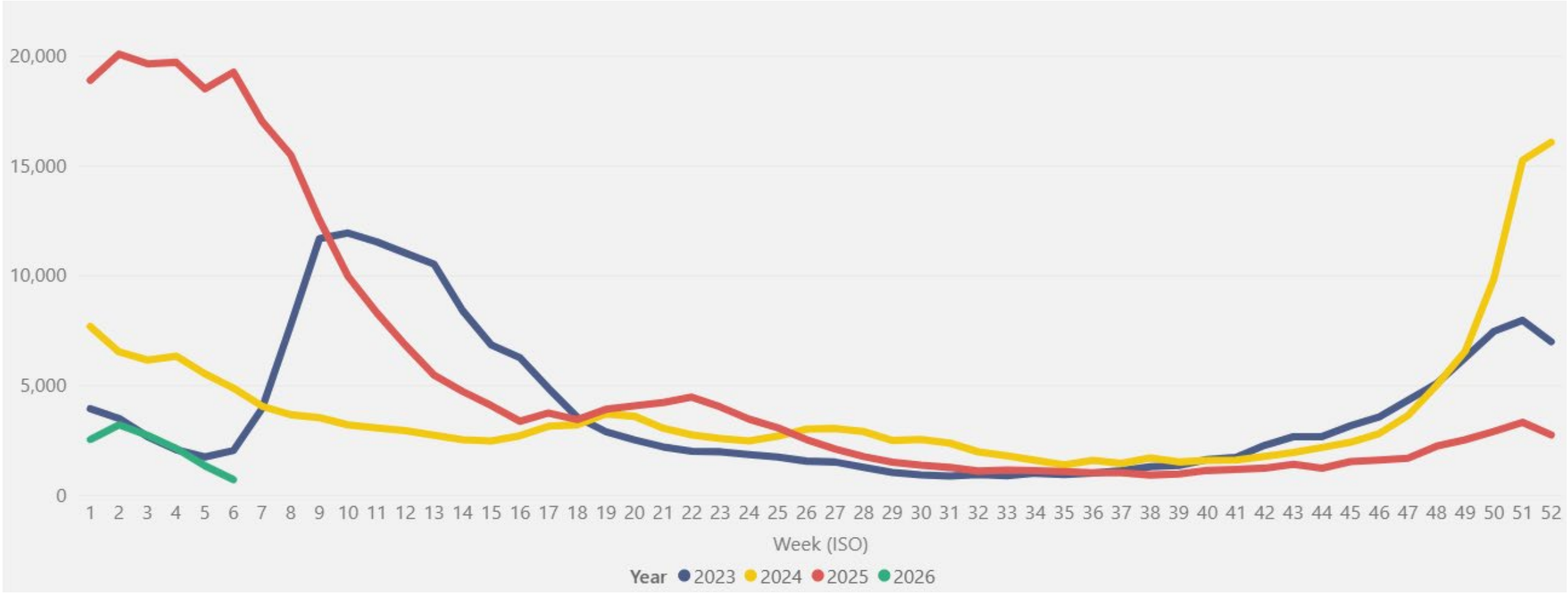
World Health Organization

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



A(H1N1)pdm09 Viruses

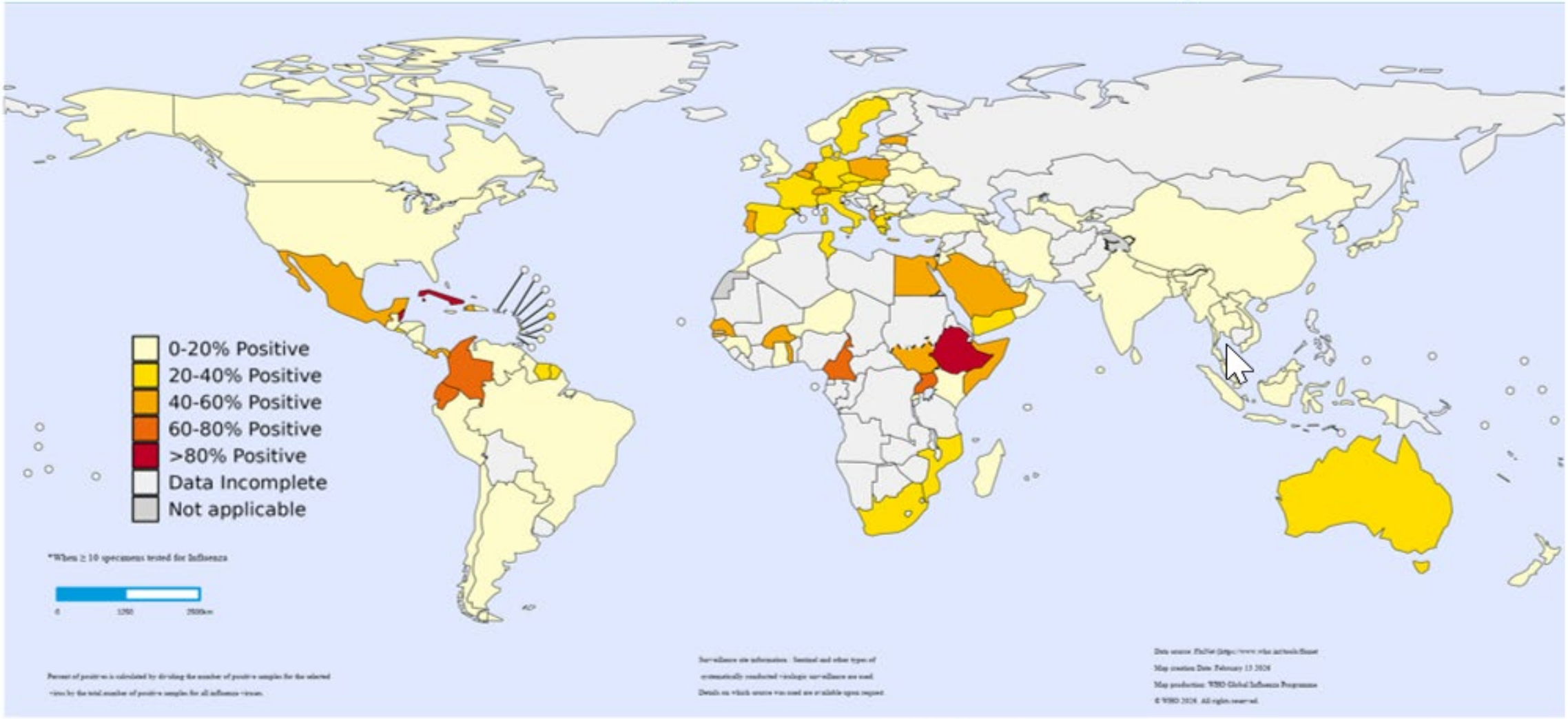
Number of A(H1N1)pdm09 viruses detected by GISRS



GISRS GLOBAL INFLUENZA SURVEILLANCE & RESPONSE SYSTEM

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

Influenza A(H1N1)pdm09 activity



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

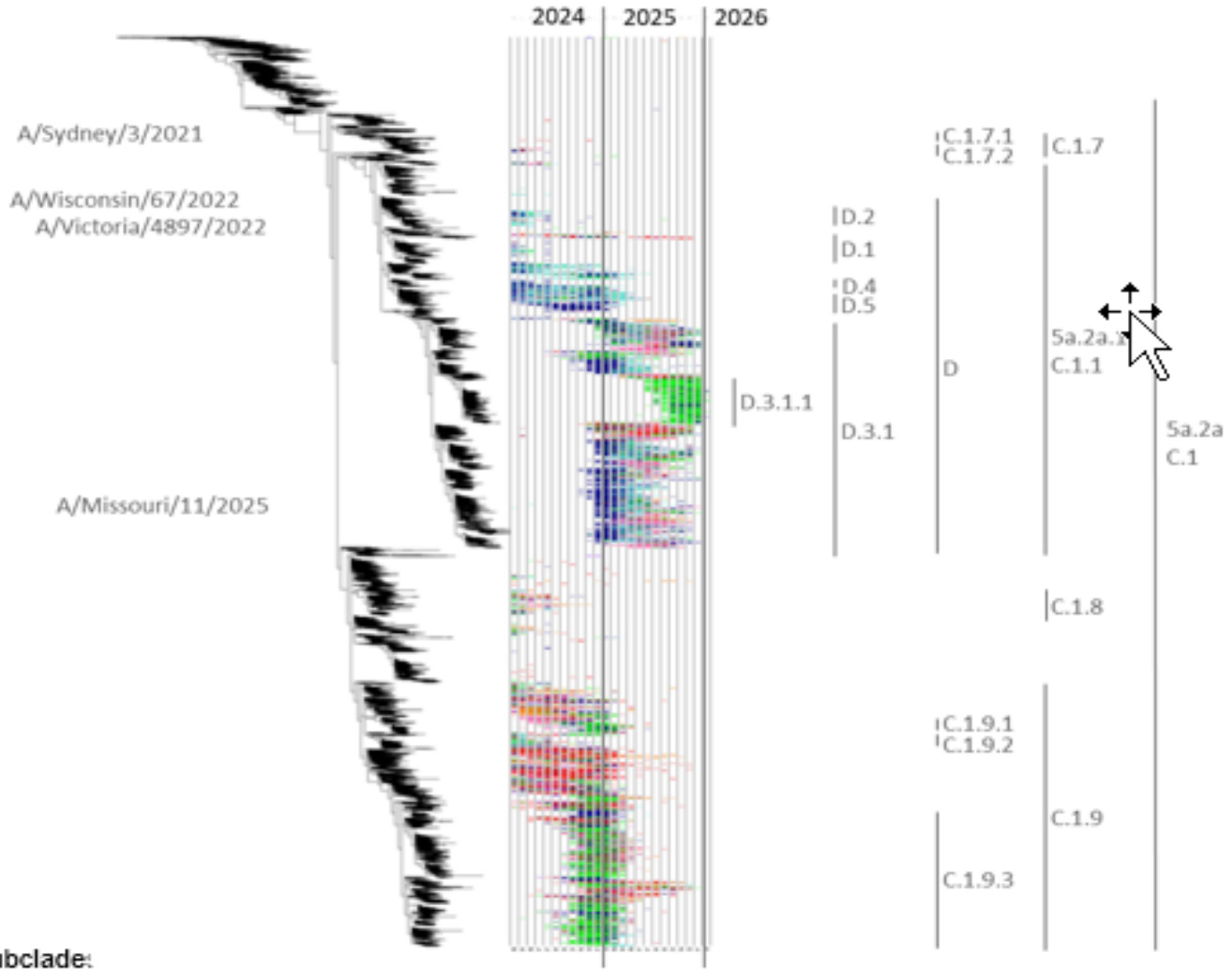
GISRS GLOBAL INFLUENZA SURVEILLANCE & RESPONSE SYSTEM

World Health Organization

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

CDC

A(H1N1)pdm09 HA phylogeography



North America
South America
Europe
Africa
Middle East
Russia
E SE Asia
Oceania

Figure Source: University of Cambridge

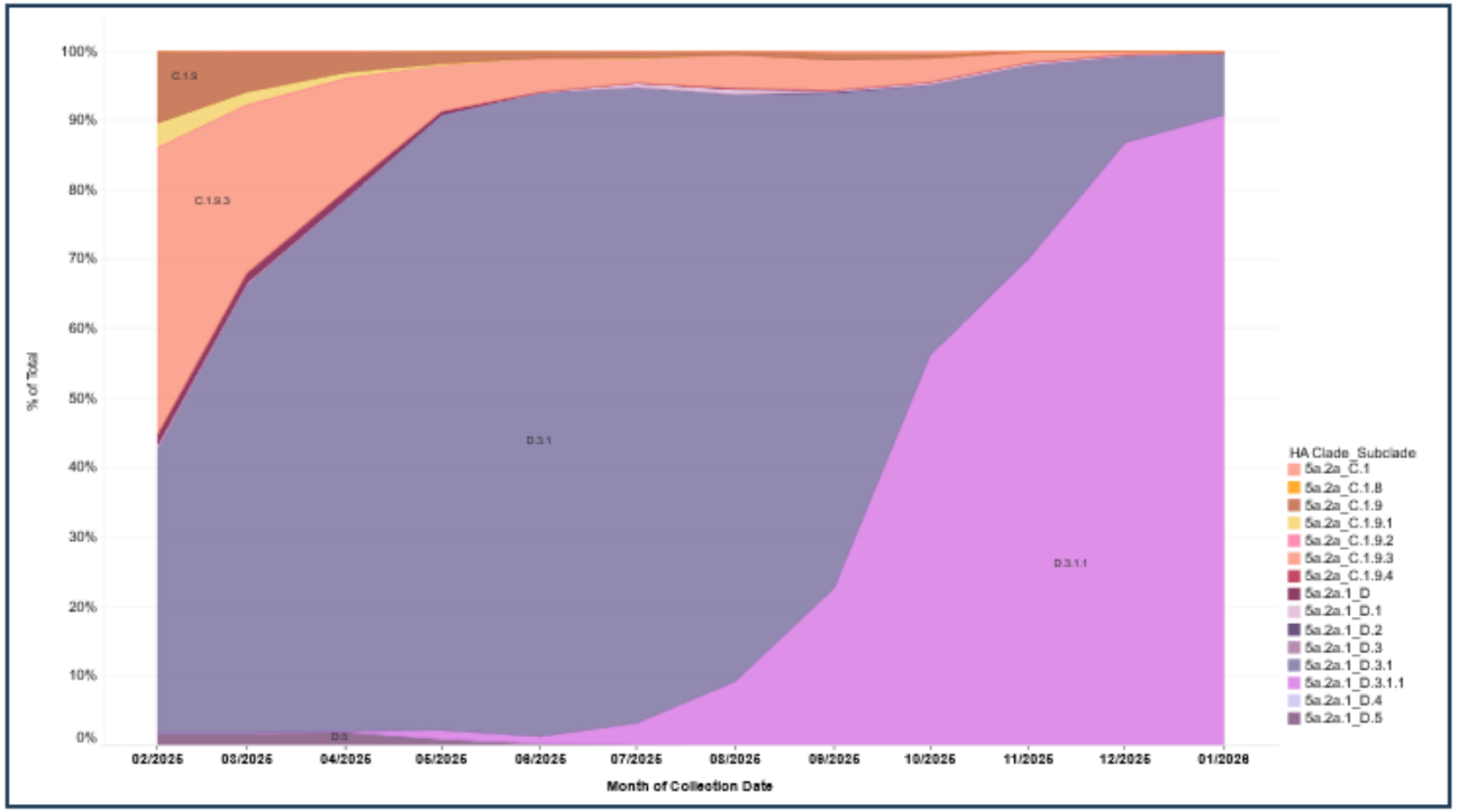
Data Source: GISAID

HA and NA clade/subclade:
https://clades.nextstrain.org/

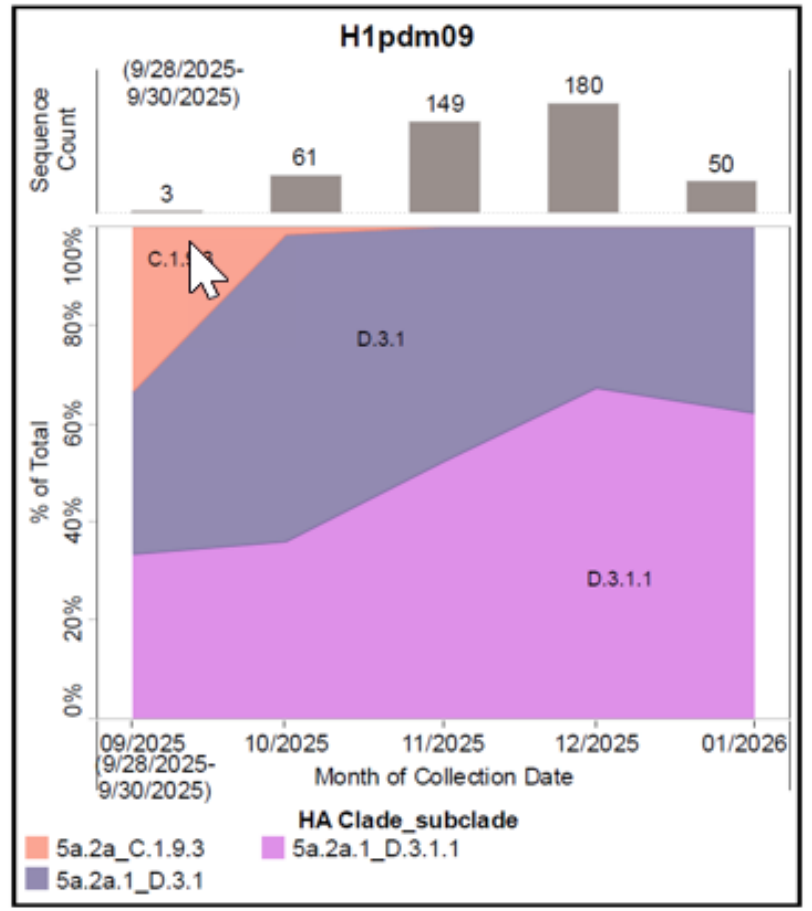
VCM Information meeting: https://www.youtube.com/@who

