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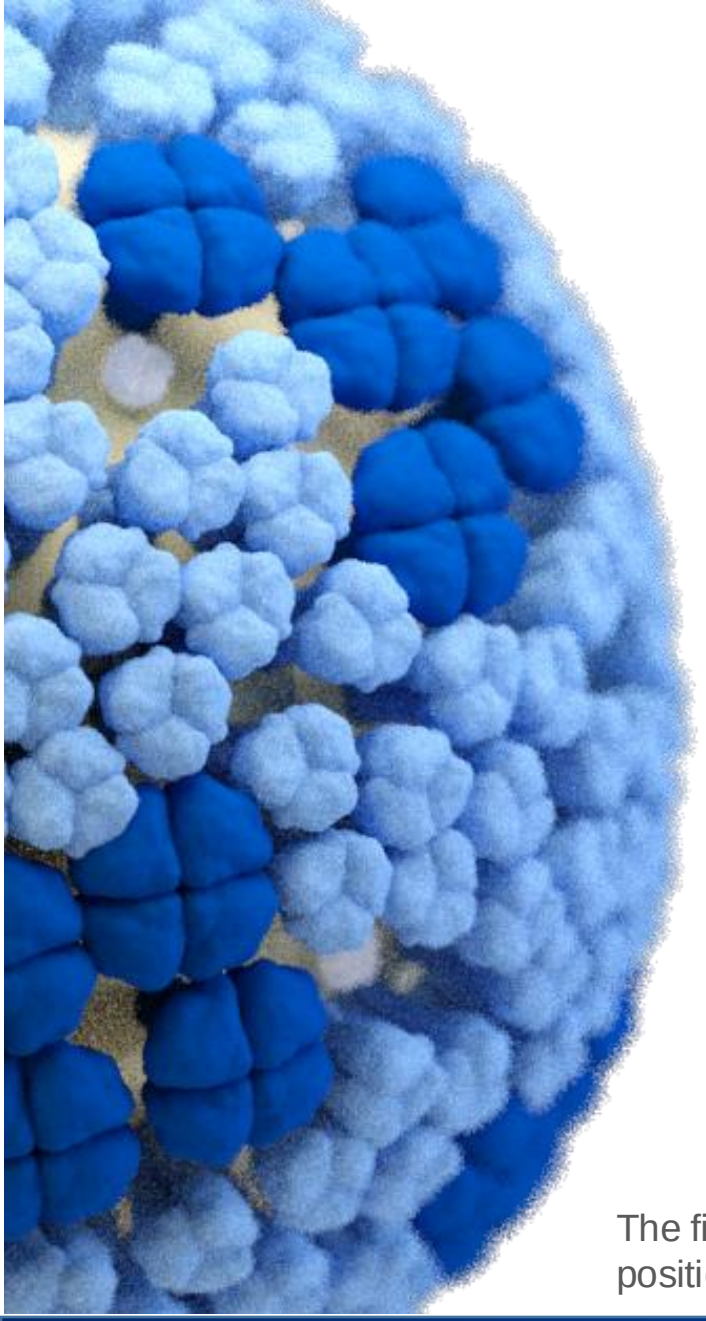


Interagency Meeting

Global Influenza Virus Surveillance and Characterization
March 13th, 2025

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

Global vaccine recommendations for the northern hemisphere 2025-2026

It is recommended that vaccines for use in the 2025-2026 northern hemisphere influenza season contain the following:

Trivalent: Egg-based Vaccines
- **an A/Victoria/4897/2022 (H1N1)pdm09-like virus antigen;**
- **an A/Croatia/10136RV/2023 (H3N2)-like virus antigen*; and**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.**

Trivalent: Cell-, recombinant protein- or nucleic acid-based Vaccines
- **an A/Wisconsin/67/2022 (H1N1)pdm09-like virus antigen;**
- **an A/District of Columbia/27/2023 (H3N2)-like virus antigen*; and**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus antigen.**

Quadrivalent: Egg- or cell culture- or recombinant-based Vaccines
- Above 3 components; and a **B/Phuket/3073/2013 (B/Yamagata lineage)-like antigen.**

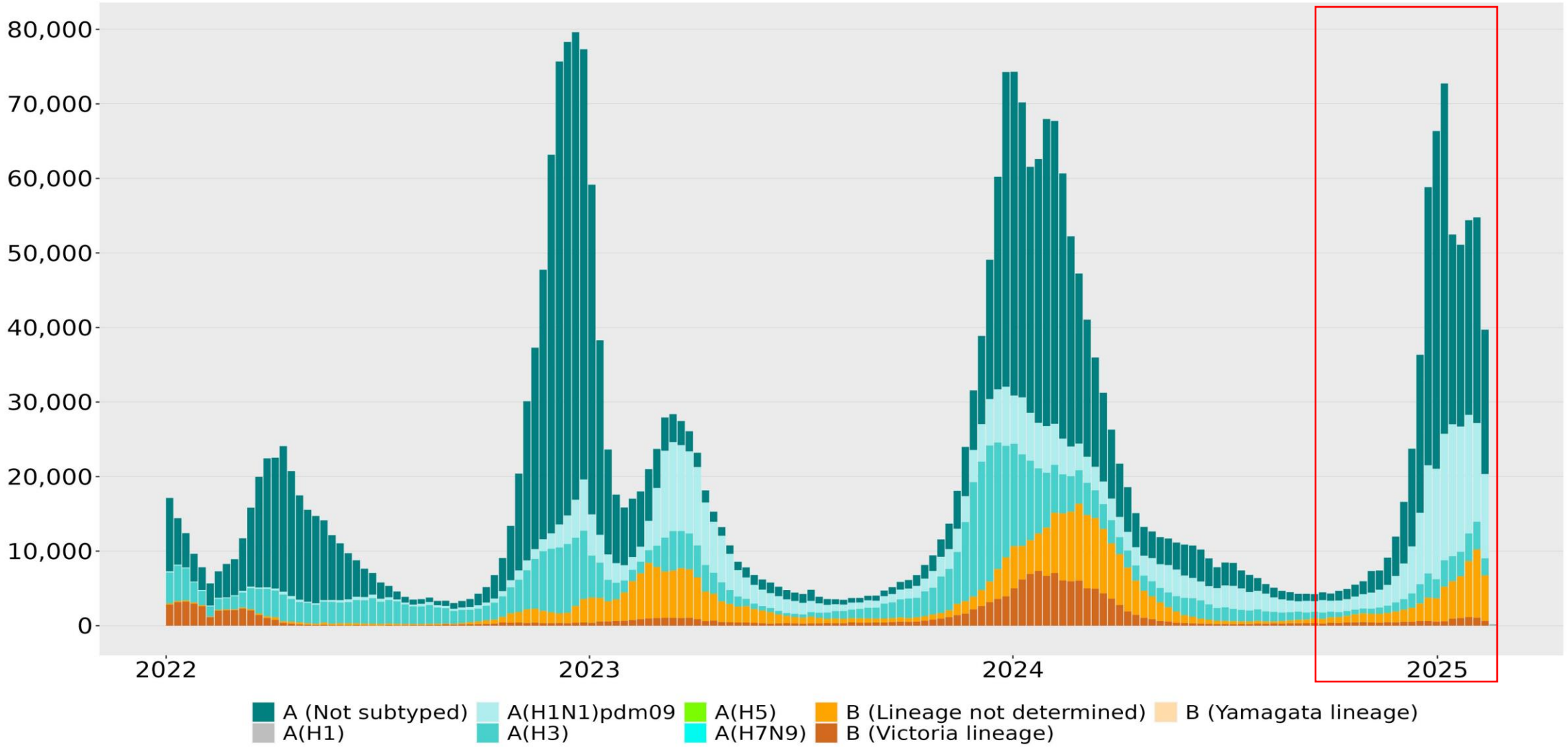
*** Different from that recommended for the 2024-25 northern hemisphere season**

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 2025-26 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

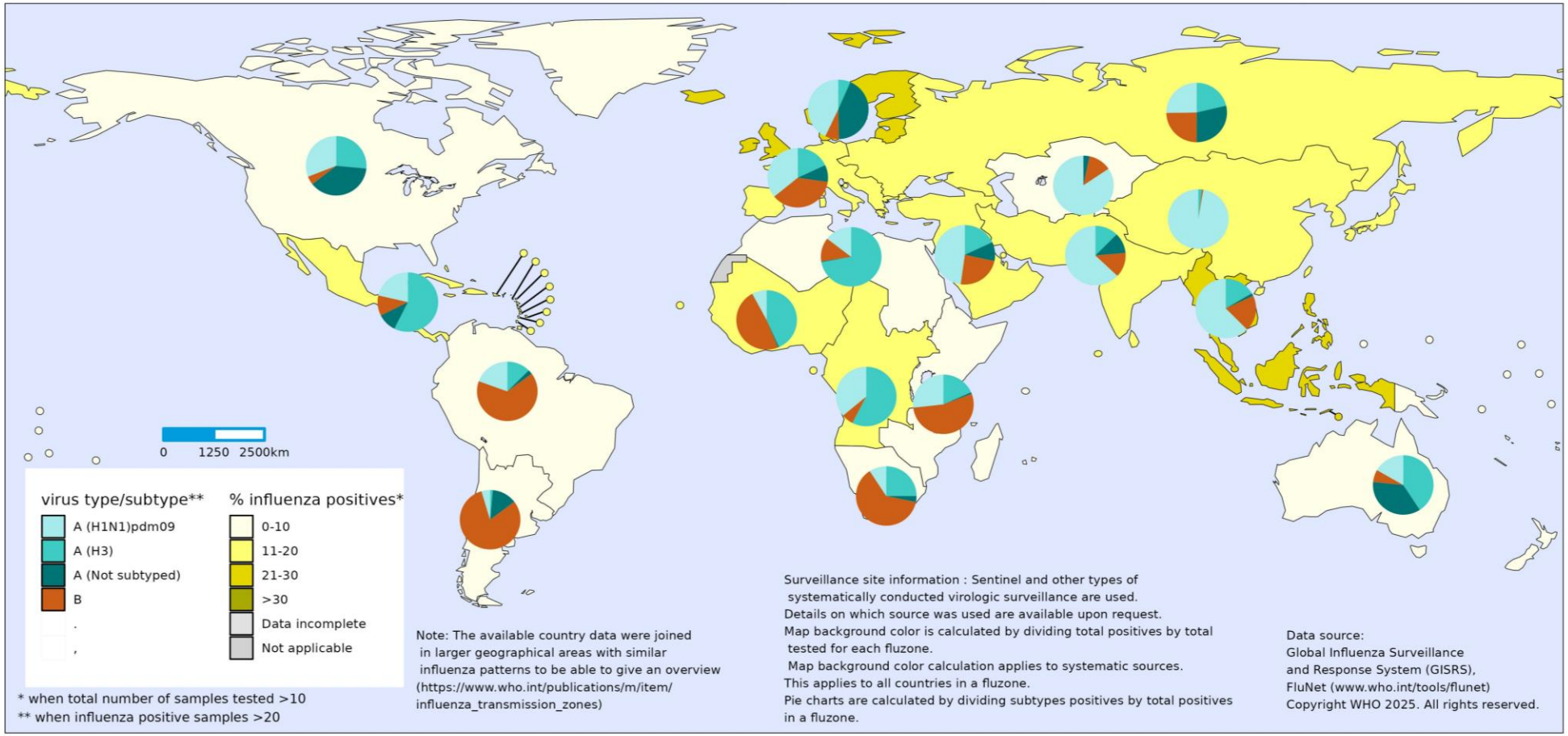
Global Circulation of Influenza Viruses Since 2022



VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

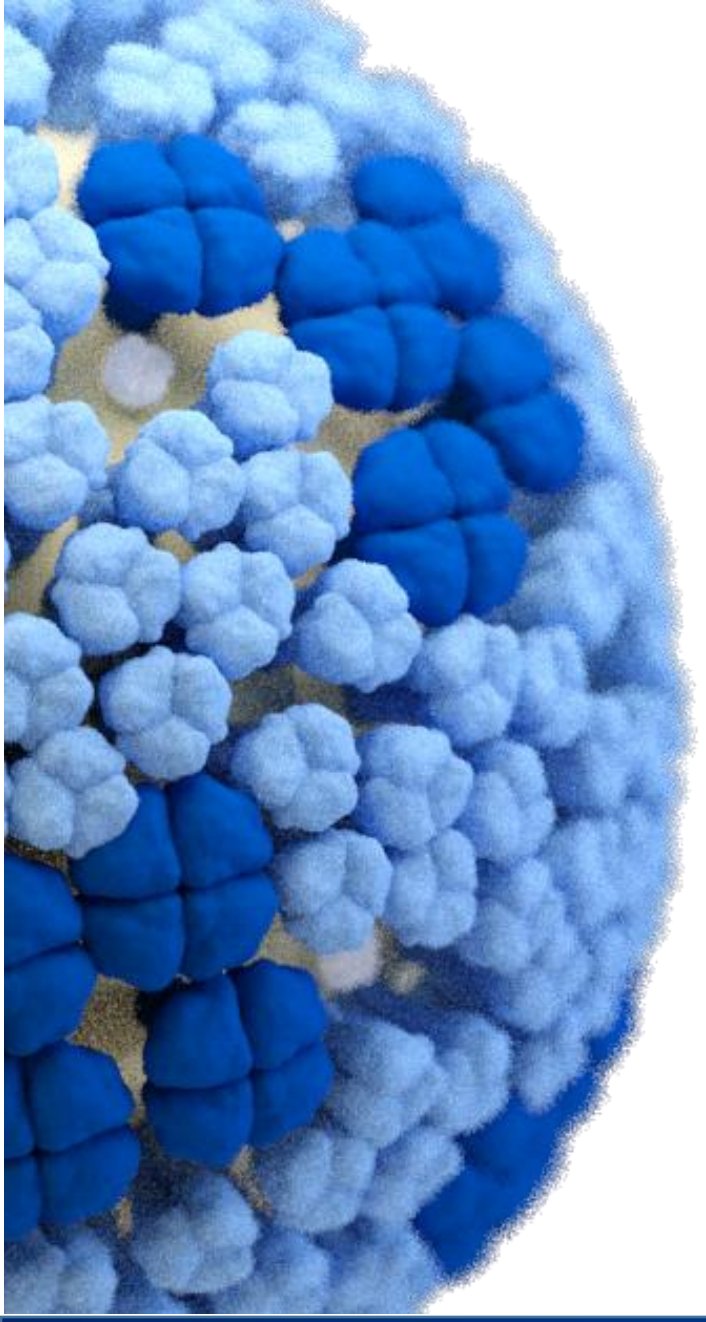
Influenza activity and global distribution of type/subtype

Distribution of Influenza virus type/subtype by influenza transmission zone, between September 01 2024 and January 31 2025



