



# OFFLU SWINE INFLUENZA REPORT

JANUARY 2022 TO JUNE 2022

## 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 Jan 1, 2022 – June 30, 2022) were downloaded from GISAID or GenBank were 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. Exploratory trees were run using FastTree (Price et al., 2009). Tabular comparisons between current CVVs or human seasonal vaccine strains and new swine data were generated using the NADC IAV bioinformatic toolkit (<https://github.com/flu-crew>). A clade representative was selected using PARNAS (<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.

# Global influenza A events in swine Epidemiology

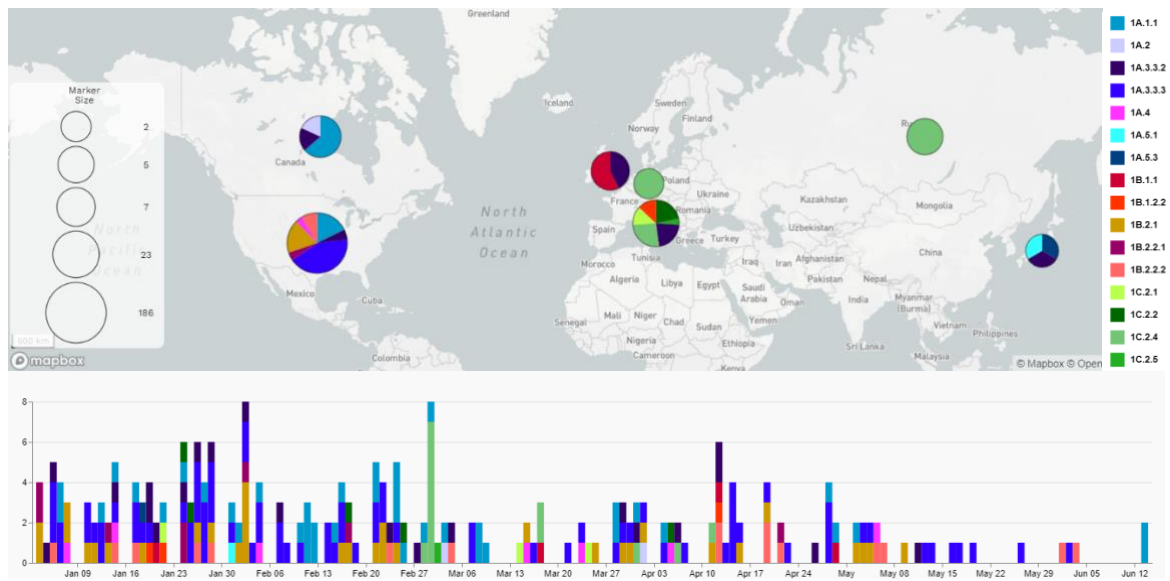


Figure 1. MicroReact map of swine IAV H1 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank between January 1, 2022 – June 30, 2022 (n=237); collection date is represented on bottom timeline. Strains submitted with only partial date were assigned a random date to preserve temporal clusters. Geographic nodes scaled to detection proportions.

