



OFFLU SWINE INFLUENZA REPORT

JULY 2024 TO DECEMBER 2024

SCOPE

In this document we present a summary of H1 and H3 swine influenza A virus evolution.

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Swine influenza A viruses: Acknowledgements and Methods

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Brief Methods for Genetic and Antigenic Analyses

Analyses were conducted by subtype and lineage or clade. Reference sequences and new data (deposited on or after July 1, 2024) downloaded from GISAID or GenBank incorporated into the USDA-ARS NADC octoFLUdb and were subsequently aligned with MAFFT (Katoh and Standley, 2013) using default settings. Alignments for each segment were inspected manually and trimmed to the start and stop codon. Phylogenetic inference was conducted with FastTree (Price et al., 2009) or IQ-Tree (Minh et al., 2020). Tabular comparisons between current CVVs or human seasonal vaccine strains and new swine data were generated using the NADC IAV bioinformatic toolkit flutile (<https://github.com/flu-crew>). A clade representative was selected using PARNAS (Markin et al., 2023: <https://github.com/flu-crew/parnas>) and the best matched available strain was selected for testing against reference ferret antisera in hemagglutination inhibition (HI) assays. All HI assays were performed with ferret anti-sera and guinea pig red blood cells. H3N2 assays were performed with the addition of oseltamivir. Phylogenies were subsampled and visualized using smot (Arendsee et al., 2022: <https://github.com/flu-crew/smot>).

Global influenza A events in swine Epidemiology

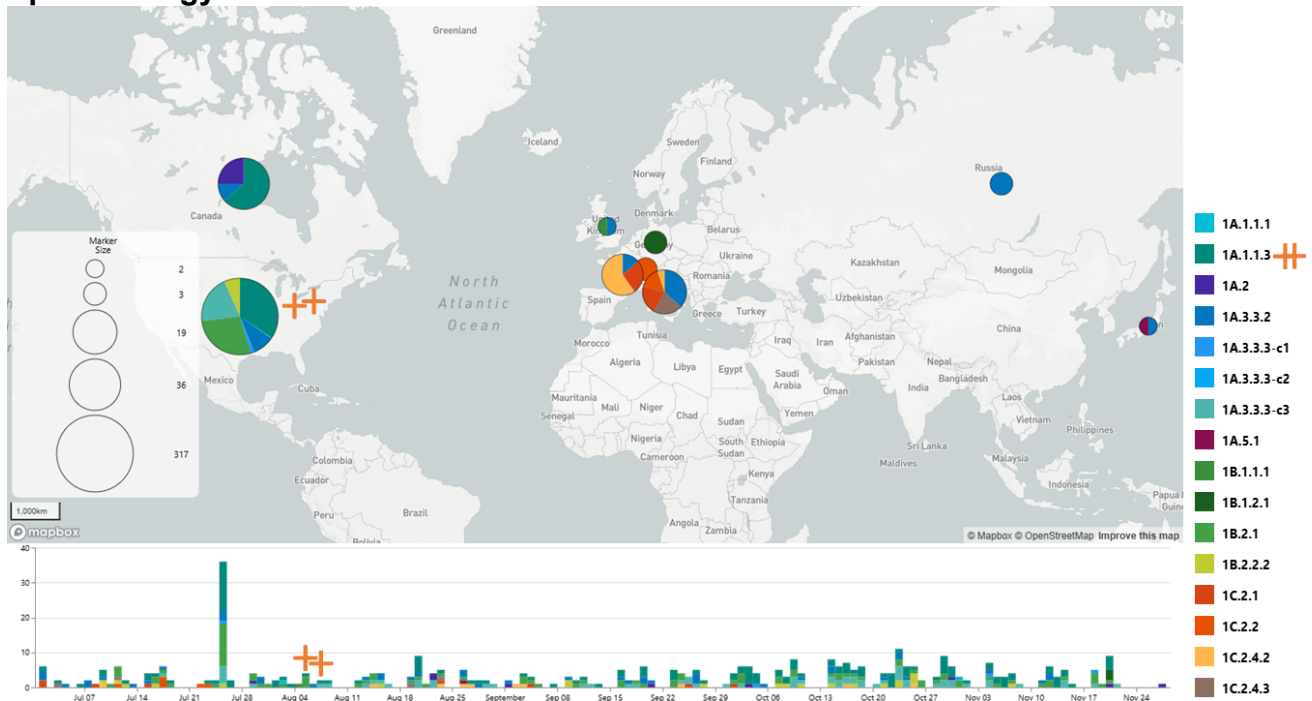


Figure 1. MicroReact map of swine IAV H1 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank on or after July 1, 2024 (n=400); collection date is represented on bottom timeline. Strains submitted with only partial date were assigned a random date to preserve temporal clusters. Geographic nodes scaled to detection proportions. Clades containing variants, location, and date of detection are marked with orange crosses.

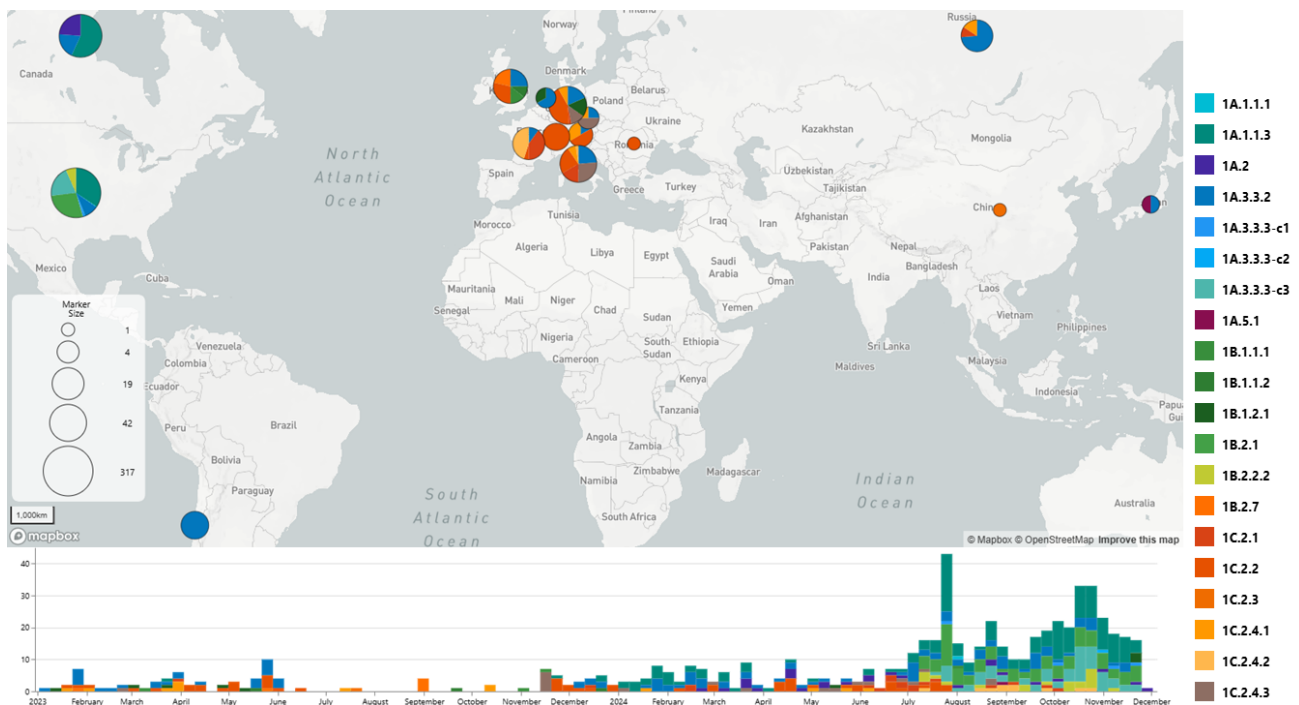


Figure 2. MicroReact map of swine IAV H1 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank on or after January 1, 2023 (n=620); collection date is represented on bottom timeline. Strains submitted with only partial date were assigned a random date to preserve temporal clusters. Geographic nodes scaled to detection proportions.

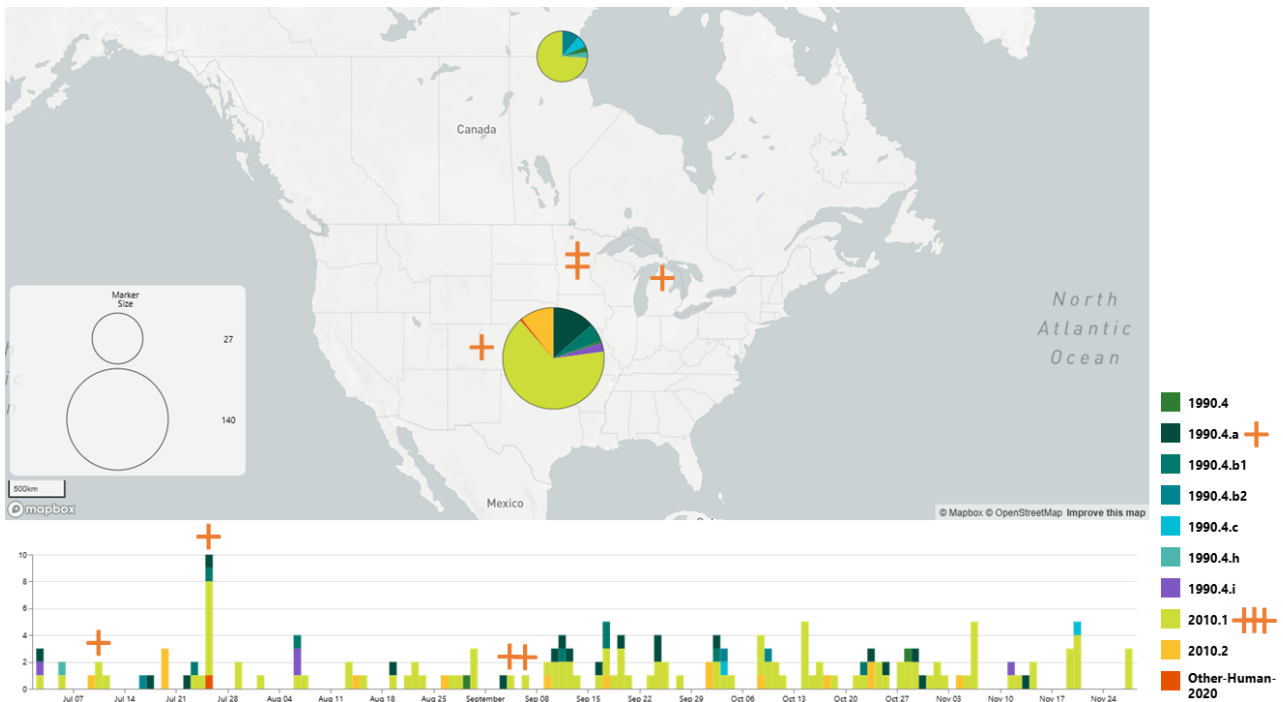


Figure 3. MicroReact map of swine IAV H3 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank on or after July 1, 2024 (n=167). Strains submitted with only partial date were assigned a random date within the provided year to preserve temporal clusters. Geographic nodes scaled to detection proportions. Clades containing variants, location, and date of detection are marked with orange crosses.

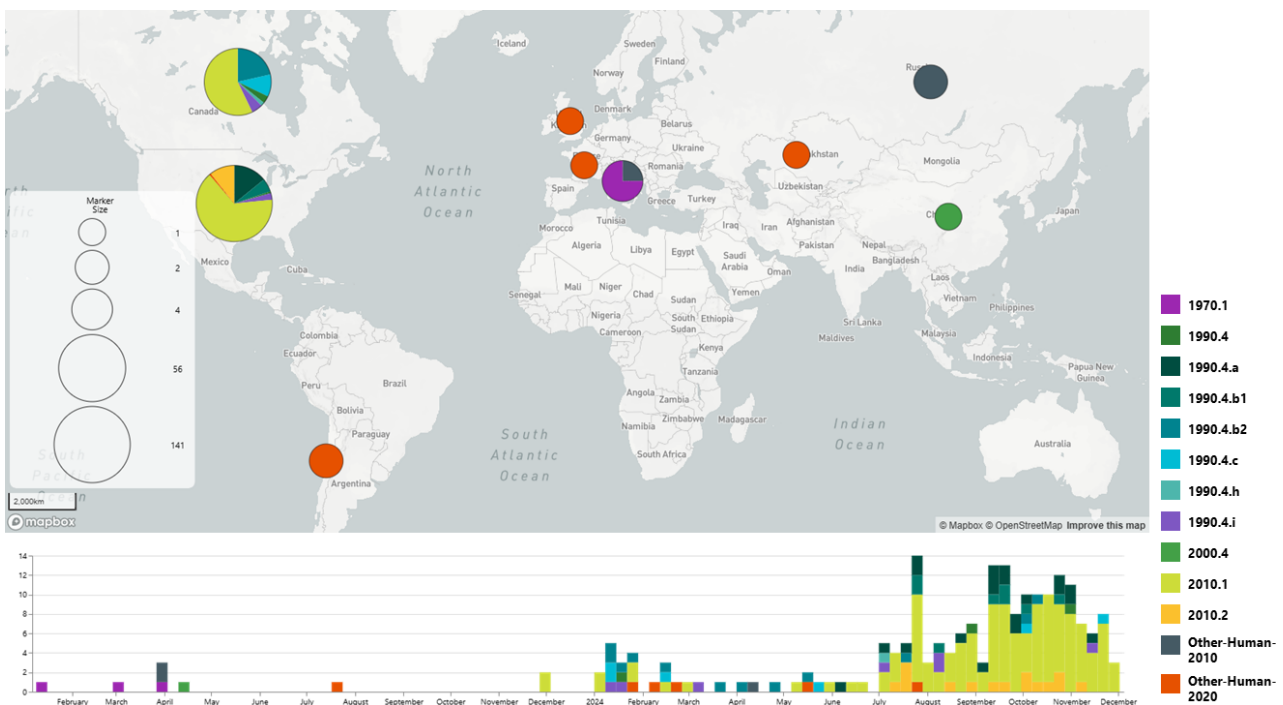


Figure 4. MicroReact map of swine IAV H3 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank on or after January 1, 2023 (n=209). Strains submitted with only partial date were assigned a random date within the provided year to preserve temporal clusters. Geographic nodes scaled to detection proportions.

Contemporary Global H1 swine IAV: genetic diversity

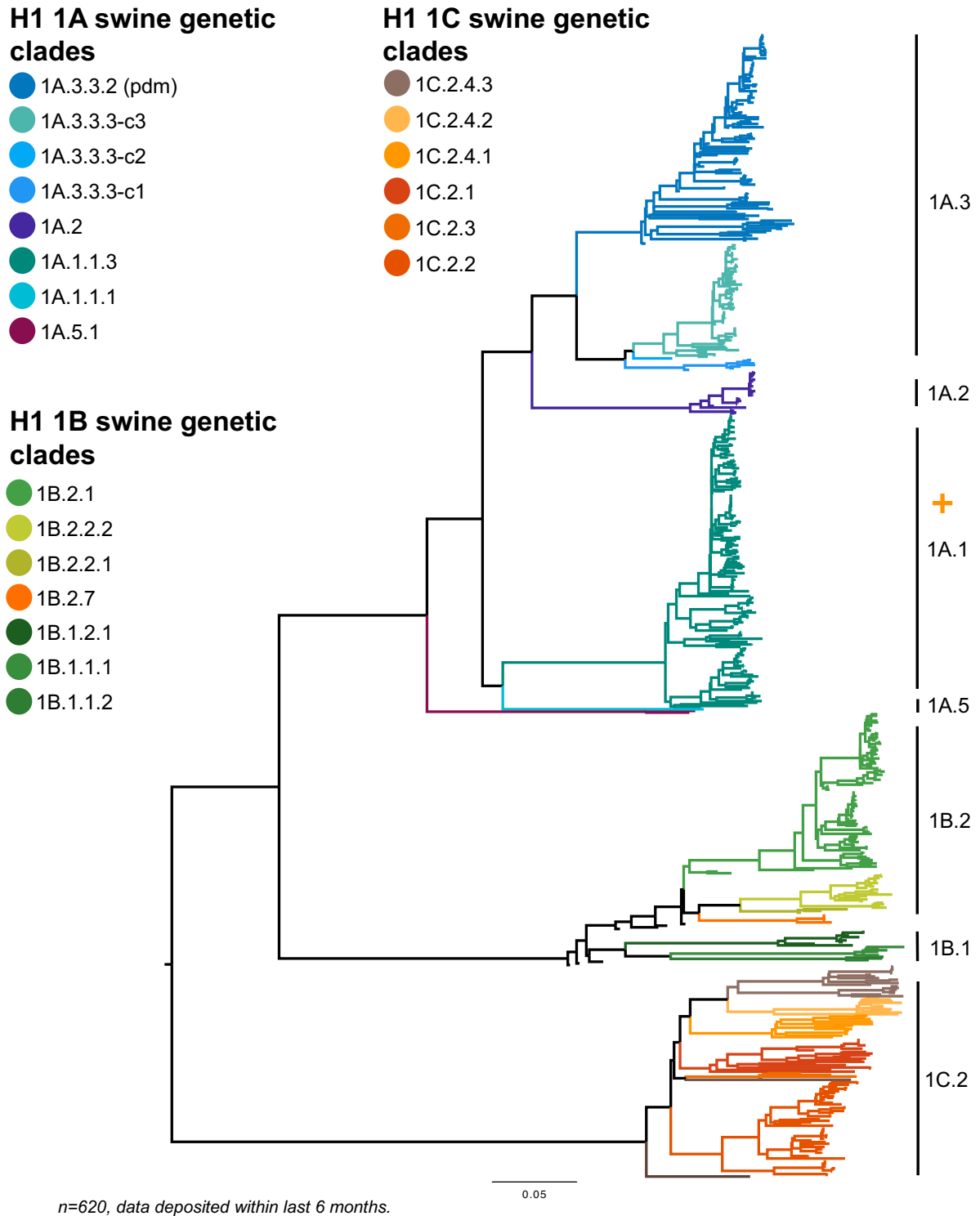


Figure 5. Global swine H1 phylogenetic tree (n=620) with reference strains (n=77) colored by clade and annotated by global H1 lineage nomenclature. Analyses were conducted with reference sequences and data (all data deposited on or after July 1, 2024) from GISAID or shared via the OFFLU swine IAV working group.