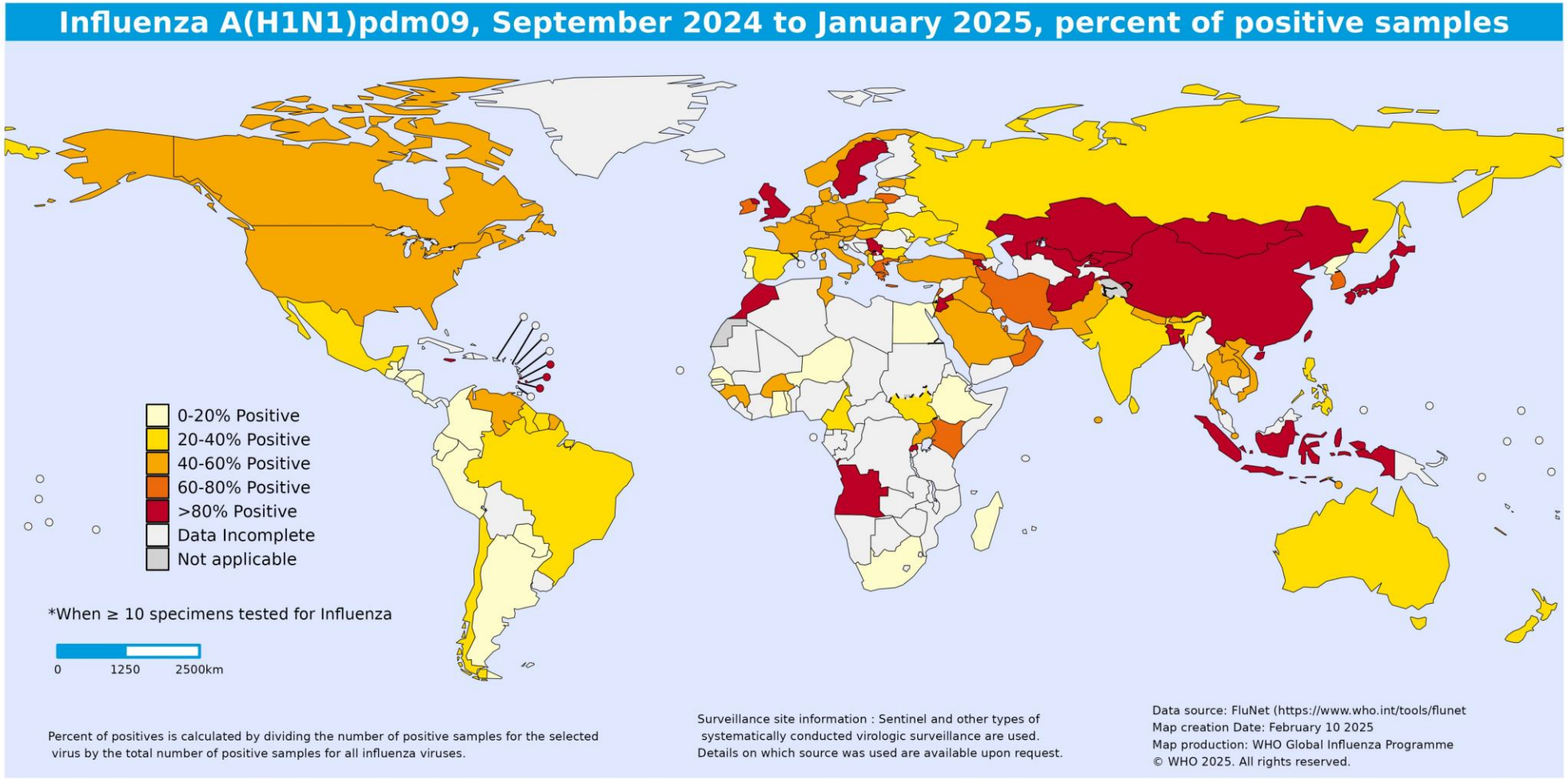
World Health Organization

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y



A(H1N1)pdm09 Viruses

Influenza A(H1N1)pdm09 activity

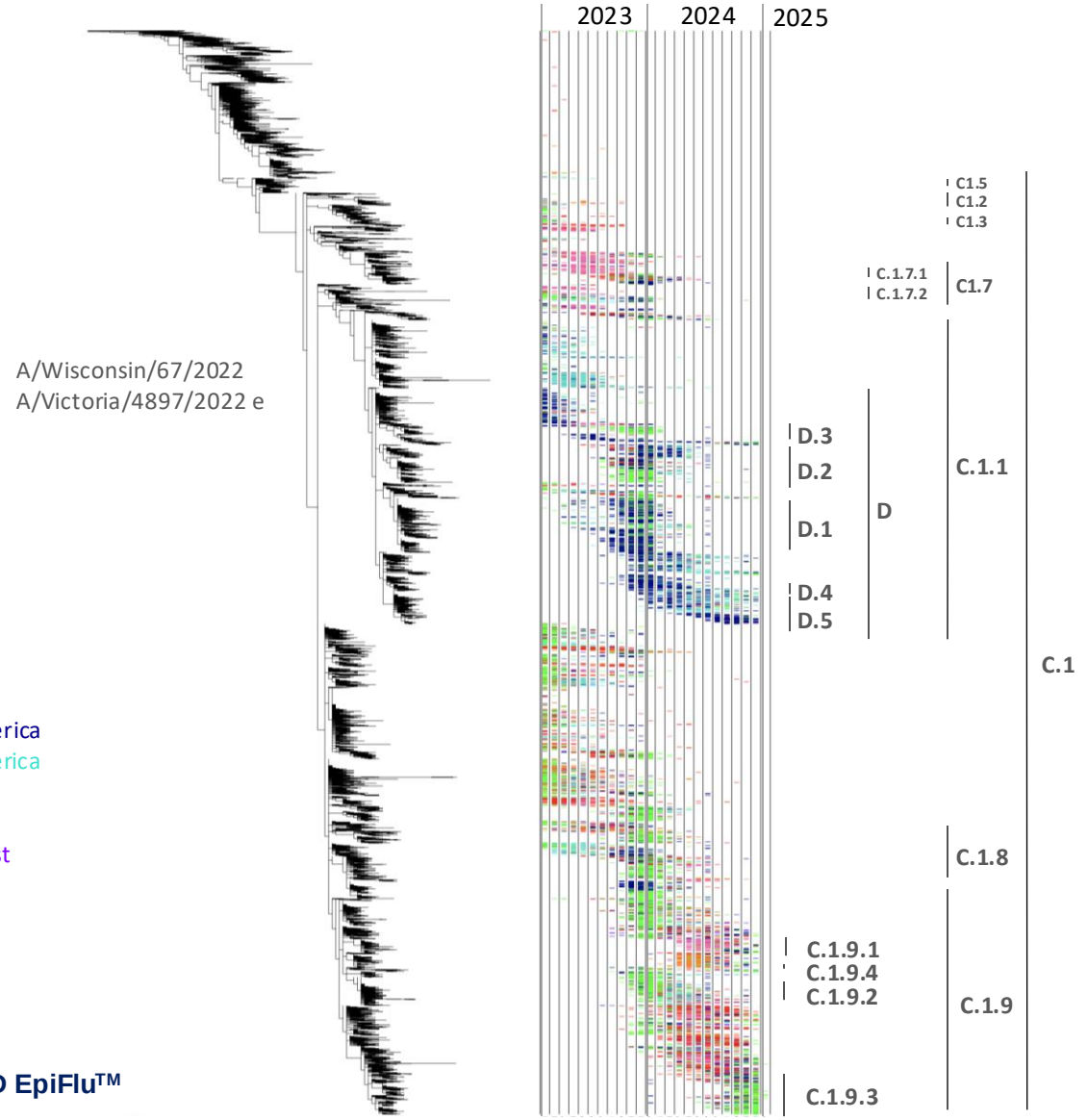


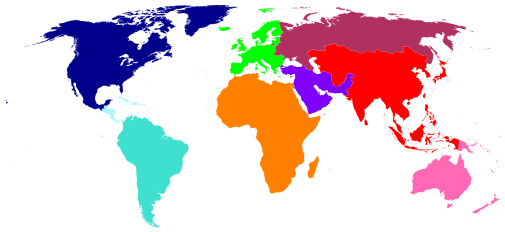
World Health Organization

Data source: FluNet, (https://www.who.int/tools/flunet), Global Influenza Surveillance and Response System (9 February 2025)

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H1N1)pdm09 HA phylogeography





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

Source: University of Cambridge, UK

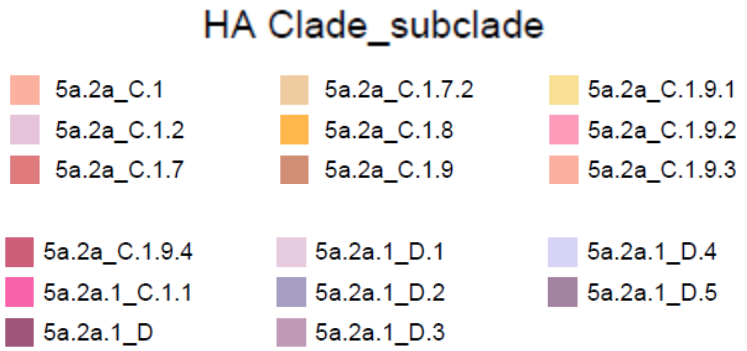
Based on HA sequence availability from GISAID EpiFlu™

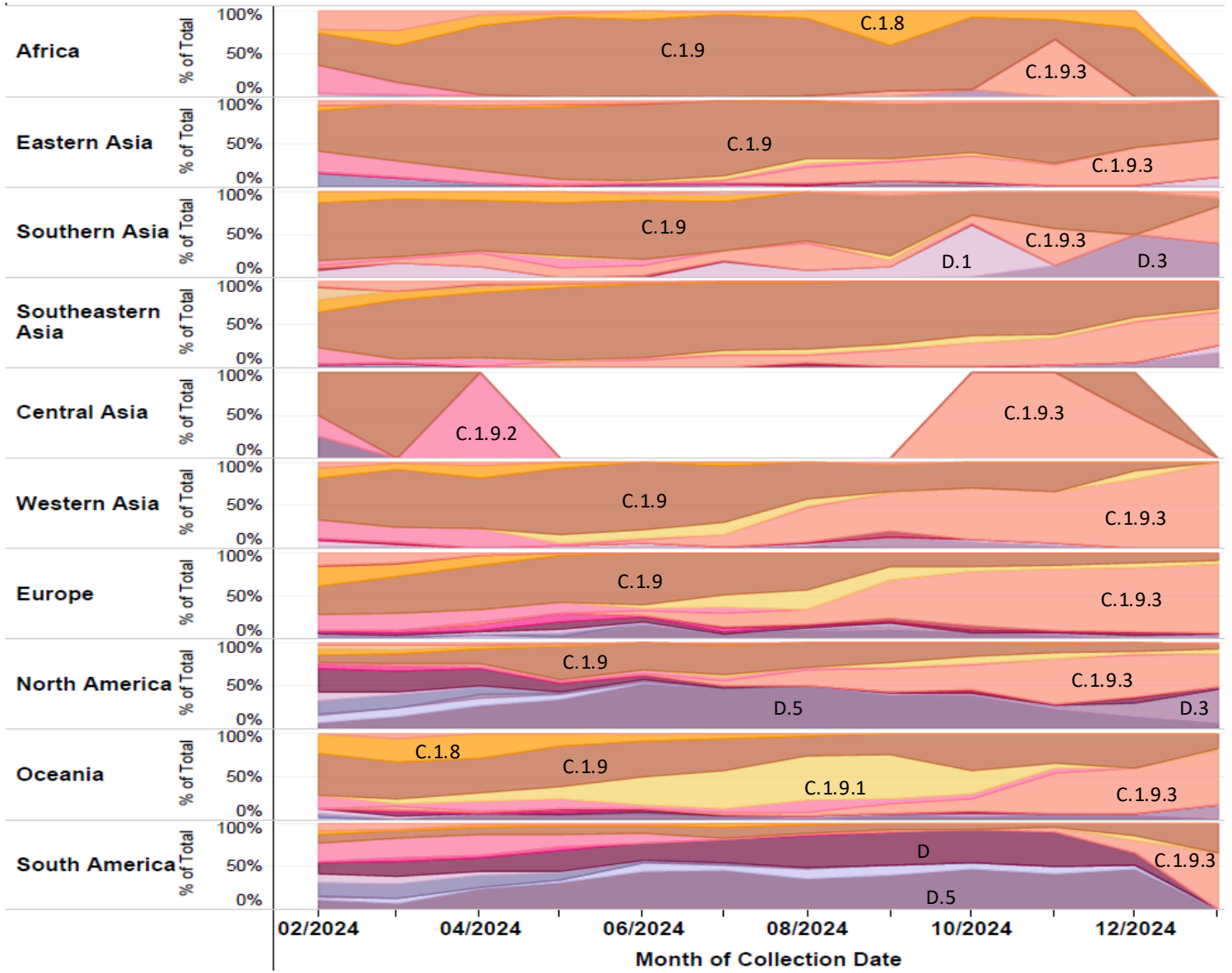
https://clades.nextstrain.org/

VCM Information meeting:
https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H1N1)pdm09 Extended Diversity Plot by Geographic Region

Feb. 1, 2024 - Present





https://clades.nextstrain.org/

Based on HA sequence availability from GISAID EpiFlu™

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

Antisera to northern hemisphere 2024-25 vaccine virus antigens

A/Wisconsin/67/2022-like (cell) D (5a.2a.1)			A/Victoria/4897/2022-like (egg) C.1.1 (5a.2a.1)		
WHO CC	Like (<8 fold)	Low (≥ 8 fold)	WHO CC	Like (<8 fold)	Low (≥ 8 fold)
CDC	219 (99%)	2 (1%)	CDC	219 (99%)	2 (1%)
CNIC	1579 (99%)	11 (1%)	CNIC	1544 (98%)	37 (2%)
FCI	396 (99%)	2 (1%)	FCI	397 (100%)	1 (0%)
NIID	153 (96%)	6 (4%)	NIID	153 (96%)	6 (4%)
VIDRL	608 (99%)	8 (1%)	VIDRL	612 (99%)	4 (1%)
TOTAL	2955 (99%)	29 (1%)	TOTAL	2925 (98%)	50 (2%)

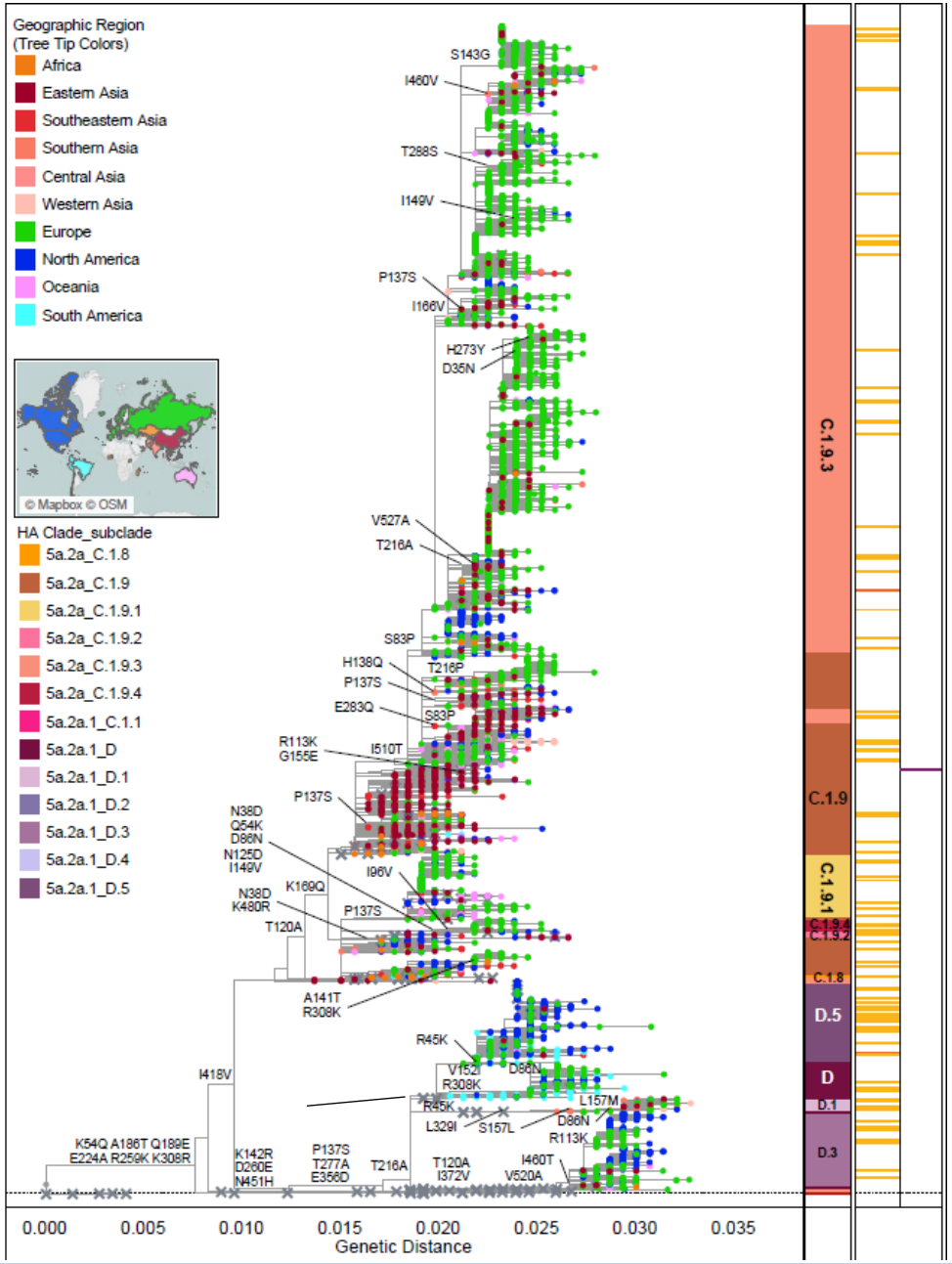
"Low" reactor represented titers ≥ 8-fold lower than vaccine strain homologous titer by HI