A(H1N1)pdm09 Extended Diversity Plot

Global view
Feb 2025-Jan 2026



US view
Sep 28 2025-Jan 2026



Data Source: GISAID

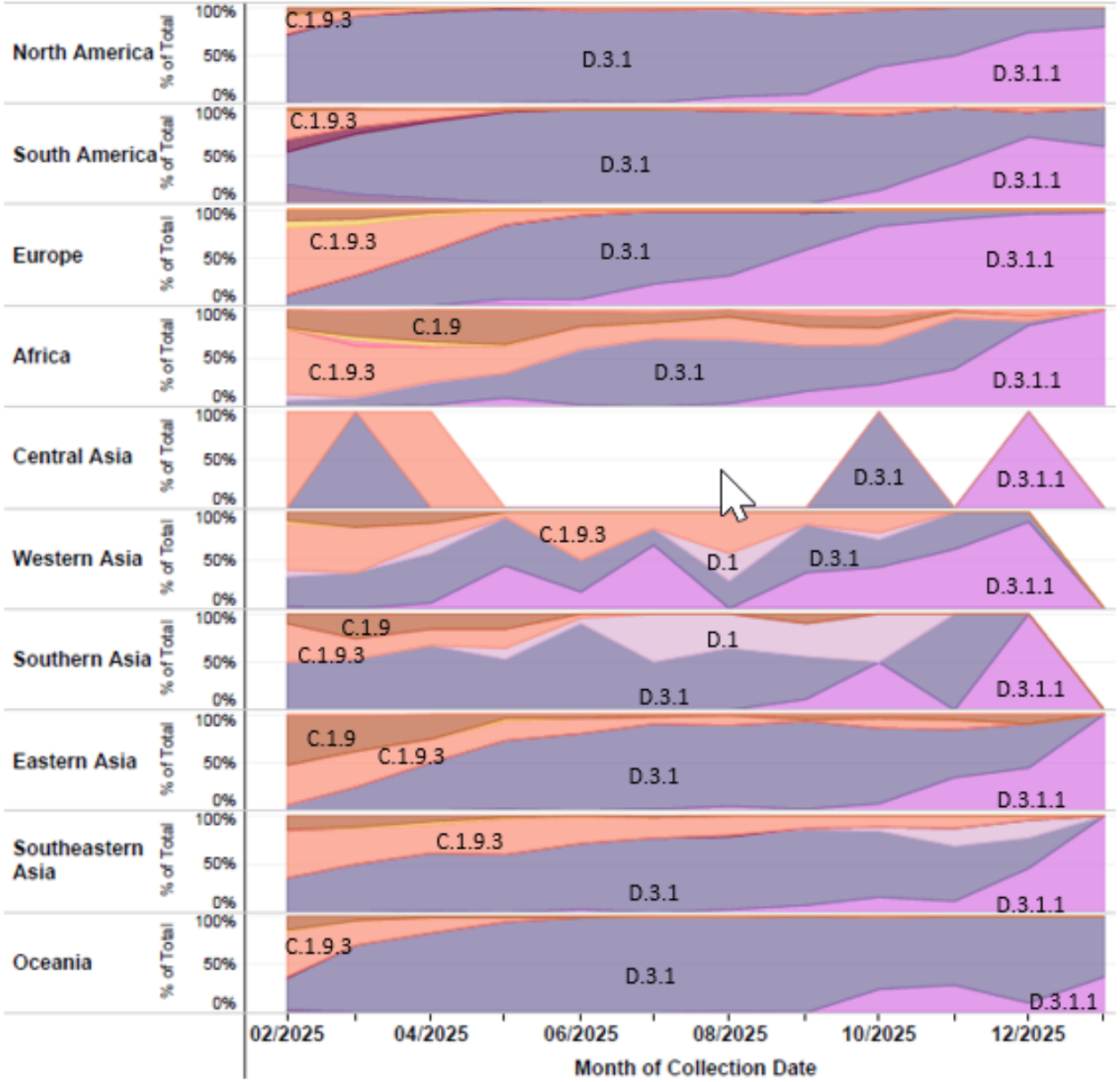
HA and NA clade/subclades:
https://clades.nextstrain.org/

A(H1N1)pdm09 Extended Diversity Plot by Geographic Region

February 2025 – February 2026

HA Clade_Subclade

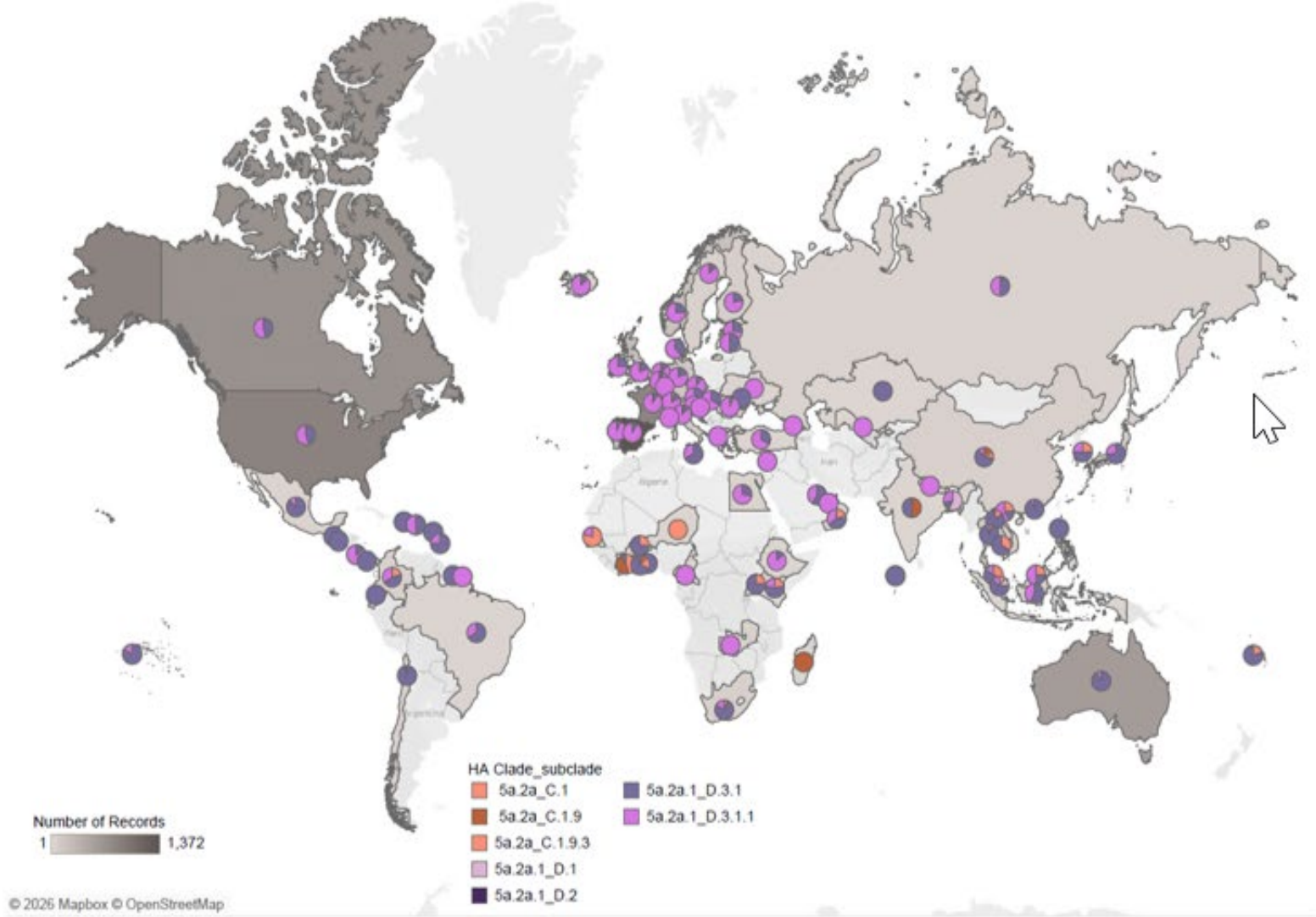
- 5a.2a_C.1
- 5a.2a_C.1.8
- 5a.2a_C.1.9
- 5a.2a_C.1.9.1
- 5a.2a_C.1.9.2
- 5a.2a_C.1.9.3
- 5a.2a_C.1.9.4
- 5a.2a.1_D
- 5a.2a.1_D.1
- 5a.2a.1_D.2
- 5a.2a.1_D.3
- 5a.2a.1_D.3.1
- 5a.2a.1_D.3.1.1
- 5a.2a.1_D.4
- 5a.2a.1_D.5



Data Source: GISAID

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

Global A(H1N1)pdm09 HA clade diversity: Sep 2025 to Jan 2026



Data Source: GISAID

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

Antigenic analysis of A(H1N1)pdm09 viruses in HI assays

Antisera to southern hemisphere 2026 vaccine virus antigens

WHO CC	A/Missouri/11/2025-like Cell 5a.2a.1 (D.3.1)	Low (≥ 8 fold)
CDC	144 (99%)	1 (1%)
CNIC	55 (98%)	1 (2%)
FCI	211 (100%)	0 (0%)
NIID	42 (100%)	0 (0%)
VIDRL	75 (99%)	1 (1%)
TOTAL	527 (99%)	3 (1%)

WHO CC	A/Missouri/11/2025-like Egg 5a.2a.1 (D.3.1)	Low (≥ 8 fold)
CDC	33 (92%)	3 (8%)
CNIC	8 (100%)	0 (0%)
FCI	209 (99%)	2 (1%)
VIDRL	74 (97%)	2 (3%)
TOTAL	324 (98%)	7 (2%)

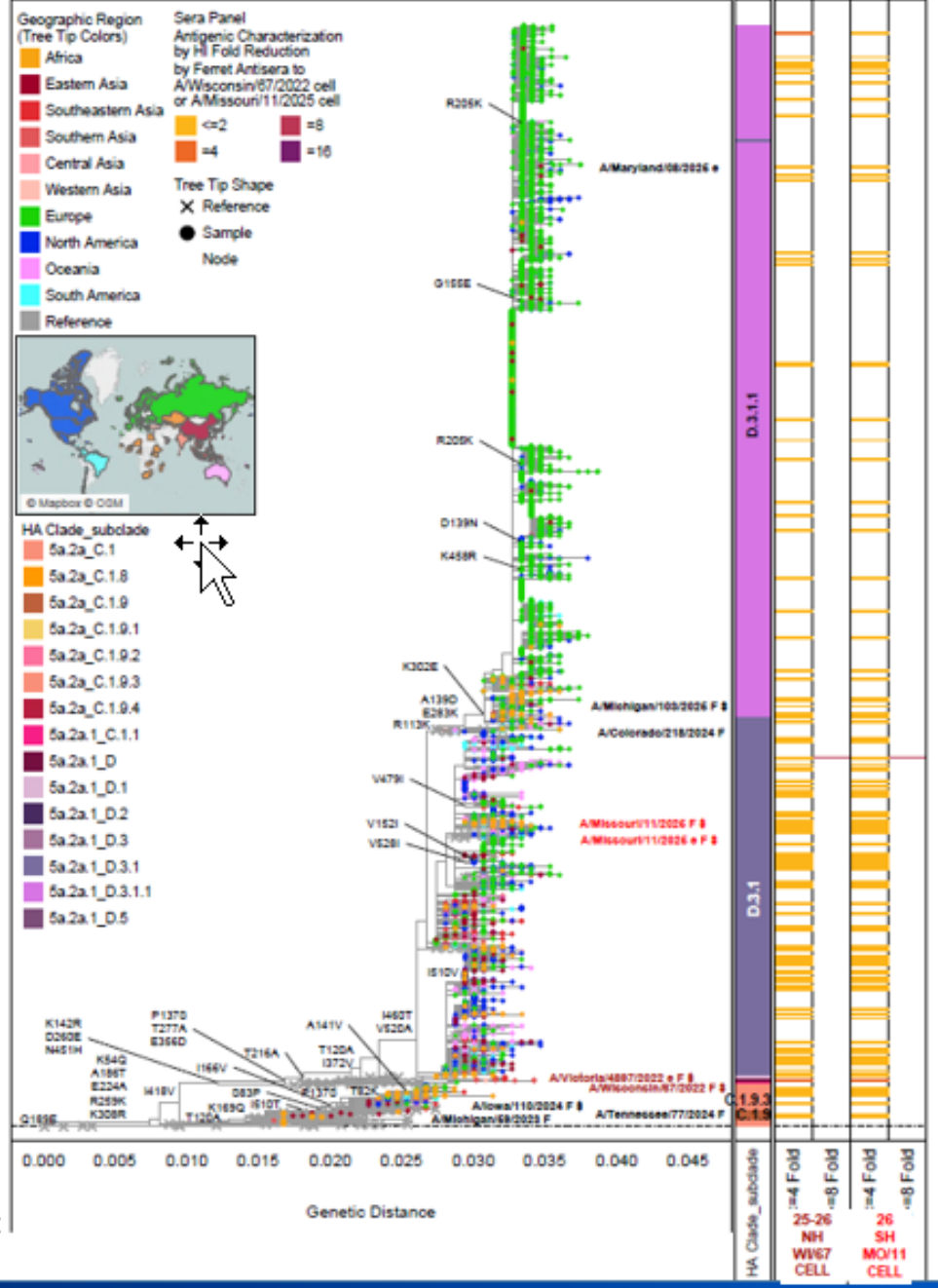
“Low” reactor represented titers ≥ 8-fold lower than vaccine strain homologous titer by HI

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

A(H1N1)pdm09 Integrated Genotype and Phenotype Analysis

Antigenic Characterization by HI using Ferret Antisera Fold Reduction to A/Wisconsin/67/2022 cell or A/Missouri/11/2025 cell

- <=2
- =4
- =8
- =16
- >=32



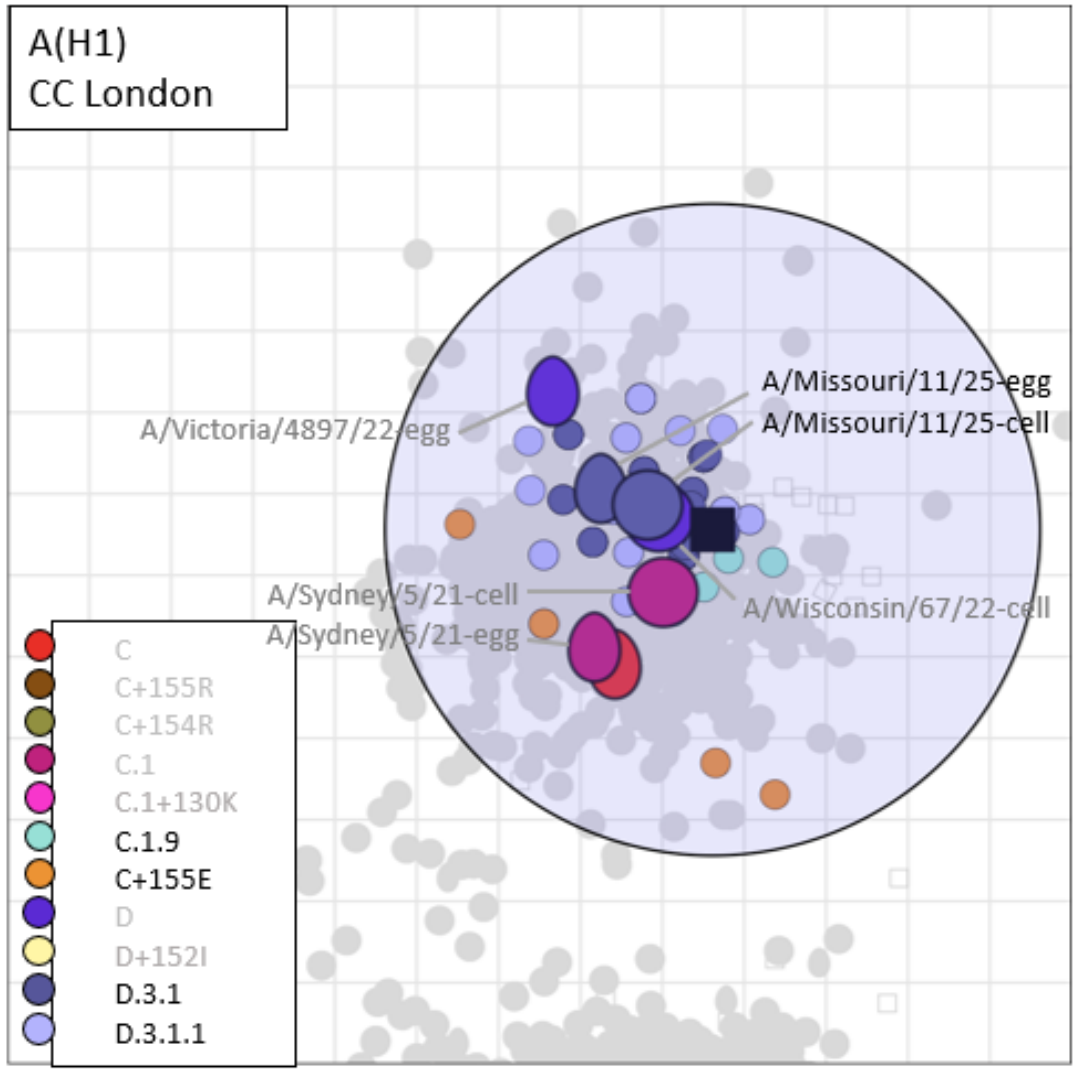
5a.2a.1 (D.3.1, D.3.1.1)

5a.2a (C.1.9, C.1.9.3)