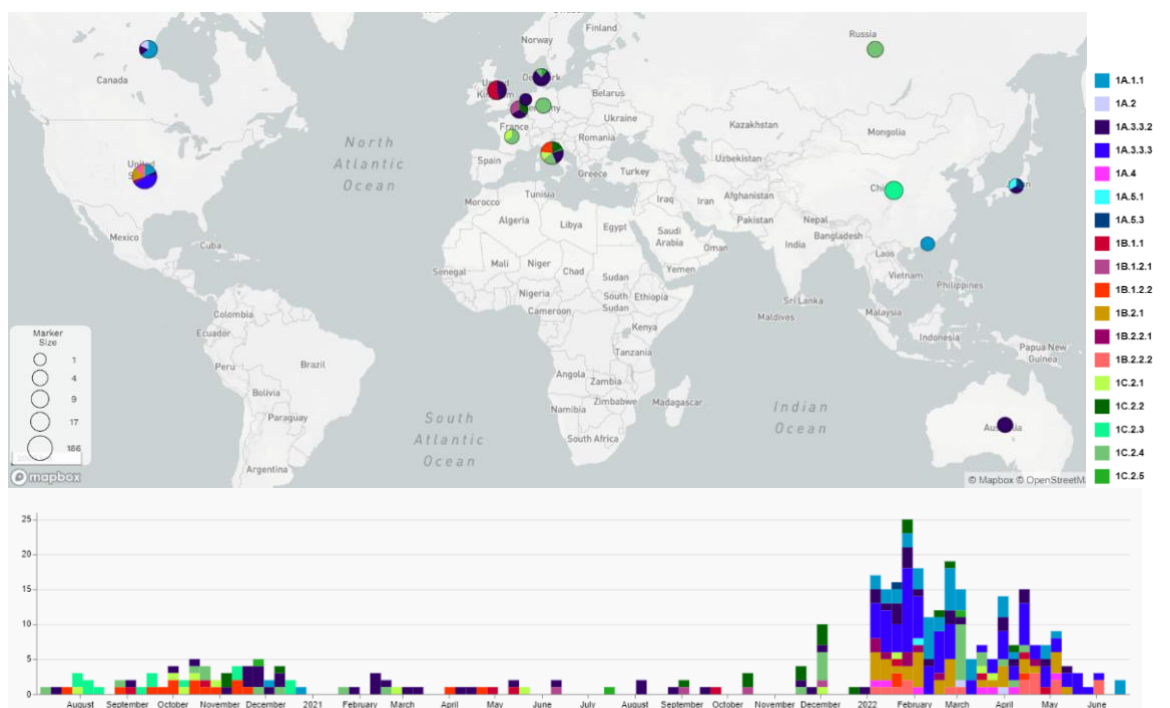


Figure 2. MicroReact map of swine IAV H1 HA genes colored by phylogenetic clade for sequences collected from June 30, 2020 – June 30, 2022 and deposited to GISAID or GenBank between June 30, 2020– June 30, 2022 (n=345); collection date is represented on bottom timeline. Strains submitted with only partial date were assigned a random date to preserve temporal clusters. Geographic nodes scaled to detection proportions.

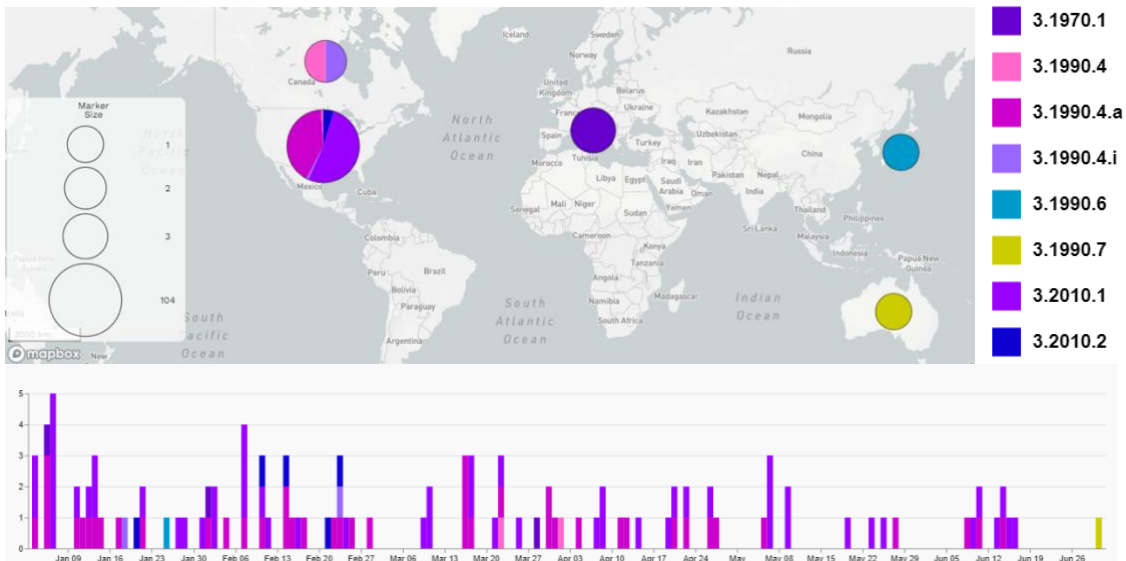


Figure 3. MicroReact map of swine IAV H3 HA genes colored by phylogenetic clade for sequences collected and deposited to GISAID or GenBank between January1, 2022– June 30, 2022 (n=111). Strains submitted with only partial date were assigned a random date within the provided year to preserve temporal clusters. Geographic nodes scaled to detection proportions.