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H1N1)pdm09 Integrated Genotype and Phenotype Analysis

Clade	Subclade	HA Amino Acid changes compared to A/Wisconsin/67/2022
5a.2a	C.1	S137P, R142K, E260D, A277T, D356E, V418I, H451N
	C.1.8	V47I, T120A, S137P, R142K, E260D, A277T, D356E, H451N
	C.1.9	T120A, S137P, R142K, K169Q, E260D, A277T, D356E, H451N
	C.1.9.1	T120A, R142K, K169Q, E260D, A277T, D356E, H451N
	C.1.9.2	N38D, T120A, S137P, R142K, K169Q, E260D, A277T, D356E, H451N, K480R
	C.1.9.3	S83P, T120A, S137P, R142K, K169Q, E260D, A277T, D356E, H451N, I510T
	C.1.9.4	N38D, Q54K, D86N, T120A, N125D, S137P, R142K, I149V, K169Q, E260D, A277T, D356E, H451N
5a.2a.1	C.1.1	None
	D	T216A
	D.1	R45K, T216A
	D.2	R113K, T216A, V427I
	D.3	T120A, T216A, I372V
	D.4	T120A, T216A
	D.5	R45K, T216A

https://clades.nextstrain.org/



Antigenic Characterization by HI using Ferret Antisera Fold Reduction into A/Wisconsin/67/2022 cell

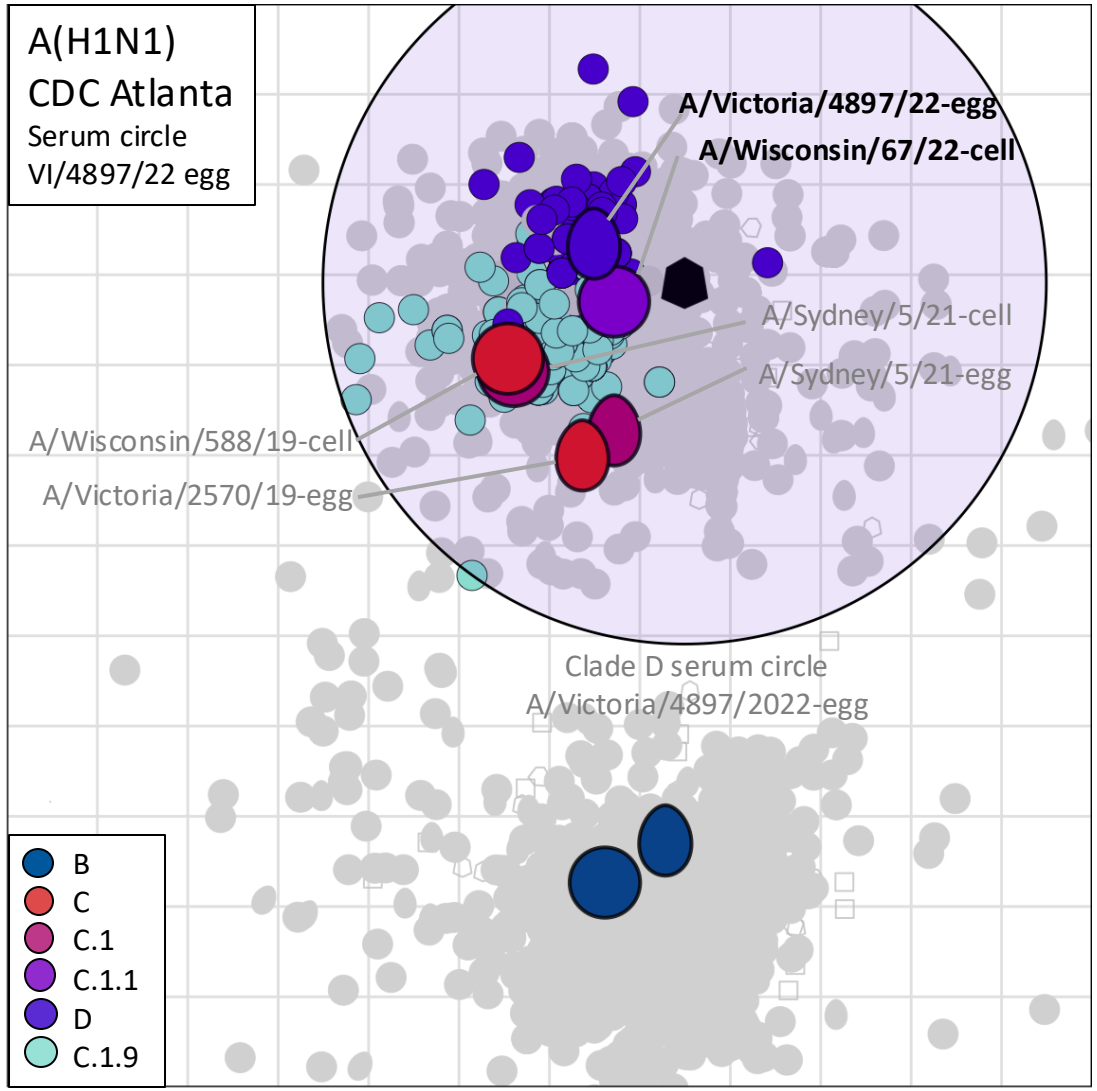
<=2
=4
=8

5a.2a
(C.1.8, C.1.9, C.1.9.1, C.1.9.2, C.1.9.3, C.1.9.4)

5a.2a.1
(C.1.1, D, D.1, D.2, D.3, D.4, D.5)

Based on HA sequence availability from GISAID EpiFlu™

A(H1N1)pdm09 antigenic cartography



Source: University of Cambridge

VCM Information meeting:
https://www.youtube.com/watch?v=kGTmLmiBL-Y

Serum circles (within 8-fold of homologous titers)

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

Vaccine: A/Wisconsin/67/2022-like C.1.1 (5a.2a.1)

				C.1.1 (5a.2a.1)	D (5a.2a.1)	D.5 (5a.2a.1)	C.1.9 (5a.2a)			C.1.9.3 (5a.2a)
				-	+V152I	+R45K +T216A	+T120A +K169Q	+T120A +P137S +K169Q	+T120A +G155E +K169Q	+T120A +I166V +K169Q
				*WI/67	MA/76	DE/83	MI/59	TN/77	MO/124	IA/110
				SIAT	SIAT	SIAT	SIAT	SIAT	SIAT	SIAT
A/WISCONSIN/67/2022 SIAT [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	175	√	√	73	73	28	101
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	686	√	√	√	√	√	√
	Pediatric (9-17Y)	USA	ccIIV3 (cell)	502	√	√	√	√	√	√
	Adult	USA	ccIIV3 (cell)	408	√	√	√	√	√	√
			RIV3 (recombinant)	502	√	√	√	√	320	√
			IIV3 (egg)	557	√	√	√	√	408	√
	Elderly (≥65Y)	USA	IIV3-HD (egg)	243	√	√	√	√	√	√

Statistically non-inferior = √

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

GMT Ratio Lower-Bound (90% CI)

0.000 — 1.000

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/DELAWARE/83/2024 (DE/83); A/IOWA/110/2024 (IA/110); A/MASSACHUSETTS/76/2024 (MA/76); A/MICHIGAN/59/2023 (MI/59); A/MISSOURI/124/2024 (MO/124); A/TENNESSEE/77/2024 (TN/77); A/WISCONSIN/67/2022 (WI/67).

A(H1N1)pdm09: antiviral susceptibility

Neuraminidase inhibitors

- Of 2,492 A(H1N1)pdm09 virus clinical samples and isolates that were examined for neuraminidase inhibitor (NAI) susceptibility by genetic and/or phenotypic analyses, 61 viruses showed evidence of reduced susceptibility to NAIs.
  - Fifty-six had NA substitution H275Y (42 of which were detected in China), two had a mixture of H275Y/H, two had I223K, one had I223V and S247N.

Endonuclease inhibitors

- Of 1,754 A(H1N1)pdm09 viruses examined by genetic and/or phenotypic analyses, four showed reduced susceptibility to the endonuclease inhibitor baloxavir marboxil.
  - One virus had an E23G PA substitution, one had a mixture of E23K/E, one had an E199G, and one had a mixture of E199K/E

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H1N1)pdm09 summary (1): global circulation and HA diversity

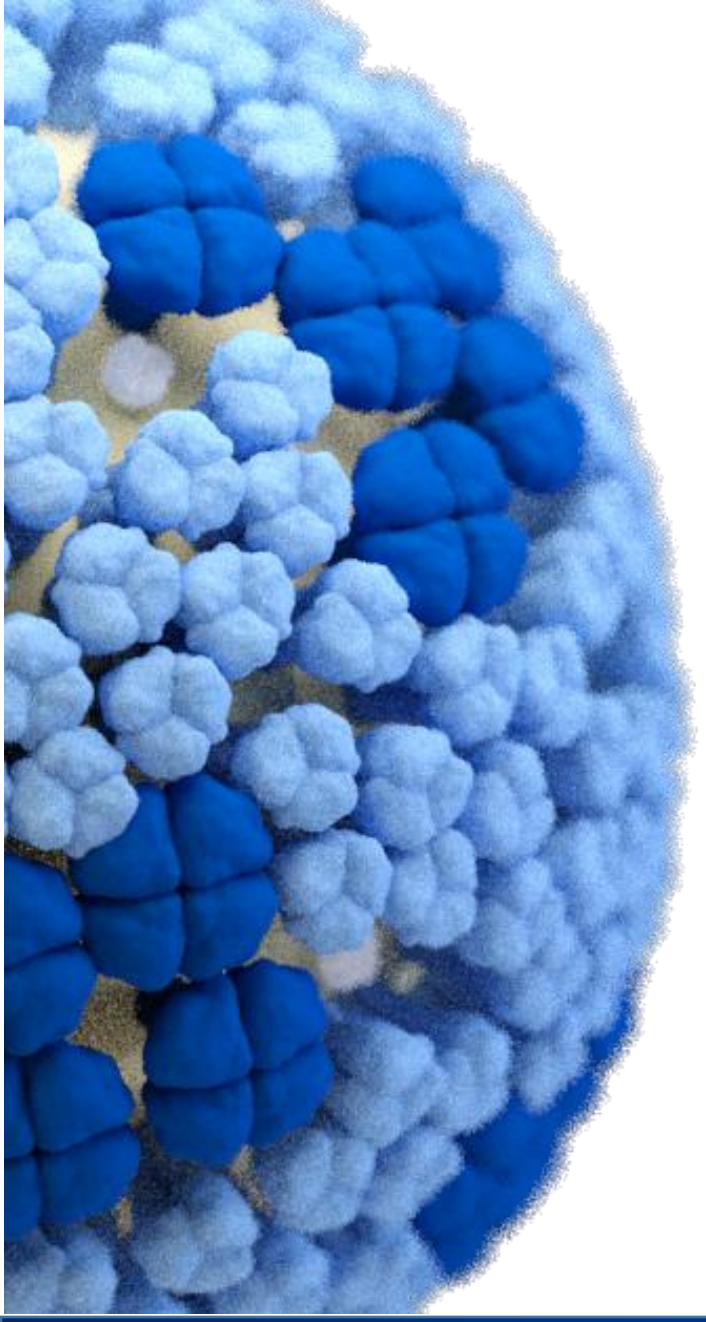
- A(H1N1)pdm09 viruses circulated globally and predominated in several geographic regions.
- The hemagglutinin (HA) genes of viruses that were genetically characterized belonged to the 6B.1A.**5a.2** clade, with further diversity within subclades 5a.2a and 5a.2a.1 and their respective emerging subclades.
- Viruses from both subclades continued to circulate:
  - 5a.2a viruses were predominant in Oceania, Asia, Europe, Africa, and the Caribbean, while 5a.2a.1 viruses were predominant in South America. In North America, both clades co-circulated.

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H1N1)pdm09 summary (2): antigenic characteristics

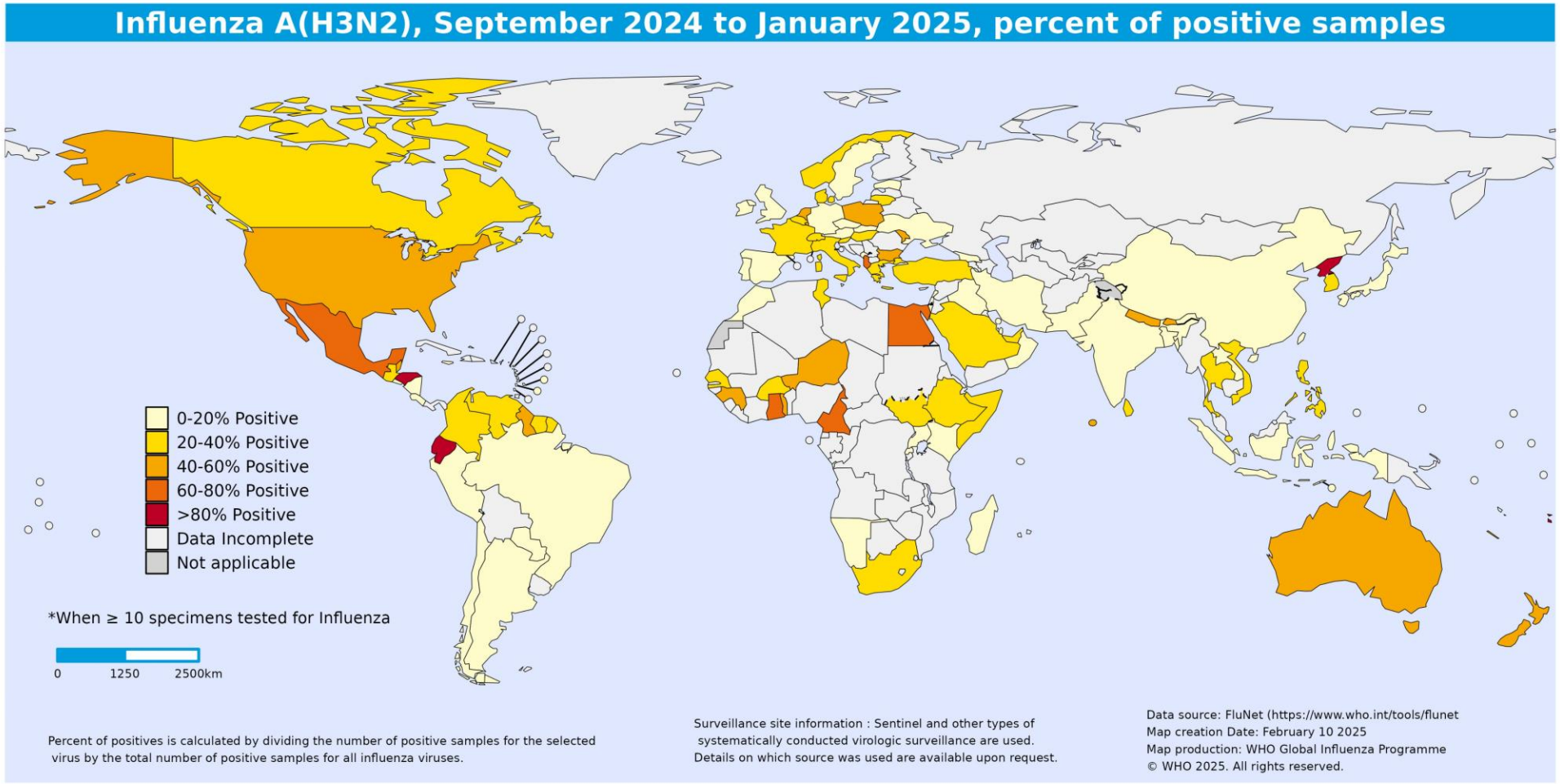
- Post-infection ferret antisera raised against the SH 2024 and NH 2024-2025 A(H1N1)pdm09 vaccine components (cell culture-propagated A/Wisconsin/67/2022 and egg-propagated A/Victoria/4897/2022) from the 5a.2a.1 subclade recognized 5a.2a and 5a.2a.1 viruses well, including emerging D and C.1.9 subclades.
- Post-vaccination GMTs were not reduced significantly for most recently circulating A(H1N1)pdm09 viruses when compared to the responses to cell culture-propagated A/Wisconsin/67/2022 (H1N1)pdm09-like vaccine reference viruses.
- **The data supported A/Wisconsin/67/2022-like (C.1.1 (5a.2a.1)) and A/Victoria/4897/2022-like (D (5a.2a.1)) to remain as the vaccine antigens for the 2025-26 northern hemisphere.**