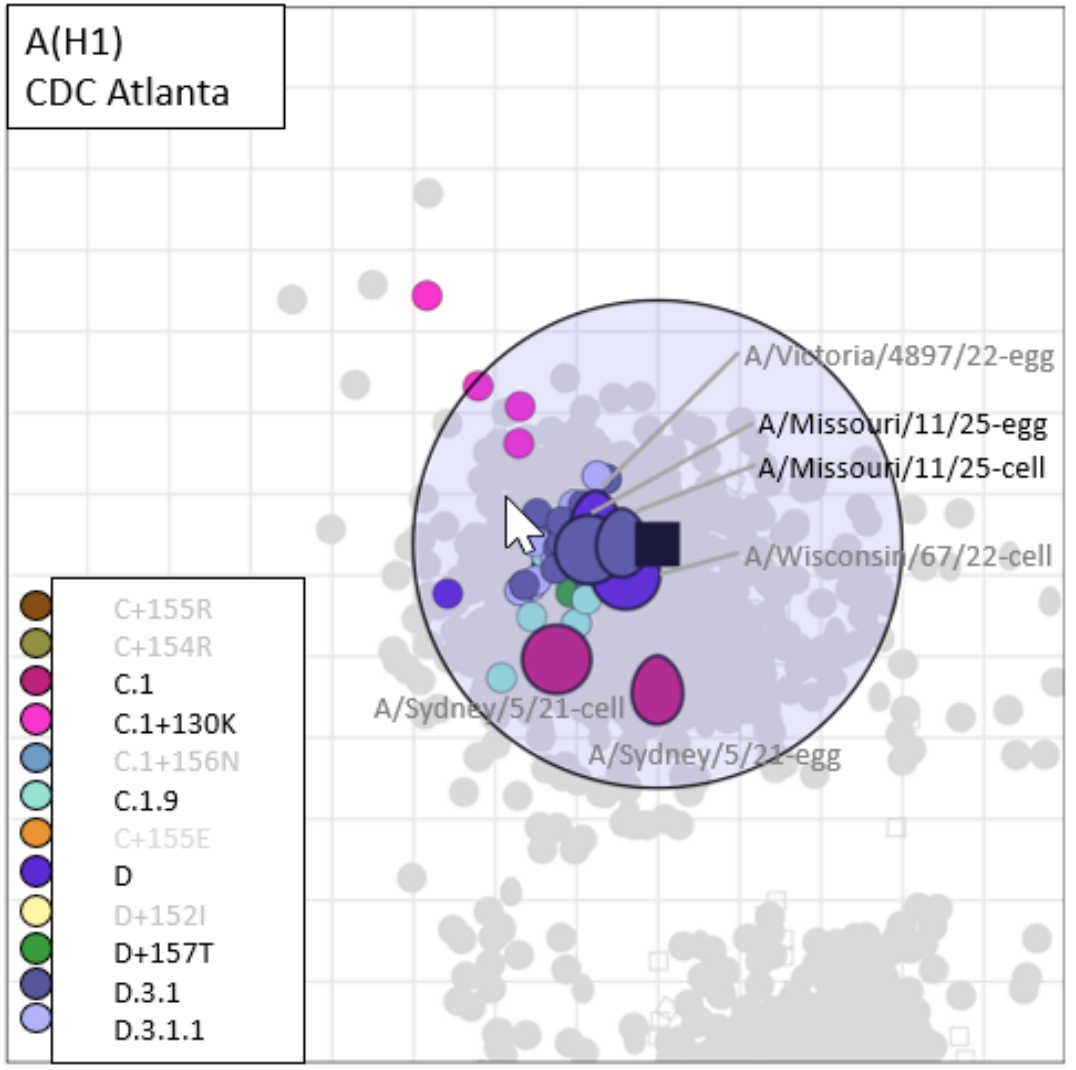
Data Source: GISAID

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

A(H1N1)pdm09 antigenic cartography (CDC and UK CC)



A/Missouri/11/25-cell serum circle (within 8-fold of homologous titer)



A/Missouri/11/25-egg serum circle (within 8-fold of homologous titer)

Source: University of Cambridge

Human post-vaccination serum analysis of A(H1N1)pdm09 viruses (CDC data)

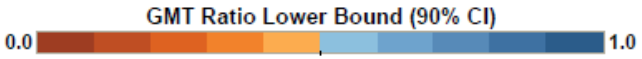
				C.1.1 (5a.2a.1)	D.3.1 (5a.2a.1)	D.3.1.1 (5a.2a.1)	C.1.9.3 (5a.2a)
				-	-	-	+T120A +I166V +K169Q
				*WI/67	MO/11	MI/103	IA/110
				SIAT	SIAT	SIAT	SIAT
A/WISCONSIN/67/2022 SIAT [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	368	√	√	√
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	437	√	√	√
	Adult (18-49Y)	USA	ccIIV3 (cell)	394	√	√	√
			RIV3 (recombinant)	920	√	√	√
	Elderly (≥65Y)	USA	HD-IIV3	95	√	√	√

				D (5a.2a.1)	C.1.1 (5a.2a.1)	D.3.1 (5a.2a.1)		D.3.1.1 (5a.2a.1)	C.1.9.3 (5a.2a)
				+T216A +Q223R	-	+Q223R	-	-	+T120A +I166V +K169Q
				*VIC/4897	WI/67	MO/11	MO/11	MI/103	IA/110
				EGG	SIAT	EGG	SIAT	SIAT	SIAT
A/VICTORIA/4897/2022 EGG [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	202	√	√	√	√	√
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	309	√	√	√	√	√
	Adult (18-49Y)	USA	ccIIV3 (cell)	299	√	√	√	√	√
			RIV3 (recombinant)	619	√	√	√	√	√
	Elderly (≥65Y)	USA	HD-IIV3	113	√	√	√	√	√

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/IOWA/110/2024 (IA/110); A/MICHIGAN/103/2025 (MI/103); A/MISSOURI/11/2025 (MO/11); A/VICTORIA/4897/2022 (VIC/4897); A/WISCONSIN/67/2022 (WI/67).

Statistically non-inferior = √
Statistically non-inferior but reference virus GMT < 40 = **X**



Influenza A(H1N1)pdm09: antiviral susceptibility

Neuraminidase inhibitors

- Of 1,161 A(H1N1)pdm09 virus clinical samples and isolates examined by genetic and/or phenotypic analyses, 15 viruses showed evidence of reduced susceptibility to neuraminidase inhibitors (NAIs):
  - 7 had an H275Y NA substitution
  - 8 had I223V and S247N substitutions.

Endonuclease inhibitors

- Of 1,331 A(H1N1)pdm09 viruses examined by genetic and/or phenotypic analyses, no viruses showed evidence of reduced susceptibility to the endonuclease inhibitor baloxavir marboxil

Influenza A(H1N1)pdm09 summary (1)

Phylogenetics of A(H1N1)pdm09 HA genes

- A(H1N1)pdm09 viruses circulated globally but did not predominate in any region.
- The vast majority of HA genes of viruses that were genetically characterized belonged to clade 5a.2a1 subclades D.3.1 and D.3.1.1.

Influenza A(H1N1)pdm09 summary (2)

Antigenic characteristics of A(H1N1)pdm09 viruses

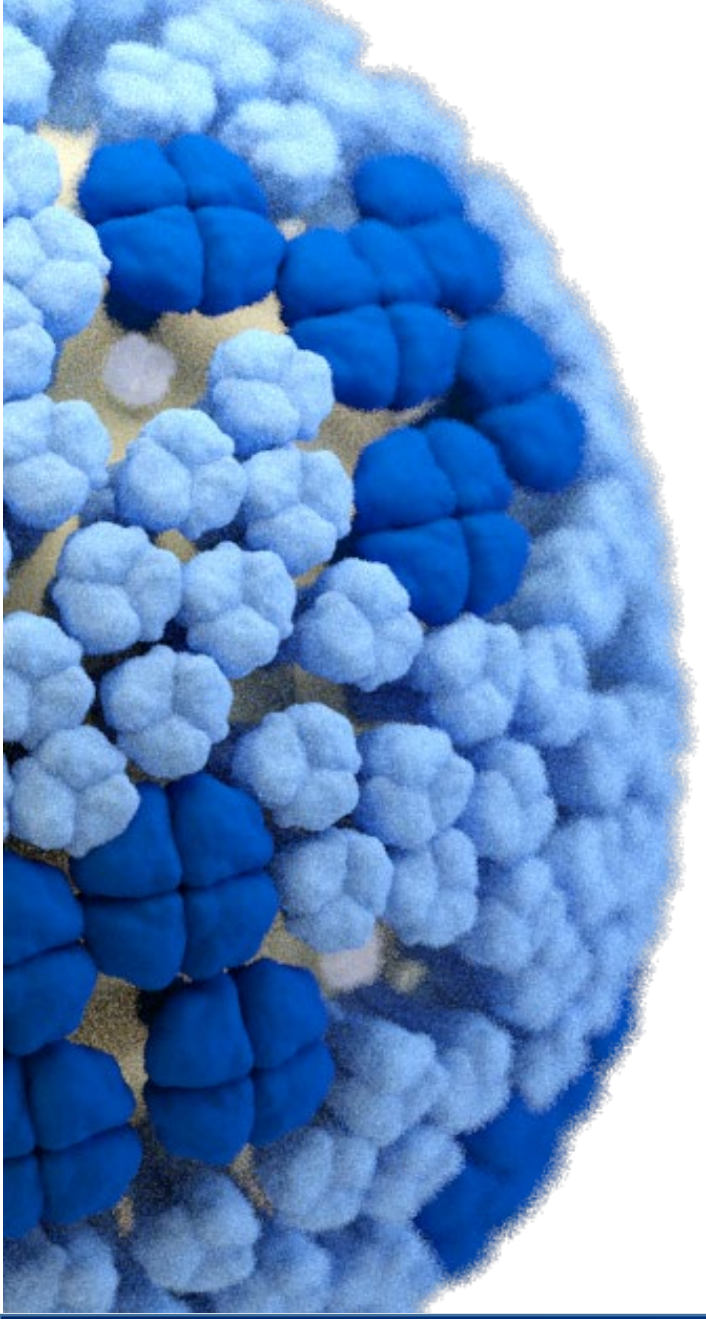
- The antigenic properties of A(H1N1)pdm09 viruses were assessed in hemagglutination inhibition (HI) assays with post-infection ferret antisera. HI results for viruses with collection dates since September 2025 showed that ferret antisera raised against cell culture-propagated A/Wisconsin/67/2022-like and egg-propagated A/Victoria/4897/2022-like viruses from the 5a.2a.1 clade recognized viruses in both 5a.2a and 5a.2a.1 clades well.
- However, post-infection ferret antisera raised against viruses from HA clade 5a.2a showed some reduction in recognition of viruses from the now predominating D.3.1 and D.3.1.1 HA subclade.
- Post-infection ferret antisera raised against viruses from HA subclade D.3.1 (e.g., A/Missouri/11/2025) recognized recently circulating viruses from both 5a.2a and 5a.2a.1 clades well.

Influenza A(H1N1)pdm09 summary (3)

Human serology studies

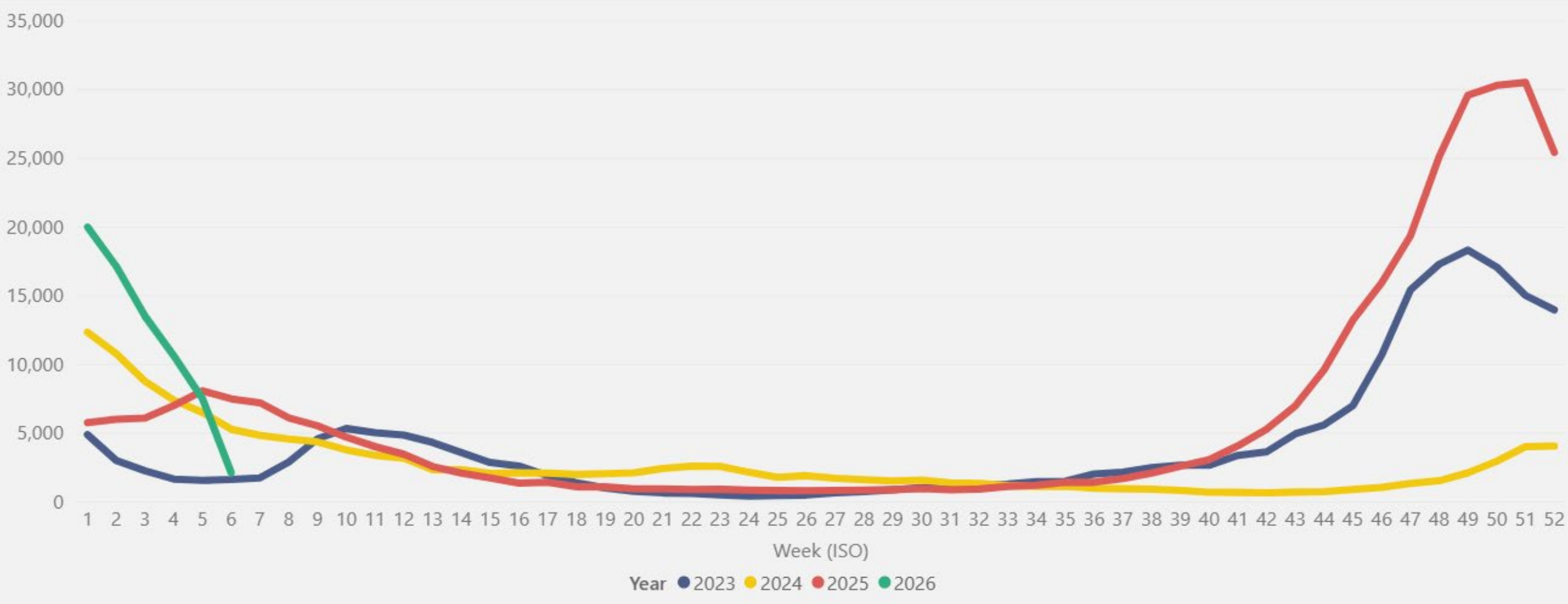
- Human serology studies were conducted using NH 2025-2026 influenza vaccine formulation vaccinated serum panels by HI assays with recent A(H1N1)pdm09 viruses with HA genes from clades 5a.2a (subclade C.1.9.3) and 5a.2a.1 (subclades D.3.1 and D.3.1.1).
- When compared to the responses to cell culture-propagated A/Wisconsin/67/2022 A(H1N1)pdm09-like vaccine reference viruses, post-vaccination geometric mean titres (GMTs) were significantly reduced for some recently circulating viruses from D.3.1 and D.3.1.1 subclades.

The data supported recommending A/Missouri/11/2025 (H1N1)pdm09-like (D.3.1) viruses as the A(H1N1)pdm09 vaccine antigens for the 2026-2027 northern hemisphere.



A(H3N2) Viruses

Number of A(H3N2) viruses detected by GISRS



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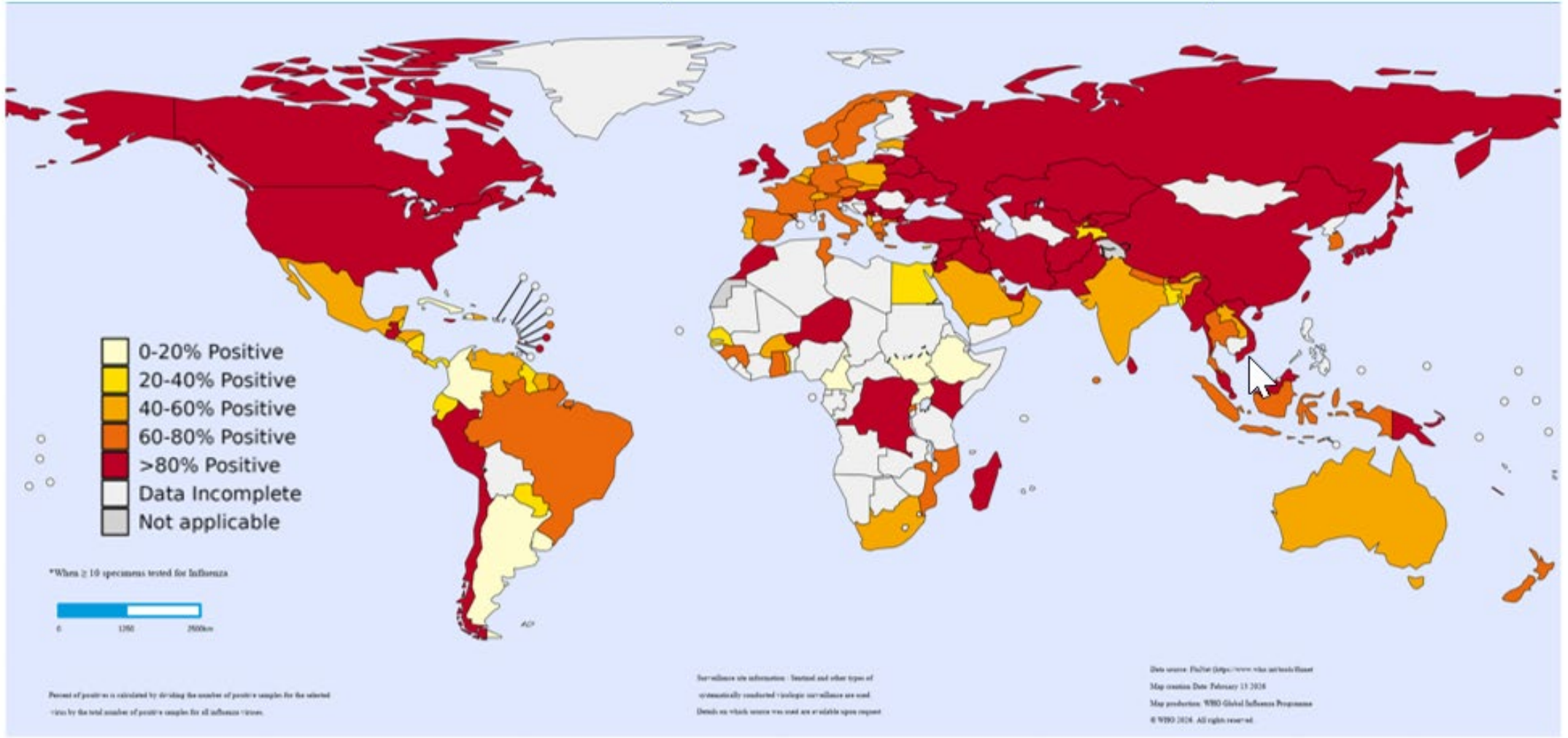
Influenza A(H3N2) virus activity