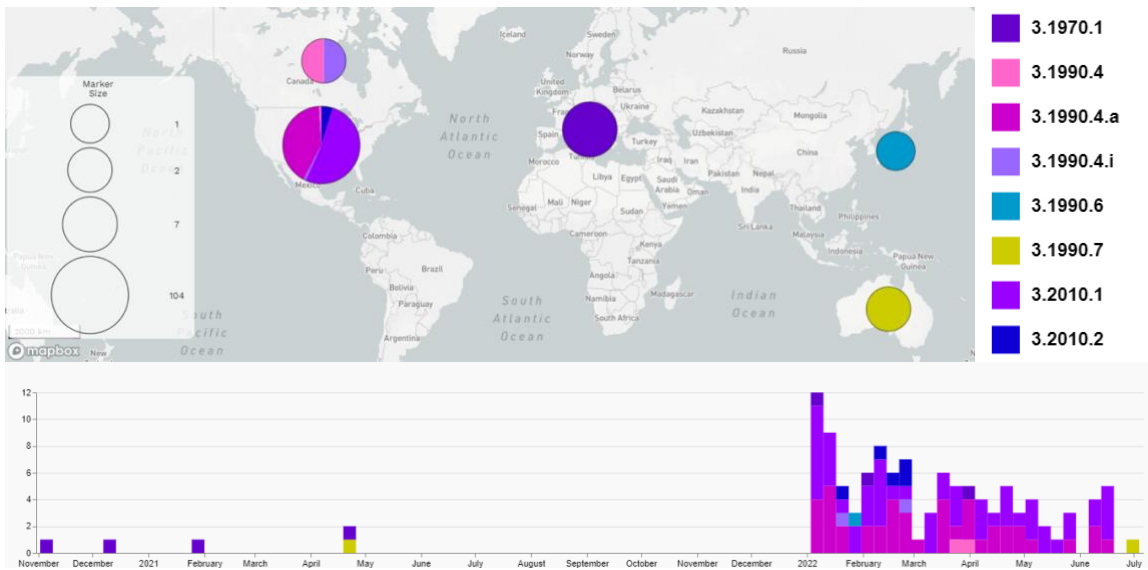


Figure 4. MicroReact map of swine IAV H3 HA genes colored by phylogenetic clade for sequences collected from June 30, 2020– June 30, 2022 and deposited to GISAID or GenBank between June 30, 2020– June 30, 2022 (n=116). Strains submitted with only partial date were assigned a random date within the provided year to preserve temporal clusters. Geographic nodes scaled to detection proportions.