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y



A(H3N2) Viruses

Influenza A(H3N2) virus activity

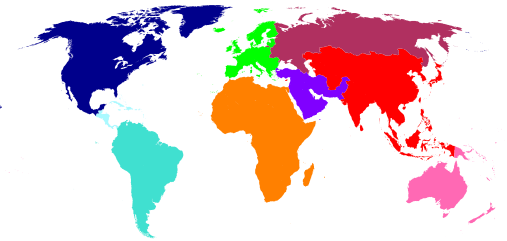


World Health Organization

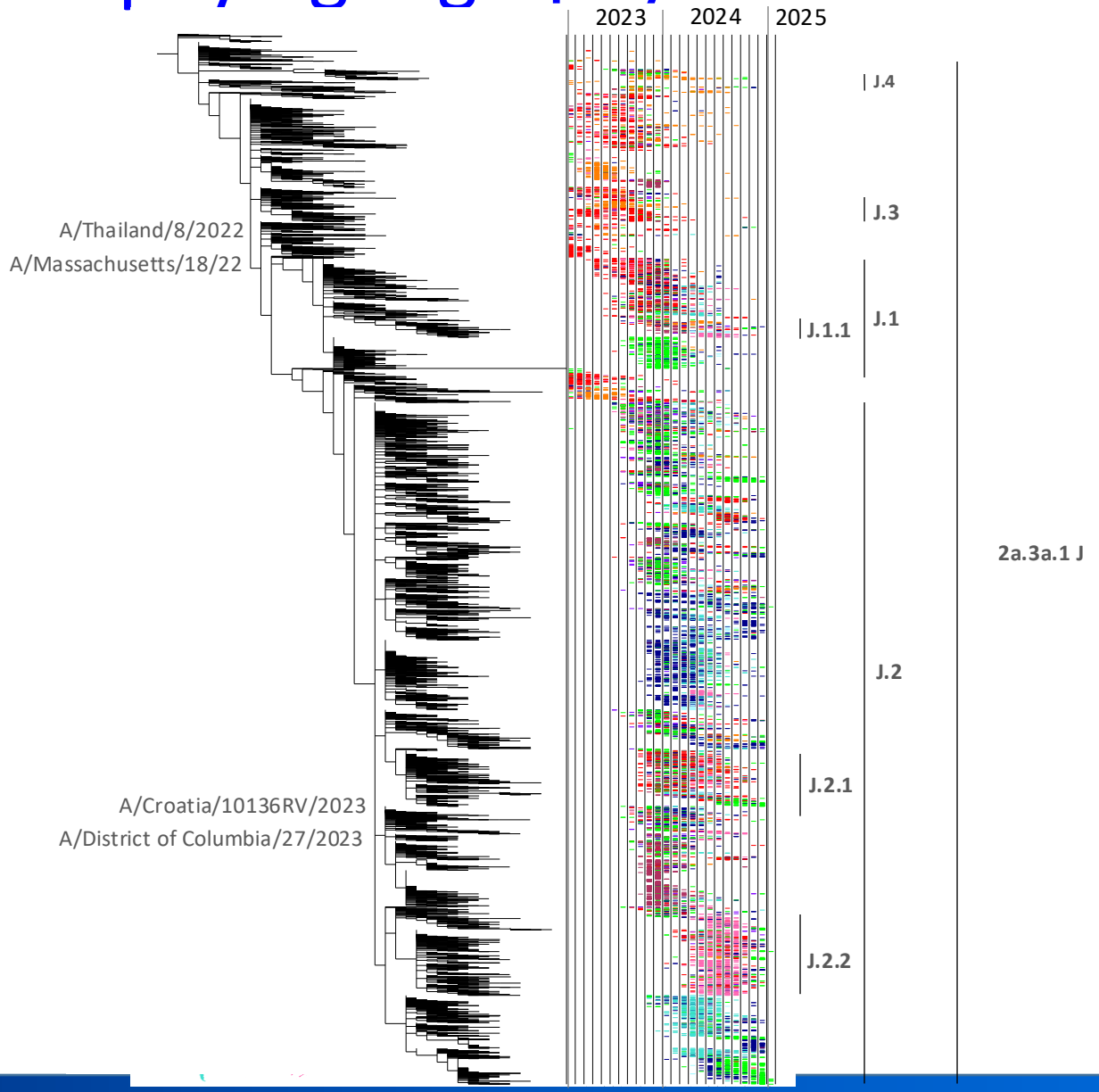
Data source: FluNet, (https://www.who.int/tools/flunet), Global Influenza Surveillance and Response System (9 February 2025)

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H3N2) HA phylogeography



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



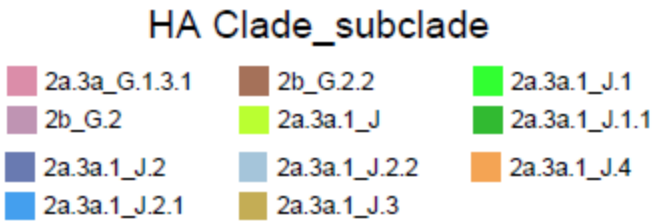
https://clades.nextstrain.org/

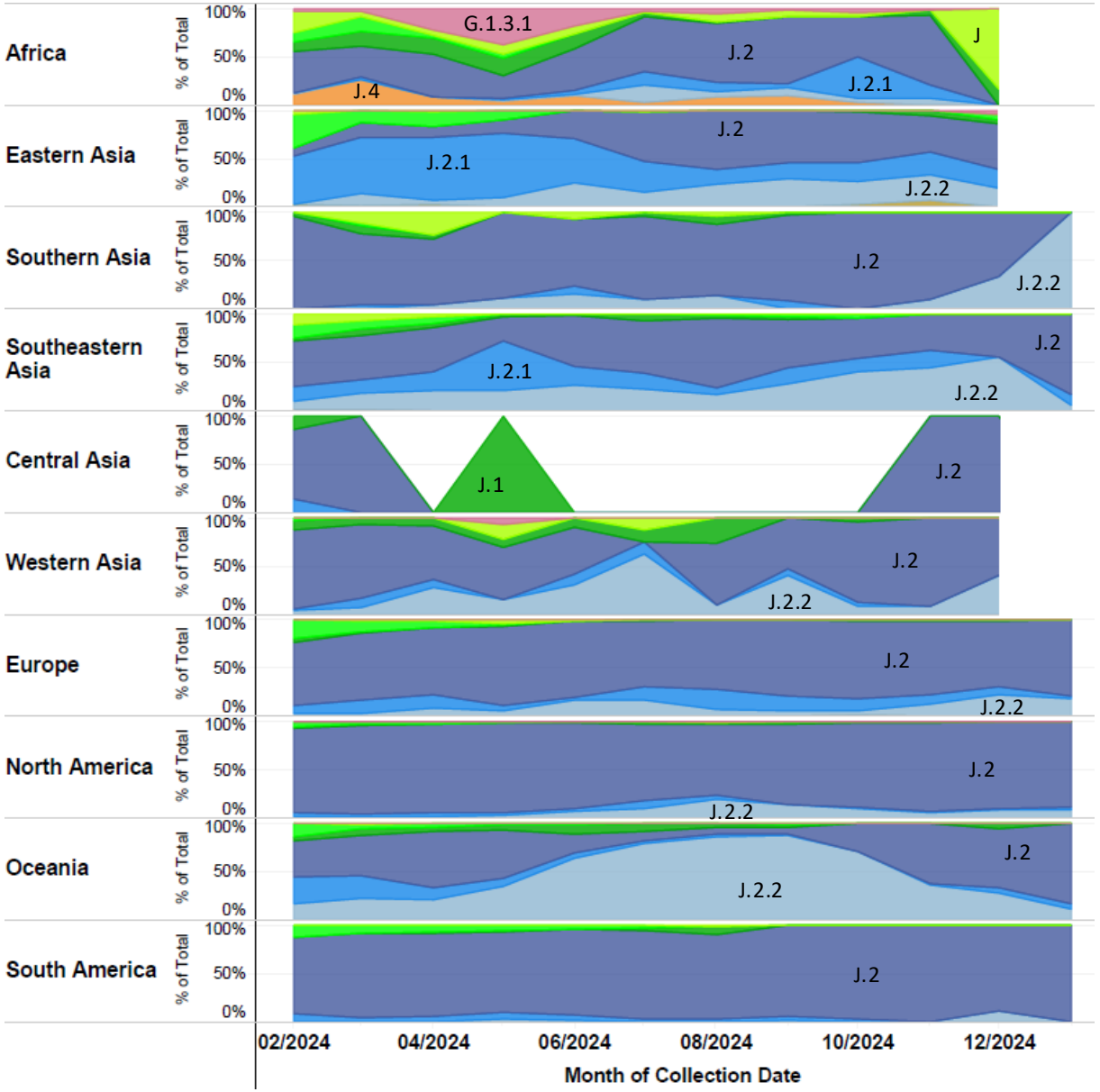
VCM Information meeting:
https://www.youtube.com/watch?v=kGTmLmiBL-Y

Source: University of Cambridge, UK

A(H3N2) Extended Diversity Plot by Geographic Region

Feb. 1, 2024 - Present





Antigenic analysis of A(H3N2) viruses in **HI** assays

HI Assay

Antisera to **northern hemisphere 2024-25 antigens** (2a.3a.1)

A/Massachusetts/18/2022-like Cell (2a.3a.1)			A/Thailand/8/2022-like Egg (2a.3a.1)		
WHO CC	Like (<8 fold)	Low (≥ 8 fold)	WHO CC	Like (<8 fold)	Low (≥ 8 fold)
CDC	121 (54%)	102 (46%)	CDC	136 (61%)	87 (39%)
CNIC	39 (63%)	23 (37%)	CNIC	37 (60%)	25 (40%)
FCI	220 (72%)	87 (28%)	FCI	227 (74%)	80 (26%)
NIID	38 (95%)	2 (5%)	NIID	36 (90%)	4 (10%)
VIDRL	487 (75%)	166 (25%)	VIDRL	187 (29%)	466 (71%)
Total	905 (70%)	380 (30%)	Total	623 (48%)	662 (52%)

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

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

Antigenic analysis of A(H3N2) viruses in **HI** assays

HI Assay

Antisera to **southern hemisphere 2025 antigens** (J.2)

A/District of Columbia/27/2023-like Cell (J.2)			A/Croatia/10136RV/2023-Like Egg (J.2)		
WHO CC	Like (<8 fold)	Low (≥ 8 fold)	WHO CC	Like (<8 fold)	Low (≥ 8 fold)
CDC	221 (99%)	2 (1%)	CDC	52 (66%)	27 (34%)
CNIC	61 (100%)	0 (0%)	CNIC	41 (67%)	20 (33%)
FCI	301 (99%)	3 (1%)	FCI	197 (64%)	110 (36%)
NIID	40 (100%)	0 (0%)	NIID	27 (68%)	13 (33%)
VIDRL	653 (100%)	0 (0%)	VIDRL	450 (69%)	203 (31%)
Total	1276 (99%)	5 (0%)	Total	767 (67%)	373 (33%)

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

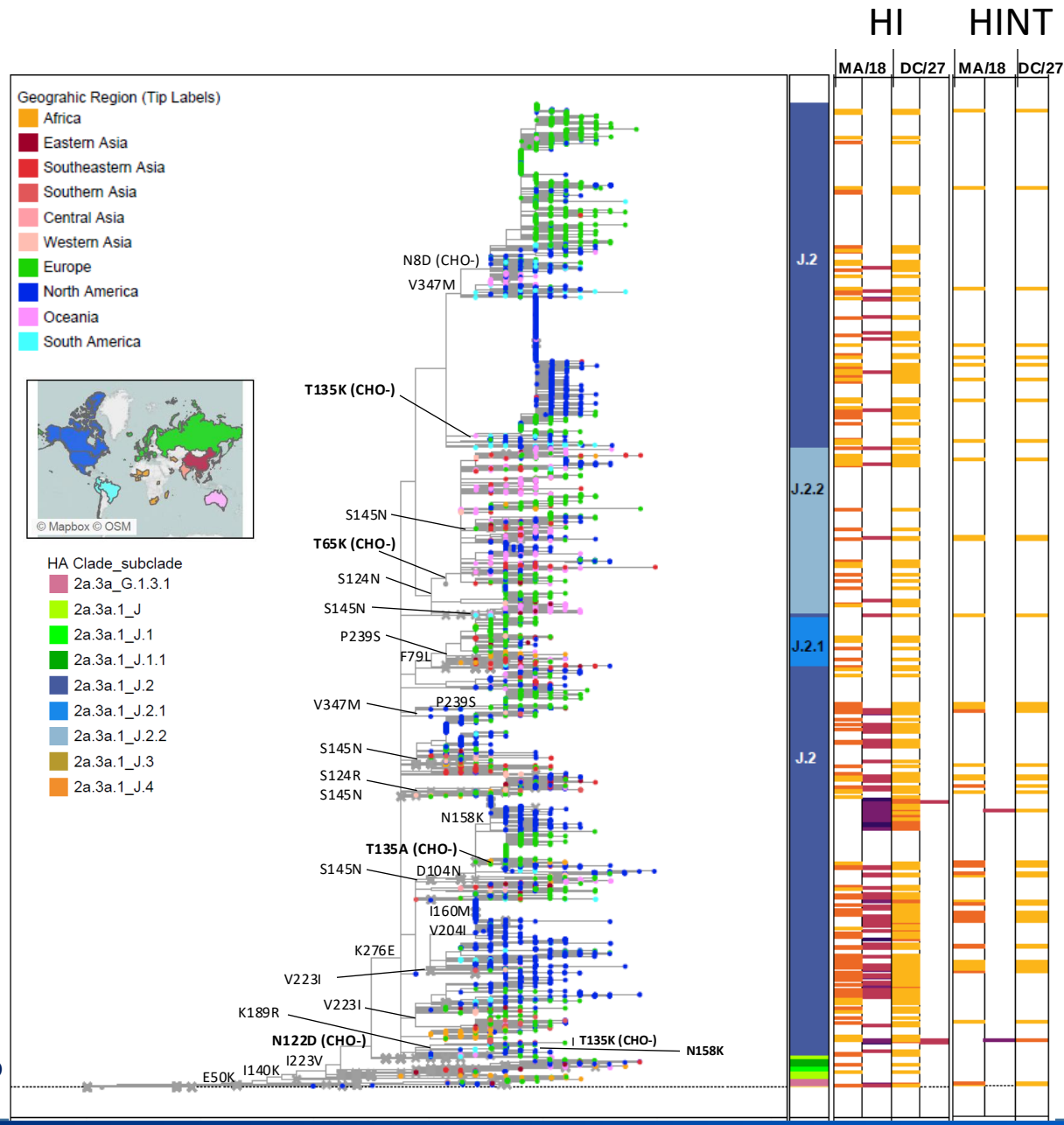
VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H3N2) Integrated Genotype and Phenotype Analysis