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

GISRS GLOBAL INFLUENZA SURVEILLANCE & RESPONSE SYSTEM

World Health Organization

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

A(H3N2) HA phylogeography

North America
South America
Europe
Africa
Middle East
Russia
E SE Asia
Oceania

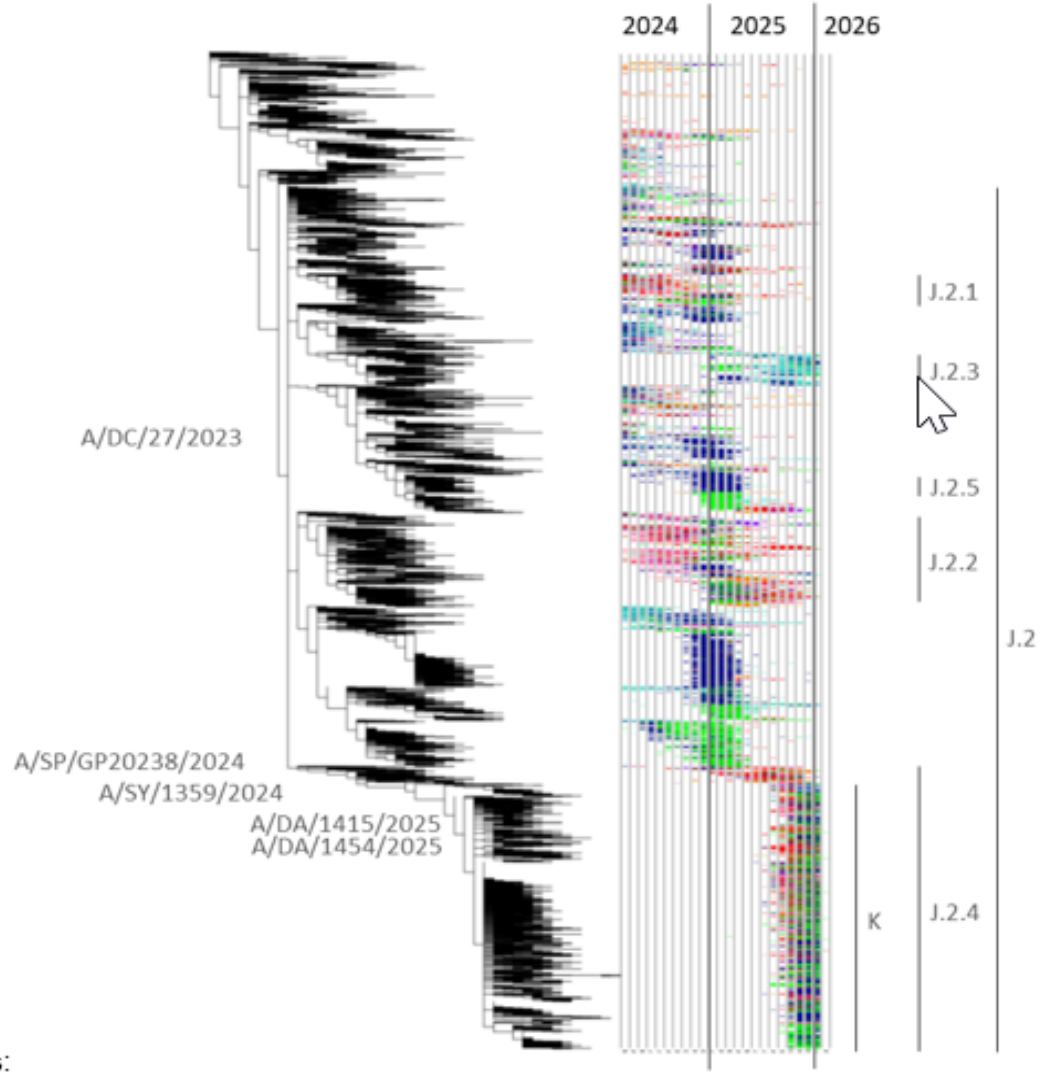


Figure Source: University of Cambridge

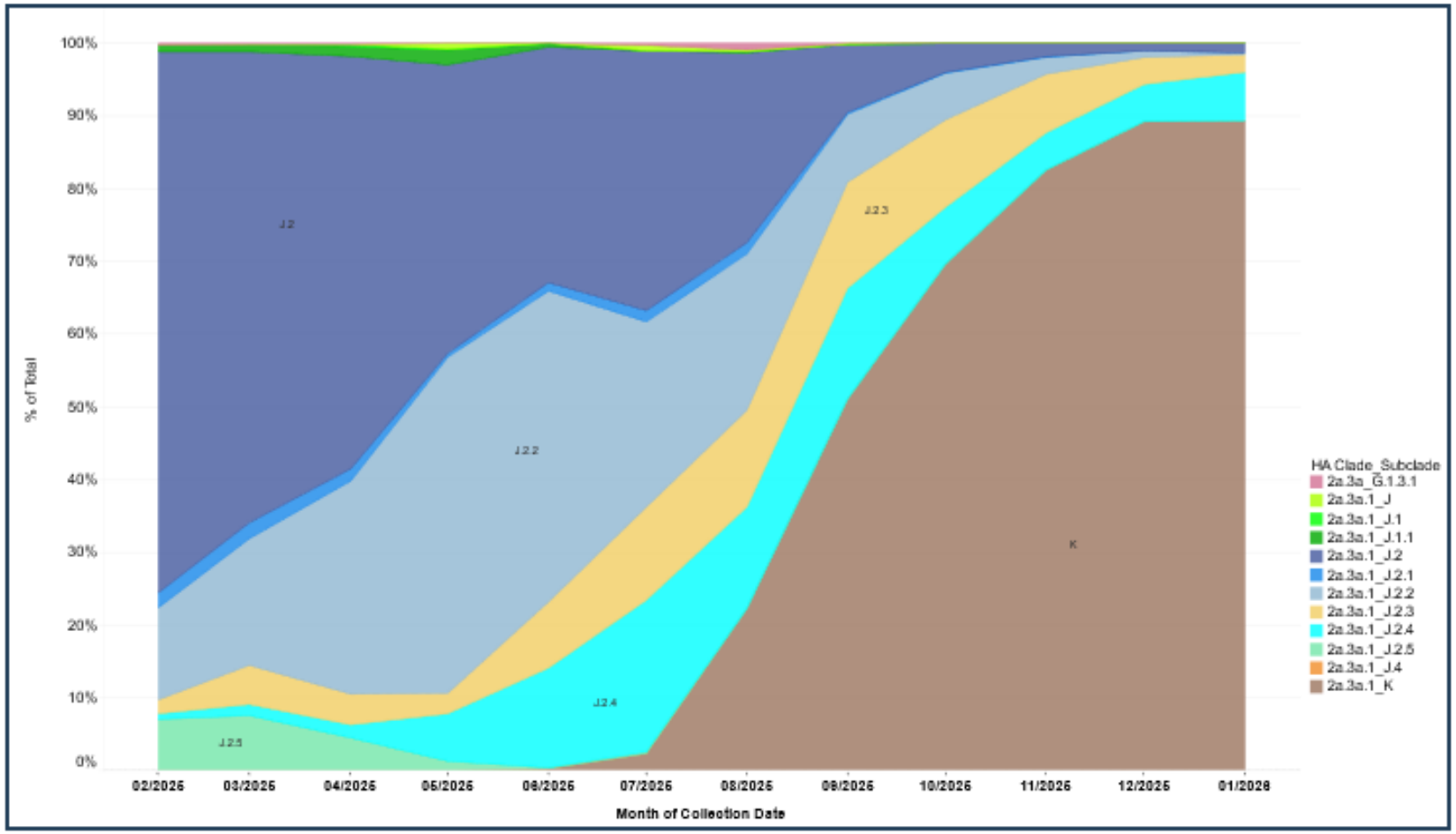
Data Source: GISAID

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

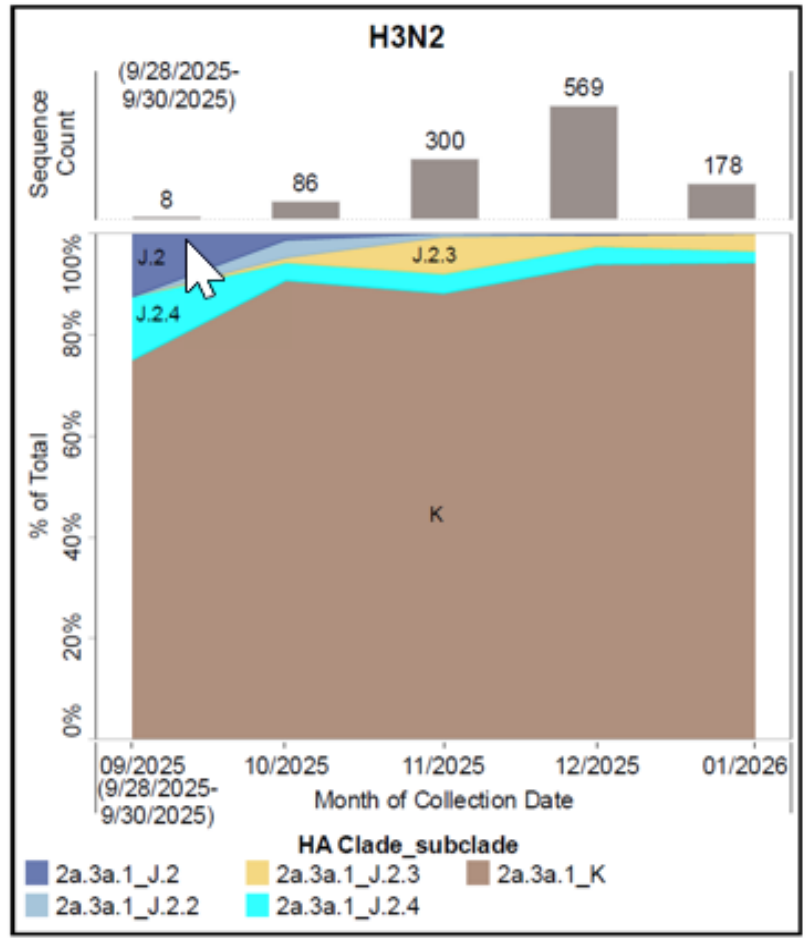
VCM Information meeting: https://www.youtube.com/@who

A(H3N2) Extended Diversity Plot

Global view
Feb 2025-Jan 2026



US view
Sep 28, 2025-Jan 2026



Data Source: GISAID

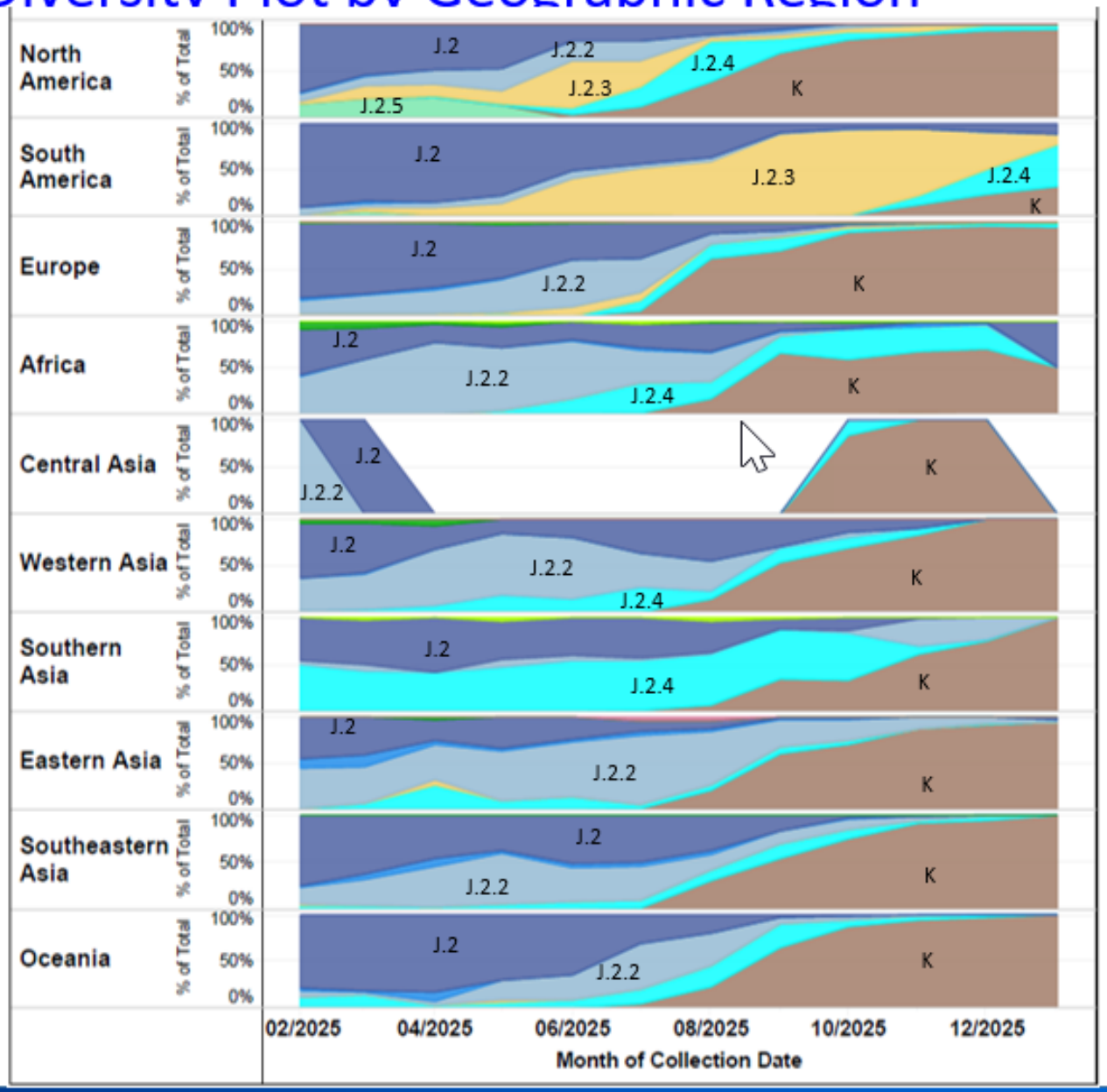
HA and NA clade/subclades:
https://clades.nextstrain.org/

A(H3N2) Extended Diversity Plot by Geographic Region

February 2025 – February 2026

HA Clade_Subclade

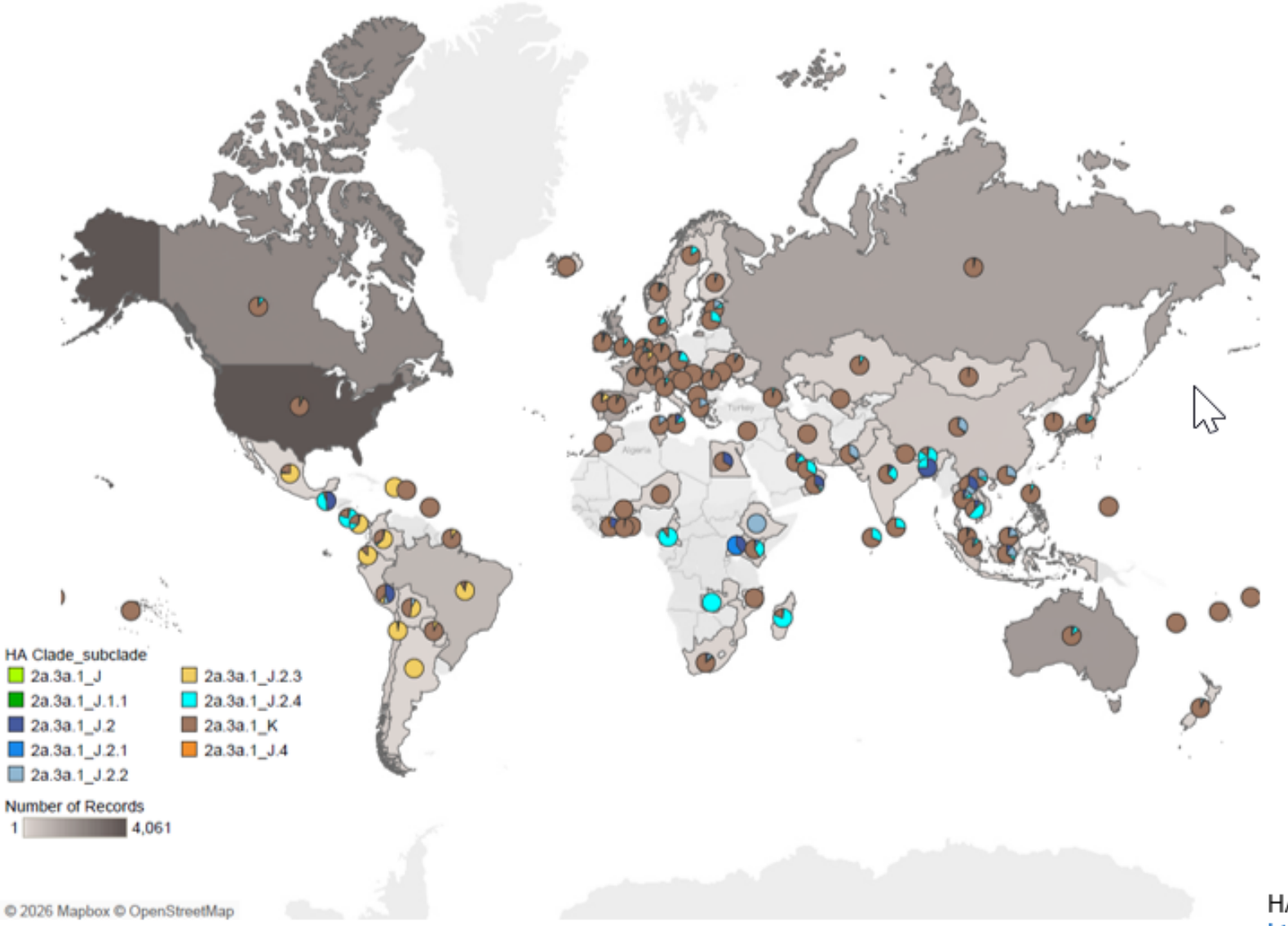
- 2a.3a_G.1.3.1
- 2a.3a.1_J
- 2a.3a.1_J.1
- 2a.3a.1_J.1.1
- 2a.3a.1_J.2
- 2a.3a.1_J.2.1
- 2a.3a.1_J.2.2
- 2a.3a.1_J.2.3
- 2a.3a.1_J.2.4
- 2a.3a.1_J.2.5
- 2a.3a.1_J.4
- 2a.3a.1_K