## Contemporary Global H1 swine IAV: genetic diversity

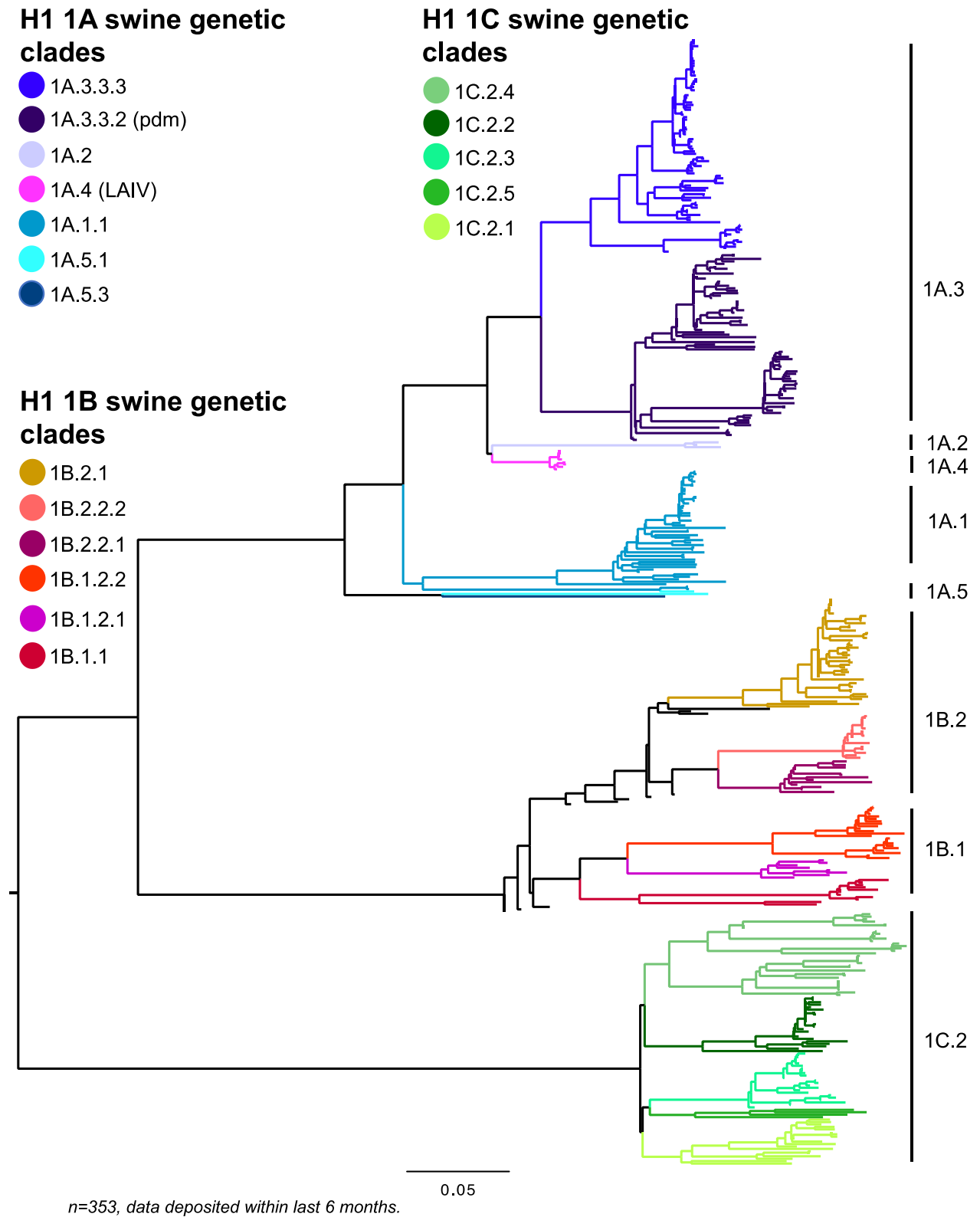
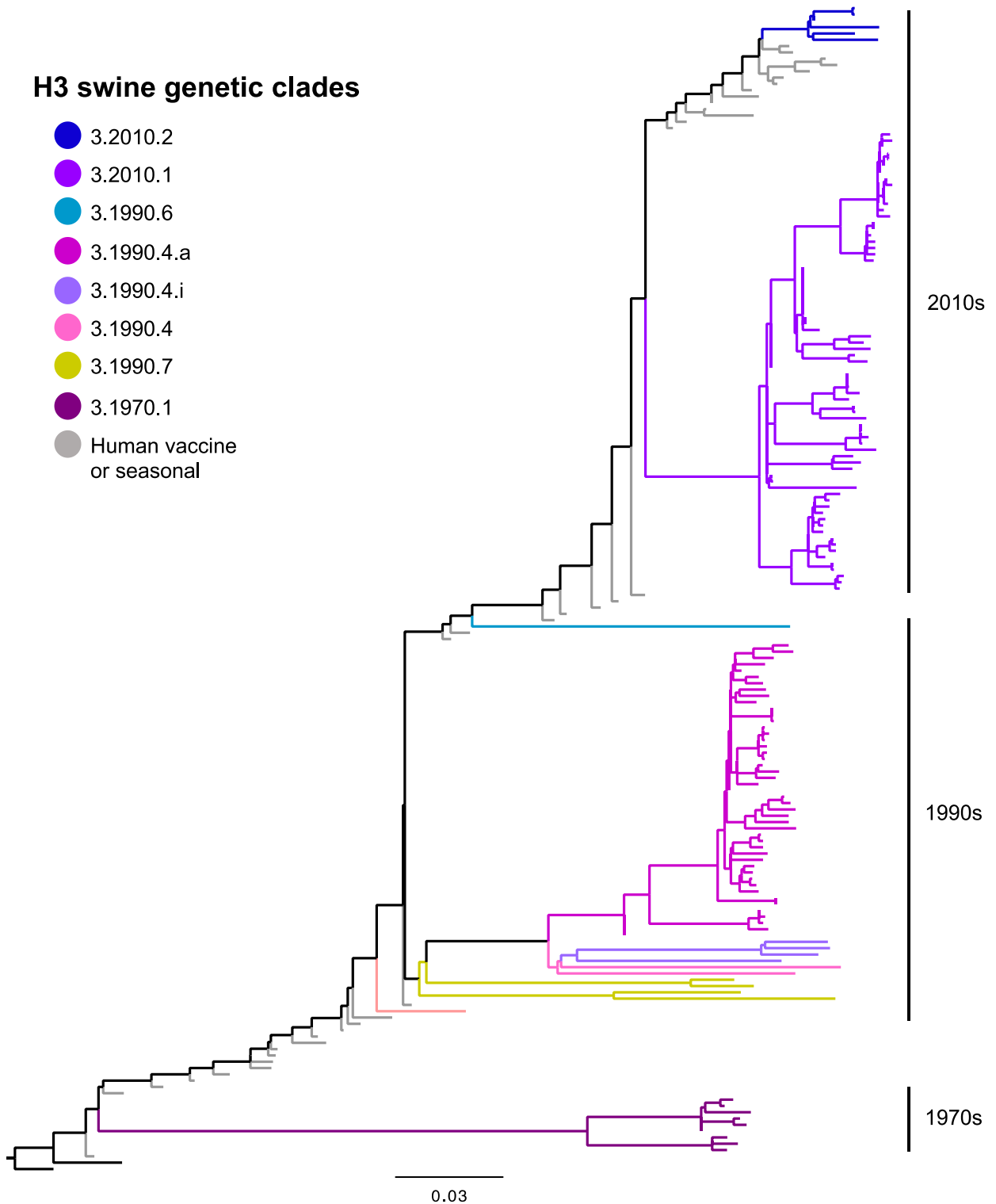


Figure 5. Global swine H1 phylogenetic tree colored by clade and annotated by global H1 lineage nomenclature. Analyses were conducted with reference sequences and data (all data deposited January 1, 2022 – June 30, 2022) from GISAID or shared via the OFFLU swine IAV working group.

## Contemporary Global H3 swine IAV: genetic diversity



*n=116, data deposited within last 6 months, and n=69 reference genes.*

Figure 6. Global swine H3 phylogenetic tree colored by clade and annotated by decade of introduction from human seasonal H3. Analyses were conducted with reference sequences and data (all data deposited January 1, 2022 – June 30, 2022) from GISAID or shared via the OFFLU swine IAV working group.