Contemporary Global H3 swine IAV: genetic diversity

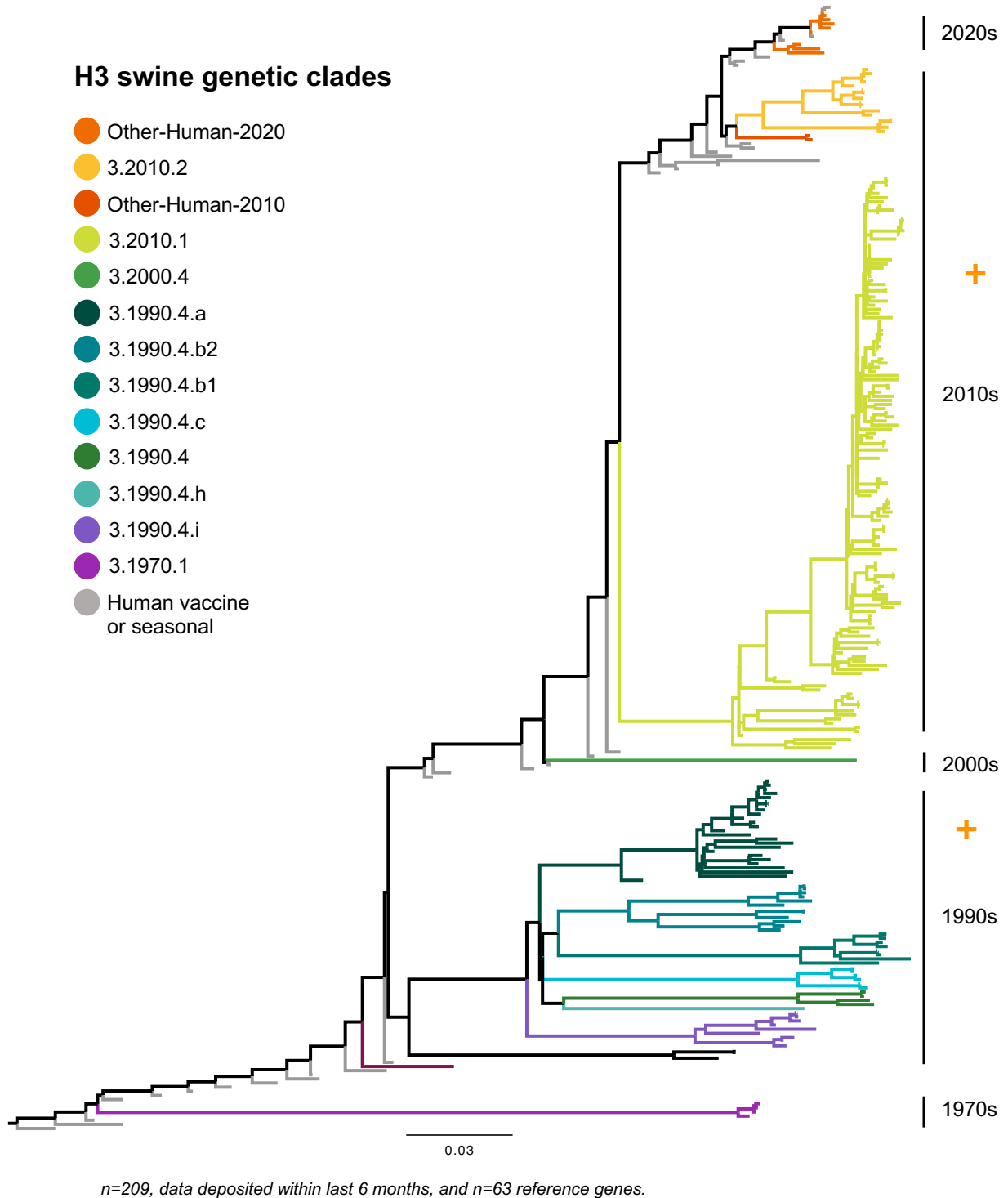


Figure 6. Global swine H3 phylogenetic tree (n=209) with reference strains (n=63) colored by clade and annotated by decade of introduction from human seasonal H3. Analyses were conducted with reference sequences and data (all data deposited on or after July 1, 2024) from GISAID or shared via the OFFLU swine IAV working group.

Regional geographic summary

Phylogenetic analysis identified 25 genetic clades from H1 and H3 IAV in swine in sequence data deposited on or after July 1, 2024.

16 clades were H1 subtype, with detections from: 1A classical swine lineage (7 clades); 1B human-seasonal lineage (4 clades); and 1C Eurasian avian lineage (4 clades).

- The 1A classical swine lineage viruses have global detection: 1A.1.1.1 in the USA; 1A.1.1.3 in USA and Canada; 1A.2 in Canada; 1A.3.3.3-c1, 1A.3.3.3-c2, and 1A.3.3.3-c3 in USA; 1A.5.1 in Japan. The 1A.3.3.2 (pdm09) circulated in all countries that deposited sequence data during this 6-month period (7 countries).
- 1B.1 human seasonal lineage (1B.1.1.1 in the UK; 1B.1.2.1 in Germany) was only in Europe, and the 1B.2 human seasonal lineage was only detected in the USA.
- The 1C.2 Eurasian avian lineage was detected in Europe.

9 H3 clades were detected in swine within 3 distinct lineages derived from human seasonal H3 virus spillovers grouped by the decade of introduction (1990.4; 2010.1; 2010.2); there was a single detection of a human seasonal spillover without evidence for onward circulation (Other-Human-2020).

- The 1990.4 and the 2010.1 lineages were detected in the USA and Canada. The 1990.4 lineage diversified into 6 co-circulating genetic clades.
- The 2010.2 were detected in the USA.
- *A human-to-swine spillover was detected in the USA associated with the 2023-24 influenza season (Other-Human-2020).*
- *Additional independent human-to-swine spillovers were detected in Chile, France, Kazakhstan, and Northern Ireland but were prior to the July-December 2024 reporting period.*

Global Variant Cases:

During the reporting period (July 1 – December 31, 2024), 6 variant cases were reported and included with the swine analyses when sequence data were available.

4 cases were reported in the September 2024 OFFLU report; 2 2010.1 variant cases are annotated as “new variants” in the phylogenetic tree:

- **USA: H1N2v (2x 1A.1.1.3); H3N2v (1x 1990.4.a, 3x 2010.1)**

1A classical swine lineage

- ★ H1v candidate vaccine virus
- A/Victoria/4897/2022
- H1N1pdm seasonal vaccines
- Reported H1v cases
- # HI tested viruses

H1 1A swine genetic clades

- 1A.3.3.2-pdm (n=107)
- 1A.3.3.3-c3 (n=64)
- 1A.3.3.3-c2 (n=1)
- 1A.3.3.3-c1 (n=4)
- 1A.2 (n=26)
- 1A.1.1.3 (n=171)
- 1A.1.1.1 (n=1)
- 1A.5.1 (n=1)

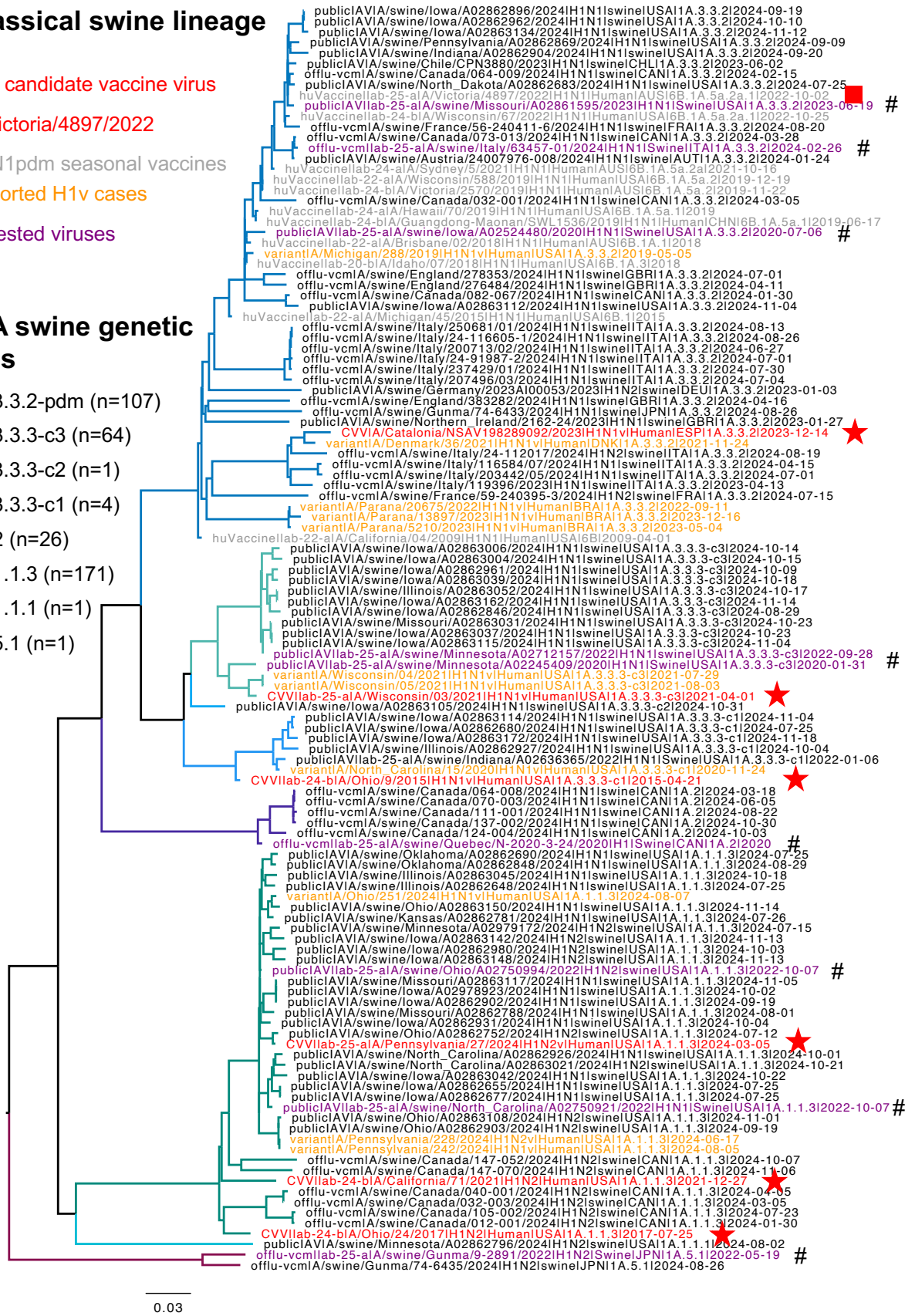


Figure 7. Swine H1 HA genes of the 1A lineage (tree was proportionally downscaled to 92 swine HA genes, excluding references). Number of detections of each clade from data deposited on or after July 1, 2024 are presented adjacent to the clade name in the figure key.

Antigenic analysis: Swine 1A Lineage

Table 1. USA Data: Hemagglutination inhibition of CVV or human seasonal vaccine ferret antisera against contemporary swine 1A lineage strains selected to represent clade consensus.

- > 8 fold reduction
- 8 fold reduction
- 4 fold reduction

	Global Clade	US Clade	A/Pennsylvania/27/2024	A/swine/North_Carolina/A02750921/2022 #61	A/swine/North_Carolina/A02750921/2022 #65	A/Victoria/4897/2022	A/swine/Iowa/A02524480/2020 #30	A/swine/Iowa/A02524480/2020 #14	A/Wisconsin/3/2021-like CVV RG76C	A/swine/Minnesota/A02245409/2020 #28	A/swine/Minnesota/A02245409/2020 #12	Human Pooled Serum
A/Pennsylvania/27/2024	1A.1.1.3	alpha-del	1280	160	320	<10	<10	<10	10	<10	<10	40
A/swine/North_Carolina/A02750921/2022	1A.1.1.3	alpha-del	320	640	1280	<10	<10	<10	20	<10	<10	80
A/swine/Ohio/A02750994/2022*	1A.1.1.3	alpha-del	1280	640	1280	<10	<10	<10	10	<10	<10	80
A/Victoria/4897/2022	1A.3.3.2, 5a.2a.1 (subclade D)	pdm09	<10	<10	<10	1280	10	20	40	<10	<10	160
A/swine/Iowa/A02524480/2020	1A.3.3.2	pdm09	10	10	10	80	320	1280	40	20	20	160
A/swine/Missouri/A02861595/2023*	1A.3.3.2	pdm09	<10	<10	<10	20	10	10	80	<10	<10	80
IDCDC-RG76 A/Wisconsin/03/2021 CVV	1A.3.3.3-c3	gamma.3	<10	<10	<10	20	<10	10	5120	40	40	160
A/swine/Minnesota/A02245409/2020	1A.3.3.3-c3	gamma.3	40	40	80	40	40	40	640	2560	640	160
A/swine/Minnesota/A02712157/2022*	1A.3.3.3-c3	gamma.3	20	20	40	20	20	20	320	320	160	80
A/swine/Quebec/N-2020-3-24/2020*	1A.2	beta	20	<10	<10	<10	640	1280	80	<10	20	80
A/Wisconsin/588/2019												320

*Previously tested in OFFLU report 2024b (September 2024); Reference CVV in red, seasonal vaccines in dark red, new in bold. Homologous titers highlighted in gray. Human sera were collected in USA with titer relative to A/Victoria/4897/2022, pool of 2 male and 2 female adults.

- The contemporary swine 1A.1.1.3 (alpha-del) had no loss in reactivity to the CVV A/Pennsylvania/27/2024 ferret anti-sera but had 4-fold loss to human pooled sera.
- The contemporary swine 1A.3.3.2 (pdm) with onward transmission in swine had >8-fold decrease to A/Victoria/4897/2022 5a.2a.1 and had a 4-fold loss to human pooled sera.
- The contemporary swine 1A.3.3.3-c3 (gamma.3) virus had >8-fold decrease from the within-clade 1A.3.3.3-c3 CVV A/Wisconsin/2021 and a 4-fold loss to human pooled sera.
- The contemporary swine 1A.2 (beta) virus has no within clade CVV, >8-fold decrease to all CVV and human seasonal vaccine ferret anti-sera and had a 4-fold loss to human pooled sera.

Table 2. EU Data: Hemagglutination inhibition of CVV or human seasonal vaccine ferret antisera against representative swine 1A lineage strain.

	Global Clade	A/California/71/21	A/California/7/2009	A/Guangdong-Maonan/SWL1536/2019	A/Victoria/2570/2019 (IVR-215)	A/Victoria/4897/2022 (IVR)-238	A/Ohio/9/2015 CVV
A/California/71/21	H1N1 1A.1.1.3	1280	20	160	160	0	40
A/California/7/2009	1A.3.3.2, pdm09	40	640	1280	320	320	0
A/Guangdong-Maonan/SWL1536/2019 (IVR-215)	1A.3.3.2, 1A.5a.1 (subclade B)	40	2560	10240	1280	320	40
A/Victoria/2570/2019 (IVR-215)	1A.3.3.2, 1A.5a.2 (subclade C)	80	160	640	10240	5120	160
A/Victoria/4897/2022 (IVR-238)	1A.3.3.2, 5a.2a.1 (subclade D)	160	80	640	10240	10240	320
A/swine/Italy/63457-01/2024*	1A.3.3.2	80	80	1280	10240	5120	80
A/Ohio/9/2015 CVV	1A.3.3.3-c1	20	40	160	80	20	320
A/swine/Gunma/9-2891/2022*	1A.5.1	80	<10	160	320	nt	80

- >8 fold reduction
- 8 fold reduction
- 4 fold reduction

*Previously tested in OFFLU report 2024b (September 2024). Reference CVV in red, reference seasonal vaccine strains in dark red. Homologous titers highlighted gray.

- The contemporary swine 1A.3.3.2 (pdm09) with onward transmission in swine retained reactivity with A/Victoria/4897/2022 5a.2a.1 ferret anti-sera.
- The contemporary swine 1A.5.1 had >8-fold decrease to all human seasonal vaccine ferret anti-sera, and a 4-fold loss in reactivity with the 1A.3.3.3-c1 CVV.

Table 3. Amino acid substitutions between representative swine 1A.1.1.3 strains compared to within-clade, HI-tested CVVs (A/Pennsylvania/27/2024 and A/California/71/2021) and recent 1A.1.1.3 variants.

site	A/Pennsylvania/27/2024	A/California/71/2021	A/swine/Ohio/A02750994/2022	A/swine/North_Carolina/A02750921/2022	A/Pennsylvania/242/2024	A/Ohio/251/2024	annotations
48	S	A					
69	S	P					
70	I					T	Cb
71	L	P					Cb
84	S	N	N	N	N	N	
97	N				D		
103	E	V					
119	I	T					
124	A	S	P	S	P	P	Sa
126	Y	H					
127	K	E					
128	K	T	T	T	T	T	
132	E	A					RBS
140	G			E			Ca2
142	G	S	S	S	S	N	Ca2
143	S				G		
149	M			V			
155	A	G					Sa
157	S			L			Sa
160	R	M		K			Sa
166	V	A					Ca1
168	N	D		D			
185	G	D		D			
186	N	S					
189	Q	R					Sb, RBS
195	A	T					Sb, RBS
222	G	N					Ca2, RBS
232	T	A					
235	E					A	
261	S					P	
272	I			T			
273	Y	H	H	H	H	H	
283	K					E	
286	L				I		
298	I	V	V	V	V	V	
308	K	R					
310	R	T					
aadiff		26	6	13	9	10	

Reference CVVs in red, HI swine strains in purple, variant detections in orange.

Table 4. Amino acid substitutions between representative swine 1A.2 clade strain compared to A/California/07/2009, the nearest HI-tested human vaccine.

site	A/California/07/2009	A/swine/Quebec/N-2020-3-24/2020	annotations
35	D	N	
61	I	L	
71	S	F	Cb
73	A	R	Cb
74	S	R	Cb
84	S	N	
85	S	P	
97	D	N	
104	Q	H	
109	S	L	
120	T	A	
121	S	N	
128	S	T	
137	P	S	Ca2
138	H	Y	
142	K	N	Ca2
168	D	N	
170	G	K	Ca1
176	L	I	
183	S	P	
186	A	T	

cont. →

site	A/California/07/2009	A/swine/Quebec/N-2020-3-24/2020	annotations
190	S	T	Sb, RBS
195	A	E	Sb, RBS
205	R	K	
216	I	A	
224	E	A	RBS
234	V	I	
235	E	D	
239	K	T	
260	N	G	
261	A	S	
270	T	K	
273	H	Q	
274	D	N	
276	N	T	
285	A	S	
298	I	V	
302	K	E	
311	K	N	
314	L	M	
aadiff		40	

Reference vaccine strain in gray, HI strain in purple.

Table 5. Amino acid substitutions between representative swine 1A.3.3.2 clade strains compared to WHO recommended human seasonal vaccine used in HI assays (A/Victoria/4897/2022) and additional HI-tested seasonal vaccine strains.

site	A/Victoria/4897/2022	A/Wisconsin/67/2022	A/California/07/2009	A/Guangdong-Maonan/SWL1536/2019	A/Victoria/2570/2019	A/swine/Iowa/A02524480/2020	A/swine/Missouri/A02861595/2023	A/swine/Italy/63457-01/2024	annotations
47	V							I	
54	Q		K	K	K	K			
74	R		S						Cb
83	S		P						
84	N		S						
96	I							T	
97	N		D						
112	E						D		
113	R					K			
120	T							A	
127	D						N		
129	D		N			N			
130	N		K	K		K			
137	S		P	P	P			P	Ca2
142	R		K	K	K	K		K	Ca2
156	K		N	N		N	Q		Sb
161	I		L	L		L			
162	N		S						Sa
163	Q		K						Sa
164	T		S						Sa
173	V					I			
183	P		S						
185	I		S			T			
186	T		A	A	A	A			
187	D			A					RBS
189	E		Q		Q	Q			Sb, RBS
203	T		S						
216	A	T	I	T	T	T		T	
217	R						X		
223	R	Q	Q	Q		Q	Q	Q	RBS
224	A		E	E	E	E			RBS
250	A		V	V		V			
256	T		A						
259	K		R	R	R	R			
260	E		N	D	D	N		D	
277	A		T	T	T	T		T	
283	E		K						
295	V		I						
308	R		K	K	K	K			
321	V		I						
aadiff		2	31	16	11	19	5	9	

Reference vaccine strains in gray (WHO recommended are bold), HI strains in purple.