Data Source: GISAID

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

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



Data Source: GISAID

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

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 (≥ 8 fold)	WHO CC	A/Croatia/10136RV/2023-Like Egg 2a.3a.1 (J2) by HI	Low (≥ 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%)
Total	1168 (27%)	3238 (73%)	Total	603 (14%)	3803 (86%)

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

"Low" represented titers ≥ 8-fold lower than vaccine strain homologous titer

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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 (≥ 8 fold)
CDC	167 (76%)	54 (24%)
CNIC	405 (72%)	154 (28%)
FCI	102 (39%)	160 (61%)
NIID	207 (92%)	18 (8%)
VIDRL	1274 (88%)	179 (12%)
Total	2155 (79%)	565 (21%)

WHO CC	A/Singapore/GP20238/2024-Like Egg 2a.3a.1 (J.2.4) by HI	Low (≥ 8 fold)
CDC	110 (85%)	19 (15%)
CNIC	368 (22%)	1279 (78%)
FCI	115 (44%)	147 (56%)
NIID	198 (88%)	27 (12%)
VIDRL	1184 (81%)	269 (19%)
Total	1975 (53%)	1741 (47%)

WHO CC	A/Sydney/1359/2024-like Cell 2a.3a.1 (J.2.4) by VN	Low (≥ 8 fold)
CDC	96 (81%)	22 (19%)
FCI	73 (84%)	14 (16%)
Total	169 (82%)	36 (18%)

WHO CC	A/Singapore/GP20238/2024-Like Egg 2a.3a.1 (J.2.4) by VN	Low (≥ 8 fold)
FCI	11 (13%)	76 (87%)
Total	11 (13%)	76 (87%)

"Low" represented titers ≥ 8-fold lower than vaccine strain homologous titer

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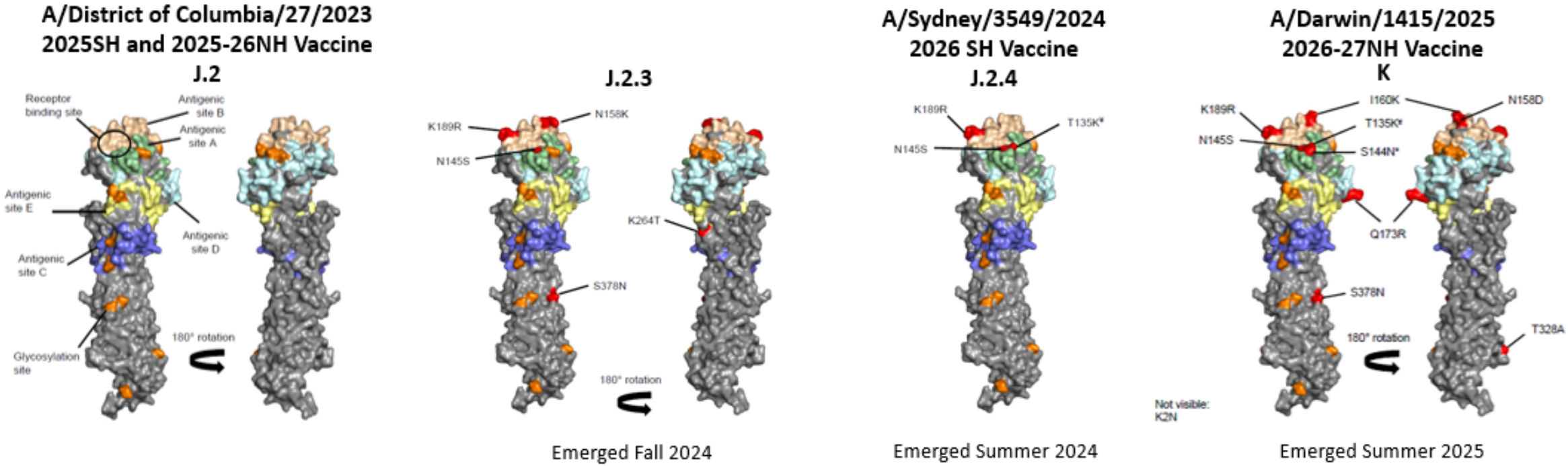
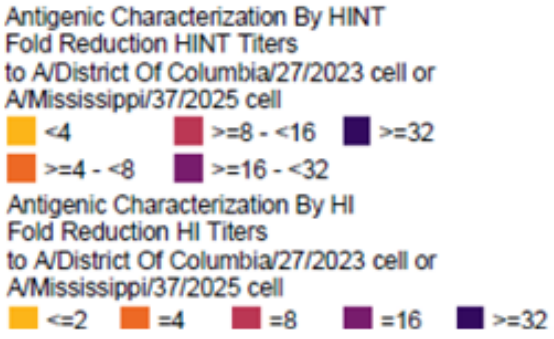
A(H3N2) Circulating Subclades

- 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

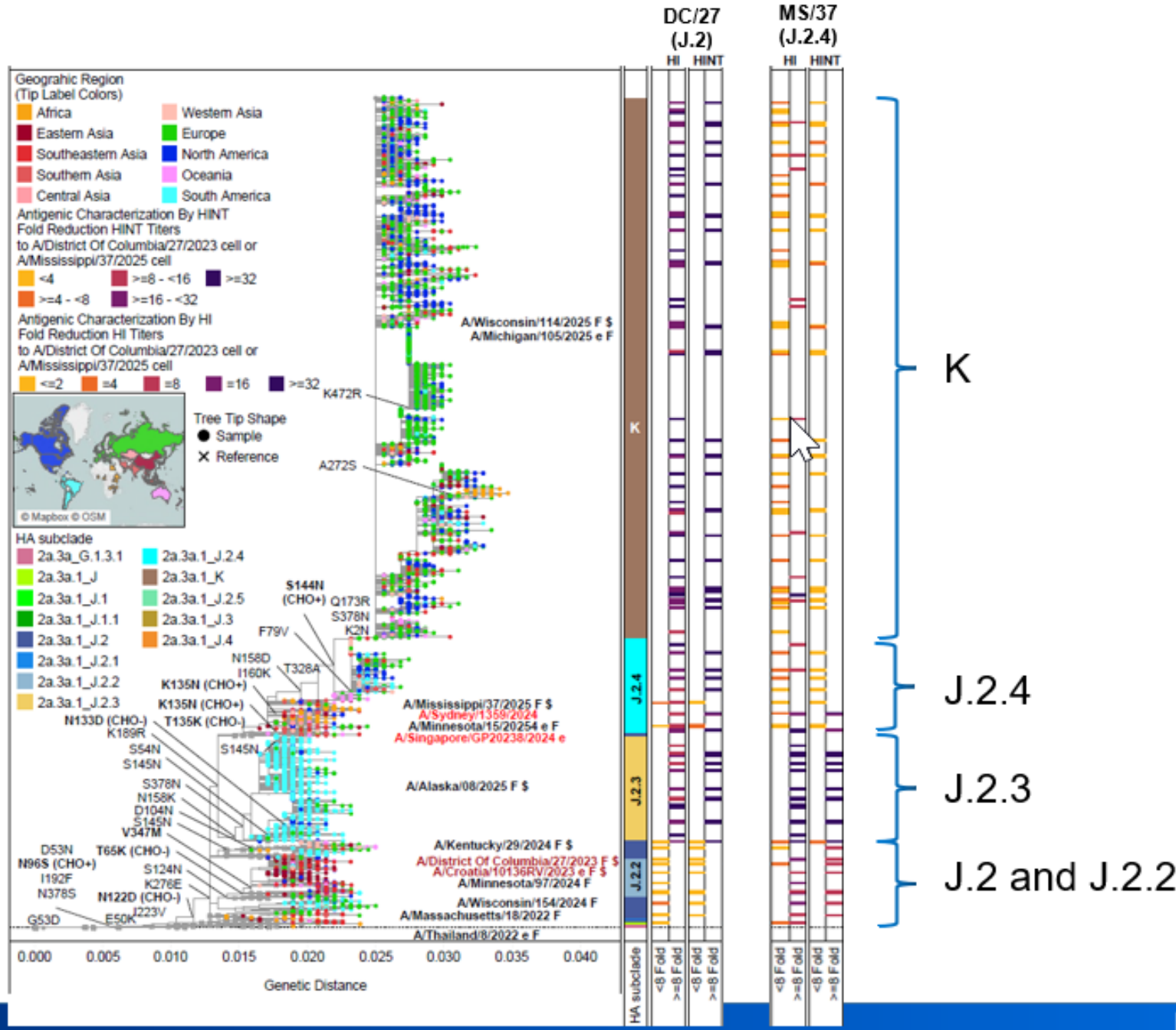


A(H3N2) Integrated Genotype and Phenotype Analysis



Data Source: GISAID

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



HI antigenic analysis of A(H3N2) viruses

		Reference Antisera					
		Cell	Cell	Cell	Egg	Cell	Egg
		Cro/10136RV	Neth/10685	Syd/1359	Sing/GP20238	Dar/1415	Dar/1454
	HA subclade	J.2	J.2.3	J.2.4	J.2.4	K	K
Reference virus							
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**
Test virus							
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

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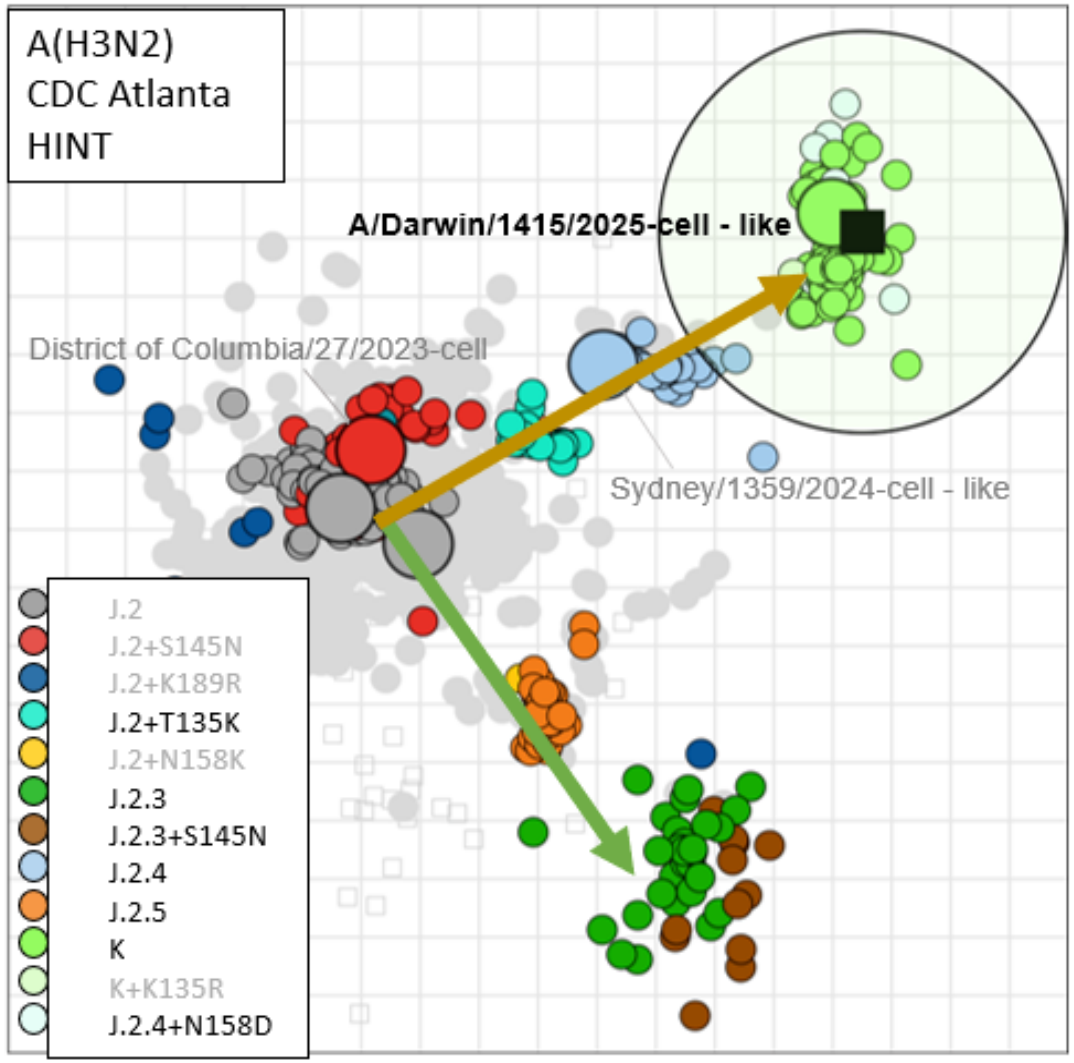
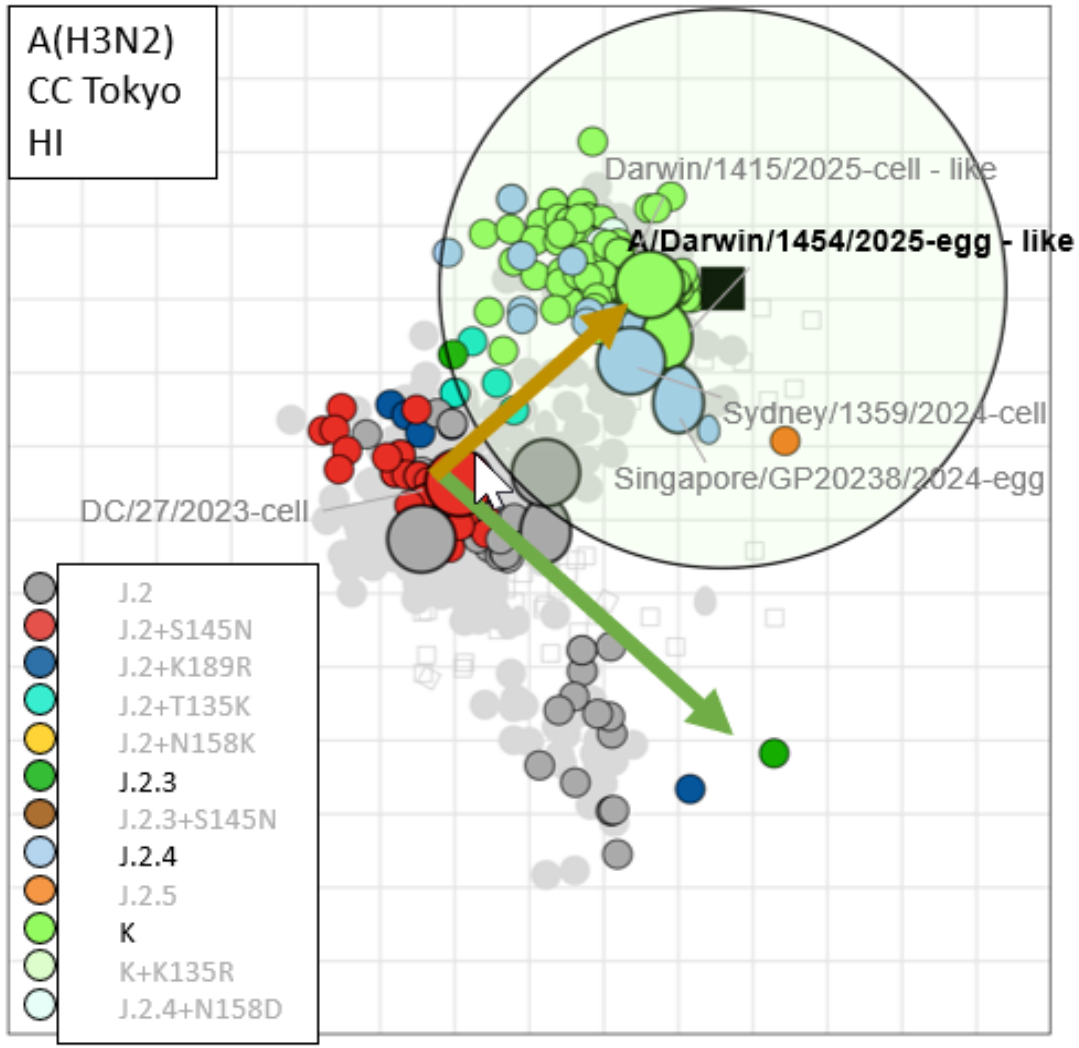
A(H3N2) antigenic cartography



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

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

				J.2 - *DC/27 SIAT	J.2.3 +N145S +N158K +K189R AK/08 SIAT	J.2.4 +T135K (CHO-) +N145S +K189R MS/37 SIAT	K +T135K (CHO-) +N145S +N158D +I160K +K189R WI/114 SIAT	J.2.5 +N158K KY/29 SIAT
A/DISTRICT OF COLUMBIA/27/2023 SIAT [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	139	50	88	61	√
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	437	197	√	279	288
	Adult (18-49Y)	USA	ccIIV3 (cell)	279	174	√	169	√
			RIV3 (recombinant)	1413	√	√	780	√
	Elderly (≥65Y)	USA	HD-IIV3 (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).

Statistically non-inferior = √
Statistically non-inferior but reference virus GMT < 40 = **X**

GMT Ratio Lower Bound (90% CI)

0.0 — 1.0

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.

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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.