## Regional geographic summary

Phylogenetic analysis identified 26 genetic clades from H1 and H3 IAV in swine in genetic sequence data deposited between January 1, 2022 – June 30, 2022.

18 clades were H1 subtype, with detections from each of the lineages: 1A classical swine lineage (7 clades); 1B human-seasonal lineage (6 clades); and 1C Eurasian avian lineage (5 clades).

- The 1A classical swine lineage viruses have global detection: 1A.1.1 in USA and Canada; 1A.2 in Canada; 1A.4 in USA; 1A.3.3.3 in USA. The 1A.1.5.1 and 1A.1.5.3 HA genes were only detected in Japan. The 1A.3.3.2/pdm circulated in all countries that deposited sequence data during this 6-month period (5 late breaker sequences from the UK not in clade counts).
- 1B.1 human seasonal lineage was only in Europe (5 late breaking sequences from the UK not in clade counts), and the 1B.2 human seasonal lineage was only in the USA.
- The 1C.2 Eurasian avian lineage was detected in Europe and Russia. The 1C.2.3 HA clade was reported in China, but these data were collected in 2020.

Eight H3 clades were detected in swine within six distinct lineages derived from human seasonal H3 virus spillovers grouped by the decade of introduction (1970.1; 1990.4; 1990.6; 1990.7; 2010.1; 2010.2). The 1990.4 lineage diversified into three co-circulating genetic clades.

- The H3 2010.1 and 2010.2 clades were only detected in the USA, the H3 1970.1 clade was only detected in Europe. The 1990.4 lineage was detected in the USA and Canada. The 1990.6 lineage was only detected in Japan.
- A novel H3 HA clade, 1990.7, was named and detected in Australia. The 1990.7 is a unique 1990s human-to-swine H3 virus spillover that has circulated exclusively in Australia. There were 2 variant cases detected within this clade in prior reports.

### Global Variant Cases:

**During the reporting period (January 1, 2022 – June 30, 2022), 1 variant case was reported and included with the swine analyses:**

- **Germany: H1N1v (1C.2.2)**

**An additional 6 variant cases were reported July 1, 2022 – present but collected following the report window. When HA sequence were available, they were included in the phylogenetic trees:**