Table 6. Amino acid substitutions between representative 1A.3.3.3-c3 clade strains compared to nearest HI-tested CVV (A/Wisconsin/03/2021).

site	A/Wisconsin/03/2021	A/swine/Minnesota/A02245409/2020	A/swine/Minnesota/A02712157/2022	annotations
35	T	N	N	
45	K	R	R	
56	N		S	
74	S		R	Cb
83	S	P		
84	N		K	
120	T	A		
127	E	D	D	
129	D	N	N	
130	K	R		
137	P	S		Ca2
142	R	N	N	Ca2
161	V		I	
163	T	K	K	Sa
168	N		D	
169	K	R		
171	K		R	
189	R	Q	Q	Sb, RBS
195	E	A	A	Sb, RBS
205	R	K	K	
224	S	A	A	RBS
252	R		I	
262	G		E	
270	A	T	T	
278	T		A	
295	I		V	
302	E		K	
326	S		T	
aadiff		16	23	

Reference CVV in red, HI swine strains in purple.

Table 7. Amino acid substitutions between representative 1A.5 clade strain compared to nearest HI-tested human vaccine (A/Victoria/2570/2019).

site	A/Victoria/2570/2019	A/swine/Gunma/9-2891/2022	annotations
2	T	I	
5	I	V	
19	V	I	
36	K	T	
39	G	K	
54	K	R	
61	I	L	
72	T	N	
73	A	V	Cb
74	R	S	Cb
84	N	K	
96	I	S	
119	K	N	
120	T	A	
127	D	K	
128	S	T	
130	N	R	
137	P	S	Ca2
138	H	K	
139	A	S	
141	A	K	
142	K	S	Ca2
152	V	L	
156	K	-	Sb
157	S	D	Sa
163	Q	K	Sa
164	T	S	Sa
166	I	V	Ca1
173	V	I	
185	I	R	
186	A	N	

cont. →

site	A/Victoria/2570/2019	A/swine/Gunma/9-2891/2022	annotations
187	D	S	RBS
190	S	F	Sb, RBS
193	Q	N	Sb, RBS
195	A	E	Sb, RBS
196	D	N	
197	A	T	
205	R	T	
207	S	N	
208	K	Q	
211	K	M	
216	T	E	
223	R	Q	RBS
224	E	A	RBS
239	K	T	
256	T	A	
257	M	V	
258	E	D	
260	D	G	
261	A	S	
270	T	V	
272	V	L	
274	D	N	
276	N	T	
278	T	E	
283	E	K	
298	I	V	
302	K	E	
310	T	A	
314	L	M	
321	V	I	
aadiff		61	

Reference vaccine strain in gray, HI swine strain in purple.

1B human-like lineage

- ★ H1v candidate vaccine virus
- A/Brisbane/59/2007
- Previous seasonal H1N1 vaccine
- Reported H1v cases
- # HI tested viruses

H1 1B swine genetic clades

- 1B.2.1 (n=88)
- 1B.2.2.2 (n=21)
- 1B.2.2.1
- 1B.2.7 (n=6)
- 1B.1.2.1 (n=9)
- 1B.1.1.1 (n=4)
- 1B.1.1.2 (n=3)

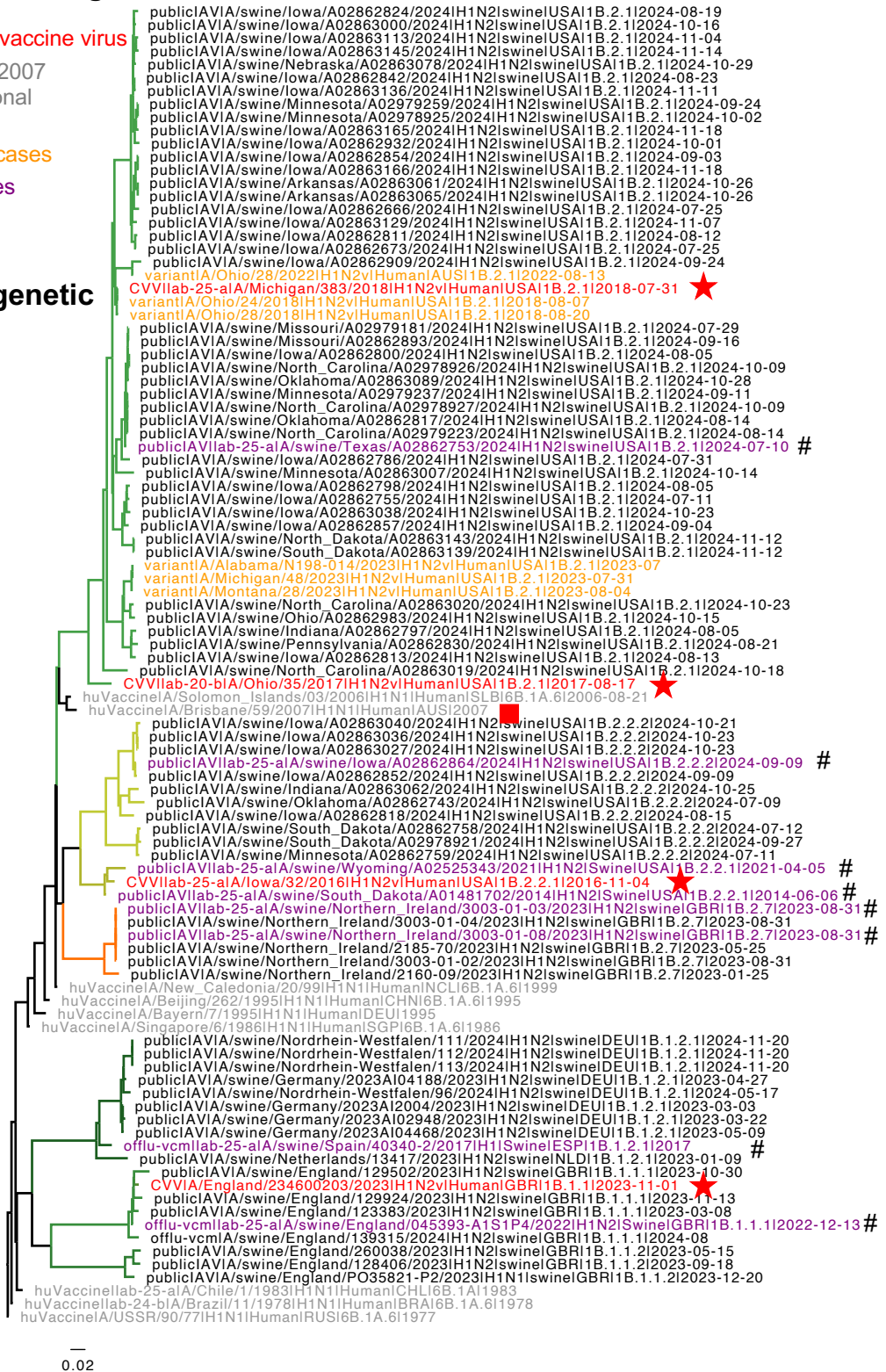


Figure 8. Swine H1 HA genes of the 1B lineage (tree was proportionally down sampled to 81 swine HA genes, excluding references). Number of detections of each clade from data deposited on or after July 1, 2024 are presented adjacent to the clade name in the figure key.

Antigenic analysis: Swine 1B Lineage

Table 8. USA Data: Hemagglutination inhibition of CVV vaccine ferret antisera against contemporary swine 1B lineage strains selected to represent clade consensus.

- > 8 fold reduction
- 8 fold reduction
- 4 fold reduction

	Global Clade	US Clade	A/Michigan/383/2018 RG58A	A/Iowa/32/2016	A/swine/Wyoming/A02525343/2021** #15	A/swine/Wyoming/A02525343/2021* #16	Human Pooled Sera
A/Michigan/383/2018 RG58A	1B.2.1	delta-2	160	20	<10	<10	80
A/swine/Texas/A02862753/2024	1B.2.1	delta-2	160	<10	<10	<10	20
A/Iowa/32/2016	1B.2.2.1	delta-1a	<10	320	40	20	80
A/swine/Wyoming/A02525343/2021	1B.2.2.1	delta-1a	<10	20	160	80	80
A/swine/South_Dakota/A01481702/2014*	1B.2.2.1	delta-1a	<10	10	20	<10	80
A/swine/Iowa/A02862864/2024	1B.2.2.2	delta-1b	<10	<10	<10	<10	40

*Previously tested in OFFLU report 2024b (September 2024); Reference CVV in red, new swine strains in bold. Homologous titers highlighted gray. Human sera were collected in USA with titer relative to A/Victoria/4897/2022 (1:320), pool of 2 male and 2 female adults.

- The 1B.2.1 (delta-2) clade swine representative had no loss of titer to the within clade CVV but had a >8-fold loss in cross-reactivity to human pooled sera.
- The 1B.2.2.1 (delta-1a) clade swine representative had >8-fold reduction from the within clade CVV A/Iowa/32/2016 a 4-fold loss to human pooled sera.
- The contemporary swine 1B.2.2.2 (delta-1b) does not have a within-clade CVV, had a >8-fold decrease from CVV A/Iowa/32/2016, and had an 8-fold loss in cross-reactivity to human pooled sera.

Table 9. EU Data: Hemagglutination inhibition of CVV vaccine ferret antisera against contemporary swine 1B lineage strains selected to represent clade consensus.

	Global Clade	A/Chile/1/1983	A/Brazil/11/1978	A/Michigan/383/2018 CVV	A/Iowa/32/2016 CVV
A/Chile/1/1983	H1N1 1B	640	640	20	320
A/Brazil/11/1978	H1N1 1B	320	1280	20	320
A/swine/England/045393-A1S1P4/2022*	1B.1.1.1	40	80	40	nt
A/swine/Spain/40340-2/2017#	1B.1.2.1	160	640	80	nt
A/Michigan/383/2018 CVV	1B.2.1	320	160	640	640
A/Iowa/32/2016 CVV	1B.2.2.1	160	40	80	2560
A/swine/Northern Ireland/3003-01-03/2023	1B.2.7	40	40	20	160
A/swine/Northern Ireland/3003-01-08/2023	1B.2.7	20	40	20	160

- >8 fold reduction
- 8 fold reduction
- 4 fold reduction

Reference CVV in red, reference seasonal vaccine strains in dark red. *Previously tested in OFFLU report 2024b (September 2024); #Previously tested in OFFLU report 2020b (September 2020). Reference CVV in red, reference seasonal vaccine strains in dark red. New swine strains are bolded. Homologous titers highlighted gray.

- There are no within-clade CVVs for 1B lineages from Europe and the 1B.2.1 CVV has ≥ 8 -fold loss in reactivity with 1B.1 representative swine strains.
- The swine 1B.1.1.1 had >8-fold loss in cross-reactivity with A/Chile/1/1983 and A/Brazil/11/1978.
- The swine 1B.1.2.1 strain retained cross-reactivity with the ancestral human seasonal reference strain but had 8-fold loss in cross-reactivity with the 1B.2.1 CVV.
- The swine 1B.2.7 clade viruses had no within-clade CVV and >8-fold loss in cross-reactivity with all seasonal vaccine and CVV anti-sera.

Table 10. Amino acid substitutions between representative swine 1B.1.x lineage strains compared to most similar HI-tested vaccine strains (A/Chile/1/1983 and A/Brazil/11/1978).

site	A/Chile/1/1983	A/Brazil/11/1978	A/swine/England/045393-A1S1P4/2022	A/swine/Spain/40340-2/2017	annotations
14	D		E		
36	N	S	S	S	
43	K	R		R	
48	A		P		
54	K		T		
66	E		K		
73	K			V	Cb
74	K		N		Cb
82	T		L		
83	P			T	
85	S		P	P	
89	T		I	I	
94	Y		H		
96	A		S	S	
120	E		D		
121	S	R			
124	P			S	Sa
125	K		G	N	Sa
128	V	I			
129	T			N	
130	K	R			
135	A	S	S	S	RBS
137	S		P		Ca2
139	K		D		
141	K			N	
149	L		V		
153	E		G		Sb
156	G		N		Sb
157	S		L	I	Sa
161	L		V		
162	S		N		Sa
169	K			R	

cont. →

site	A/Chile/1/1983	A/Brazil/11/1978	A/swine/England/045393-A1S1P4/2022	A/swine/Spain/40340-2/2017	annotations
170	E			D	Ca1
171	K			E	
185	I			M	
189	K			R	Sb, RBS
190	T		A	A	Sb, RBS
193	R		H		Sb, RBS
194	K		N		RBS
196	N			T	
197	A		T		
205	H	N			
208	R			K	
209	R		K		
211	T			I	
216	K		R	R	
220	V		I	I	RBS
222	N	G			Ca2, RBS
237	G		D	K	Ca1
238	D		E		
239	T		E		
248	L			F	
252	W		Q	L	
260	G		S		
262	G			E	
267	T		I	V	
270	A		T		
272	M			V	
273	D			N	
276	D		N		
277	A	T	T	T	
308	R		K		
310	T			K	
aadiff		9	39	33	

Reference human seasonal vaccines in gray, HI swine strains in purple.

Table 11. Amino acid substitutions between representative 1B.2.1 strain compared to within-clade, HI-tested CVV (A/Michigan/383/2018 RG58A).

site	A/Michigan/383/2018	A/swine/Texas/A02862753/2024	annotations
35	D	N	
36	S	N	
71	N	T	Cb
102	R	K	
169	E	K	
170	G	E	Ca1
173	V	I	
196	N	T	
203	S	T	
205	H	Q	
211	T	I	
260	S	G	
272	M	I	
310	A	T	
aadiff		14	

Reference CVV strain in red, HI swine strain in purple.

Table 12. Amino acid substitutions between representative swine 1B.2.2.x strains compared to within-lineage, HI-tested CVV (A/Iowa/32/2016).

site	A/Iowa/32/2016	A/swine/Wyoming/A02525343/2021	A/swine/South_Dakota/A01481702/2014	A/swine/Iowa/A02862864/2024	annotations
19	L	V	V	V	
50	L			I	
69	S			T	
72	S	P			
74	K	E	E		Cb
82	A			T	
85	S			P	
86	D			E	
94	Q			D	
96	T	A	A		
106	S	N			
119	R			K	
127	T			N	
128	V			T	
130	T	D			
132	K	T	V		RBS
141	E		K		
142	G			R	Ca2
149	I			V	
153	V			E	Sb
157	L	R			Sa
166	K		E		Ca1
168	E	D	D	N	
170	G			E	Ca1
175	I	V			

cont. →

site	A/Iowa/32/2016	A/swine/Wyoming/A02525343/2021	A/swine/South_Dakota/A01481702/2014	A/swine/Iowa/A02862864/2024	annotations
176	L			I	
183	S			P	
184	N			D	
186	G			E	
187	D			N	RBS
193	H			R	Sb, RBS
194	T			K	RBS
202	M			S	
208	R	K		E	
215	T	A		I	
222	D	N		N	Ca2, RBS
228	N			K	
236	P			A	
241	I	V		M	
244	T			A	
256	A			T	
269	K			N	
271	P			S	
274	E			K	
277	A			T	
283	K			Q	
287	N	T			
298	V			A	
310	T	R		A	
aadiff		16	7	38	

Reference CVV strain in red, HI swine strains in purple.

Table 13. Amino acid substitutions between representative swine 1B.2.7 clade strains compared to the nearest HI-tested CVV (A/Iowa/32/2016) and the most similar human seasonal strain (A/New_Caledonia/20/1999). Amino acid substitutions between representative swine 1B.2.7 clade strains compared to the nearest HI-tested CVV (A/Iowa/32/2016) and the most similar human vaccine (A/New_Caledonia/20/1999).

Nearest tested CVV					Most similar vaccine				
site	A/Iowa/32/2016	A/swine/Northern_Ireland/3003-01-03/2023	A/swine/Northern_Ireland/3003-01-08/2023	annotations	site	A/New_Caledonia/20/1999	A/swine/Northern_Ireland/3003-01-03/2023	A/swine/Northern_Ireland/3003-01-08/2023	annotations
19	L	V	V		43	L	S	S	
43	L	S	S		44	L	I	I	
44	L	I	I		68	E	K	K	
68	E	K	K		69	L	S	S	
72	S	P	P		72	S	P	P	
73	K	Q	Q	Cb	73	K	Q	Q	Cb
74	K	E	E	Cb	84	N	D	D	
82	A	T	T		86	E	K	K	
84	N	D	D		89	T	A	A	
85	S	P	P		94	Y	H	H	
86	D	K	K		96	A	D	D	
94	Q	H	H		112	E	K	K	
96	T	D	D		125	T	N	N	Sa
112	E	K	K		132	V	K	K	RBS
119	R	K	K		141	K	E	E	
142	G	S	S	Ca2	153	G	E	E	Sb
149	I	L	L		166	V	S	S	Ca1
153	V	E	E	Sb	169	K	E	E	
166	K	S	S	Ca1	175	V	I	I	
168	E	N	N		186	G	E	E	
169	K	E	E		187	D	N	N	RBS
170	G	E	E	Ca1	189	R	K	K	Sb, RBS
183	S	P	P		190	A	T	T	Sb, RBS
186	G	E	E		193	H	R	R	Sb, RBS
187	D	N	N	RBS	210	F	L	L	
189	R	K	K	Sb, RBS	215	A	T	T	
193	H	R	R	Sb, RBS	237	G	R	R	Ca1
202	M	V	V		258	S	N	N	
210	F	L	L		260	G	S	S	
237	G	R	R	Ca1	273	D	G	G	
244	T	A	A		289	S	G	G	
258	S	N	N		295	V	I	I	
260	G	S	S		306	Y	F	F	
261	L	F	F		321	I	T	T	
269	K	N	N		aadiff		34	34	
273	D	G	G						
283	K	Q	Q						
289	N	G	G						
295	V	I	I						
306	Y	F	F						
310	T	A	A						
321	I	T	T						
aadiff		42	42						

Reference CVV in red, human seasonal vaccine strain in gray, HI swine strains in purple.