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Influenza A(H3N2) summary (3)

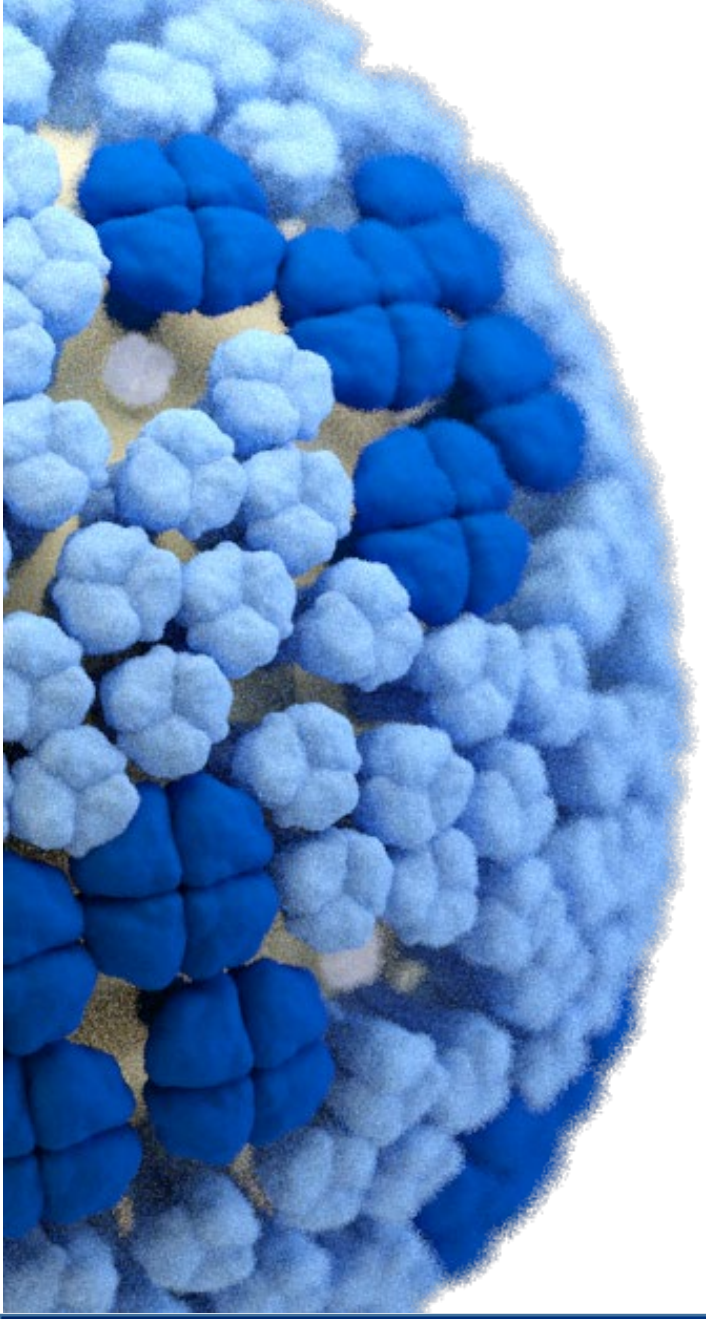
Human serology studies

- 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.

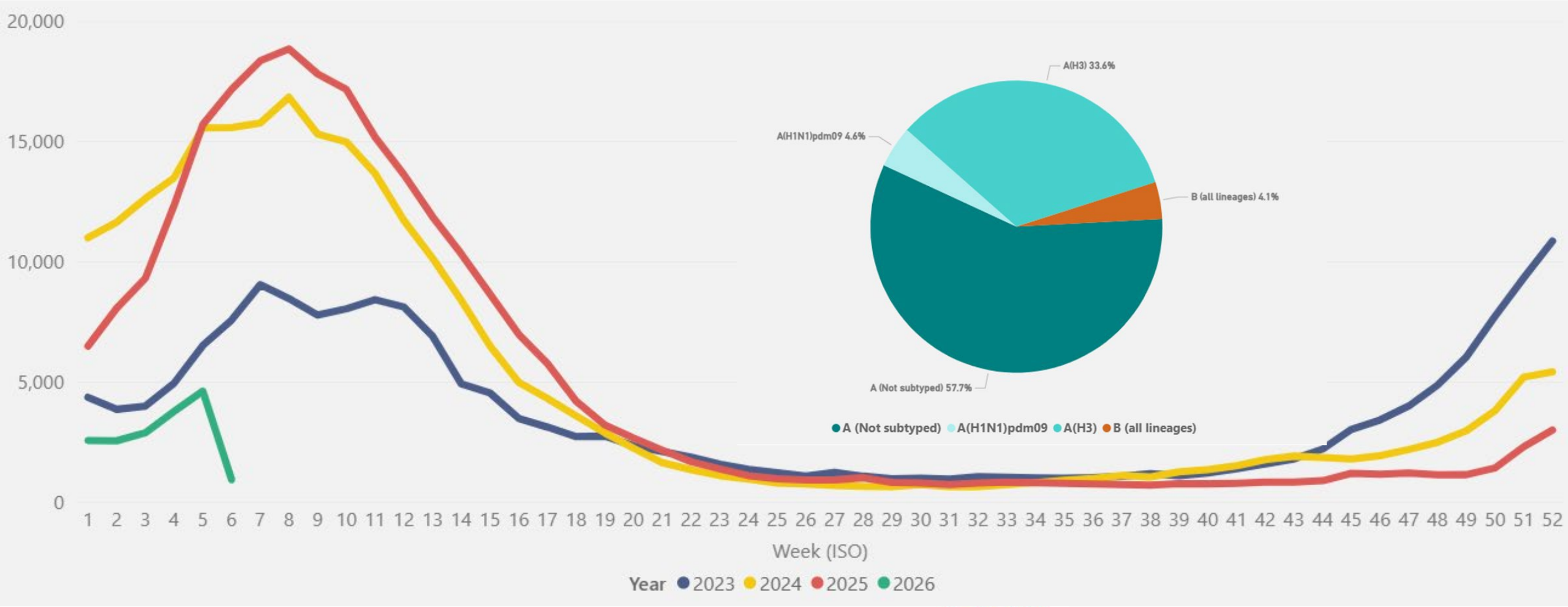
The data supported recommending a cell-propagated A/Darwin/1415/2025 (H3N2)-like (K) virus and an egg-propagated A/Darwin/1454/2025 (H3N2)-like (K) virus as the A(H3N2) vaccine antigens for the 2026-2027 northern hemisphere.

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



Influenza B Viruses

Number and Percentage of B viruses detected by GISRS

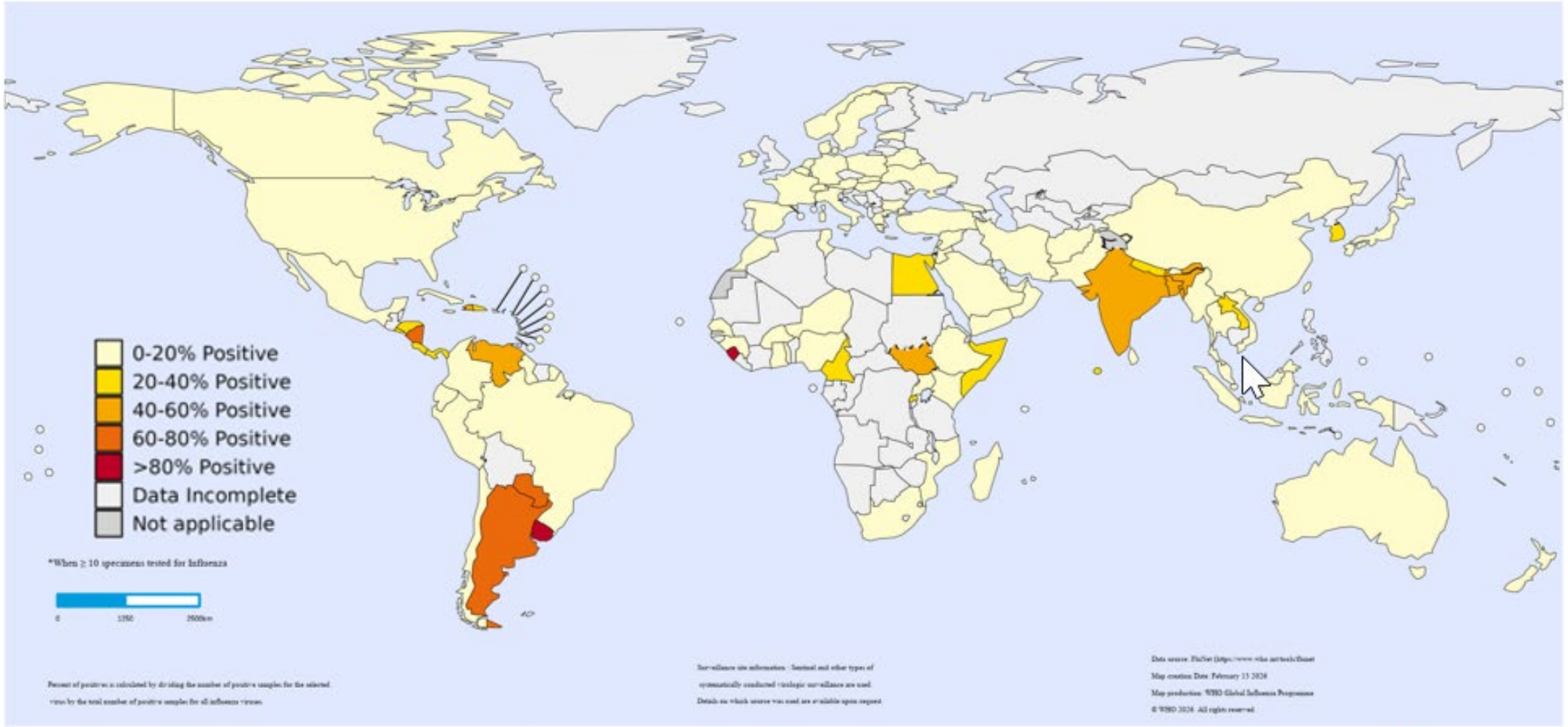


Data reported to FluNet by GISRS National Influenza Centers in 135 member states

GISRS GLOBAL INFLUENZA SURVEILLANCE & RESPONSE SYSTEM

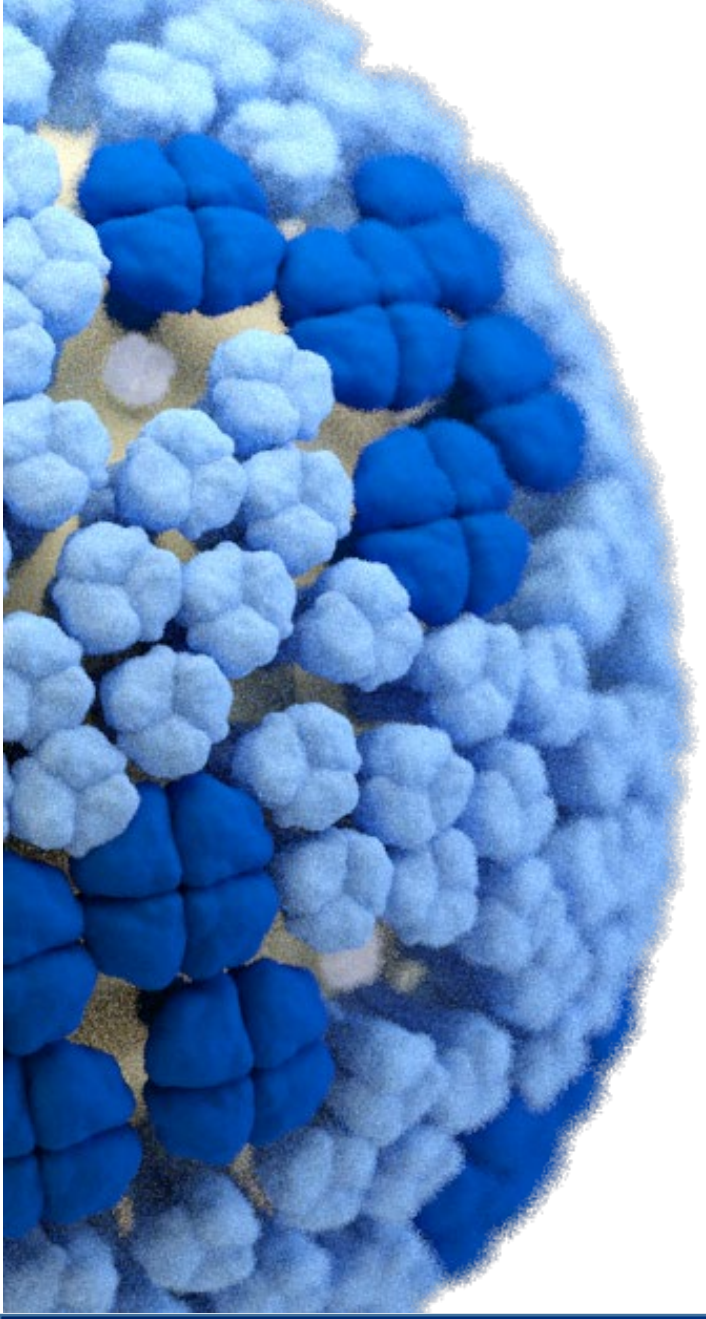
VCM Information meeting: https://www.youtube.com/@who

Influenza B virus activity



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

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



Influenza B/Victoria Viruses

B/Victoria HA phylogeography

C3:
- E128K, A154E, S208P
- recent subset = S255P, I267V & D197N (+CHO)

C3.1:
- P208S & D197N (+CHO)