- **USA: H1N2v (1 1A.1.1; 1 1A.3.3.2; 1B.2.1 no sequence); H3N2v (3 2010.1)**

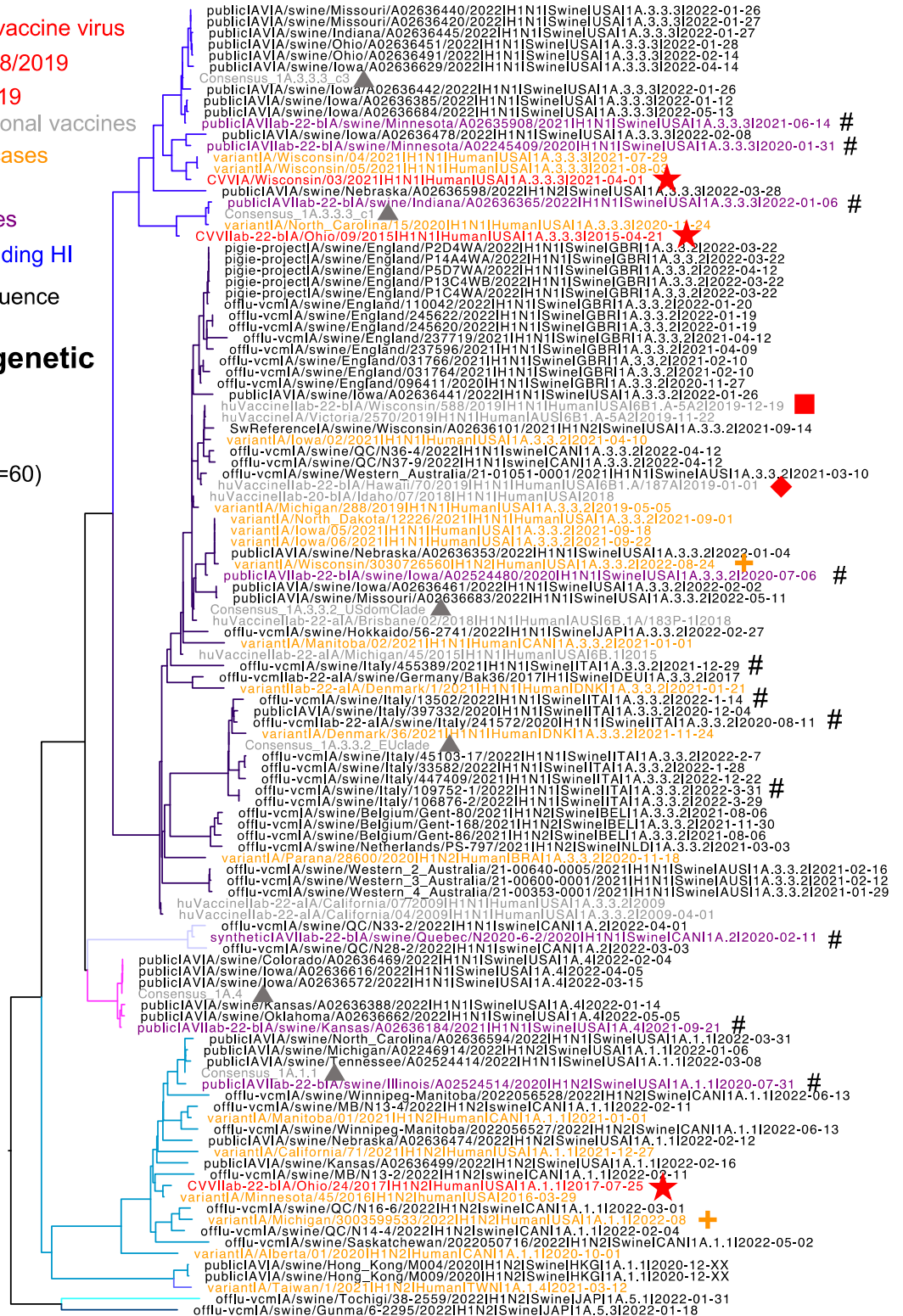


# 1A classical swine lineage

- ★ H1v candidate vaccine virus
- A/Wisconsin/588/2019
- ◆ A/Hawaii/70/2019
- H1N1pdm seasonal vaccines
- Reported H1v cases
- + New variant(s)
- # HI tested viruses
- Requested/pending HI
- ▲ Consensus sequence

## H1 1A swine genetic clades

- 1A.3.3.3 (n=79)
- 1A.3.3.2/pdm (n=60)
- 1A.2 (n=3)
- 1A.4/LAIV (n=5)
- 1A.1.1 (n=42)
- 1A.1.5.1 (n=1)
- 1A.1.5.3 (n=1)



0.03

Figure 7. Swine H1 HA genes of the 1A lineage (tree was proportionally down-sampled to 71 swine HA genes, excluding references). Number of detections of each clade from data deposited between January 1, 2022 - June 30, 2022 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	IDCDC-RG59 A/Ohio/24/2017-like CVV	A/swine/Illinois/A02524514/2020 #26	A/swine/Illinois/A02524514/2020 #27	A/Wisconsin/588/2019	rg-A/Hawaii/70/2019 #9	rg-A/Hawaii/70/2019 #11	A/swine/Iowa/A02524480/2020*#30	A/swine/Iowa/A02524480/2020* #14	A/Ohio/9/2015 CVV RG48A	A/swine/Minnesota/A02245409/2020 #28	A/swine/Minnesota/A02245409/2020 #12
IDCDC-RG59 A/Ohio/24/2017 CVV	1A.1.1	alpha-del	640	320	160	<10	160	160	160	320	<10	20	20
A/swine/Illinois/A02524514/2020*	1A.1.1	alpha-del	<10	2560	2560	<10	<10	<10	<10	10	<10	<10	<10
rg-A/swine/Quebec/N2020-6-2/2020*	1A.2	beta	<10	<10	10	nt	10	<10	10	20	40	40	20
A/Wisconsin/588/2019 6B1.A-5A2	6B1.A-5a.2	H1N1pdm09	<10	10	20	640	80	80	80	80	20	20	20
rg-A/Hawaii/70/2019	6B.1A.5a.1	H1N1pdm09	nt	<10	<10	10	1280	1280	1280	2560	10	20	10
A/swine/Iowa/A02524480/2020*	1A.3.3.2	H1N1pdm09	20	<10	10	80	1280	640	1280	2560	20	20	20
A/Ohio/9/2015 CVV RG48A	1A.3.3.3	gamma.1	<10	<10	20	10	<10	10	40	20	640	40	20
A/swine/Minnesota/A02245409/2020*	1A.3.3.3-c3	gamma.3	<10	<10	<10	nt	10	10	40	40	20	1280	640
A/swine/Indiana/A02636365/2022	1A.3.3.3-c1	gamma.1	nt	10	10	10	<10	10	20	10	80	20	10
A/swine/Minnesota/A02635908/2021*	1A.3.3.3-c3	gamma.3	<10	20	10	40	10	10	80	40	40	320	320
A/swine/Kansas/A02636184/2021	1A.4	gamma-2-beta-like	<10	10	10	20	10	10	20	40	20	40	20

Reference CVV in red, seasonal vaccine strains in dark red, new swine strains in bold. Homologous titers highlighted in grey. \*Previously tested; rg=synthetic HA/NA on PR8 backbone.