1C Eurasian avian lineage

★ H1v candidate vaccine virus

Reported H1v cases

HI tested viruses

H1 1C swine genetic clades

● 1C.2.4.3 (n=19)

● 1C.2.4.2 (n=10)

● 1C.2.4.1 (n=13)

● 1C.2.1 (n=88)

● 1C.2.3 (n=1)

● 1C.2.2 (n=53)

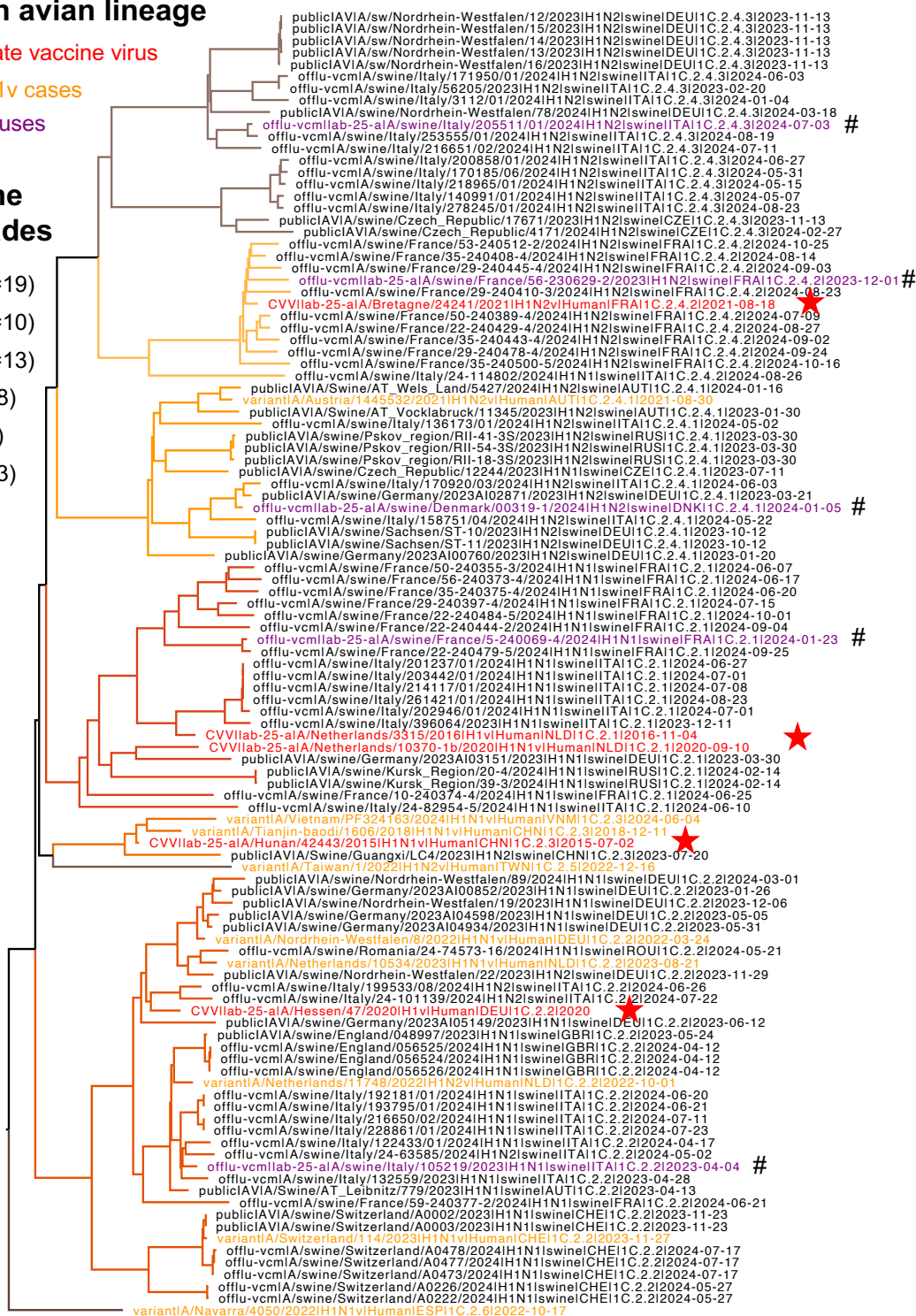


Figure 9. Swine H1 HA genes of the 1C lineage (tree was proportionately downsampled to 95 swine HA sequences, excluding references). Number of detections of each clade from data deposited on or after July 1, 2024 are presented adjacent to the clade name in the figure key.

Antigenic analysis: Swine 1C Lineage

Table 14. EU data: Hemagglutination inhibition of CVV vaccine ferret antisera against contemporary swine 1C lineage strains selected to represent clade consensus.

Global Clade		A/Netherlands/3315/2016 CVV	A/Netherlands/10370-1b/2020 CVV	A/Hessen/47/2020-like CVV	A/Hunan/42443/2015 CNIC-1601 CVV	A/Bretagne/24241/2021 CVV
A/Netherlands/3315/2016 CVV	1C.2.1	1280	160	320	160	40
A/Netherlands/10370-1b/2020 CVV	1C.2.1	160	640	320	640	0
A/swine/France/5-240069-4/2024	1C.2.1	320	320	80	160	0
A/swine/Italy/133898-3/2022	1C.2.1	640	320	160	640	20
A/Hessen/47/2020-like CVV	1C.2.2	160	320	1280	1280	40
A/swine/Italy/105219/2023	1C.2.2	160	320	640	1280	40
A/Hunan/42443/2015 CNIC-1601 CVV	1C.2.3	160	320	320	2560	0
A/Bretagne/24241/2021 CVV	1C.2.4.2	80	20	40	160	1280
A/swine/Denmark/00319-1/2024	1C.2.4.1	80	80	80	160	20
A/swine/France/56-230629-2/2023	1C.2.4.2	160	160	160	160	1280
A/swine/Italy/205511-01/2024	1C.2.4.3	80	80	40	80	20

- > 8 fold reduction
- 8 fold reduction
- 4 fold reduction

Reference CVV in red, reference seasonal vaccine strains in dark red. New swine strains are bolded. Homologous titers highlighted gray.

- The 1C.2.1 strains retained cross-reactivity to the 1C.2.1 CVV A/Netherlands/10370-1b/2020.
- The 1C.2.2 strain retained cross-reactivity to the within-clade CVV A/Hessen/47/2020-like.
- The 1C.2.4.1 swine strain from Denmark had no within-clade CVV and demonstrated >8-fold loss to the 1C.2.4.2 CVV A/Bretagne/24241/2021.
- The 1C.2.4.2 swine strains retained reactivity to the within-clade CVV A/Bretagne/24241/2021.
- The representative swine 1C.2.4.3 had no within-clade CVV and demonstrated >8-fold loss to available 1C CVV strains.

Table 15. Amino acid substitutions between representative swine 1C.2.1 strain compared to within-clade, HI-tested CVVs (A/Netherlands/3315/2016 and A/Netherlands/10370-1b/2020) and similar 1C.2.3 CVV (A/Hunan/42443/2015) used in HI assays.

site	A/Netherlands/3315/2016	A/Netherlands/10370-1b/2020	A/Hunan/42443/2015	A/swine/France/5-240069-4/2024	annotations
20	M		L	L	
31	N	D			
44	L	M			
48	A		I		
56	N		S		
66	E		K		
69	L			S	
71	I	L	L		Cb
74	N	K			Cb
83	S	P			
84	N			K	
96	A			T	
97	D	N		N	
102	R		K		
120	E	A	A	A	
125	N			S	Sa
127	E		D		
130	K		R		
132	S	T	T		RBS
134	V			I	RBS
137	S	P		T	Ca2
141	I	A	A	V	
142	K	N	N	N	Ca2
152	V			I	
155	E	G	G	A	Sa
161	I	L	L		
163	T	K	K	K	Sa
175	I	V	V	V	
179	V			I	
199	V	I			
202	G	E		E	
204	S			P	Ca1
208	K	Q			
215	V	A		I	
220	V			I	RBS
253	Y	H	H		
258	N	D	K		
262	N		S		
267	M	I	R		
271	N	H	Q		
288	S		G		
298	I		V		
311	Q	R			
321	T	I	I	V	
324	V	I	I	I	
aadiff		26	25	22	

Reference CVVs in red, HI swine strain in purple.

Table 16. Amino acid substitutions between representative swine 1C.2.2 strain compared to within-clade, HI-tested CVV (A/Hessen/47/2020).

site	A/Hessen/47/2020	A/swine/Italy/105219/2023	annotations
3	I	L	
53	K	R	
97	D	N	
116	I	V	
118	P	S	
161	L	I	
163	N	K	Sa
175	V	I	
185	D	E	
214	T	I	
235	D	N	
253	Y	H	
267	M	I	
269	N	D	
302	E	K	
aadiff		15	

Reference CVV in red, HI swine strain in purple.

Table 17. Amino acid substitutions between representative swine 1C.2.4.x strains compared to the within-lineage, HI-tested CVV (A/Bretagne/24241/2021) and similar 1C.2.1 CVV (A/Netherlands/10370-1b/2020) used in HI assays.

site	A/Bretagne/24241/2021	A/Netherlands/10370-1b/2020	A/swine/Denmark/00319-1/2024	A/swine/France/56-230629-2/2023	A/swine/Italy/205511/01/2024	annotations
5	I	V	V		V	
20	M		L		L	
31	N	D			D	
35	T	N				
36	N	S	S		S	
39	G		E			
44	L	M				
54	N				K	
56	D	N	N	N	N	
57	V			I		
69	L				R	
71	V	L	L		L	Cb
74	N	K	S			Cb
80	I			V		
83	S	P	P			
84	N		S		D	
86	K		E		E	
89	T	A			I	
96	A		S		S	
97	D	N				
102	R				K	
104	L	Q	R			
106	S				G	
111	F		L			
116	I				V	
119	K				D	
120	-	A	A		A	
121	N	T	T		A	
124	P				E	Sa
125	S	N	D		N	Sa
127	E				K	
128	A	T	T		T	
129	-	T	T			
130	-	K	Q		D	
134	V		I		G	RBS
135	S	A	A			RBS
137	S	P				Ca2
138	K	H	H	R	H	
141	A				T	
142	N		K	S	K	Ca2
146	R				Q	
152	T	V	V			
153	S	K			K	Sb

cont. →

site	A/Bretagne/24241/2021	A/Netherlands/10370-1b/2020	A/swine/Denmark/00319-1/2024	A/swine/France/56-230629-2/2023	A/swine/Italy/205511/01/2024	annotations
155	G				-	Sa
156	K	N	G		N	Sb
157	P	S	S		S	Sa
159	S	P	P		P	Sa
161	L				I	
162	S		N			Sa
163	K		G			Sa
166	K	T	T		T	Ca1
169	K				R	
172	E				K	
185	Y	D				
186	S		R			
190	T				A	Sb, RBS
194	N		H		S	RBS
199	V	I				
202	V	E	E			
203	S				T	
208	Q		R			
215	V	A				
216	P	A	T		D	
218	P		Q			RBS
219	E	K	R		K	RBS
220	I	V				RBS
222	E			K		Ca2, RBS
224	R	A	A		A	RBS
237	E	G	G		G	Ca1
239	T				N	
252	R	W	W			
253	Y	H				
258	E	D	D	D	D	
259	K				I	
260	G				S	
261	S		L	Y		
262	N				S	
266	M		V		L	
267	K	I	I			
269	D		E			
288	S		G			
289	D	N	N		N	
290	R	L	L			
311	Q	R	R			
aadiff		43	49	8	51	

Reference CVVs in red, HI swine strains in purple.

H3 swine lineage

- ★ H3v candidate vaccine virus
- A/DistrictOfColumbia/27/2023
- Previous H3N2 seasonal vaccines
- Reported H3N2v cases
- + New variant(s)
- # HI tested viruses

H3 swine genetic clades

- Other-Human-2020 (n=6)
- 3.2010.2 (n=15)
- Other-Human-2010 (n=3)
- 3.2010.1 (n=124)
- 3.2000.4 (n=1)
- 3.1990.4.a (n=20)
- 3.1990.4.b2 (n=12)
- 3.1990.4.b1 (n=8)
- 3.1990.4.c (n=6)
- 3.1990.4 (n=3)
- 3.1990.4.h (n=1)
- 3.1990.4.i (n=7)
- 3.1970.1 (n=3)
- Human vaccine or seasonal

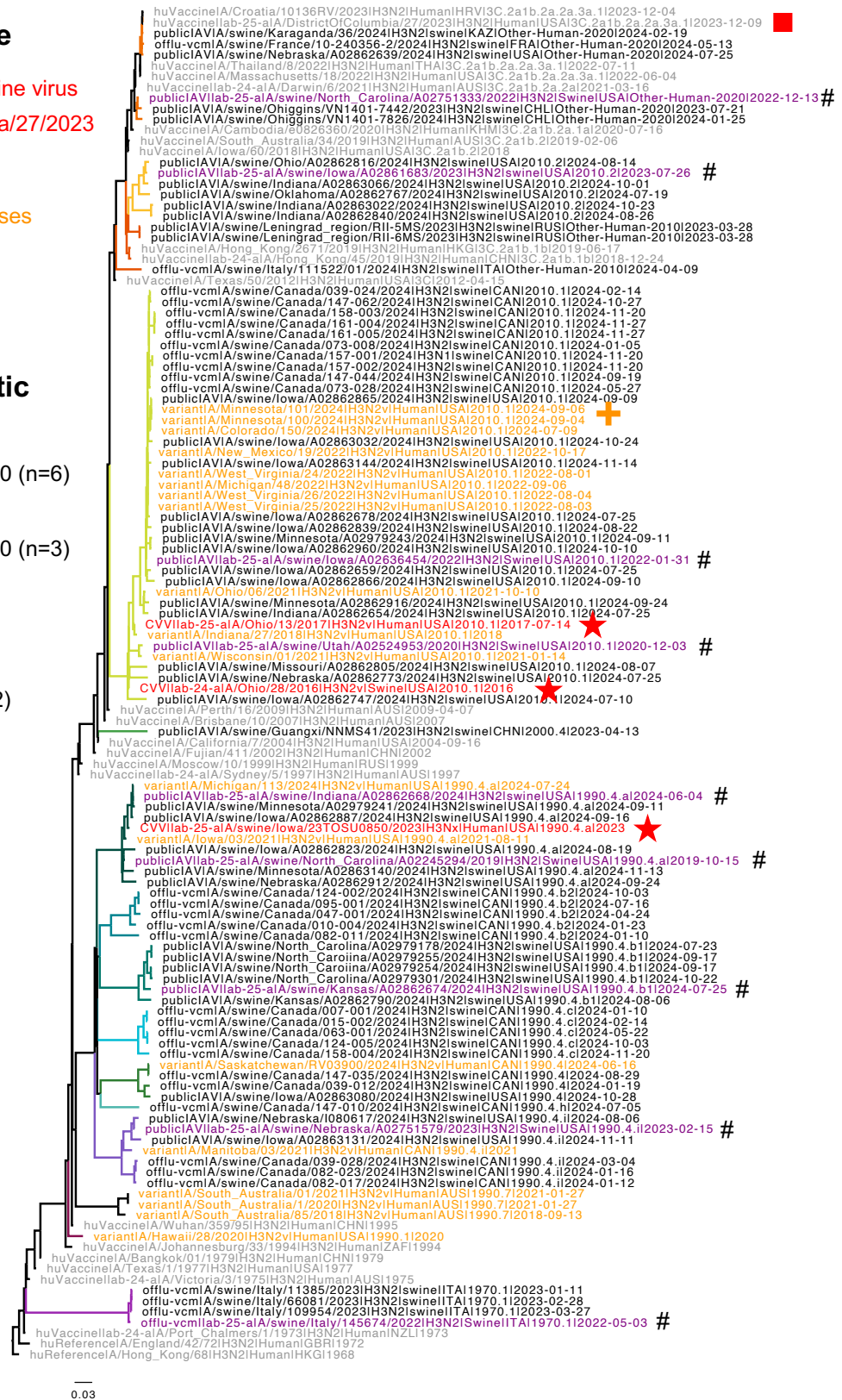


Figure 10. Swine H3 HA genes (tree was proportionally down sampled to 79 swine HA genes, excluding references). Number of detections of each clade from data deposited on or after July 1, 2024 are presented adjacent to the clade name in the figure key.

Antigenic analysis: Swine H3

Table 18. USA Data: Hemagglutination inhibition of CVV or human seasonal vaccine ferret antisera against contemporary swine H3 strains selected to represent clade consensus.

- > 8 fold reduction
- 8 fold reduction
- 4 fold reduction

	Global Clade	A/swine/Iowa/23TOSU0850/2023 CVV	A/swine/North_Carolina/A02245294/2019 (H3N2) #32	A/swine/North_Carolina/A02245294/2019 (H3N2) #18	IDCDC-RG60A A/Ohio/13/2017 CVV	A/swine/Utah/A02524953/2020 (H3N2) #19	A/swine/Utah/A02524953/2020 (H3N2) #20	A/DistrictofColumbia/27/2023	Human pooled sera
A/swine/Iowa/23TOSU0850/2023 CVV	1990.4.a	640	40	40	<10	<10	<10	<10	160
A/swine/North_Carolina/A02245294/2019	1990.4.a	160	640	640	20	20	40	<10	40
A/swine/Indiana/A02862668/2024	1990.4.a	320	640	640	20	20	20	10	160
A/swine/Kansas/A02862674/2024	1990.4.b1	20	40	<10	<10	10	10	<10	320
A/swine/Nebraska/A02751579/2023*	1990.4.i	40	10	10	<10	10	10	<10	40
IDCDC-RG60A A/Ohio/13/2017 CVV	2010.1	80	20	80	1280	160	160	<10	640
A/swine/Utah/A02524953/2020	2010.1	20	40	40	160	640	640	20	80
A/swine/Iowa/A02636454/2022*	2010.1	<10	20	40	160	320	320	<10	160
A/swine/Iowa/A02861683/2023*	2010.2	<10	10	10	<10	10	20	<10	80
A/swine/North_Carolina/A02751333/2022*	2020.1	<10	10	10	<10	<10	<10	80	320
A/District_of_Columbia/27/2023	J.2	<10	20	<10	<10	20	<10	80	320
A/Darwin/6/2021	G.1								640

*Previously tested in OFFLU report 2024b (September 2024); Reference CVV in red, seasonal vaccine strains in dark red, new swine strains in bold. Homologous titers highlighted in gray. Human sera were collected in USA with titer relative to A/Darwin/6/2021, pool of 2 male and 2 female adults. nt=not tested.

- The contemporary swine 1990.4.a retained reactivity to the CVV A/swine/Iowa/23TOSU0850/2023 but had > 4-fold reduction in reactivity in adult human pooled sera.
- The contemporary swine 1990.4.b1 does not have a CVV contained within clade and demonstrated a >8-fold decrease from CVV but retained reactivity in adult human pooled sera.
- The contemporary swine 1990.4.i does not contain a within clade CVV and demonstrated a >8-fold decrease from available CVV and had >8-fold reduction in reactivity to adult human pooled sera.
- The contemporary swine 2010.1 representative strain had an 8-fold loss to A/Ohio/13/2017 and a 4-fold loss in reactivity with adult human pooled sera.
- The contemporary swine 2010.2 does not contain within clade CVV and demonstrated 8-fold or greater loss to the human vaccine strain and had 8-fold loss in reactivity against adult human pooled sera.
- The contemporary swine 2020.1 does not contain within clade CVV but had no loss to the human vaccine strain or adult human pooled sera.