C.5, C.5.1, C.5.6, C.5 and C.5.7:
- various substitutions, all have D197E

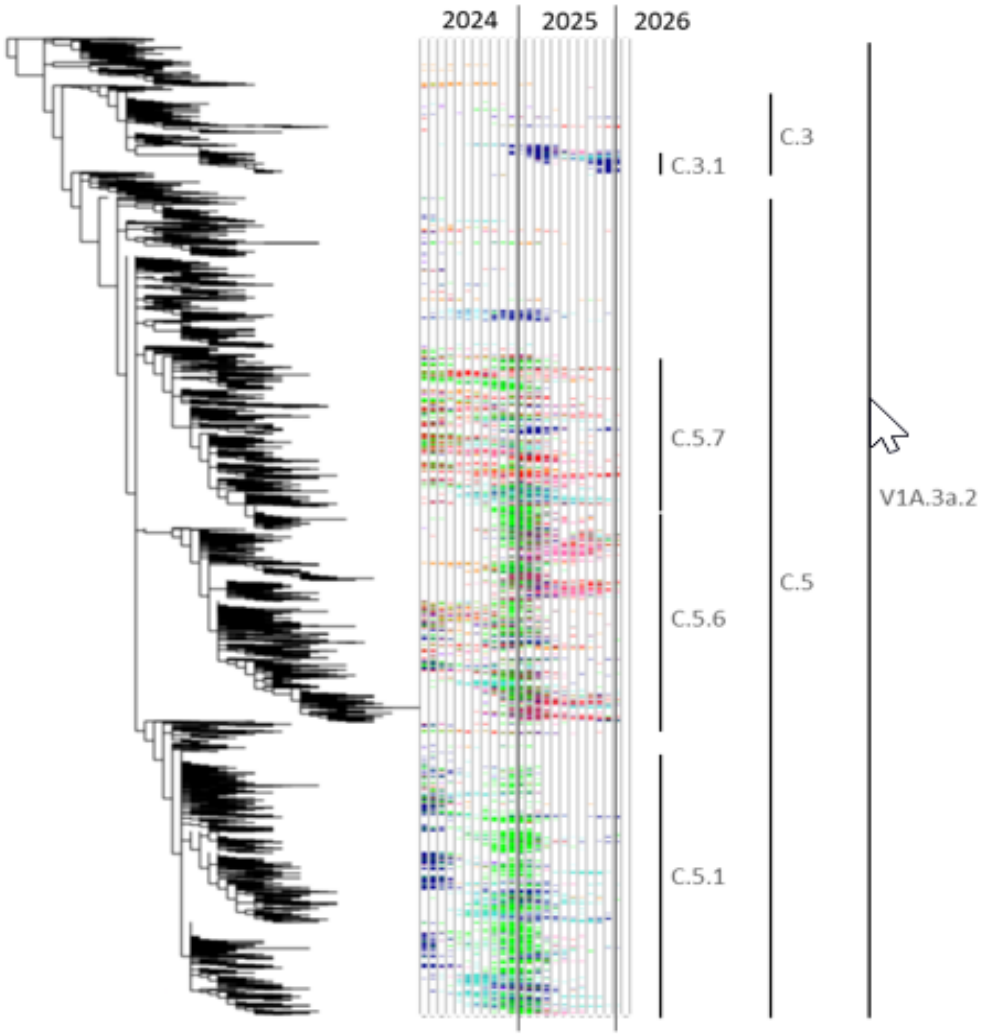


Figure Source: *University of Cambridge*

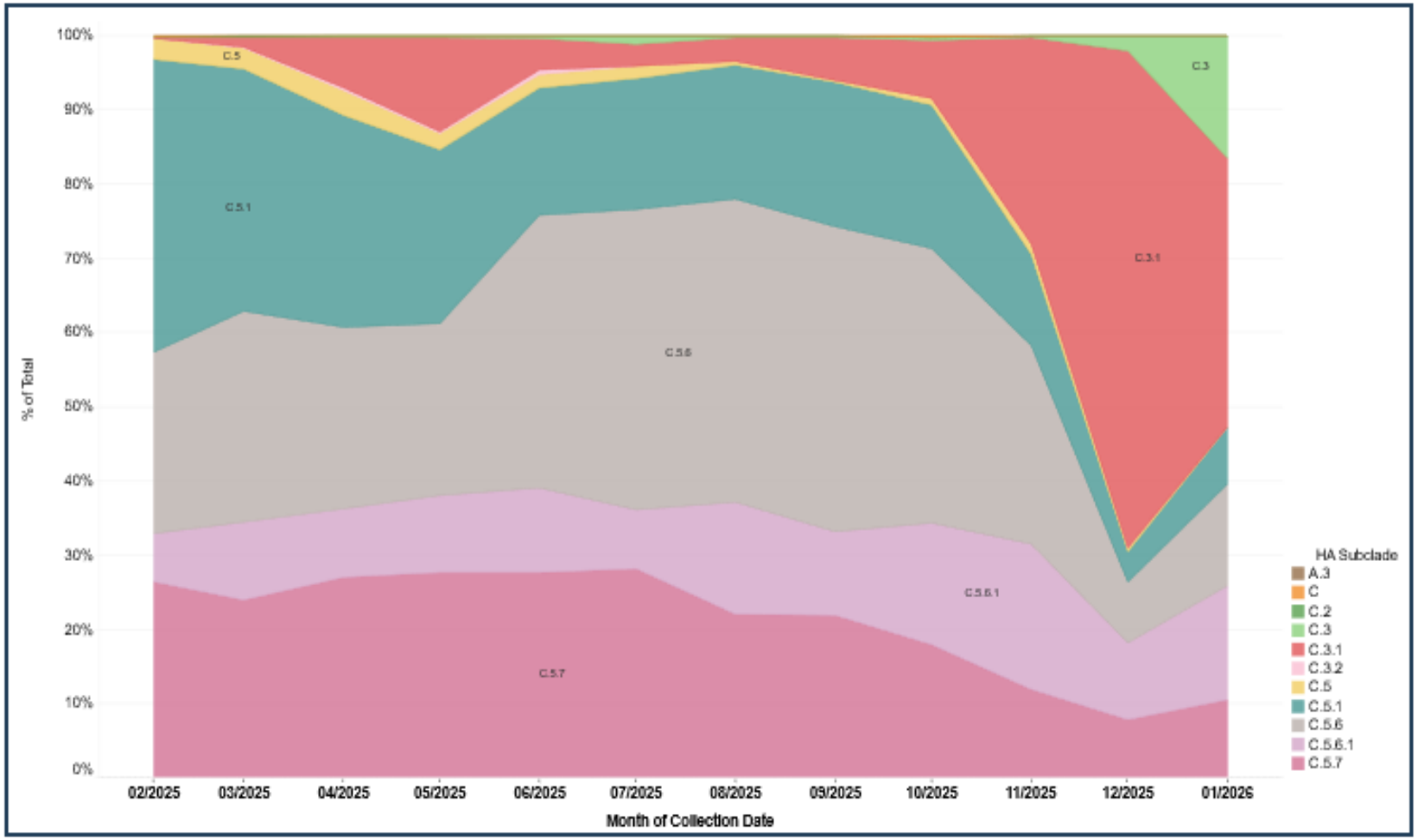
Data Source: GISAID

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

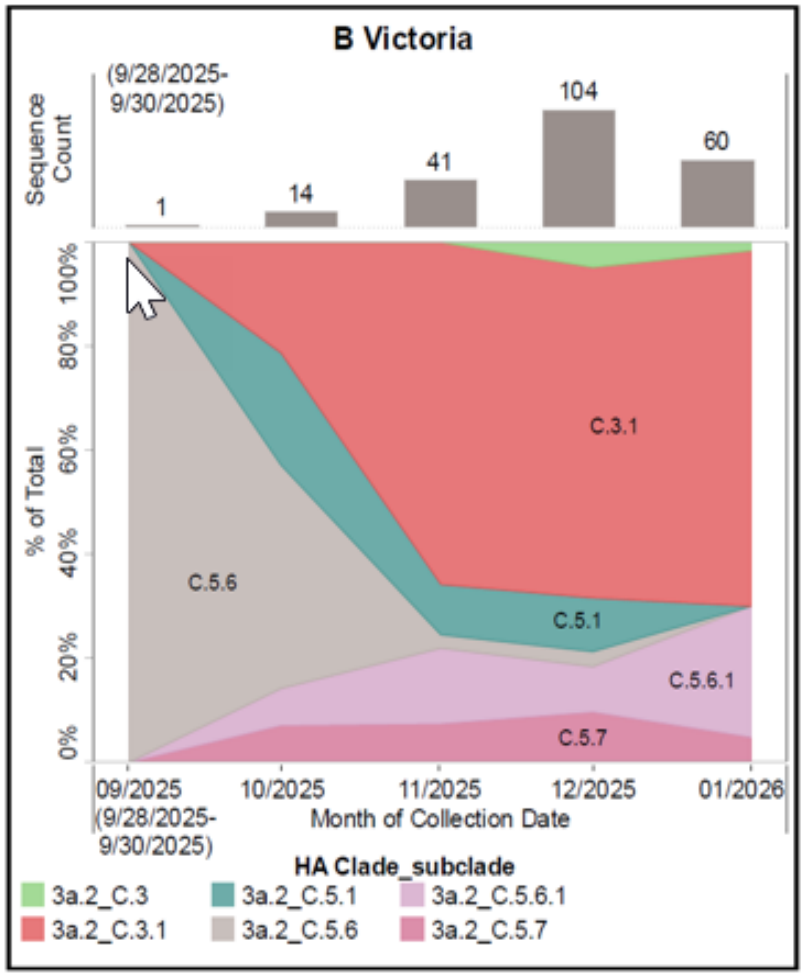
VCM Information meeting: https://www.youtube.com/@who

B/Victoria Extended Diversity Plot

Global view
Feb 2025-Jan 2026



US view
Sep 28, 2025-Jan 2026



Data Source: GISAID

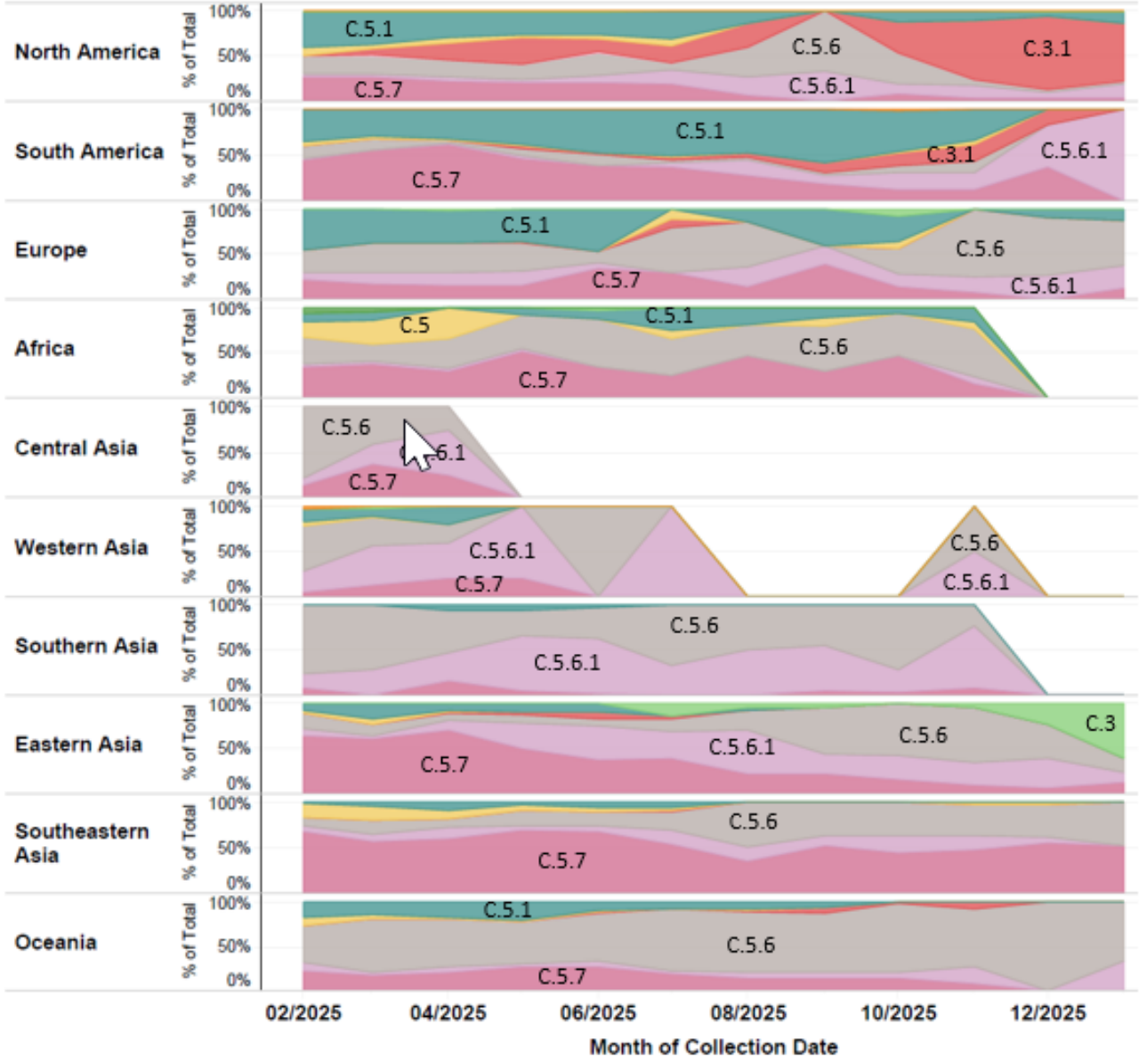
HA and NA clade/subclades:
https://clades.nextstrain.org/

B/Victoria Extended Diversity Plot by Geographic Region, February 1, 2025-Present

February 2025 – February 2026

HA Subclade

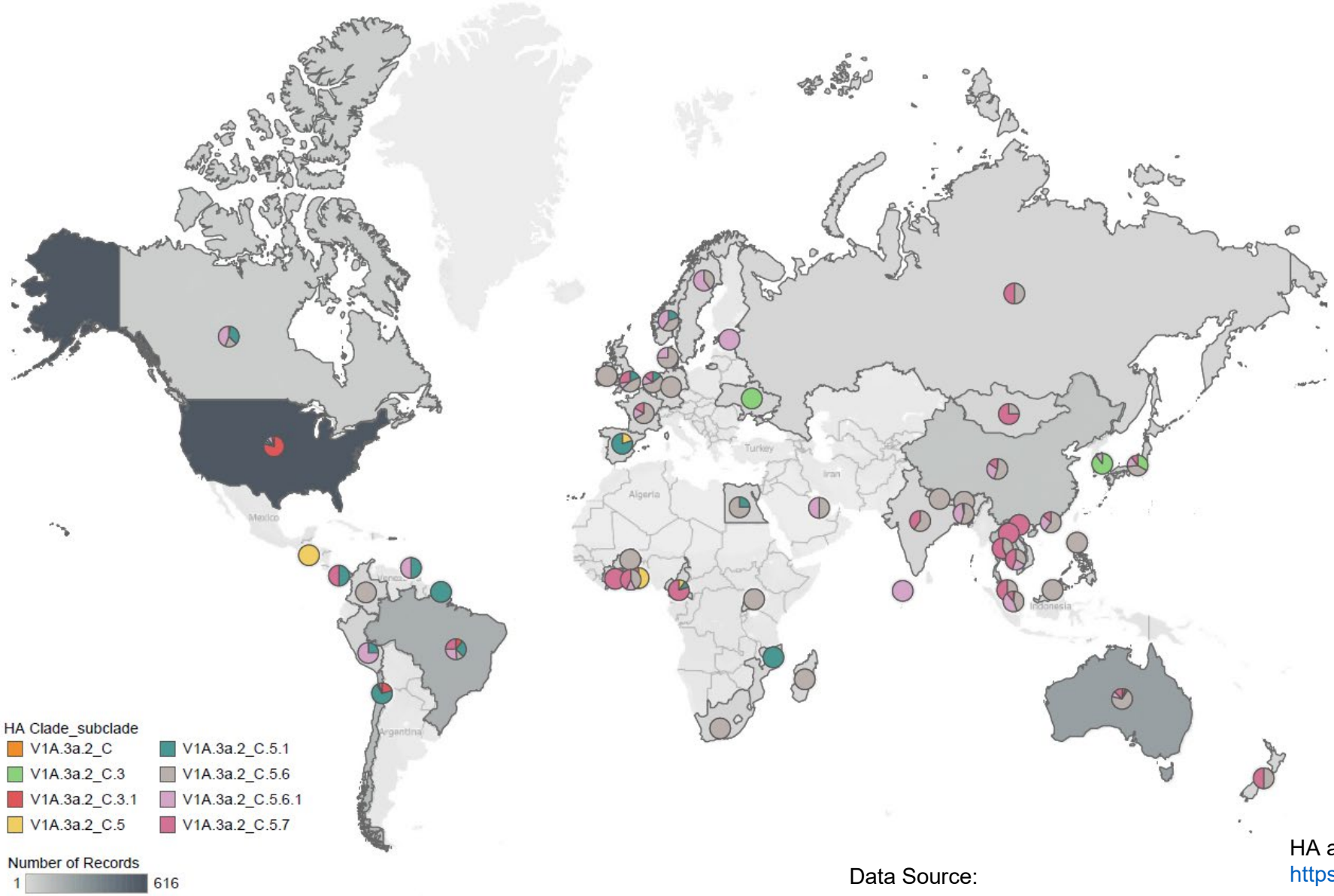
- A.3
- C
- C.2
- C.3
- C.3.1
- C.3.2
- C.5
- C.5.1
- C.5.6
- C.5.6.1
- C.5.7



Data Source: GISAID

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

Global B/Victoria HA clade diversity: Sep 2025 to Jan 2026



Data Source:

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

Antigenic analysis of B/Victoria viruses in **HI** assays

Antisera to northern hemisphere 2025-26 & southern hemisphere 2026 vaccine virus antigens

WHO CC	B/Austria/1359417/2021-like Cell Clade V1A.3a.2	Low (≥ 8 fold)	WHO CC	B/Austria/1359417/2021-like Egg Clade V1A.3a.2	Low (≥ 8 fold)
CDC	43 (57%)	33 (43%)	CDC	43 (57%)	33 (43%)
CNIC	218 (98%)	4 (2%)	CNIC	215 (97%)	7 (3%)
FCI	33 (97%)	1 (3%)	FCI	1 (3%)	33 (97%)
NIID	16 (53%)	14 (47%)	NIID	16 (53%)	14 (47%)
VIDRL	284 (96%)	13 (4%)	VIDRL	285 (96%)	12 (4%)
TOTAL	594 (90%)	65 (10%)	TOTAL	560 (85%)	99 (15%)

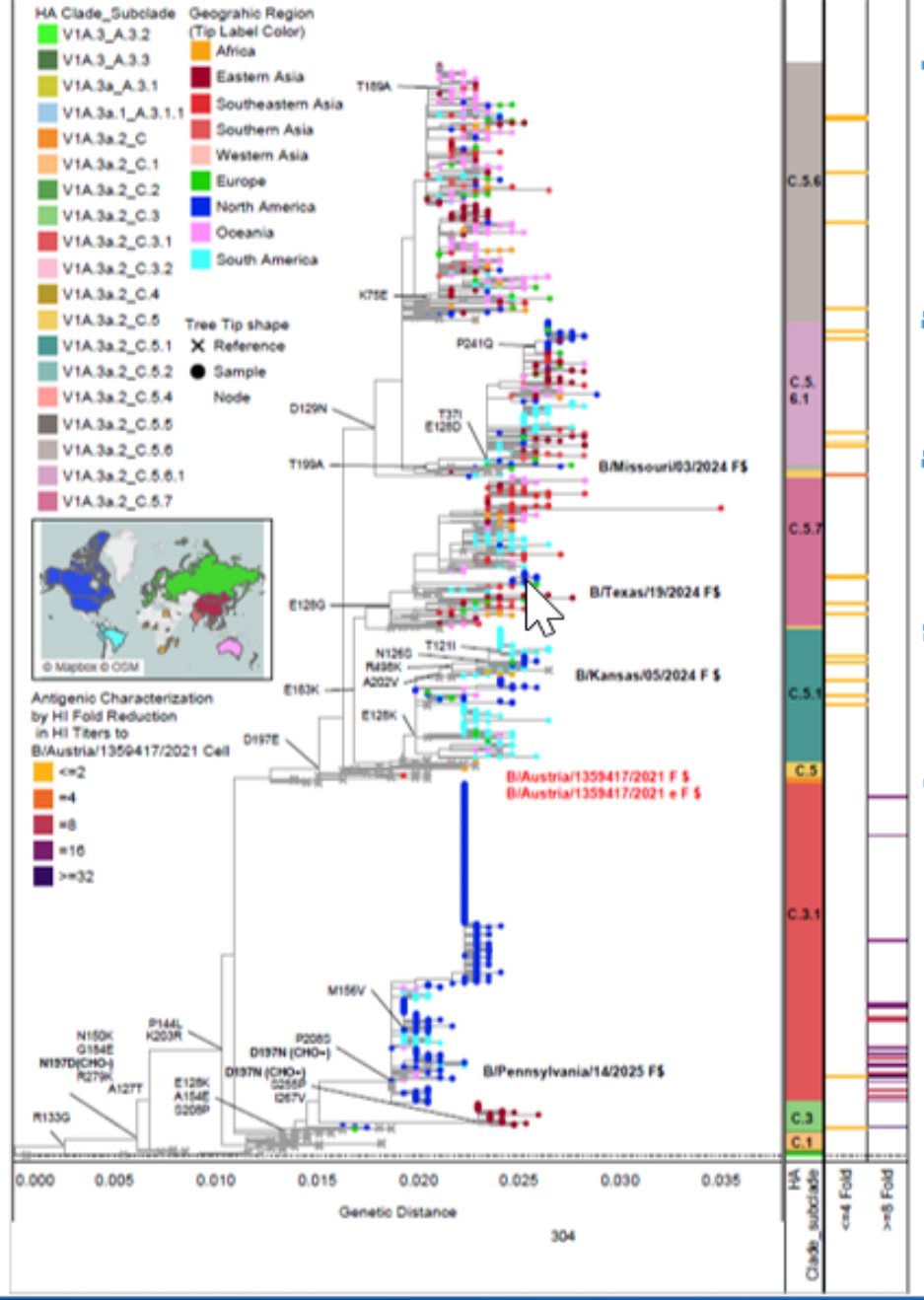
"Low" represented titers ≥ 8-fold lower than vaccine strain homologous titer