Clade	Subclade	HA Amino Acid changes compared to A/Massachusetts/18/2022
2a.3a	G.1.3.1	K140I, V223I
2a.3a.1	J	
	J.1	I25V, V347M
	J.1.1	I25V, S145N, V347M
	J.2	N122D(CHO-), K276E
	J.2.1	F79L, N122D(CHO-), P239S, K276E
	J.2.2	N122D(CHO-), S124N(CHO-), K276E
	J.3	V505I
	J.4	Q173R, K276E

https://clades.nextstrain.org/

Based on HA sequence availability from GISAID EpiFlu™



Antigenic Characterization by HI using Ferret Antisera Fold Reduction

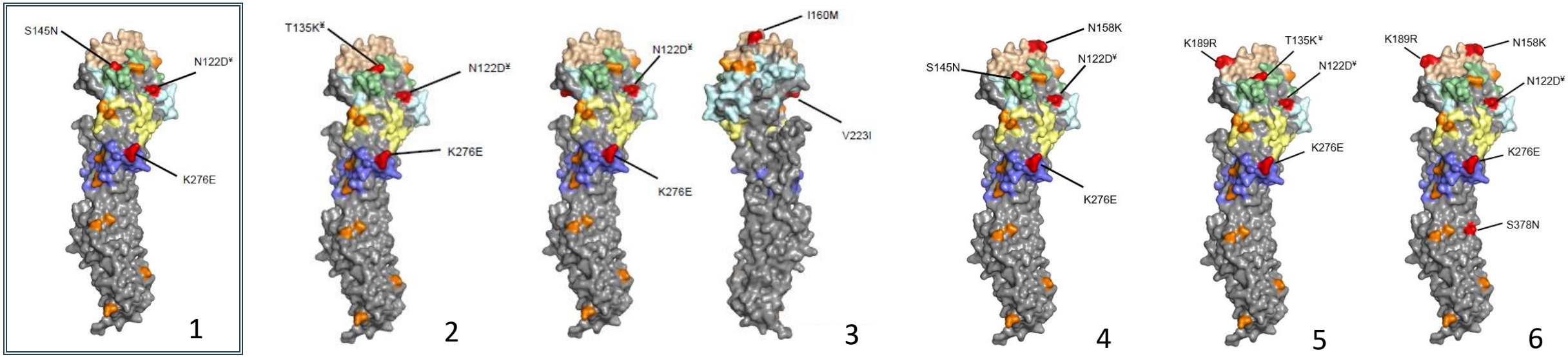
<=2 =4 =8 =16 >=32

Antigenic Characterization by HINT using Ferret Antisera Fold Reduction

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

A(H3N2) Integrated Genotype and Phenotype Analysis

- Multiple additional HA substitutions have emerged, with several positions showing convergent evolution (e.g., HA substitutions S145N, T135K (CHO-), N158K, K189R and V223I)
- Ferret antisera to A/Massachusetts/18/2022-like viruses show reduced to poor reactivity with J.2 viruses with additional HA substitutions
  - Greater reductions for viruses with either N158K or K189R HA substitutions or both.
- Reference viruses from subclade J.2+S145N (e.g., A/District of Columbia/27/2023 and A/Croatia/10136RV/2023) (boxed below) recognized the majority circulating viruses well

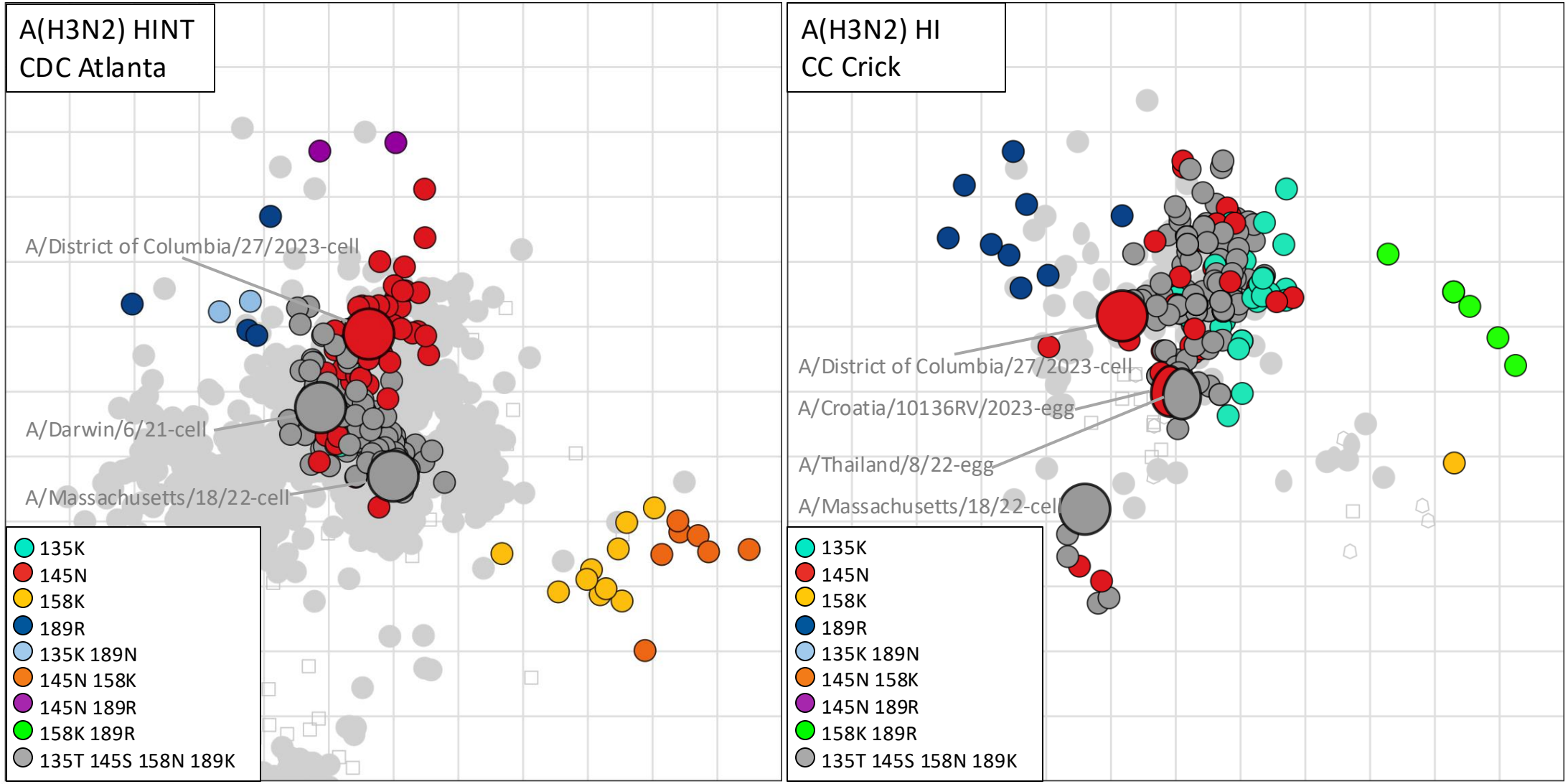


Emerging subclades in J.2 September 2024 through January 2025

A(H3N2) HI Assay

						2024-25 NH Antigens		2025 SH Antigens						
						J				J.2			Post VX Human Sera 2023/2024	
		HA Subclade		DATE COLLECTED	PASSAGE	SIAT	EGG	SIAT	EGG	SIAT	SIAT	SIAT	CELL	
REFERENCE VIRUSES						MA/18	THA/8	DC/27	CRO/ 10136RV	OK/05	ID/69	WI/154	ADULT	HA AA changes vs. J.2 Base consensus
2	A/MASSACHUSETTS/18/2022	J		2022/06/04	S3	**2560**	1280	640	640	320	80	320	320	D122N(CHO+), E276K
3	A/THAILAND/8/2022	J		2022/07/11	E3/E2	2560	**2560**	1280	1280	640	160	640	320	D122N(CHO+), V182X, F195Y, E276K
5	A/DISTRICT OF COLUMBIA/27/2023	J.2	S145N	2023/12/09	S2	320	160	**320**	640	320	160	320	160	S145N
6	A/CROATIA/10136RV/2023	J.2	S145N	2023/12/04	E2/E2	1280	1280	1280	**1280**	640	640	640	320	S145N, D186A
8	A/OKLAHOMA/05/2024	J.2	N158K	2024/02/08	S2	160	160	160	160	**5120**	40	160	160	N158K
9	A/IDAHO/69/2023	J.2	S145N + K189R	2023/12/27	S2	160	80	160	320	80	**160**	80	160	S145N, K189R
11	A/WISCONSIN/154/2024	J.2	T135K	2024/10/26	S2	320	640	640	320	320	80	**1280**	160	T135K(CHO-)
TEST VIRUSES														
16	A/COLORADO/245/2024	J.1.1	S145N	2024/12/01	S1	320	160	160	160	160	80	160	80	I25V, S54N, S145N, I214T, V347M, S400T
29	A/MISSOURI/209/2024	J.2		2024/12/02	S1	640	320	320	320	320	80	320	160	N8D(CHO-), V347M
12	A/COLORADO/209/2024	J.2		2024/10/10	S2	640	640	320	320	320	80	320	160	I160M, V204I, V223I
30	A/NEVADA/224/2024	J.2		2024/11/22	S1	320	160	320	160	160	80	160	160	R92K, V223I
24	A/HAWAII/41/2024	J.2		2024/11/22	S1	320	160	160	320	160	80	320	160	I48M, N63S(CHO-), V112I, V223I
10	A/MICHIGAN/32/2024	J.2	S145N	2024/02/20	S2	640	320	640	640	320	160	320	160	D104N, S145N
20	A/OKLAHOMA/06/2024	J.2	S145N	2024/10/03	S1	640	320	320	320	320	160	320	160	F79V, S124R(CHO-), S145N
25	A/CALIFORNIA/229/2024	J.2	S145N	2024/12/20	S1	160	80	160	160	160	80	160	80	I48V, Q80R, K82R, S145N
31	A/VIRGINIA/41/2024	J.2	S145N	2024/12/01	S1	320	160	320	320	320	80	320	160	S145N, R261Q, V347M
17	A/DELAWARE/97/2024	J.2	S145N + N158K	2024/11/18	S1	80	80	160	80	1280	20	80	80	D104N, S145N, N158K, Q173H
18	A/MINNESOTA/09/2025	J.2	S145N + N158K	2025/01/09	S1	80	80	160	160	1280	20	80	40	D104N, V112I, S145N, N158K
32	A/WISCONSIN/193/2024	J.2	T135K	2024/12/15	S1	640	320	320	640	320	80	1280	160	T135K(CHO-)
33	A/OREGON/03/2025	J.2	T135K + K189R	2025/01/02	S1	80	80	80	160	80	40	640	80	T135K(CHO-), K189R
13	A/COLORADO/06/2024	J.2.1		2024/01/02	S1	640	320	640	320	320	160	320	320	F79L, P239S
15	A/PENNSYLVANIA/234/2024	J.2.2		2024/07/02	S2	640	320	320	320	320	80	320	160	T65K(CHO-), S124N(CHO-)
36	A/MINNESOTA/117/2024	J.2.2	S145N	2024/09/21	S1	320	160	320	320	320	160	320	160	T65K(CHO-), S124N(CHO-), S145N, Q327L
14	A/MINNESOTA/97/2024	J.2.2	S145N	2024/08/05	S2	640	320	640	320	320	160	320	160	T65K(CHO-), S124N, S145N

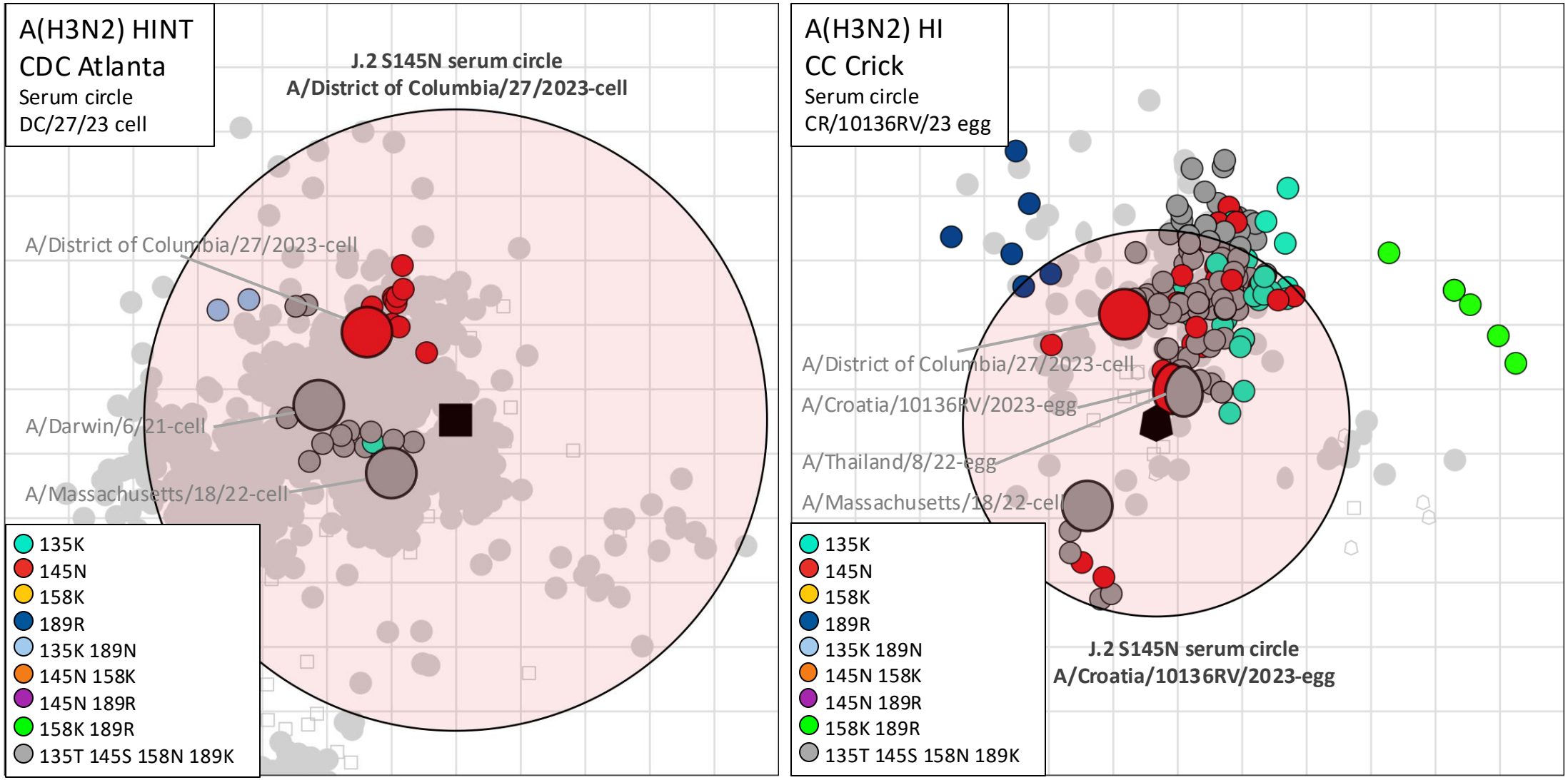
A(H3N2) antigenic cartography



Source: University of Cambridge

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H3N2) antigenic cartography



Serum circles (within 8-fold of homologous titers)

Source: University of Cambridge

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

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

Vaccine: A/Massachusetts/18/2022-like (2a.3a.1 J)

				J	J.2					J.2.2	
				-	+S145N	+D104N +S145N	+N158K	+I160M +V204I +V223I	+T135K	+T65K +S124N	+T65K +S124N +S145N
				*MA/18	DC/27	MI/32	OK/05	CO/209	WI/154	PA/234	VIC/478
				SIAT	SIAT	SIAT	SIAT	SIAT	SIAT	SIAT	SIAT
A/MASSACHUSETTS/18/2022 SIAT [REF]	Pediatric (6-35M)	USA	ccIIV3 (cell)	28	11	X	10	X	X	X	X
	Pediatric (3-8Y)	USA	ccIIV3 (cell)	557	√	√	149	√	√	√	√
	Pediatric (9-17Y)	USA	ccIIV3 (cell)	735	331	288	422	√	√	√	√
	Adult	USA	ccIIV3 (cell)	520	299	190	269	299	343	√	√
			RIV3 (recombinant)	686	279	299	368	√	√	√	343
			IIV3 (egg)	408	184	160	260	197	√	√	√
	Elderly (≥65Y)	USA	IIV3-HD (egg)	299	130	95	117	139	√	92	190

Statistically non-inferior = √

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

GMT Ratio Lower-Bound (90% CI)

0.000 — 1.000

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/COLORADO/209/2024 (CO/209); A/DISTRICT OF COLUMBIA/27/2023 (DC/27); A/MASSACHUSETTS/18/2022 (MA/18); A/MICHIGAN/32/2024 (MI/32); A/OKLAHOMA/05/2024 (OK/05); A/PENNSYLVANIA/234/2024 (PA/234); A/VICTORIA/478/2024 (VIC/478); A/WISCONSIN/154/2024 (WI/154).