- The contemporary swine 1A.1.1 (alpha-del) was not detected by the 1A.1.1 CVV A/Ohio/24/2017 ferret anti-sera.
- The 1A.2 swine strain was not significantly detected by any CVV or vaccine anti-sera.
- The contemporary swine 1A.3.3.2 (pdm) with onward transmission in swine had significant 16-fold decrease in cross-reactivity to the A/Wisconsin/588/2019 6B1.A-5a.2 vaccine strain, but maintained cross-reactivity to A/Hawaii/70/2019-like 6B.1A.5a.1 vaccine strain.
- The contemporary swine 1A.3.3.3 (gamma) clade 3 virus had a 16-fold decrease with the 1A.3.3.3-clade 1 CVV A/Ohio/09/2015. The contemporary swine 1A.3.3.3 (gamma) clade 1 virus had an 8-fold decrease with the within-clade 1A.3.3.3-clade 1 CVV A/Ohio/09/2015.
- The swine 1A.4 (gamma-2-beta-like) virus was not detected by any CVV or vaccine anti-sera.

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

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

	Global Clade	A/California/7/2009	A/Michigan/45/2015	A/Brisbane/02/2018	A/Guangdong-Maonan/SWL1536/2019	A/Victoria/2570/2019
A/California/7/2009	H1N1pdm09 (1A.3.3.2)	10240	1280	2560	5120	640
A/Michigan/45/2015	6B.1 H1N1pdm09 (1A.3.3.2)	10240	20480	20480	20480	640
A/Brisbane/02/2018	6B.1A/183-P1 H1N1pdm09 (1A.3.3.2)	2560	2560	10240	5120	1280
A/Guangdong-Maonan/SWL1536/2019	1A.3.3.2	2560	5120	5120	20480	640
A/Victoria/2570/2019	6B1.A-5A2 H1N1pdm09 (1A.3.3.2)	640	640	1280	1280	10240
A/swine/Italy/241572/2020*	1A.3.3.2	80	80	20	160	40
A/Swine/Germany/AR2279/2016	1A.3.3.2	320	320	640	320	320
A/Swine/Republic of Ireland/AR6853/2016	1A.3.3.2	20480	5120	10240	2560	1280
A/Swine/Germany/BAK36/2017	1A.3.3.2	320	80	160	80	40
A/Swine/Denmark/SIR1570/2017	1A.3.3.2	160	160	640	320	160
A/SWINE/SPAIN/45690-9/2018	1A.3.3.2	5120	5120	2560	10240	1280
A/swine/Italy/455389/2021/H1N1	1A.3.3.2	320	640	320	640	320
A/swine/Italy/109752-1/2022	1A.3.3.2	80	160	80	80	40
A/swine/Italy/13502/2022/H1N1	1A.3.3.2	80	40	0	0	20

Reference seasonal vaccine strains in dark red, variant in orange, new swine strains in bold. Homologous titers highlighted gray.

- The contemporary swine 1A.3.3.2 (pdm) with onward transmission in European swine were poorly recognized by the panel of human seasonal vaccine strains with the exception of two viruses, where there was good recognition.

Table 3. Amino acid substitutions between representative swine 1A.1.1 clade strain compared to the within-clade CVV (A/Ohio/24/2017).

site	A/Ohio/24/2017	A/swine/Illinois/A0252451 4/2020	annotations
48	A	S	
69	S		
71	L		Cb
103	E		
119	I		
124	P		Sa
127	K		
132	V	E	RBS
138	D	Y	
141	A	Q	
149	I	M	
155	G	D	Sa
156	N	D	Sb
160	R		Sa
166	V		Ca1
168	N		
170	R	G	Ca1
185	G		
186	N		
189	Q		Sb, RBS
195	A		Sb, RBS
209	E	K	
222	G		Ca2, RBS
224	T	A	RBS
232	T		
252	K	R	
308	K		
310	T	R	
311	K	R	
<b>aadiff</b>		<b>13</b>	

Reference CVV in red, HI swine strains in purple.

Table 4. Amino acid substitutions between 1A.2 compared to the nearest human H1 vaccine (A/Wisconsin/588/2019) in HI assays and the most similar vaccine (A/California/07/2009).

Relative to HI			
site	A/Wisconsin/588/2019	A/swine/Quebec/N2020-6-2/2020	annotations
35	D	N	
61	I	L	
71	S	F	
73	A	R	Cb
83	S	P	
85	S	P	
104	Q	H	
109	S	L	
120	T	A	
121	S	N	
128	S	T	
129	D	N	
130	N	K	
137	P	S	
138	H	Y	
142	K	N	
156	K	N	Sb
161	I	L	
162	N	S	Sa
163	Q	K	Sa
164	T	S	Sa
168	D	N	
170	G	K	Ca2
176	L	I	
185	I	S	
186	A	T	
190	S	T	Sb, RBS