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

B/Victoria Integrated Genotype and Phenotype Analysis

Antigenic Characterization by HI Fold Reduction to B/Austria/1359417/2021 Cell

- <=2
- =4
- =8
- =16
- >=32



C.5.6

C.5.6.1

C.5.7

C.5, C.5.1

C.3, C.3.1

Data Source: GISAID

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

HI antigenic analysis of B/Victoria lineage viruses

		REFERENCE ANTISERA			
		Cell B/Austria/ 1359417/2021	Cell B/Missouri/ 03/2024	Cell B/Texas/ 19/2024	Cell B/Pennsylvania/ 14/2025
	HA subclade	C	C.5.6	C.5.7	C.3.1
REFERENCE VIRUSES					
B/Austria/1359417/2021	C	320	1280	2560	40
B/Missouri/03/2024	C.5.6	320	2560	1280	40
B/Texas/19/2024	C.5.7	320	2560	2560	40
B/Pennsylvania/14/2025	C.3.1	20	80	80	80
TEST VIRUSES					
B/Shandong-Huancui/11058/2025	C.3	20	80	160	160
B/Colorado/65/2025	C.3	40	80	160	160
B/Pennsylvania/01/2026	C.3	40	80	160	160
B/Virginia/20/2025	C.3.1	40	80	320	320
B/Sao Paulo/358687134-IAL/2025	C.3.1	20	80	160	160
B/Hawaii/03/2026	C.3.1	40	80	160	160
B/Michigan/04/2026	C.3.1	40	80	160	160
B/Oklahoma/02/2026	C.3.1	40	80	160	160
B/New Hampshire/27/2025	C.3.1	20	40	80	80
B/Bangladesh/2898/2025	C.5.6	320	2560	5120	80
B/New York/43/2025	C.5.6	320	1280	2560	40
B/Kanagawa/Ac2504/2025	C.5.6	320	2560	2560	80
B/Tokyo/EIS13-776/2025	C.5.6.1	320	2560	2560	80
B/Bangladesh/2857/2025	C.5.6.1	320	2560	2560	80
B/North Dakota/02/2026	C.5.6.1	160	1280	1280	40
B/Vietnam/5315/2025	C.5.7	320	2560	5120	80
B/Cameroon/1888/2025	C.5.7	320	1280	5120	40
B/Missouri/36/2025	C.5.7	160	1280	1280	40

Source: CDC, USA

		REFERENCE ANTISERA	
		Egg B/Austria/ 1359417/2021	Egg B/Tokyo/ EIS13-175/2025
	HA subclade	C	C.3.1
REFERENCE VIRUSES			
B/Austria/1359417/2021	C	640	640
B/Austria/1359417/2021	C	640	320
B/Tokyo/EIS13-175/2025	C.3.1	160	1280
TEST VIRUSES			
B/Okinawa/491/2025	C.3	80	160
B/Tokyo/EIS14-299/2025	C.3	80	160
B/Kanagawa/AC2536/2026	C.3	80	160
B/Kanagawa/AC2542/2026	C.3	80	80
B/Sendai/1/2025	C.3	80	160
B/Yamaguchi/48/2025	C.3	80	160
B/Seoul/2678/2025	C.3	80	160
B/Kanagawa/AC2535/2026	C.3	80	160
B/Taiwan/C22327/2025	C.3.1	80	160
B/Tokyo/EIS13-175/2025	C.3.1	80	160
B/Tokyo/EIS13-011/2025	C.3.1	80	80
B/Pennsylvania/14/2025	C.3.1	80	160
B/Tokyo/EIS13-715/2025	C.5.7	640	1280
B/Taiwan/S27751/2025	C.5.7	640	640
B/Kanagawa/AC2504/2025	C.5.6	640	640
B/Taiwan/S28160/2025	C.5.6	640	640
B/Gifu-C/1/2025	C.5.6	320	640
B/Kanagawa/IC2536/2025	C.5.6.1	320	640

Source: WHO CC, Japan

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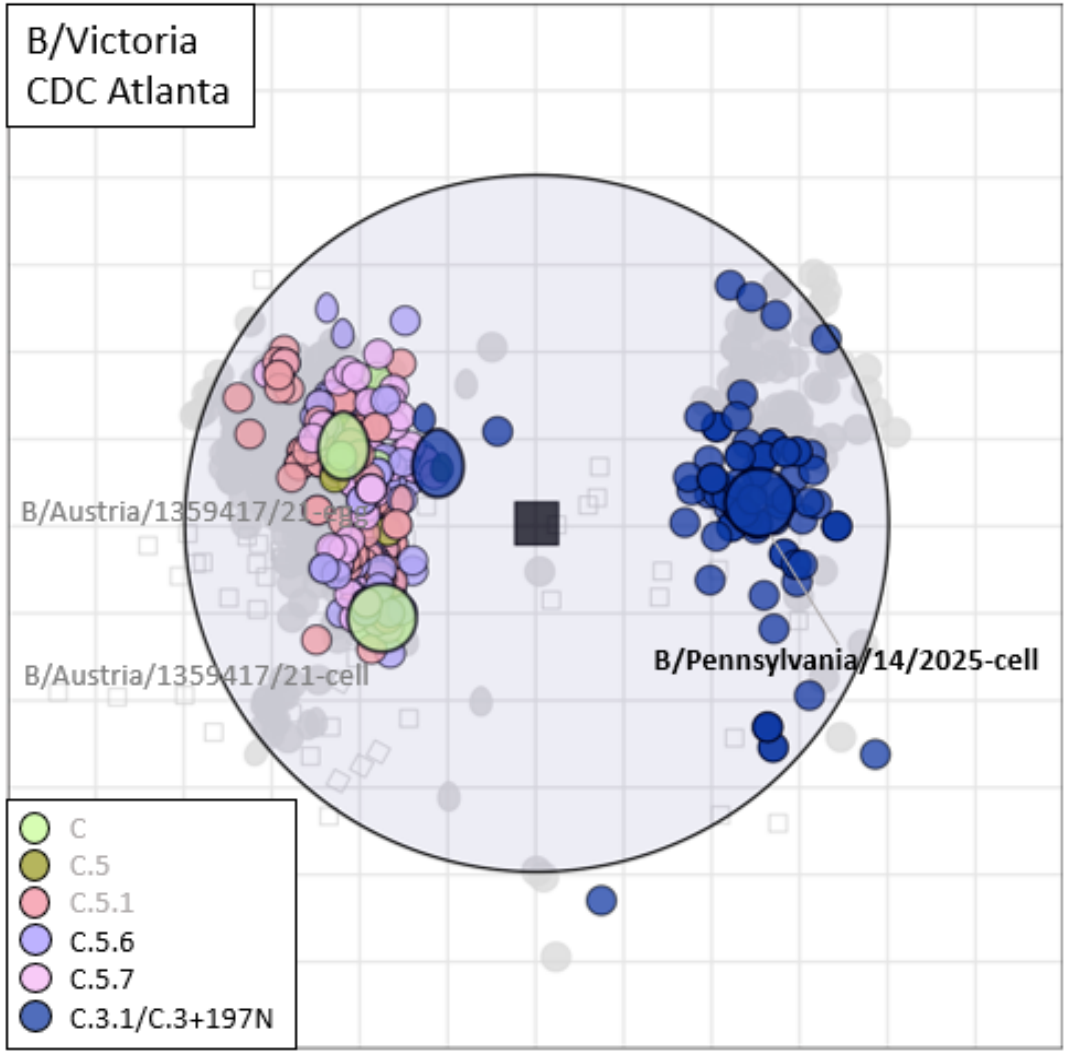
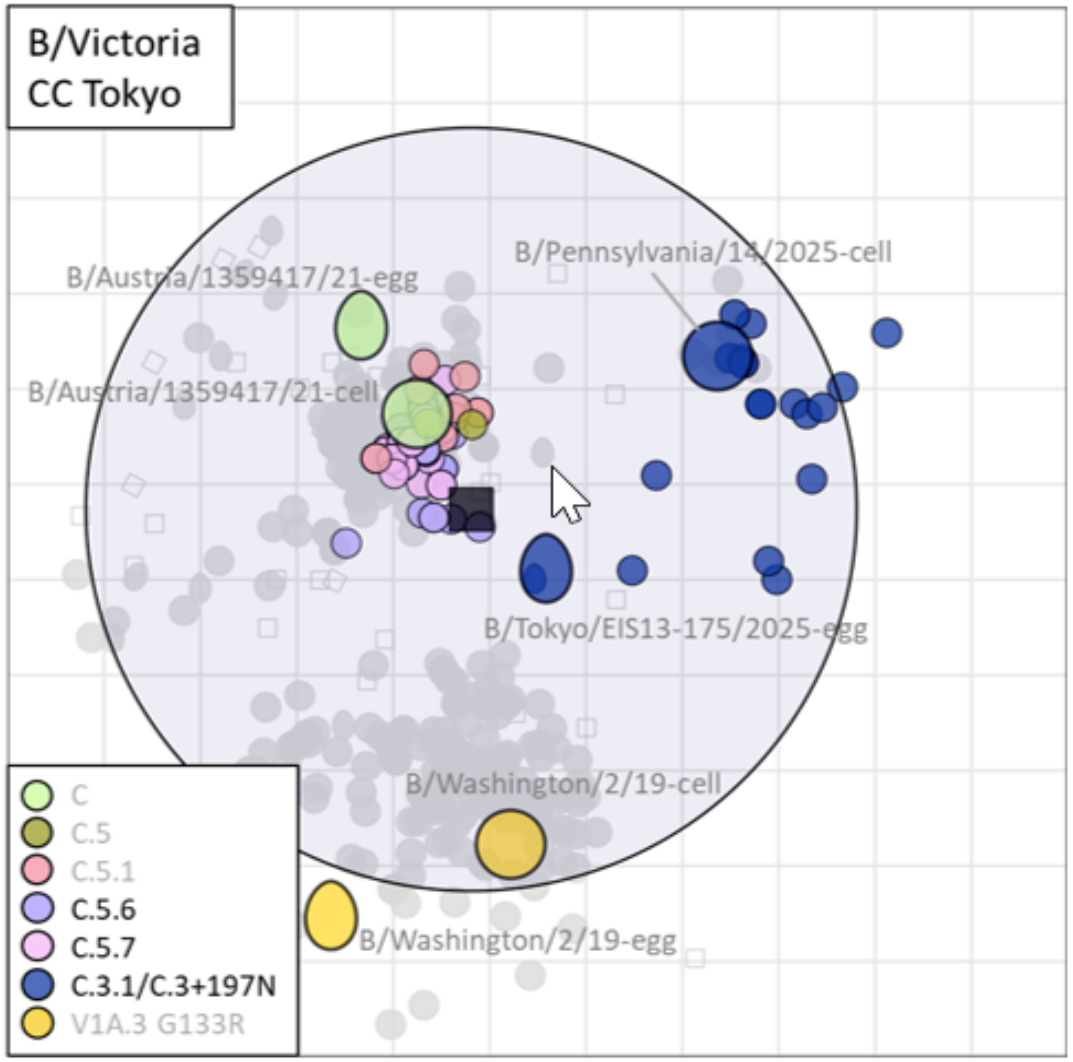
B/Victoria antigenic cartography



B/Pennsylvania/14/2025-cell-like serum circle
(within 8-fold of homologous titer)



B/Tokyo/EIS13-175/2025-egg-like serum circle
(within 8-fold of homologous titer)

Source: University of Cambridge

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Human post-vaccination serum analysis of B/Victoria viruses (CDC data)

				C - *AUT/1359417 MDCK	C.3.1 +D197N (CHO+) - PA/14 MDCK	C.5.1 - KS/05 MDCK	C.5.6 - MO/03 MDCK	C.5.7 - TX/19 MDCK
B/AUSTRIA/1359417/ 2021 MDCK [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	192	24	√	116	√
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	260	17	√	√	√
	Adult (18-49Y)	USA	ccIIV3 (cell)	437	77	√	√	√
			RIV3 (recombinant)	491	108	√	√	√
	Elderly (≥65Y)	USA	HD-IIV3 (egg)	204	44	√	√	√

				C - *AUT/1359417 EGG	 AUT/1359417 MDCK	C.3.1 +D197N (CHO+) - PA/14 MDCK	C.5.1 - KS/05 MDCK	C.5.6 - MO/03 MDCK	C.5.7 - TX/19 MDCK
B/AUSTRIA/1359417/ 2021 EGG [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	168	√	24	√	√	√
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	279	√	17	√	√	√
	Adult (18-49Y)	USA	ccIIV3 (cell)	437	√	77	√	√	√
			RIV3 (recombinant)	445	√	108	√	√	√
	Elderly (≥65Y)	USA	HD-IIV3 (egg)	226	√	44	√	√	√

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: B/AUSTRIA/1359417/2021 (AUT/1359417); B/KANSAS/05/2024 (KS/05); B/MISSOURI/03/2024 (MO/03); B/PENNSYLVANIA/14/2025 (PA/14); B/TEXAS/19/2024 (TX/19).

Statistically non-inferior = √
Statistically non-inferior but reference virus GMT < 40 = X

GMT Ratio Lower Bound (90% CI)
0.0 — 1.0

B/Victoria lineage antiviral susceptibility

Neuraminidase inhibitors

- Of 549 influenza B/Victoria lineage viruses collected since September 1, 2025, and examined by genetic and/or phenotypic analyses, only two showed evidence of reduced or highly reduced susceptibility by NAIs; both had an NA M464T substitution.

Endonuclease inhibitors

- Of 760 B/Victoria lineage viruses examined by genetic and/or phenotypic analyses in this period, none showed evidence of reduced susceptibility to baloxavir marboxil

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Influenza B/Victoria lineage summary (1)

Phylogenetics of B/Victoria lineage HA genes

- All viruses characterized belong to clade 3a.2 with further diversification into several subclades (C.1-C.5).
- Viruses designated as C.5, C.5.1, C.5.6, C.5.6.1 and C.5.7, all of which had the HA substitution D197E, circulated at varying proportions in different regions.
- Viruses designated as C.3 have HA substitutions E128K, A154E and S208P.
- Subclade C.3.1 viruses shared additional mutations D197N (addition of a potential N-glycosylation site) and P208S.
- Recent C.3 viruses which had additional changes D197N (addition of a potential N-glycosylation site), S255P and I267V and C.3.1 viruses have been detected in increasing proportions in Eastern Asia and North America in recent weeks.

Influenza B/Victoria lineage summary (2)

Antigenic characteristics of B/Victoria lineage viruses

- Post-infection ferret antisera against B/Austria/1359417/2021-like viruses (3a.2 HA) inhibited the recently circulating C.5.1, C.5.6, C.5.6.1 and C.5.7 viruses well.
  - C.3 and C.3.1 subclade viruses with HA substitution D197N were recognized poorly.
- Post-infection ferret antisera raised against cell culture-propagated viruses from subclade C.3.1 (e.g., B/Pennsylvania/14/2025) recognized recently circulating viruses from C.3, C.3.1 and other 3a.2 subclades well.
- All available egg isolates for subclade C.3 and C.3.1 viruses (e.g., B/Tokyo/EIS13-175/2025) acquired egg-adaptive mutations that remove the potential N-glycosylation site at HA 197 to 199.
- Post-infection ferret antisera raised against egg-propagated viruses from subclade C.3.1 (e.g., B/Tokyo/EIS13-175/2025) showing reduced recognition of recently circulating viruses from C.3 and C.3.1 subclades.

Influenza B/Victoria lineage summary (3)

Human serology studies

- Human serology studies were conducted using NH 2025-2026 influenza vaccine formulation vaccinated serum panels by HI assays with recent B/Victoria viruses with HA genes from subclades C.3, C.3.1, C.5, C.5.6, C.5.6.1 and C.5.7.
- When compared to the responses to egg or cell culture-propagated B/Austria/1359417/2021-like vaccine reference viruses, post-vaccination geometric mean titres (GMTs) were significantly reduced for recently circulating viruses from C.3 and C.3.1 subclades.

The data supported recommending a cell-propagated B/Pennsylvania/14/2025-like (C.3.1) virus and an egg-propagated B/Tokyo/EIS13-175/2025-like (C.3.1) virus as the B/Victoria vaccine antigens for the 2026-2027 northern hemisphere.

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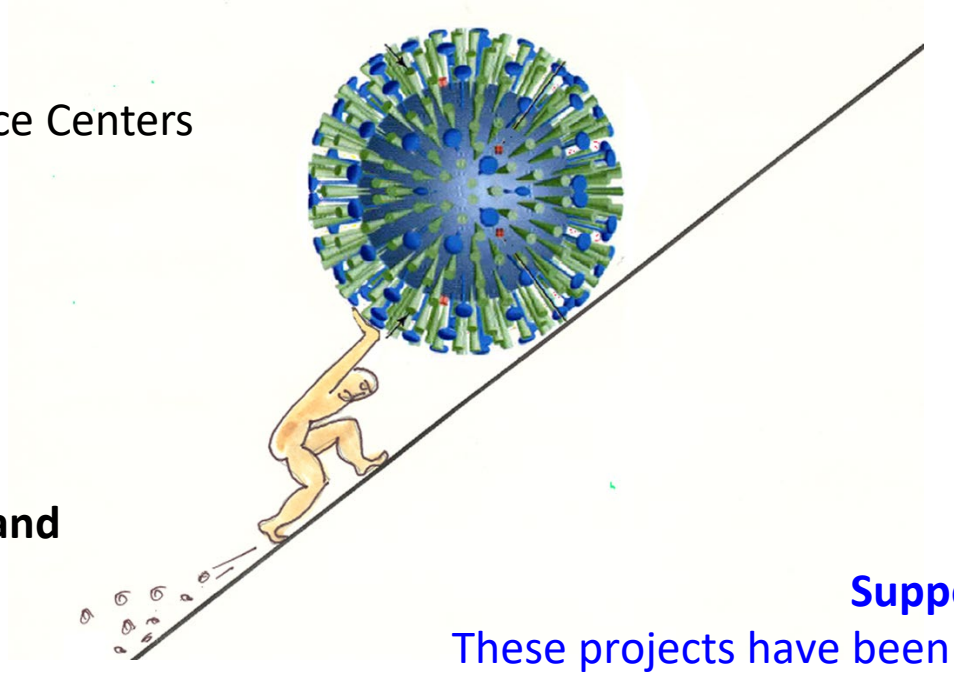
- National Influenza Reference Centers
- APHL

Global Influenza Surveillance and Response System

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



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