A(H3N2): antiviral susceptibility

Neuraminidase inhibitors

- Of 1,844 A(H3N2) viruses that were examined for neuraminidase inhibitor (NAI) susceptibility by genetic and/or phenotypic analyses, **none** showed genetic or phenotypic evidence of reduced inhibition to neuraminidase inhibitors

Endonuclease inhibitors

- Of 1,846 A(H3N2) viruses examined by genetic and/or phenotypic analyses, 3 showed genetic or phenotypic evidence of reduced susceptibility to endonuclease inhibitor baloxavir marboxil
  - Each had an I38T, I38T/I or I38T/M/I substitution in PA, respectively

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H3N2) summary (1): global circulation and HA diversity

- In some countries, areas and territories reporting influenza A viruses, A(H3N2) predominated
- Significant H3 activity was observed in North America, Central America and the Caribbean, and Oceania Melanesia and Polynesia

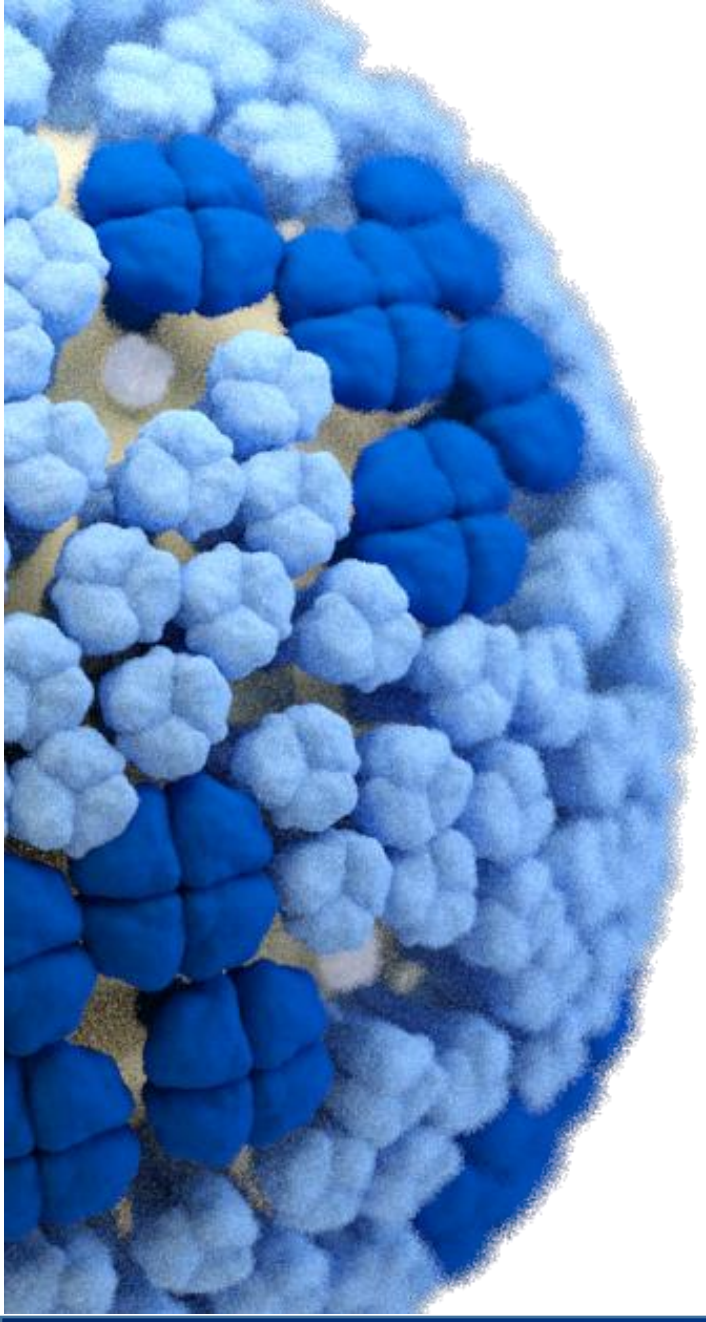
- **HA phylogenetics:**
  - Clade 2a.3a.1 HA genes continued to diversify
    - Viruses expressing HA from 2a.3.1 J.2 subclade predominated
    - Multiple additional HA substitutions have emerged, with several positions showing convergent evolution
      - S145N, T135K (CHO-), N158K, K189R, and V223I
        - Emerging subgroups with T135K and K189R
        - Emerging subgroups with N158K and K189R

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

A(H3N2) summary (2): antigenic characteristics

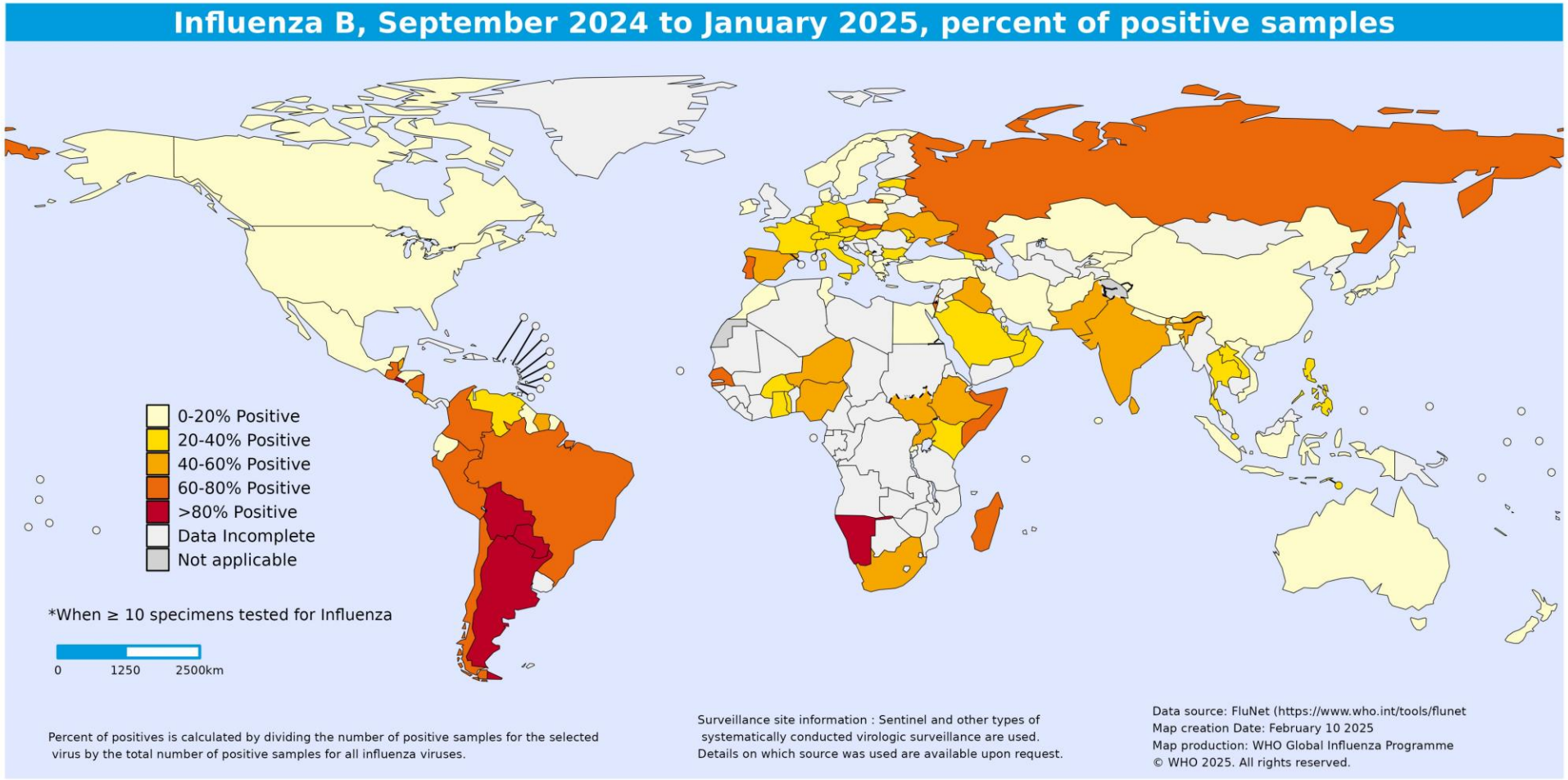
- A/Massachusetts/18/2022-cell and A/Thailand/8/2022-egg (2a.3a.1 vaccine viruses)
  - Showed reduced reactivity against many recent viruses, with greater reductions observed for viruses with either N158K or K189R HA substitutions or both.
- Reference viruses from subclade J.2+S145N (e.g., A/District of Columbia/27/2023 and A/Croatia/10136RV/2023)
  - Recognized the majority circulating viruses well
- Human serology studies with serum panels from individuals vaccinated with A/Massachusetts/18/2022-like (2a.3a.1) viruses:
  - Post vaccination GMTs to many recent A(H3N2) viruses from the J.2 subclades were significantly reduced in most serum panels
- **The data supported recommending A/District of Columbia/27/2023-like (J.2+S145N) and A/Croatia/10136RV/2023-like (J.2+S145N) as the vaccine antigens for the 2025-26 northern hemisphere.**

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y



Influenza B Viruses

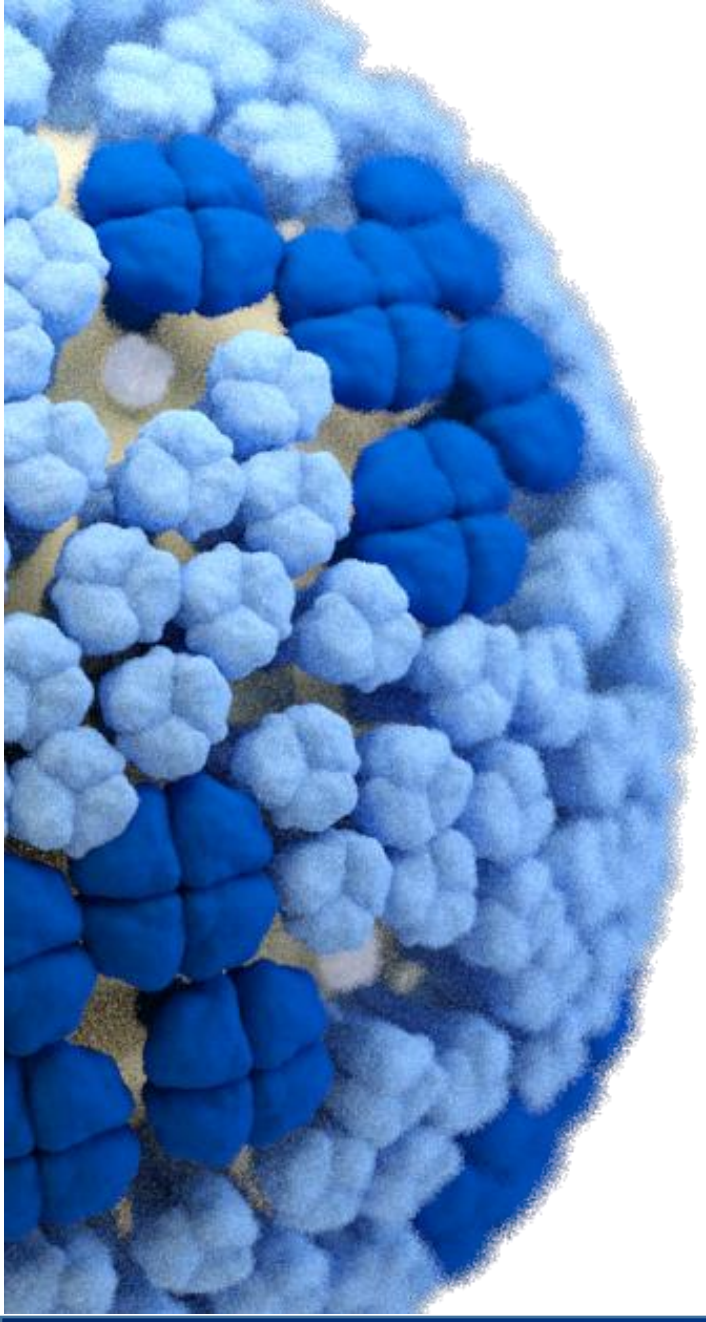
Influenza B virus activity



World Health Organization

Data source: FluNet, (https://www.who.int/tools/flunet), Global Influenza Surveillance and Response System (9 Feb 2025)

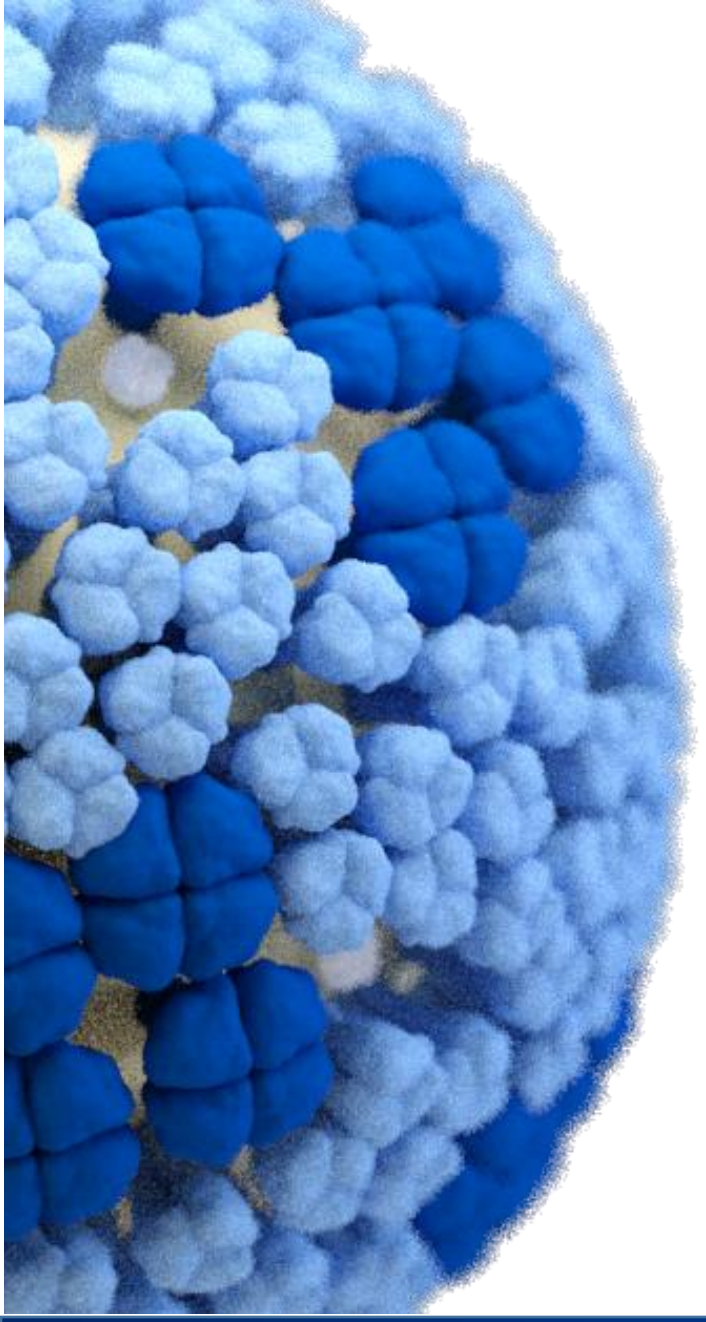
VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y