Table 19. EU data: Hemagglutination inhibition of CVV or human seasonal vaccine ferret antisera against contemporary swine H3 strains selected to represent clade consensus.

- > 8 fold reduction
- 8 fold reduction
- 4 fold reduction

Global Clade		A/Port Chalmers/1/1973	A/Ohio/28/2016 CVV	A/Victoria/3/1975	A/Sydney/5/1997
A/Port Chalmers/1/1973	Human Seasonal	5120	160	160	80
A/Ohio/28/2016 CVV	H3N2 2010.1	20	2560	<10	40
A/Victoria/3/1975	Human Seasonal	2560	160	5120	80
A/Sydney/5/1997	Human Seasonal	<10	40	<10	640
A/swine/Italy/145674/2022*	1970.1	80	320	160	80

*Previously tested in OFFLU report 2024a (February 2024). Reference CVV in red, reference seasonal vaccine strains in dark red. Homologous titers highlighted gray.

- The 1970.1 representative swine strain contains no within clade CVV and demonstrated 8-fold or greater loss in reactivity with human seasonal vaccine anti-sera.

Table 20. Amino acid substitutions between representative swine 1990.4.x strains compared to within-lineage, HI-tested CVV (A/swine/Iowa/23TOSU0850/2023), nearest tested human vaccine (A/Sydney/5/1997), and recent variant.

cont.

site	A/swine/Iowa/23TOSU0850/2023	A/Sydney/5/1997	A/swine/Indiana/A02862668/2024	A/swine/North_Carolina/A02245294/2019	A/swine/Kansas/A02862674/2024	A/swine/Nebraska/A02751579/2023	A/Michigan/113/2024	annotations
1	Q				K			
2	K				N			
3	L	I						
6	N		S	S	S	S	S	
7	D				Y			
8	N					K		
10	M	T				T		
31	D	N						
46	S				T			
48	T				K			
49	G					D		
50	R				E			
53	N	D			S			Site C
57	Q	R			K	K		
58	I					V		
62	K	E				G		
78	D	G						
80	Q					E		
81	N				D			
82	K				R			
83	E		K		T		K	
92	T	K						
96	S	N			D	N		
101	Y	D						
104	D				E			
105	Y		H				H	
107	T	S			S	S		
117	N	T			T	T		
119	E			K				
121	T	N				N		
122	Q	N				P		Site A
124	I	S			N	N		
131	A			T	N	G		
133	D	N				N		Site A
135	S	T			A			
137	Y					F		Site A
138	S	A						
140	R	K				K		
142	G	S			E	N		
144	V	I			K			Site A
145	N	K				K		Site A

site	A/swine/Iowa/23TOSU0850/2023	A/Sydney/5/1997	A/swine/Indiana/A02862668/2024	A/swine/North_Carolina/A02245294/2019	A/swine/Kansas/A02862674/2024	A/swine/Nebraska/A02751579/2023	A/Michigan/113/2024	annotations
155	Y	H			H	H		Site B
156	H	Q			S			
158	N	K			K			
159	Y					H		
163	E	A			A	A		
164	Q	L			L			
172	E	D		D	G	D		
174	F				S			
186	G	S						Site B
188	D				N			Site B
189	K	S			V	M		Site B
193	N	S			S	S		Site B
194	L	I						
196	I	A		V	A	V		
198	A					E		
201	R				G			Site D
202	V				I			
203	I	T			T	T		
207	R	K			K	K		Site D
210	Q					L		
217	I				V			Site D
220	R				K			Site D
226	V	I						
228	S				G			
229	I	R						
233	Y	H			H			
260	I					M		
261	Q	R				R		
262	S					I		
269	R				K	K		
273	H	P				L		
275	D	G			G	G		Site C
276	E	K			N	N		
278	N				K			Site C
279	S		F				F	
289	P		S	S			S	
299	K	R			R	R		
312	N				S	G		
323	V			I				
aadiff		43	5	7	45	41	5	

Reference CVV in red, human seasonal vaccine strain in gray, HI swine strains in purple, variant detection in orange.

Table 21. Amino acid substitutions between representative swine 1990.7 strains compared to most similar HI-tested vaccine strains (A/Port_Chalmers/1/1973 and A/Victoria/3/1975).

site	A/Port_Chalmers/1/1973	A/Victoria/3/1975	A/swine/Italy/145674/2022	annotations
3	F	L		
6	N		K	
7	D		G	
7+1	-	N		
9	S		N	
31	N		D	
45	S		N	
46	S		F	
48	T		M	
53	N		R	Site C
62	I		A	
67	I		V	
69	A		S	
80	Q		R	
83	T	K	K	
88	V		I	
92	K		R	
104	D		E	
106	A		T	
117	T		S	
121	I		T	
124	G		N	
126	T	N	N	
137	N		S	Site A
144	D		N	Site A
145	S		N	Site A
146	G		S	Site A
159	S		N	
160	A	T	T	
163	V		M	
164	L	Q		
171	N		S	
173	N		D	
174	F	S		
189	Q	K	R	Site B
196	V		I	
198	A		T	
201	R	K	K	Site D
202	V		I	
203	T		I	
217	I	V		Site D
244	V		I	
260	M		I	
261	R		Q	
267	I		V	
269	R		K	
278	I	S	D	Site C
299	K		R	
307	K		H	
309	V		I	
323	V		I	
aadiff		11	46	

Reference human seasonal vaccine strain in gray (WHO recommended is bold), HI swine strain in purple.

Table 22. Amino acid substitutions between representative swine 2010.1 strains compared to the within-clade, HI-tested CVVs (A/Ohio/13/2017 and A/Ohio/28/2016) and recent variants.

site	A/Ohio/13/2017	A/Ohio/28/2016	A/swine/Utah/A02524953/2020	A/swine/Iowa/A02636454/2022	A/Colorado/150/2024	A/Minnesota/101/2024	A/Minnesota/100/2024	annotations
25	I				M	M	M	
30	T				M	M	M	
31	N			D	D	D	D	
45	S			N	N	N	N	
56	Y	H	H					
62	E			G	G	G	G	
88	V		I					
92	K		R					
96	N			D	D	D	D	
106	A			V				
112	V		A					
122	N			K	K	K	K	Site A
138	S	A						
142	R				K	K	K	
144	S		T					Site A
145	N	K						Site A
156	H		Q					
158	N				D	D	D	
167	T		A					
202	I			T	T	T	T	
209	N	S	G					
212	A			T	T	T	T	
216	N				I	I	I	
223	V			I	I	I	I	
238	R			K	K	K	K	
264	K			R	R	R	R	
309	V					I	I	
312	N		K					
aadiff		4	9	11	15	16	16	

Reference CVVs in red, HI swine strains in purple, variant detections in orange (new are bold).

Table 23. Amino acid substitutions between representative swine 2010.2 clade strain compared to HI-tested CVV (A/Ohio/13/2017). A separate comparison was also made against the most similar human vaccine (A/Stockholm/6/2014).

Nearest tested CVV				Most similar vaccine			
site	A/Ohio/13/2017	A/swine/Iowa/A02861683/2023	annotations	site	A/Stockholm/6/2014	A/swine/Iowa/A02861683/2023	annotations
3	L	I		3	L	I	
9	N	G		9	S	G	
10	M	T		31	N	D	
31	N	D		53	D	N	Site C
33	Q	R		58	I	V	
45	S	N		67	I	V	
46	F	S		83	K	Q	
48	T	I		92	K	R	
56	Y	H		106	A	V	
58	I	V		121	N	K	
67	I	V		128	A	T	
82	N	K		135	T	I	
83	K	Q		140	I	K	
92	K	R		144	N	K	Site A
94	H	Y		156	H	Q	
106	A	V		158	N	D	
121	N	K		159	S	Y	
133	D	N	Site A	167	T	I	
135	A	I		174	F	X	
142	R	G		189	K	S	Site B
144	S	K	Site A	192	I	T	
145	N	S	Site A	193	F	S	Site B
156	H	Q		197	Q	R	
158	N	D		203	T	I	
159	F	Y		242	I	T	
165	E	N		291	D	N	
167	T	I		aadiff		26	
174	F	X					
186	A	G	Site B				
189	K	S	Site B				
192	I	T					
197	Q	R					
198	A	S					
199	A	S					
209	N	S					
223	V	I					
238	R	K					
242	I	T					
278	N	K	Site C				
280	A	E					
291	D	N					
312	N	S					
323	I	V					
aadiff		43					

Reference CVV in red, human seasonal vaccine strain in gray, HI swine strain in purple.

Table 24. Amino acid substitutions between representative swine 2020.1 clade strain compared to HI-tested human vaccine (A/District_of_Columbia/27/2023) and additional WHO recommended vaccines.

site	A/District_of_Columbia/27/2023	A/Thailand/8/2022	A/Massachusetts/18/2022	A/Croatia/10136RV/2023	A/swine/North_Carolina/A02751333/2022	annotations
53	N				D	Site C
79	F				V	
96	S				N	
122	D	N	N		N	Site A
145	N	S	S		S	Site A
156	S				H	
186	D			A		Site B
192	F				I	
223	V				I	
276	E	K	K		K	
aadiff		3	3	1	9	

Reference vaccine in gray (WHO recommended are bold), HI swine strain in purple.

Summary and Risk Assessment

Global Variant Cases:

During the reporting period (July 1 – December 31, 2024), 6 variant cases were reported and included with the swine analyses when sequence data were available.

4 cases were reported in the September 2024 OFFLU report; 2x 2010.1 variant cases were not previously reported (detected September 2024), and have been annotated as “new variants” in the phylogenetic tree:

- USA: H1N2v (2x 1A.1.1.3); H3N2v (1x 1990.4.a, 3x 2010.1);

Europe Swine:

- H1 1A: The contemporary swine 1A.3.3.2 retained cross-reactivity with recent human seasonal H1 vaccines. The contemporary 1A.5.1 had >8-fold decrease to all human seasonal vaccine ferret anti-sera and a 4-fold loss in reactivity to the 1A.3.3.3-c1 CVV sera.
- H1 1B: There were no within-clade CVVs tested for 1B lineages from Europe and the 1B.2.1 CVV has significant loss in reactivity with the 1B.1 representative swine strains. The swine 1B.1.1.1 had significant loss in cross-reactivity with A/Chile/1/1983 and A/Brazil/11/1978. The swine 1B.1.2.1 strain retained cross-reactivity with the ancestral human seasonal reference strains but had >8-fold loss in cross-reactivity to the tested 1B.2.1 CVV. A newly detected group of viruses, 1B.2.7, had no within-clade CVV and >8-fold loss in cross reactivity to ancestral human seasonal reference strains.
- H1 1C: The 1C.2.1 strain retained cross-reactivity to the 1C.2.1 CVV A/Netherlands/10370-1b/2020. The 1C.2.2 strain retained cross-reactivity to the within-clade CVV A/Hessen/47/2020-like. The 1C.2.4.1 swine strain had no within-clade CVV and demonstrated >8-fold loss to the 1C.2.4.2 CVV A/Bretagne/24241/2021. The 1C.2.4.2 swine strains retained reactivity to the within-clade CVV. The representative swine 1C.2.4.3 had no within-clade CVV and demonstrated >8-fold loss to available 1C CVV strains.
- H3: The 1970.1 representative swine strain from Italy demonstrated 8-fold or greater loss in reactivity with human seasonal vaccine anti-sera.

North America Swine:

- H1 1A: The contemporary swine 1A.1.1.3 (alpha-del) had no loss in reactivity to the CVV A/Pennsylvania/27/2024 ferret anti-sera but had 4-fold loss to human pooled sera. The contemporary swine 1A.3.3.2 (pdm) with onward transmission in swine had >8-fold decrease to A/Victoria/4897/2022 5a.2a.1 and had a 4-fold loss to human pooled sera. The contemporary swine 1A.3.3.3-c3 (gamma.3) virus had >8-fold decrease from the within-clade 1A.3.3.3-c3 CVV A/Wisconsin/2021 and a 4-fold loss to human pooled sera. The contemporary swine 1A.2 (beta) virus has no within clade CVV, had a >8-fold decrease to all CVV and human seasonal vaccine ferret anti-sera, and had a 4-fold loss to human pooled sera.
- H1 1B: The 1B.2.1 (delta-2) clade swine representative had no loss of titer to the within clade CVV but had a >8-fold loss in cross-reactivity to human pooled sera. The 1B.2.2.1 (delta-1a) clade swine representative had >8-fold reduction from the within clade CVV A/Iowa/32/2016 a 4-fold loss to human pooled sera. The contemporary swine 1B.2.2.2 (delta-1b) does not have a within-clade CVV, had a >8-fold decrease from CVV A/Iowa/32/2016, and had an 8-fold loss in cross-reactivity to human pooled sera.
- H3: The contemporary swine 1990.4.a retained reactivity to the CVV A/swine/Iowa/23TOSU0850/2023 but had >4-fold reduction in reactivity in adult human pooled sera. The contemporary swine 1990.4.b1 does not have a CVV contained within clade and demonstrated a >8-fold decrease from CVV but retained reactivity in adult human pooled sera. The contemporary swine 1990.4.i does not contain a within clade CVV and demonstrated a >8-fold decrease from available CVV and had >8-fold reduction in reactivity to adult human pooled sera. The contemporary swine 2010.1 representative strain had an 8-fold loss to A/Ohio/13/2017

and a 4-fold loss in reactivity with adult human pooled sera. The contemporary swine 2010.2 does not contain within clade CVV and demonstrated 8-fold or greater loss to the human vaccine strain and had 8-fold loss in reactivity against adult human pooled sera. The contemporary swine 2020.1 does not contain within clade CVV but had no loss to the human vaccine strain or adult human pooled sera.

Annex 1. Geographic Distribution of swine HA phylogenetic clades by country

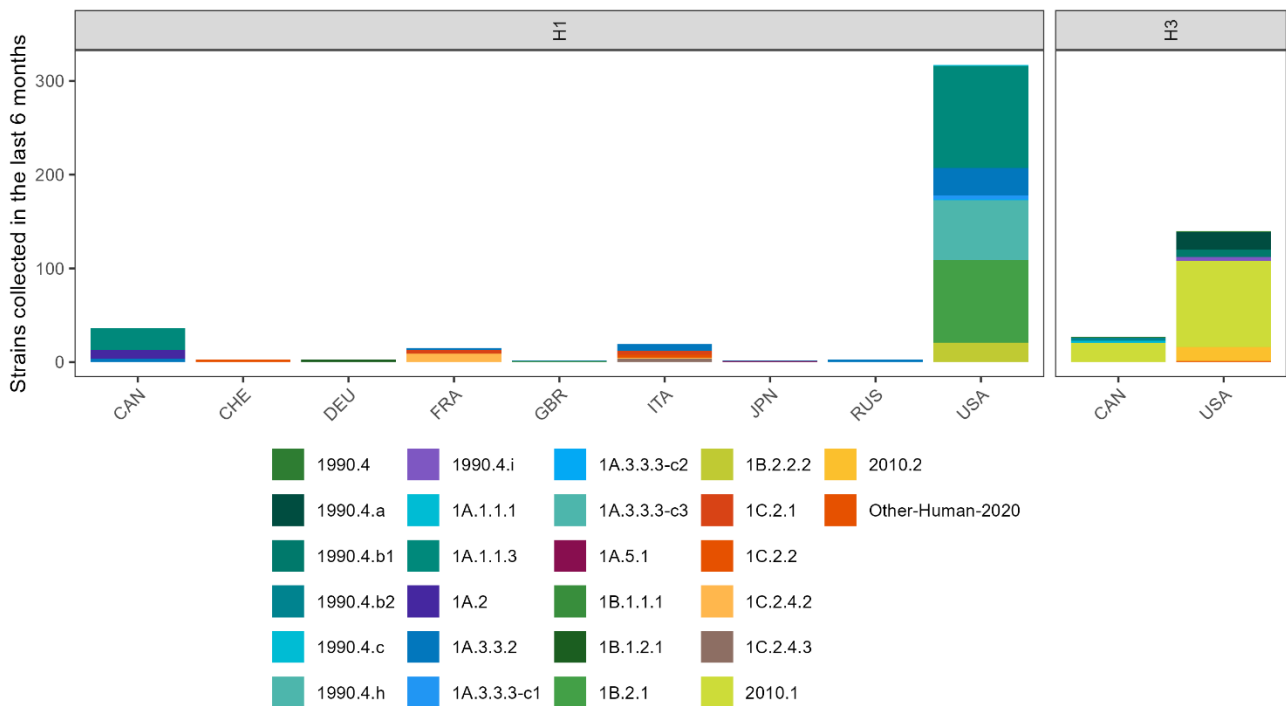


Figure A1. Summary of swine HA genes colored by phylogenetic clade for sequences deposited between July 1 2024 and January 1 2025 (n = 567).

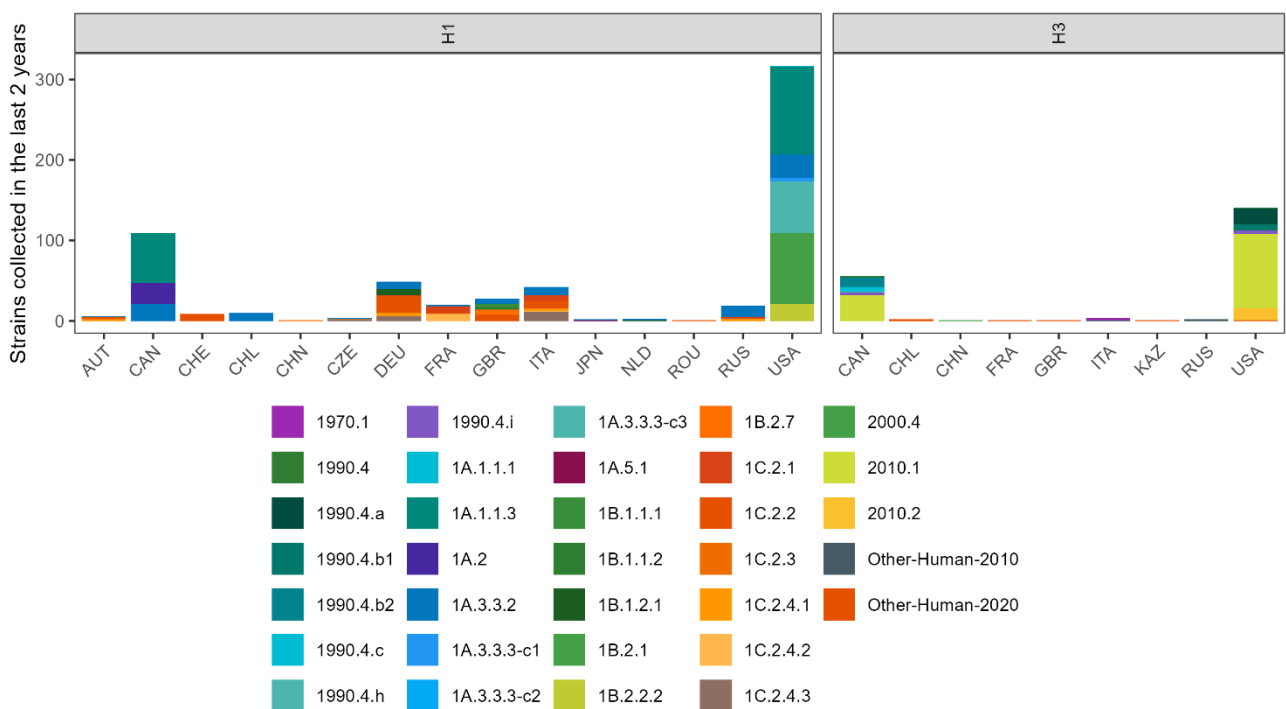


Figure A2. Summary of swine HA genes colored by phylogenetic clade. Expanded collection date criteria for non-USA sequences to a 24-month window from January 1 2023 to December 31 2024 (n = 829).