Influenza B/Yamagata Viruses

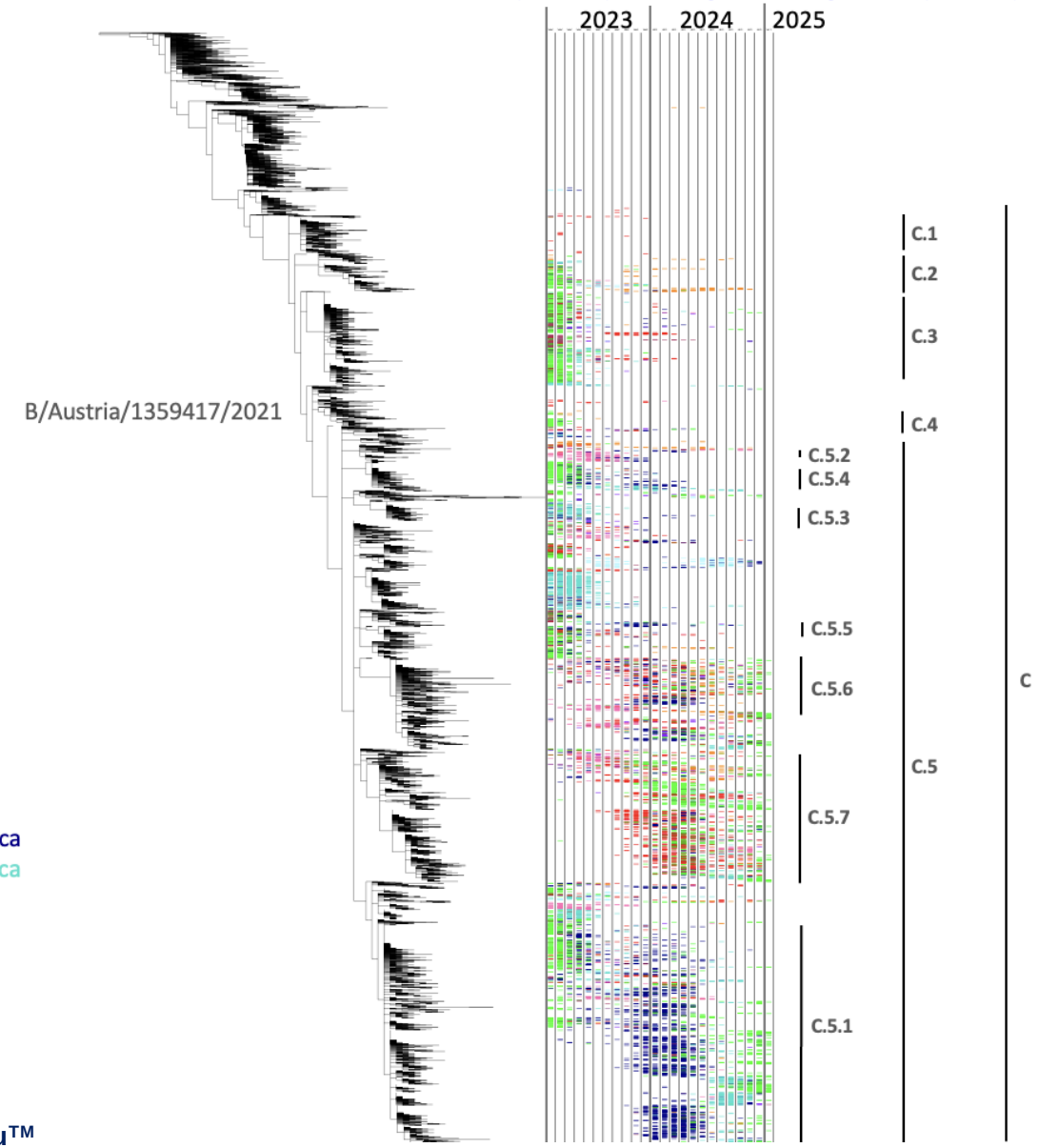
B/Yamagata lineage summary

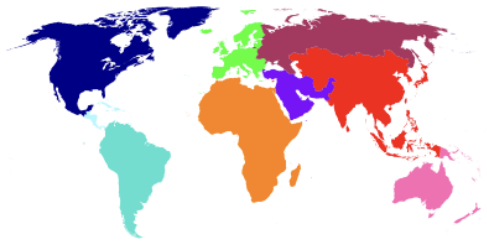
- There have been no confirmed detections of circulating B/Yamagata/16/88 lineage viruses after March 2020.
- It continues to be recommended globally that the B/Yamagata lineage antigen should be excluded from influenza vaccines as it is no longer warranted.
- Where quadrivalent vaccines are still used, the B/Yamagata lineage component remains unchanged from previous recommendations:
  - B/Phuket/3073/2013 (B/Yamagata lineage)-like virus



Influenza B/Victoria Viruses

B/Victoria HA phylogeography





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

Source: University of Cambridge, UK

Based on HA sequence availability from GISAID EpiFlu™

https://clades.nextstrain.org/

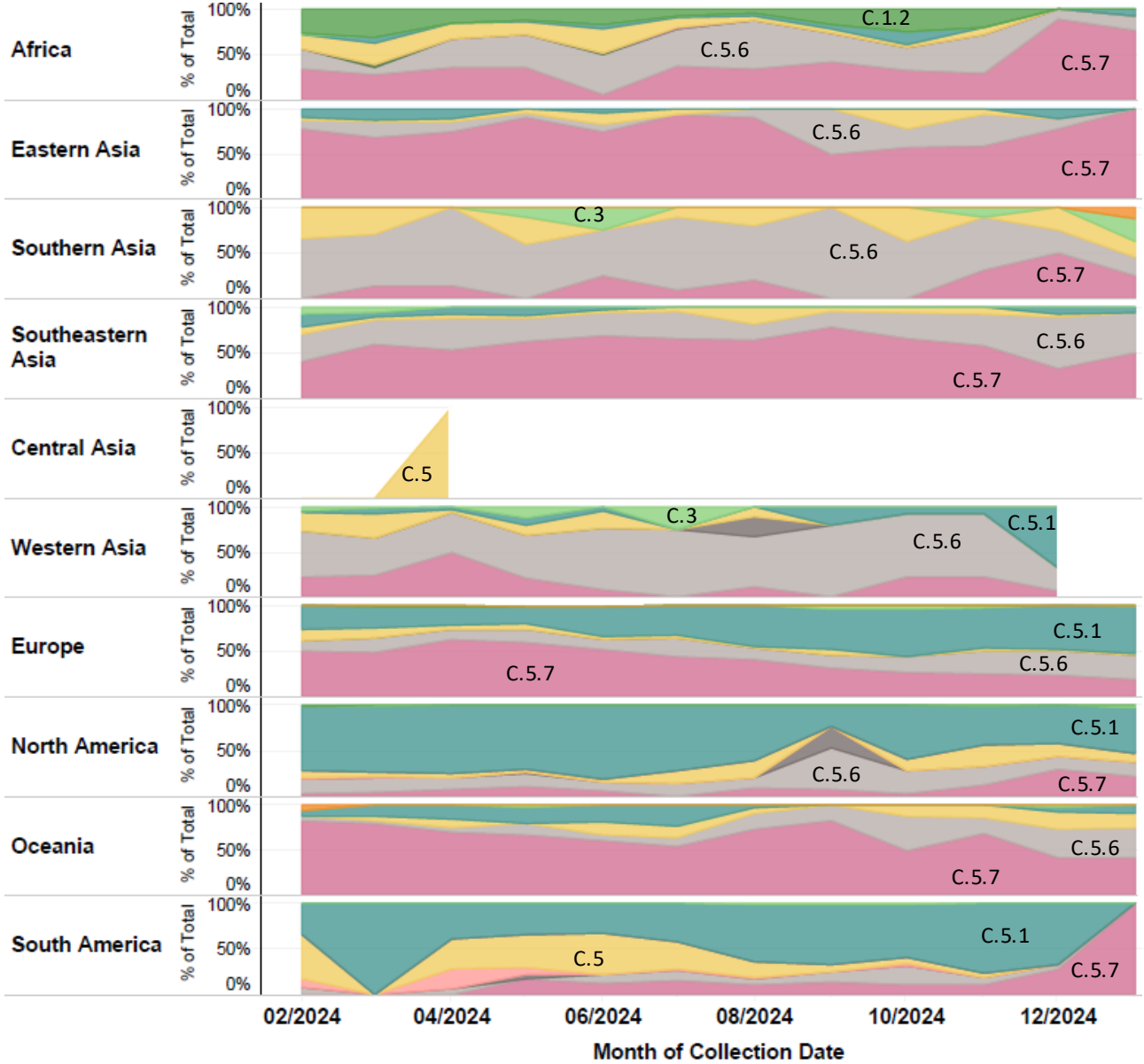
VCM Information meeting:
https://www.youtube.com/watch?v=kGTmLmiBL-Y

B/Victoria Extended Diversity Plot by Geographic Region

Feb. 1, 2024 - Present

HA Clade_subclade

- V1A.3a.2_C
- V1A.3a.2_C.2
- V1A.1_A.1
- V1A.3_A.3.3
- V1A.3a.2_C.3
- V1A.3a.2_C.5.1
- V1A.3a.2_C.5.4
- V1A.3a.2_C.5.5
- V1A.3a.2_C.5.3
- V1A.3a.2_C.5
- V1A.3a.2_C.5.6
- V1A.3a.2_C.5.7



https://clades.nextstrain.org/

Based on HA sequence availability from GISAID EpiFlu™

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

Antisera to northern hemisphere 2024-25 vaccine virus antigens

B/Austria/1359417/2021-like (cell) V1A.3a.2			B/Austria/1359417/2021-like (egg) V1A.3a.2		
WHO CC	Like (<8 fold)	Low (≥ 8 fold)	WHO CC	Like (< 8-fold)	Low (≥ 8-fold)
CDC	104 (100%)	0 (0%)	CDC	104 (100%)	0 (0%)
CNIC	33 (100%)	0 (0%)	CNIC	32 (97%)	1 (3%)
FCI	253 (100%)	0 (0%)	FCI	253 (100%)	0 (0%)
NIID	10 (100%)	0 (0%)	NIID	10 (100%)	0 (0%)
VIDRL	239 (100%)	0 (0%)	VIDRL	238 (100%)	1 (0%)
TOTAL	639 (100%)	0 (0%)	TOTAL	637 (100%)	2 (0%)

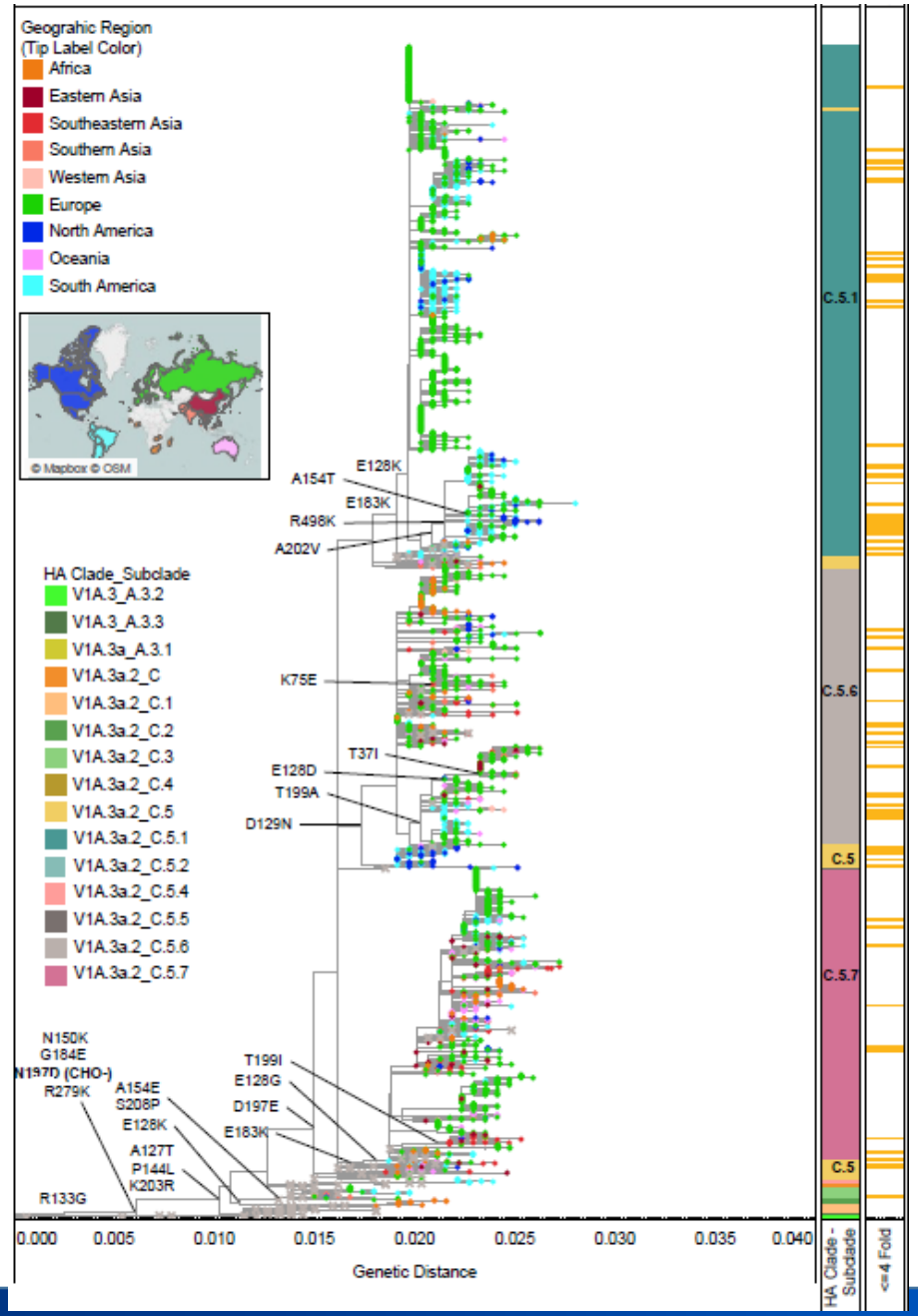
"Low" represented titers ≥ 8-fold lower than vaccine strain homologous titer