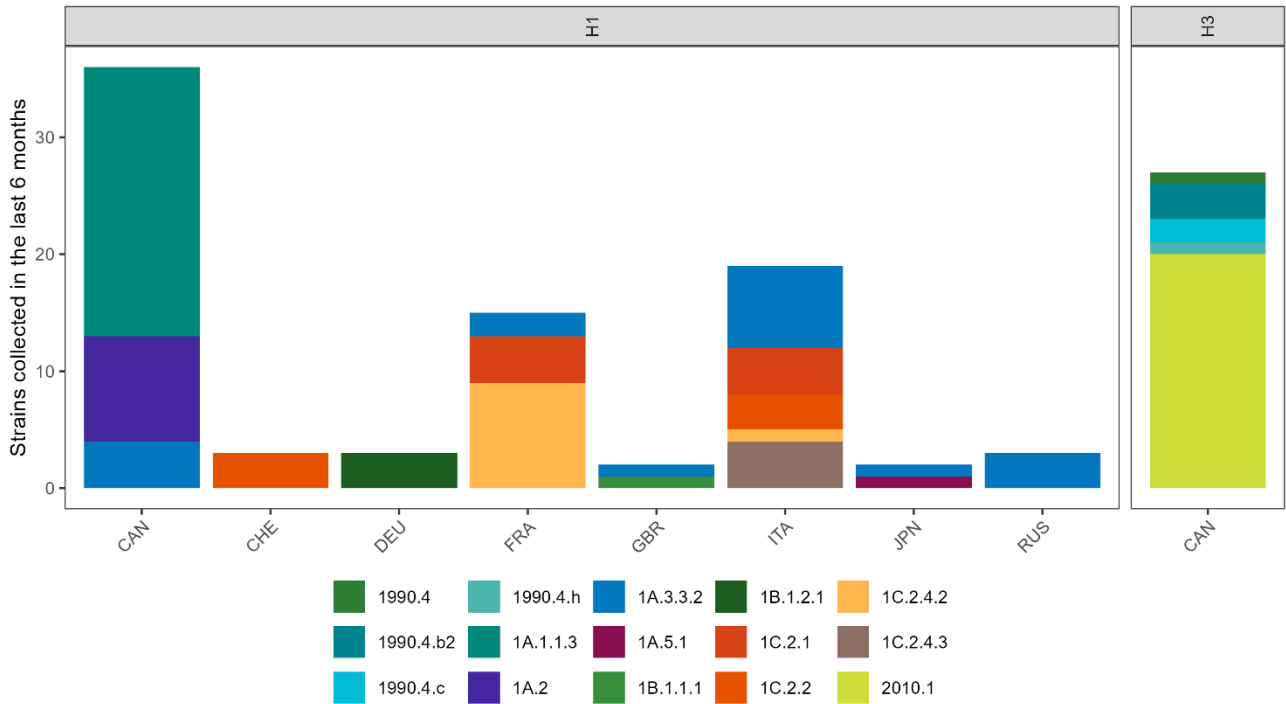


Figure A3. Summary of swine HA genes colored by phylogenetic clade for sequences deposited between July 1 2024 and January 1 2025, in any country other than the United States of America (n = 110).

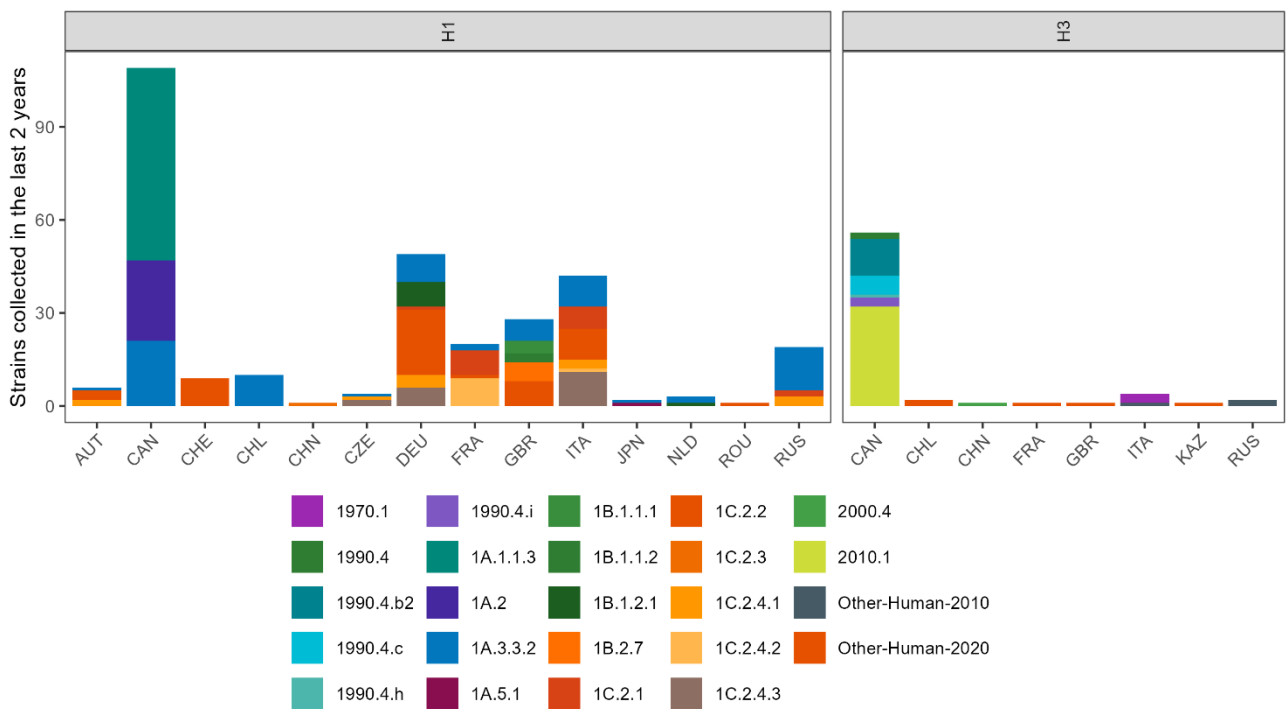


Figure A4. Summary of swine HA genes colored by phylogenetic clade. Expanded collection date criteria for non-USA sequences to a 24-month window from January 1 2023 to December 31 2024, in any country other than the United States of America (n = 371).

Table A1a. Summary of swine H1 clades by country collected in the past 6 months and deposited on or after July 2024.

clade	Country	count
1A.1.1.3	CAN	23
1A.2	CAN	9
1A.3.3.2	CAN	4
1C.2.2	CHE	3
1B.1.2.1	DEU	3
1A.3.3.2	FRA	2
1C.2.1	FRA	4
1C.2.4.2	FRA	9
1A.3.3.2	GBR	1
1B.1.1.1	GBR	1
1A.3.3.2	ITA	7
1C.2.1	ITA	4
1C.2.2	ITA	3
1C.2.4.2	ITA	1
1C.2.4.3	ITA	4
1A.3.3.2	JPN	1
1A.5.1	JPN	1
1A.3.3.2	RUS	3
1A.1.1.1	USA	1
1A.1.1.3	USA	109
1A.3.3.2	USA	29
1A.3.3.3-c1	USA	4
1A.3.3.3-c2	USA	1
1A.3.3.3-c3	USA	64
1B.2.1	USA	88
1B.2.2.2	USA	21

Table A1b. Summary of swine H1 clades by country collected in the past 24 months and deposited on or after January 2023.

cont.

clade	country	count
1A.3.3.2	AUT	1
1C.2.2	AUT	3
1C.2.4.1	AUT	2
1A.1.1.3	CAN	62
1A.2	CAN	26
1A.3.3.2	CAN	21
1C.2.2	CHE	9
1A.3.3.2	CHL	10
1C.2.3	CHN	1
1A.3.3.2	CZE	1
1C.2.4.1	CZE	1
1C.2.4.3	CZE	2
1A.3.3.2	DEU	9
1B.1.2.1	DEU	8
1C.2.1	DEU	1
1C.2.2	DEU	21
1C.2.4.1	DEU	4
1C.2.4.3	DEU	6
1A.3.3.2	FRA	2
1C.2.1	FRA	8
1C.2.2	FRA	1
1C.2.4.2	FRA	9
1A.3.3.2	GBR	7
1B.1.1.1	GBR	4
1B.1.1.2	GBR	3

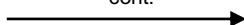
clade	country	count
1B.2.7	GBR	6
1C.2.2	GBR	8
1A.3.3.2	ITA	10
1C.2.1	ITA	7
1C.2.2	ITA	10
1C.2.4.1	ITA	3
1C.2.4.2	ITA	1
1C.2.4.3	ITA	11
1A.3.3.2	JPN	1
1A.5.1	JPN	1
1A.3.3.2	NLD	2
1B.1.2.1	NLD	1
1C.2.2	ROU	1
1A.3.3.2	RUS	14
1C.2.1	RUS	2
1C.2.4.1	RUS	3
1A.1.1.1	USA	1
1A.1.1.3	USA	109
1A.3.3.2	USA	29
1A.3.3.3-c1	USA	4
1A.3.3.3-c2	USA	1
1A.3.3.3-c3	USA	64
1B.2.1	USA	88
1B.2.2.2	USA	21

Table A2a. Summary of swine H3 clades by country collected in the past 6 months and deposited on or after July 2024.

clade	country	count
1990.4	CAN	1
1990.4.b2	CAN	3
1990.4.c	CAN	2
1990.4.h	CAN	1
2010.1	CAN	20
1990.4	USA	1
1990.4.a	USA	19
1990.4.b1	USA	8
1990.4.i	USA	4
2010.1	USA	92
2010.2	USA	15
Other-Human-2020	USA	1

Table A2b. Summary of swine H3 clades by country collected in the past 24 months and deposited on or after January 2023.

cont.



clade	country	count
1990.4	CAN	2
1990.4.b2	CAN	12
1990.4.c	CAN	6
1990.4.h	CAN	1
1990.4.i	CAN	3
2010.1	CAN	32
Other-Human-2020	CHL	2
2000.4	CHN	1
Other-Human-2020	FRA	1
Other-Human-2020	GBR	1
1970.1	ITA	3

clade	country	count
Other-Human-2010	ITA	1
Other-Human-2020	KAZ	1
Other-Human-2010	RUS	2
1990.4	USA	1
1990.4.a	USA	20
1990.4.b1	USA	8
1990.4.i	USA	4
2010.1	USA	92
2010.2	USA	15
Other-Human-2020	USA	1

Table A3a. Recent swine and variant A(H1) activity shared with international agencies and collected from sequence repositories.

Country, area or territory	Host [#]	Genetic clade
Canada	Swine	1A.1.1.3; 1A.2; 1A.3.3.2
France	Swine	1A.3.3.2; 1C.2.1; 1C.2.4.2
Germany	Swine	1B.1.2.1
Italy	Swine	1A.3.3.2; 1C.2.1; 1C.2.2; 1C.2.4.2; 1C.2.4.3
Japan	Swine	1A.3.3.2; 1A.5.1
Russia	Swine	1A.3.3.2
Switzerland	Swine	1C.2.2
United Kingdom of Great Britain and Northern Ireland	Swine	1A.3.3.2; 1B.1.1.1
United States of America	Human (2)*	1A.1.1.3
United States of America	Swine	1A.1.1.1; 1A.1.1.3; 1A.3.3.2; 1A.3.3.3-c1; 1A.3.3.3-c2; 1A.3.3.3-c3; 1B.2.1; 1B.2.2.2

[#]Swine H1 clades by country collected in the past 6 months and deposited on or after July 1, 2024.

*Number of cases and/or detections.

Table A3b. Recent swine and variant A(H3) activity shared with international agencies and collected from sequence repositories.

Country, area or territory	Host [#]	Genetic clade
Canada	Swine	1990.4; 1990.4.b2; 1990.4.c; 1990.4.h; 2010.1
United States of America	Human (4)*	1990.4.a; 2010.1
United States of America	Swine	1990.4; 1990.4.a; 1990.4.b1; 1990.4.i; 2010.1; 2010.2; Other-Human-2020

[#]Swine H3 clades by country collected in the past 6 months and deposited on or after July 1, 2024.

*Number of cases and/or detections.

Annex 2. Phylogenies annotated by amino acid changes

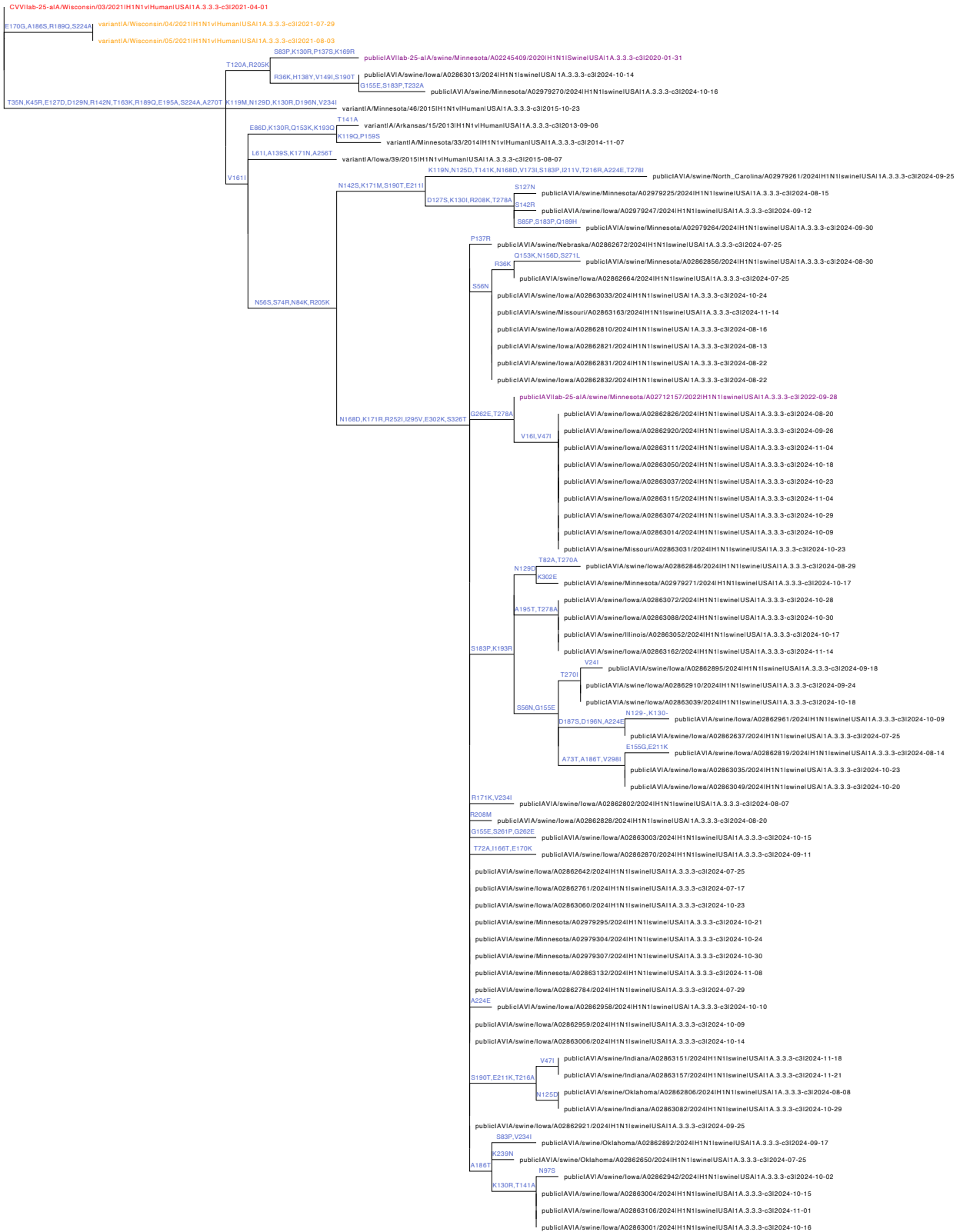


Figure A5. A phylogeny of the **1A.3.3.3-c3** clade displaying sequences deposited on or after July 1, 2024 and collected in 2024 (n=64), and 9 reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Wisconsin/03/2021) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 7.