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

B/Victoria Integrated Genotype and Phenotype Analysis

Clade	Subclade	HA Amino Acid changes compared to B/Austria/1359417/2021
V1A.3a.2	C	
	C.1	H122Q
	C.2	T182A, D197E, T221A
	C.3	E128K, A154E, S208P
	C.5	D197E
	C.5.1	E183K, D197E
	C.5.3	V87A, D129G, E183K, D197E
	C.5.4	V117I, E128K, A154T, D197E, K326R
	C.5.5	R80G, E184K, D197E
	C.5.6	D129N, D197E
	C.5.7	E128G, E183K, D197E

https://clades.nextstrain.org/



C.5.1

C.5 and C.5.6

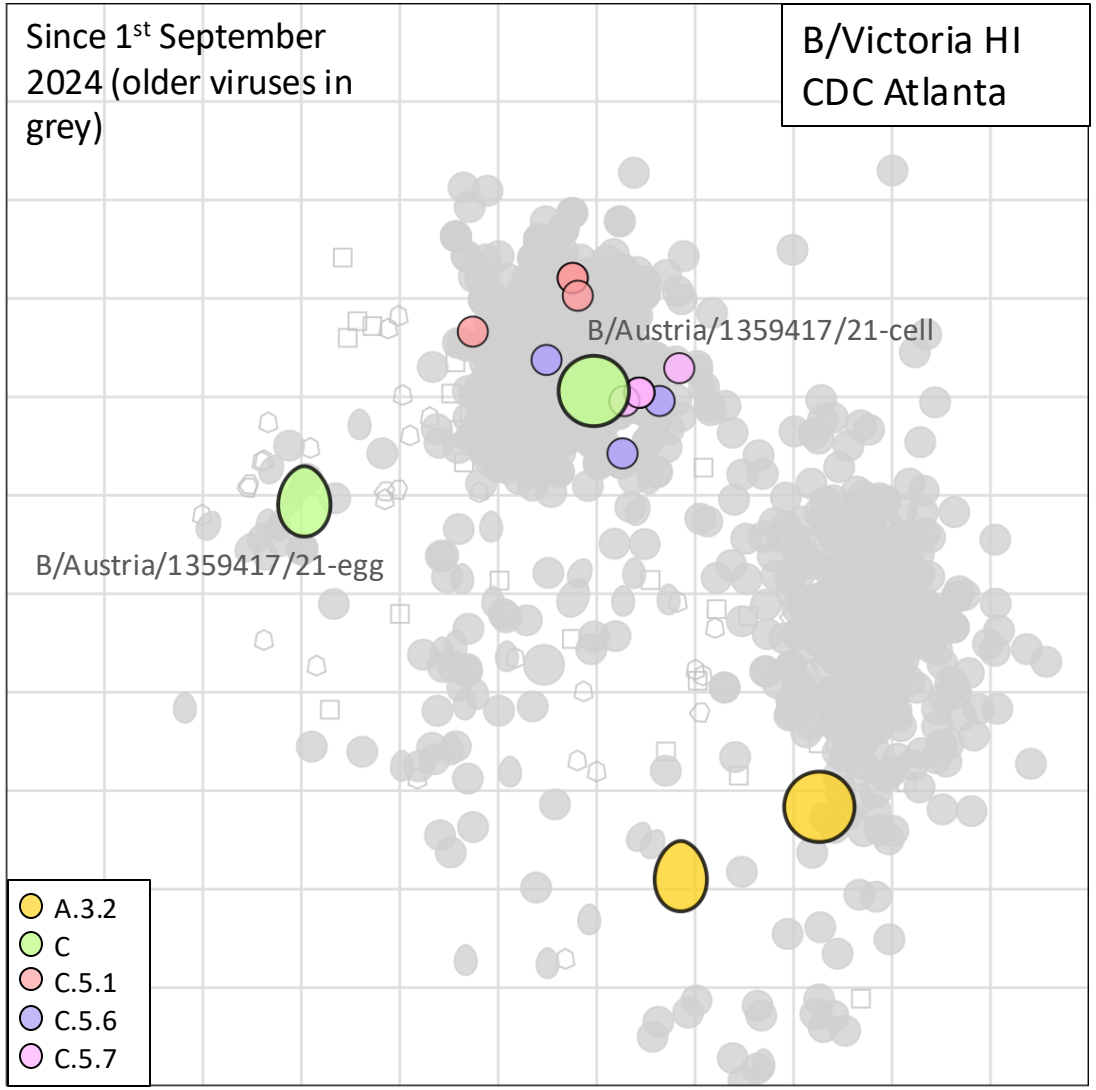
C.5.7

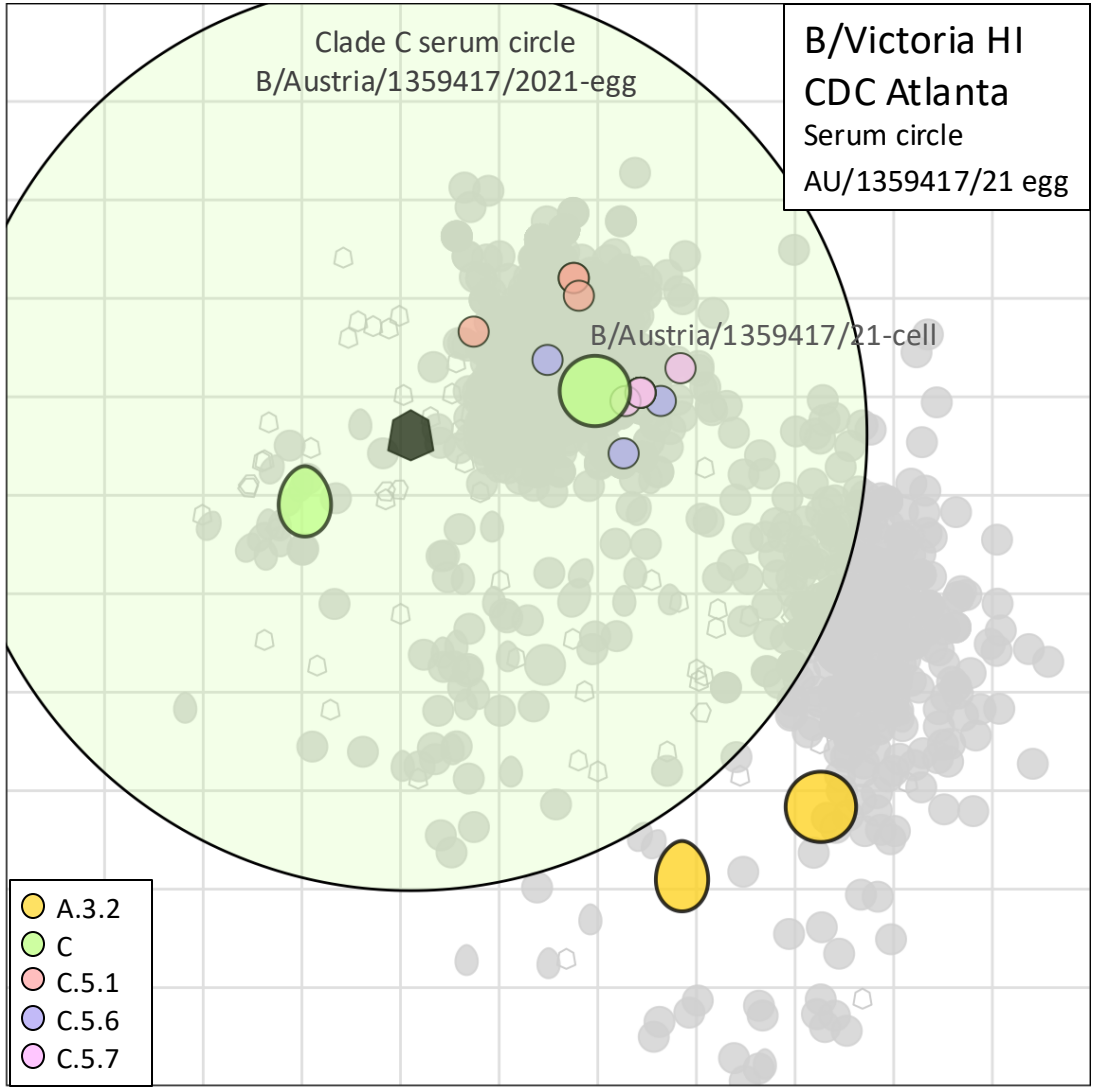
Antigenic Characterization by HI using Ferret Antisera Fold Reduction into B/Austria/1359417/2021 cell

<=2
=4
=8

Based on HA sequence availability from GISAID EpiFlu™

B/Victoria antigenic cartography





Source: University of Cambridge, UK

VCM Information meeting:
https://www.youtube.com/watch?v=kGTmLmiBL-Y

Serum circles (within 8-fold of homologous titers)

Human post-vaccination serum analysis of B/Victoria viruses

Vaccine: B/Austria/1359417/2021-like (3a.2 C)

B/AUSTRIA/1359417/2021 MDCK [REF]

			C (V1A.3a.2)	C.5.1 (V1A.3a.2)		C.5.6 (V1A.3a.2)	C.5.7 (V1A.3a.2)
			*AUT/1359417	UT/11	KS/05	AL/07	RAN/373
			MDCK	MDCK	MDCK	MDCK	MDCK
Pediatric (6-35M)	USA	ccIIV3 (cell)	44	√	√	√	√
Pediatric (3-8Y)	USA	ccIIV3 (cell)	126	√	√	√	√
Pediatric (9-17Y)	USA	ccIIV3 (cell)	130	√	√	√	√
Adult	USA	ccIIV3 (cell)	160	√	√	√	√
		RIV3 (recombinant)	184	√	√	√	√
		IIV3 (egg)	117	√	√	√	√
Elderly (≥65Y)	USA	IIV3-HD (egg)	234	√	√	√	√

Statistically non-inferior = √

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

GMT Ratio Lower-Bound (90% CI)

0.000 — 1.000

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/ALABAMA/07/2023 (AL/07); B/AUSTRIA/1359417/2021 (AUT/1359417); B/KANSAS/05/2024 (KS/05); B/RANONG/373/2023 (RAN/373); B/UTAH/11/2023 (UT/11).

B/Victoria lineage antiviral susceptibility

Neuraminidase inhibitors

- Of 671 influenza B/Victoria lineage viruses collected since 1 September 2024 that were examined for neuraminidase inhibitor (NAI) susceptibility by genetic and/or phenotypic analyses, **none** showed evidence of reduced or highly reduced inhibition by NAIs.

Endonuclease inhibitors

- Of 673 B/Victoria lineage viruses collected and analyzed in this period, **none** showed evidence of reduced susceptibility to baloxavir.

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

Influenza B/Victoria lineage summary (1): global circulation and HA diversity

- **Only influenza B/Victoria lineage viruses were available for analysis (no B/Yamagata viruses confirmed after March 2020)**

- **Phylogenetics of B/Victoria lineage HA genes**
  - Only 3a.2 HA clade viruses circulated (no 3a.1)

  - HA subclades C.5.1, C.5.6 and C.5.7 predominated

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

Influenza B/Victoria lineage summary (2): antigenic characteristics

- **Antigenic characteristics of B/Victoria lineage viruses**
  - Post-infection ferret antisera raised against B/Austria/1359417/2021-like viruses (**3a.2 HA**) inhibited the vast majority of recently circulating **3a.2** viruses well
  - **Human serology studies, using serum panels from the SH 2024 or NH 2024-2025 vaccine**
    - Recent representative B/Victoria lineage viruses expressing various clade 3a.2 HA genes were well inhibited by NH 2024-25 post vaccination human sera

- **The data supported B/Austria/1359417/2021-like (3a.2) to remain as the vaccine antigens for the 2025-26 northern hemisphere.**

VCM Information meeting: https://www.youtube.com/watch?v=kGTmLmiBL-Y

Support and Disclaimer

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.

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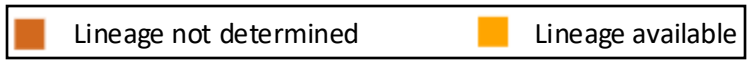
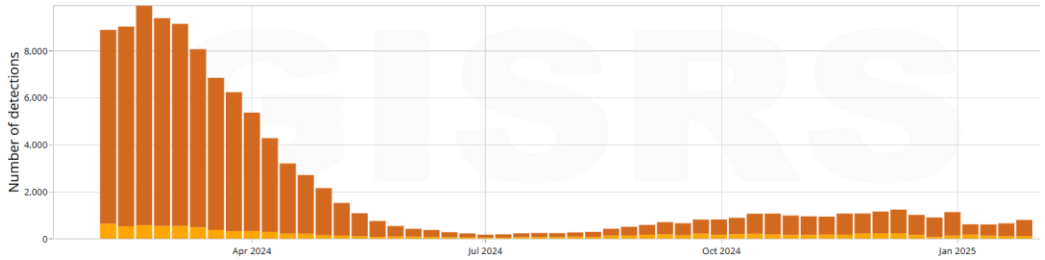
Additional Slides

Influenza B Lineage Determination by WHO Region from Feb 1, 2024 – Feb 1, 2025



PAHO



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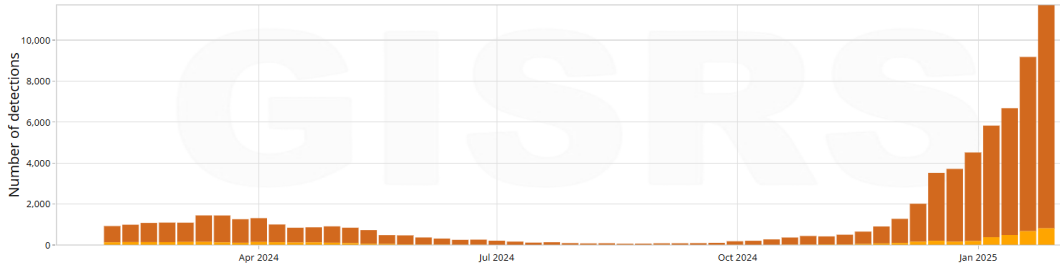

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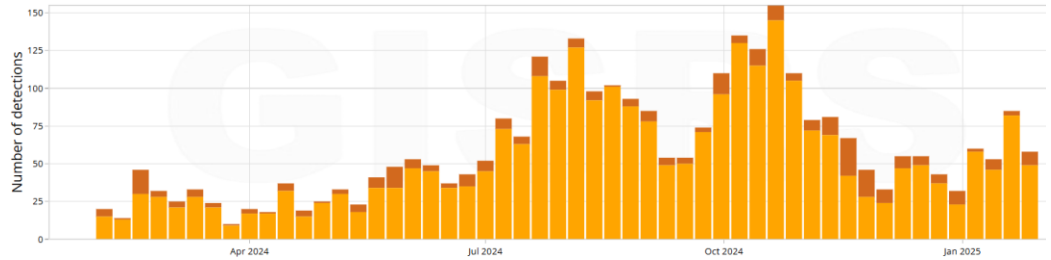

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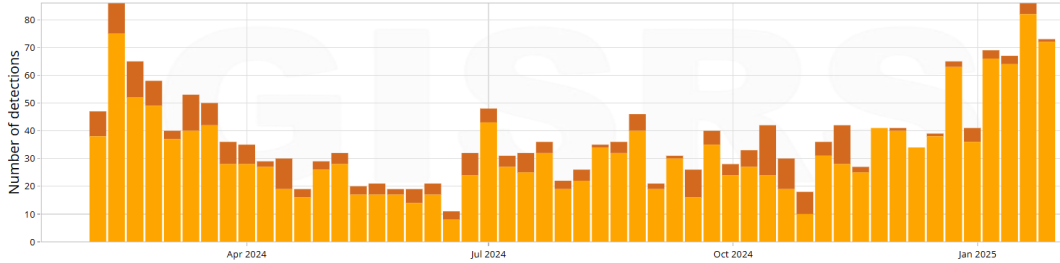
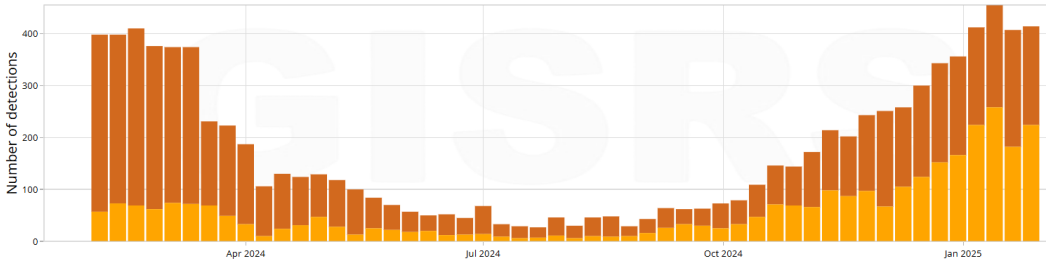
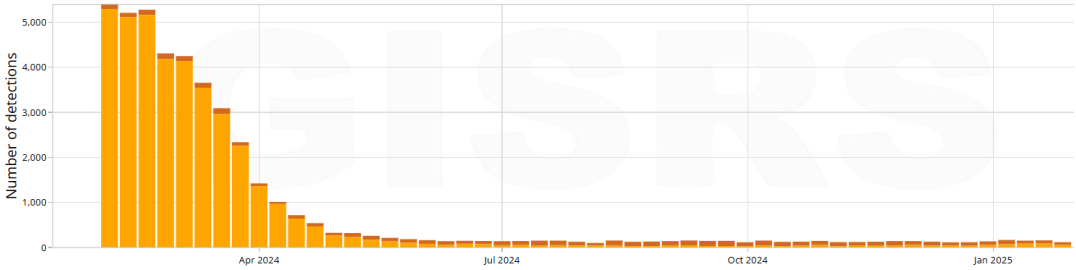


EMRO



WPRO



Data source: FluNet (https://www.who.int/tools/flunet)