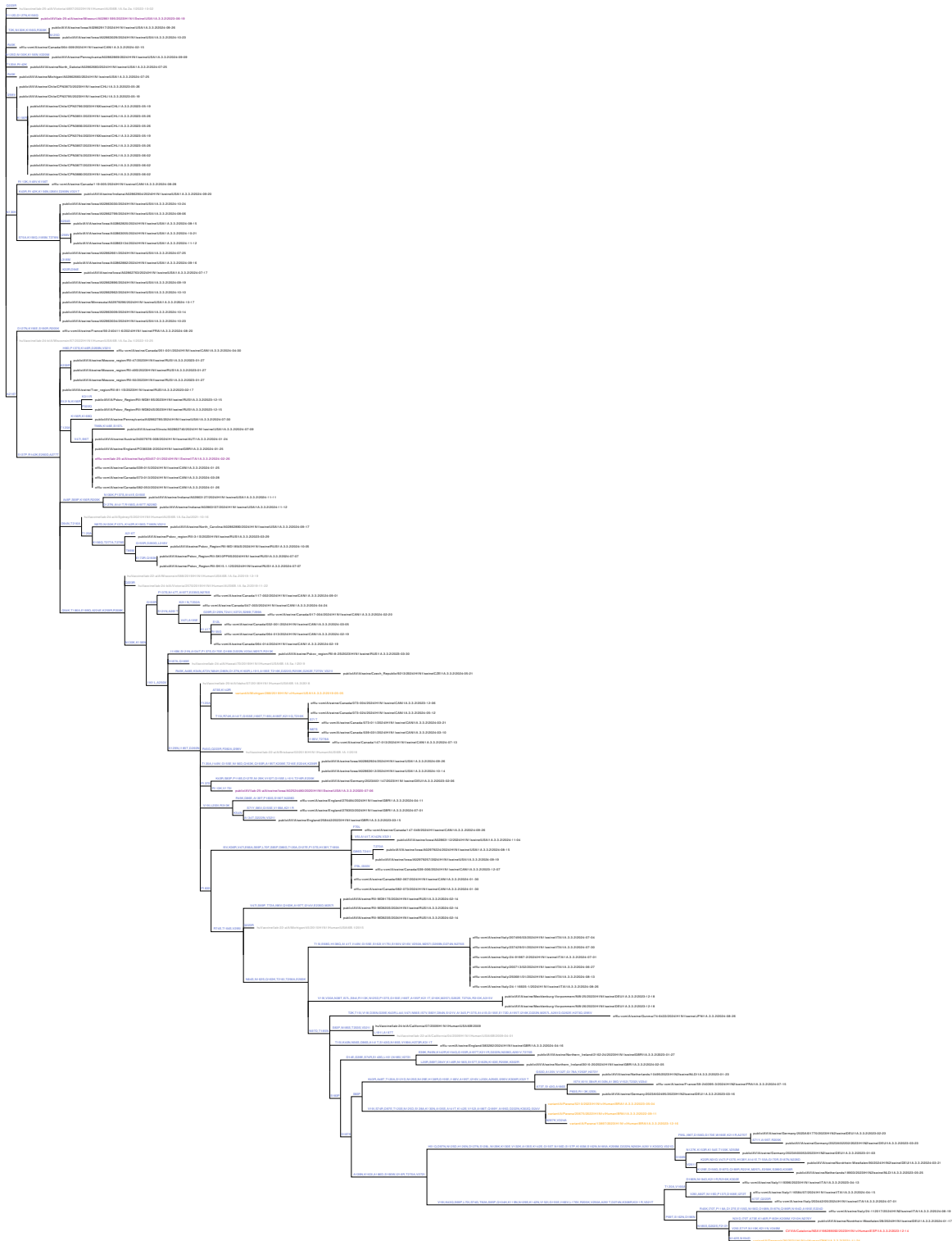


Figure A6. A phylogeny of the **1A.3.3.2 (pdm)** clade displaying n=108 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=19 reference genes. The clade is rooted relative to the most recent human vaccine strain (*A/Victoria/4897/2022*) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 7.

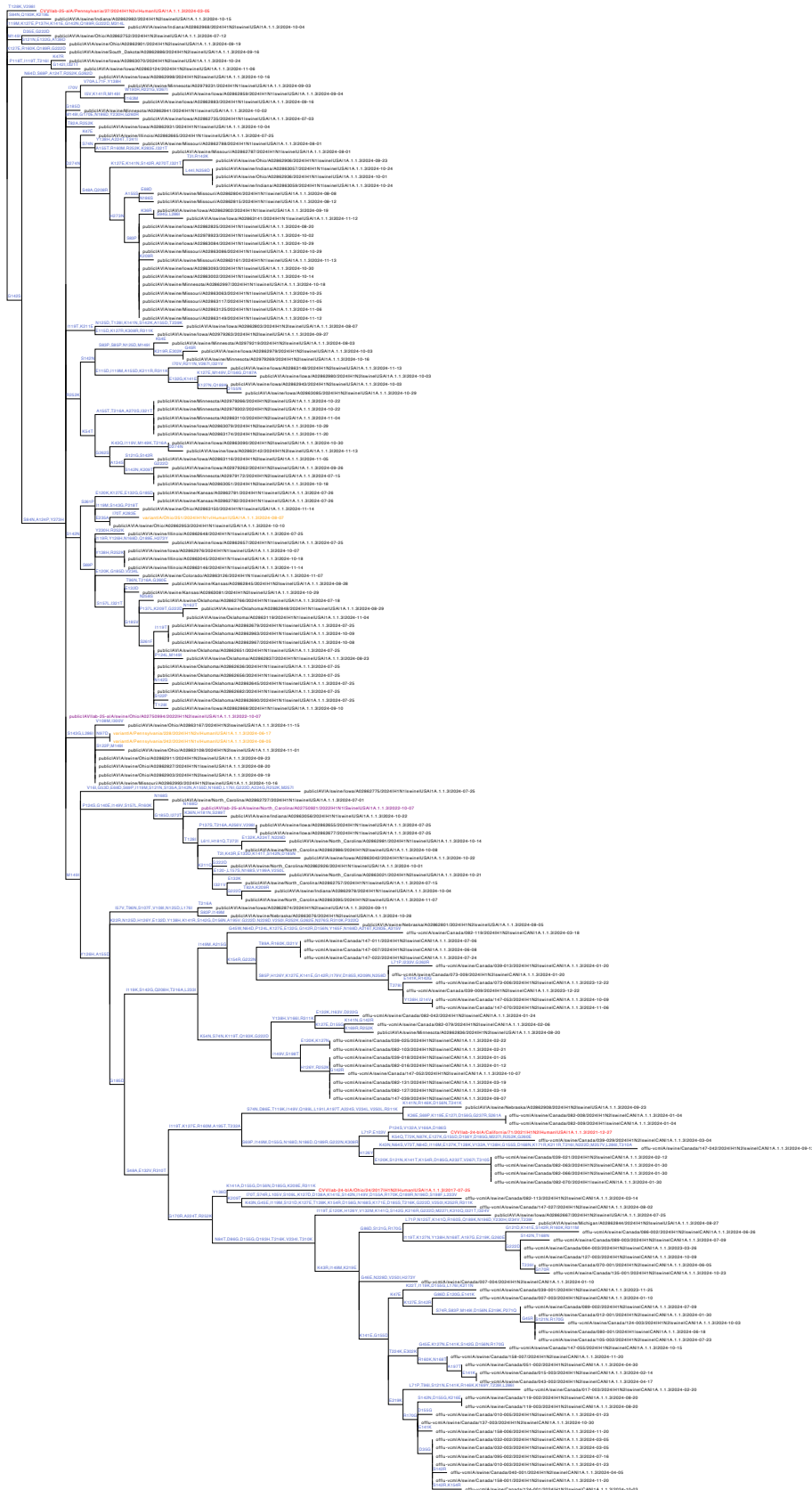


Figure A7. A phylogeny of the 1A.1.1.3 clade displaying n=171 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=8 reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Pennsylvania/27/2024) and all branches are annotated with the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 7.

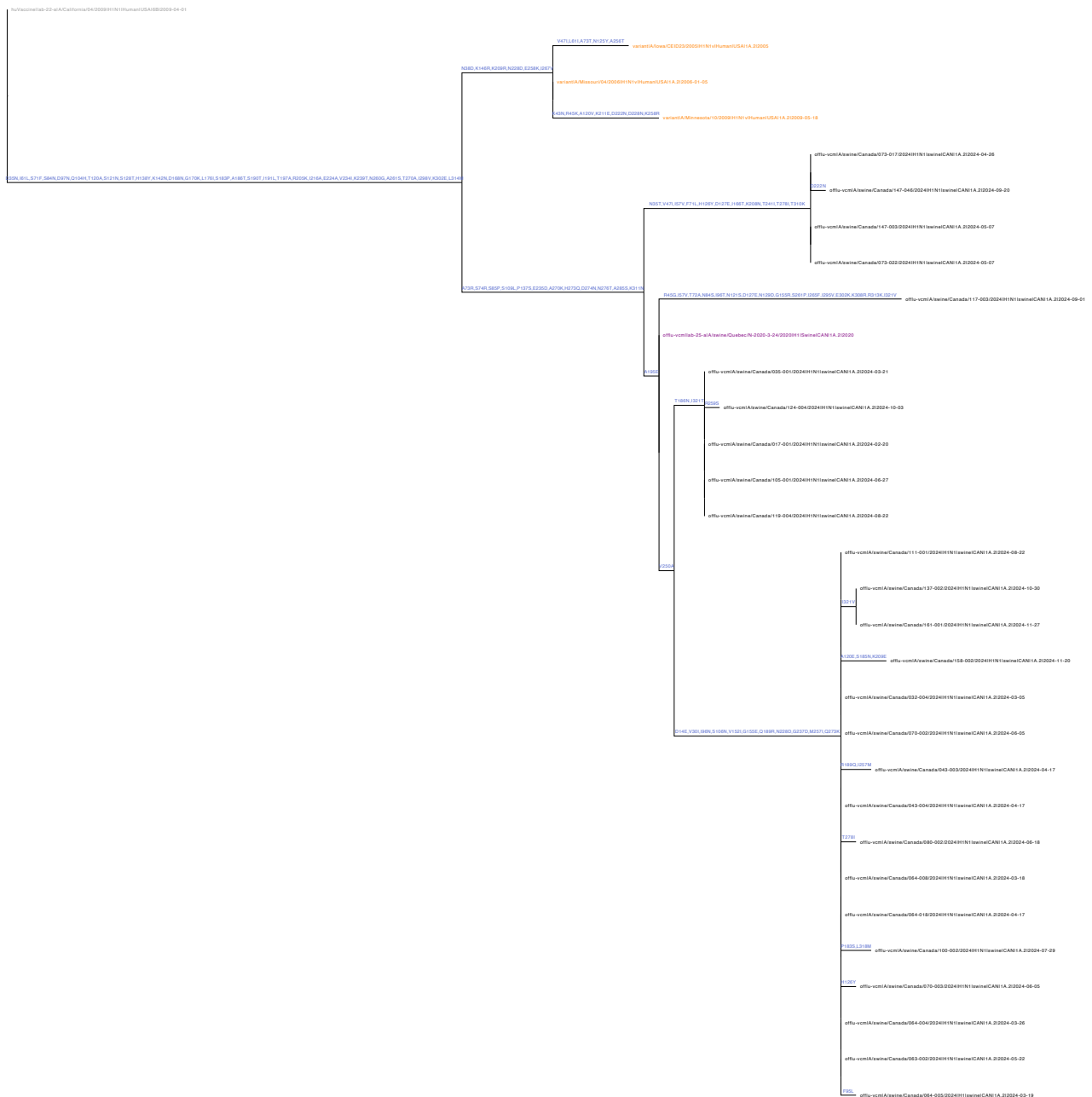


Figure A8. A phylogeny of the **1A.2** clade displaying n=26 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=5 reference genes. The clade is rooted relative to the closest human-seasonal vaccine virus (*A/California/04/2009*) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 7.

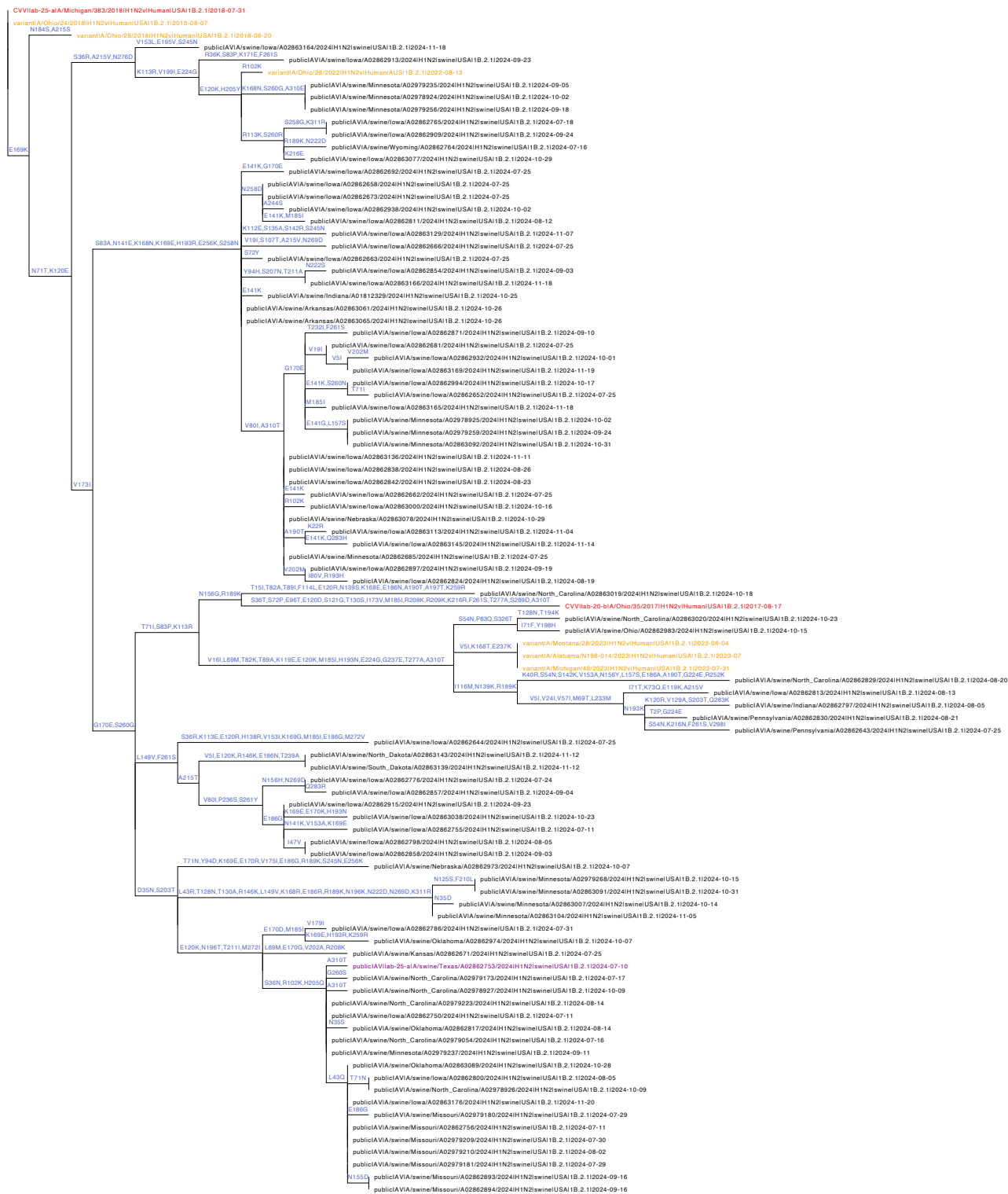


Figure A9. A phylogeny of the **1B.2.1** clade displaying n=88 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=8 reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Michigan/383/2018) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 8.

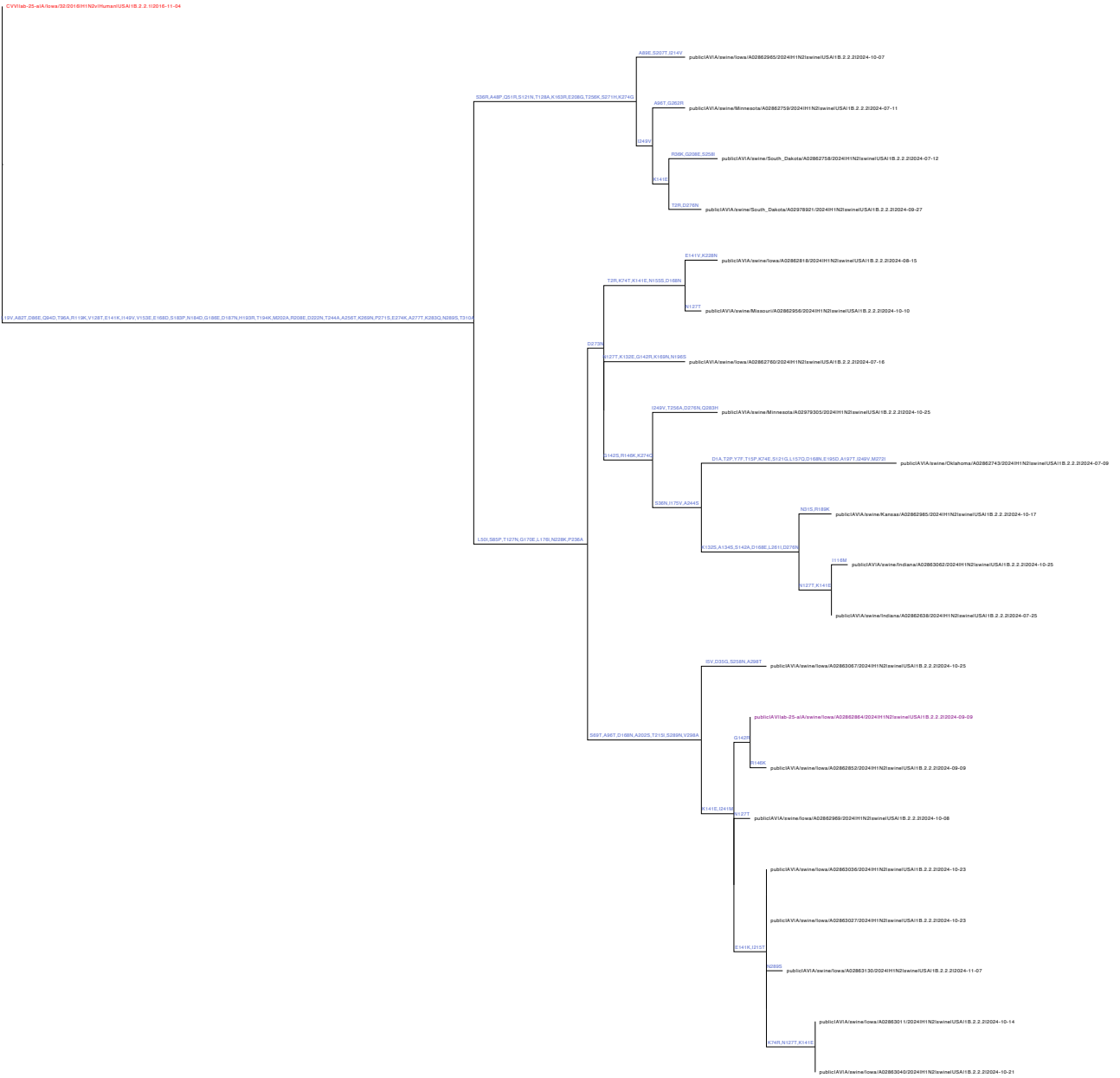


Figure A10. A phylogeny of the **1B.2.2.2** clade displaying n=21 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=1 reference genes. The clade is rooted relative to the closest CVV (*A/Iowa/32/2016*) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 8.

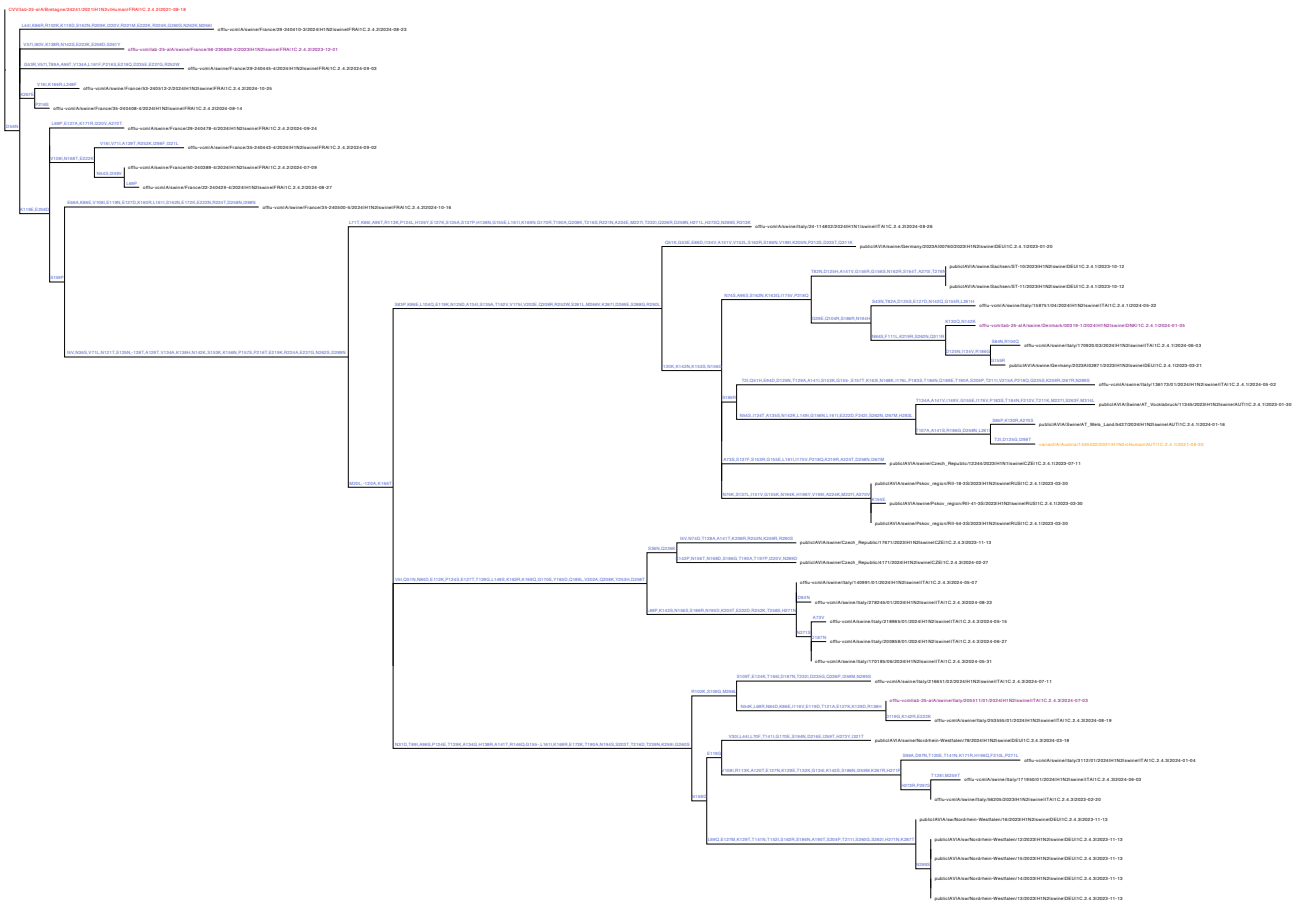


Figure A11. A phylogeny of the **1C.2.4** clade displaying n=44 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=2 reference genes. The clade is rooted relative to the closest CVV (A/Bretagne/24241/2021) and all branches are annotated with the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 9.

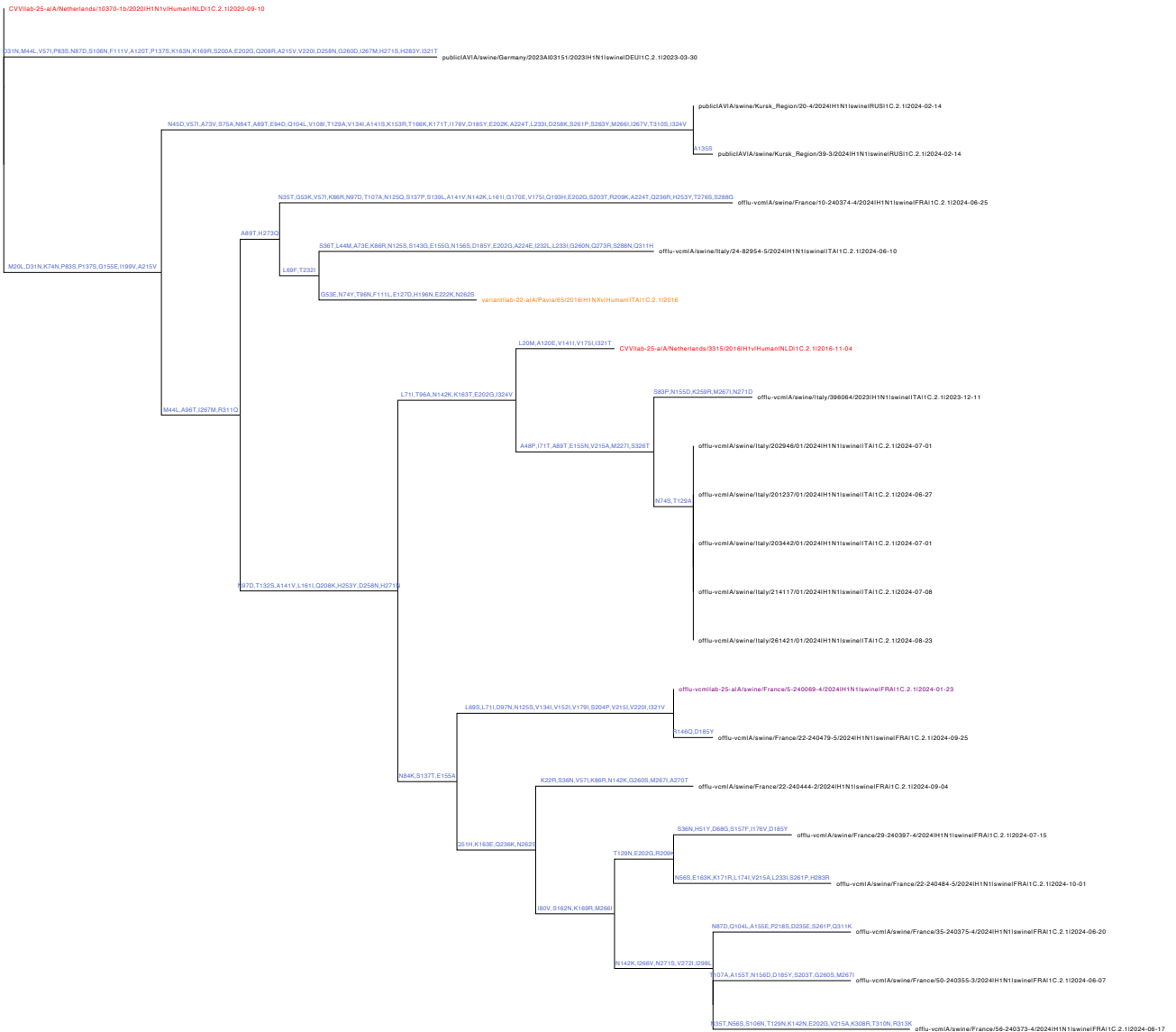


Figure A12. A phylogeny of the **1C.2.1** clade displaying n=19 sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=3 reference genes. The clade is rooted relative to the closest CVV (A/Netherlands/10370-1b/2020) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 9.

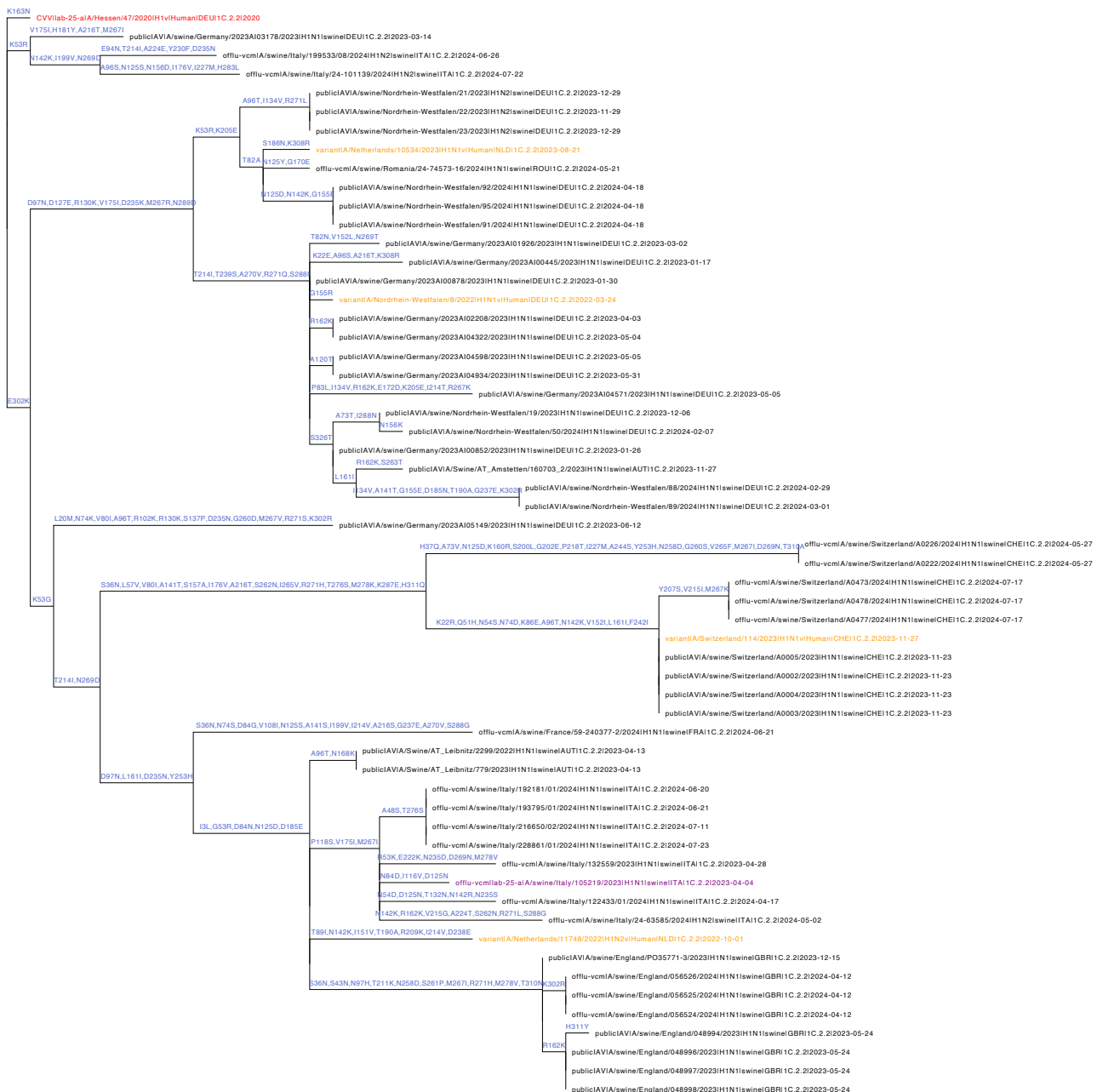


Figure A13. A phylogeny of the **1C.2.2** clade displaying $n=53$ sequences deposited on or after July 1, 2024 and collected in 2023-2024, and $n=5$ reference genes. The clade is rooted relative to the in-clade CVV (A/Hessen/47/2020) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 9.

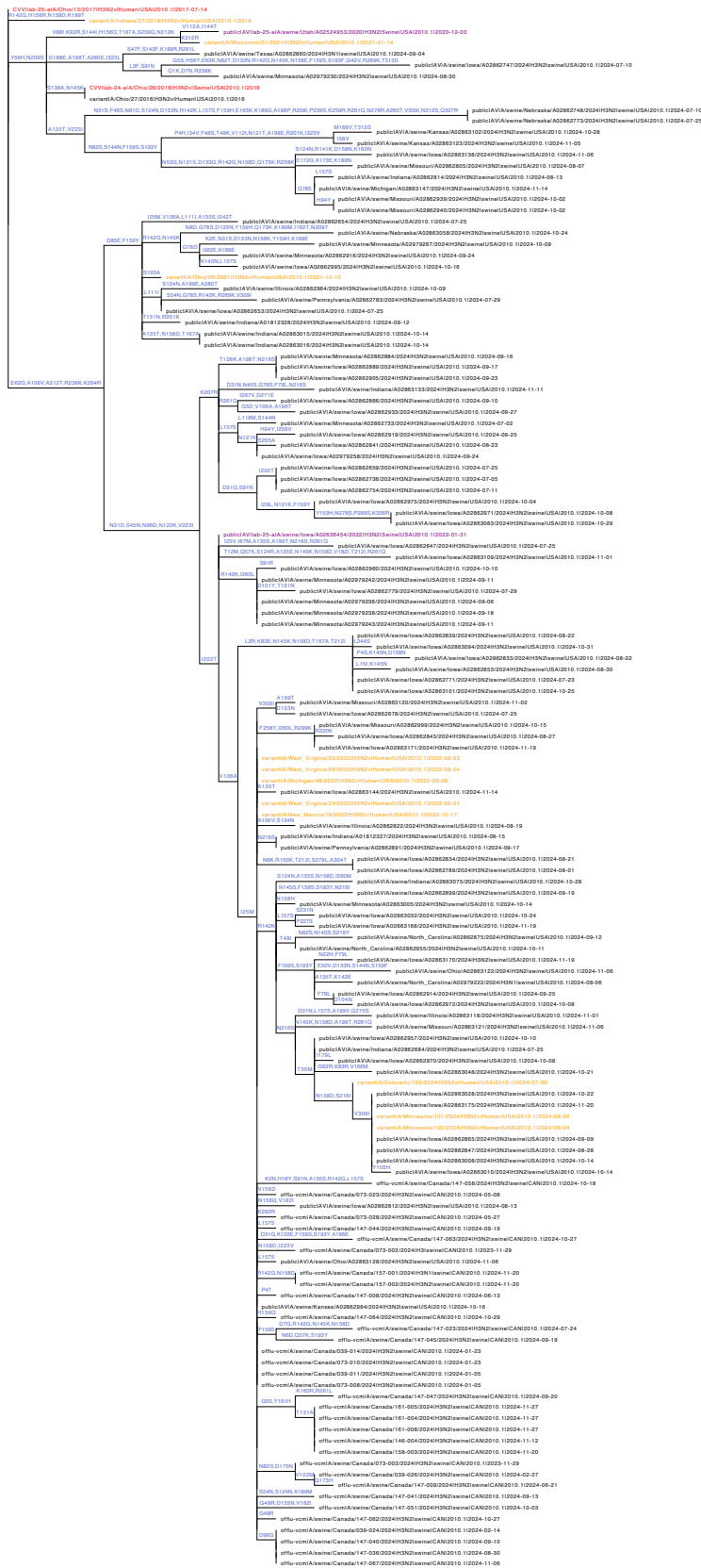


Figure A14. A phylogeny of the **3.2010.1** clade displaying $n=124$ sequences deposited on or after July 1, 2024 and collected in 2023-2024, and $n=16$ reference genes. The clade is rooted relative to the most representative in-clade C/VV (A/Ohio/13/2017) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 10.

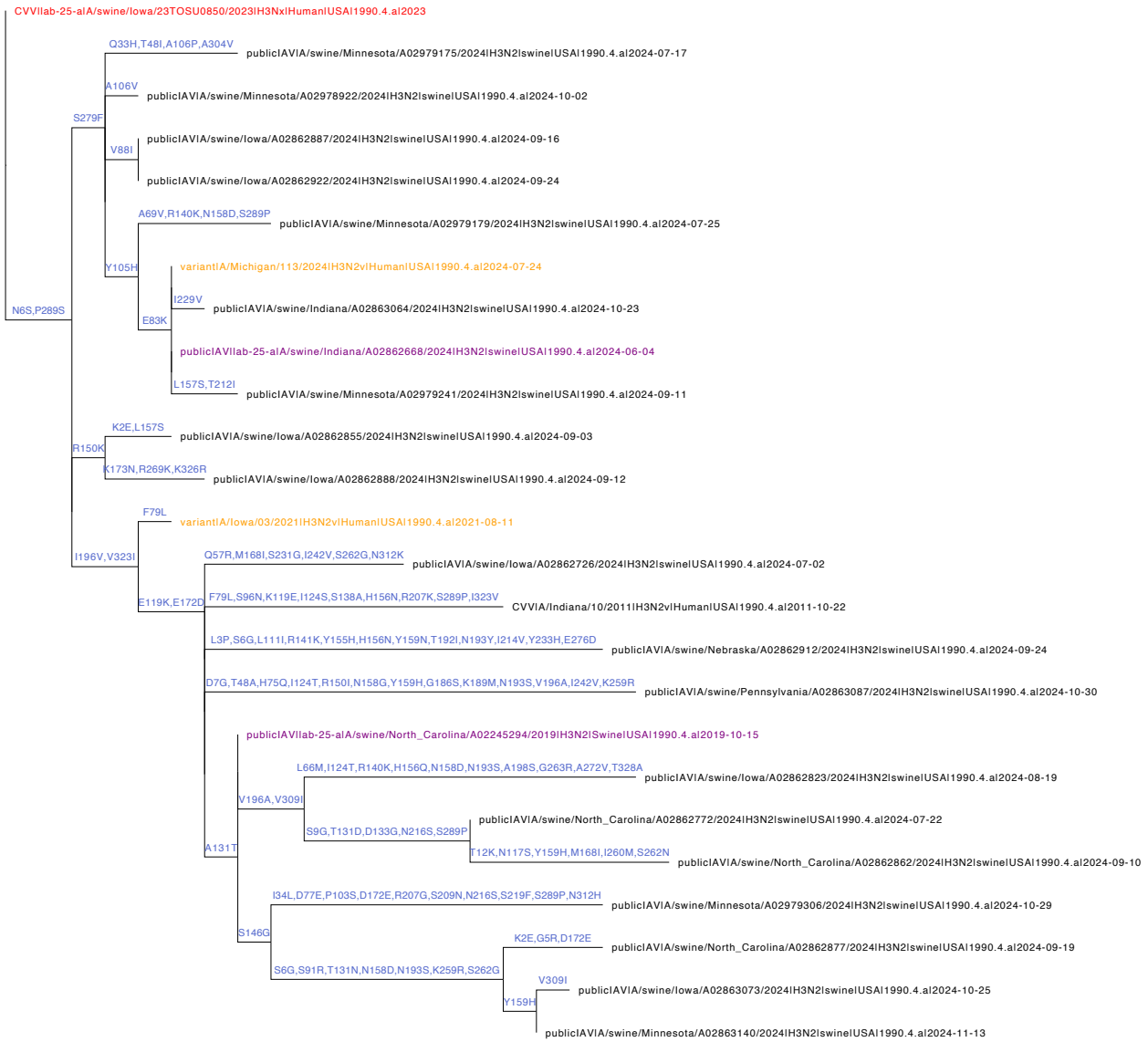


Figure A15. A phylogeny of the **3.1990.4.a** clade displaying n=20 swine sequences deposited on or after July 1, 2024 and collected in 2023-2024, and n=5 reference genes. The clade is rooted relative to the most representative in-clade CVV (A/swine/lowa/23TOSU0850/2023) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored to be consistent with Figure 10.