Relative to most similar vaccine			
site	A/California/07/2009	A/swine/Quebec/N2020-6-2/2020	annotations
35	D	N	
61	I	L	
71	S	F	
73	A	R	Cb
74	S	R	
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	
138	H	Y	
142	K	N	
168	D	N	
170	G	K	Ca2
176	L	I	
183	S	P	
186	A	T	
190	S	T	Sb, RBS
195	A	E	Sb, RBS
205	R	K	
216	I	A	
224	E	A	RBS
234	V	I	

195	A	E	Sb, RBS
203	T	S	
205	R	K	
216	T	A	
224	E	A	RBS
234	V	I	
235	E	D	
239	K	T	
250	A	V	
256	T	A	
260	D	G	
261	A	S	
270	T	K	
273	H	Q	
274	D	N	
276	N	T	
283	E	K	
285	A	S	
295	V	I	
298	I	V	
302	K	E	
311	K	N	
314	L	M	
321	V	I	
<b>aadiff</b>		<b>51</b>	

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	
<b>aadiff</b>		<b>40</b>	

Reference vaccine strain in gray, swine strains in black

Table 5. Amino acid substitutions between a representative swine 1A.3.3.2 clade strains compared to a human seasonal H1 vaccine strain (A/Wisconsin/588/2019|6B1.A-5A2) used in HI assays.

site	A/Wisconsin/588/2019	A/Hawaii/70/2019	A/swine/lowa/A02524480/2020	A/swine/Italy/455389/2021	A/swine/Italy/13502/2022	A/swine/Italy/109752-1/2022	annotations
2	T				K		
15	T			I			
19	V				I	I	
43	K				Q	Q	
68	E			G			
69	S				P	P	
70	L				I	I	Cb
74	R			S	G	G	Cb
82	T				A	A	
84	N				S	S	
85	S				P	P	
97	N				D	D	
104	Q				H	H	
113	R		K				
119	K				N	N	
120	T				A	A	
129	D		N	I	S	S	
130	N	K	K	K	K	K	
137	P		S			L	Ca2
138	H			Q			
139	A				N	N	
141	A			T			
142	K				N	N	Ca2
146	K				R		
149	I			V			
152	V				I	I	
155	G			E	E	E	Sa
156	K	N	N	N	N	N	Sb
161	I	L	L	L	L	L	

162	N			I	S	S	Sa
163	Q			K	I	I	Sa
164	T			S	S	S	Sa
166	I				V	A	Ca1
173	V		I				
175	V			I			
176	L				V	V	
183	P			S			
185	I		T	T	N	N	
186	A				D	D	
187	D	A			S	S	RBS
189	Q	E					Sb, RBS
190	S			V	W	W	Sb, RBS
194	N				D	D	RBS
196	D				N	N	
202	G				S		
205	R			K	K	K	
210	F				Y		
216	T			V	R	R	
222	D			G			Ca2, RBS
241	T				I		
250	A	V	V				
256	T			A	A	A	
257	M			I			
260	D		N	N	N	N	
261	A				T	T	
269	D			N			
270	T				A	A	
272	V				I	I	
274	D			N	N	N	
276	N			S			
283	E			K	K		
295	V			I	I	I	
308	K				R	R	
311	K				R	R	
321	V				T	T	
<b>aadiff</b>		<b>6</b>	<b>10</b>	<b>29</b>	<b>49</b>	<b>44</b>	

Reference vaccine strain in gray, HI strains in purple, requested/pending HI strains in blue.



Table 6a. Amino acid substitutions between representative swine 1A.3.3.3-clade 1 strain compared to the within-clade CVV (A/Ohio/09/2015 RG48A) used in the HI assay.

site	A/Ohio/09/2015	A/swine/Indiana/A02636365/2022	annotations
22	K	R	
48	X	A	
68	E	D	
72	T	R	
82	T	N	
83	S	P	
125	N	K	Sa
169	R	K	
204	S	P	Ca1
222	G	D	Ca2, RBS
269	E	G	
278	T	I	
283	N	S	
295	I	V	
<b>aadiff</b>		<b>14</b>	

Reference CVV in red, HI strain in purple.

Table 6b. Amino acid substitutions between representative swine 1A.3.3.3-clade 3 strains compared to the within-clade CVV (A/Wisconsin/03/2021).

site	A/Wisconsin/03/2021	A/swine/Minnesota/A02635908/2021	A/swine/Minnesota/A02245409/2020	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	S	N	Ca2
161	V	I		
163	T	K	K	Sa
169	K		R	
171	K	M		
189	R	Q	Q	Sb, RBS
190	S	T		Sb, RBS
195	E	A	A	Sb, RBS
205	R	K	K	
211	E	V		
224	S	A	A	RBS
270	A	T	T	
323	S	X		
<b>aadiff</b>		<b>19</b>	<b>16</b>	

Reference CVV in red, HI strains in purple.

Table 7. Amino acid substitutions between 1A.4 compared to the human H1 vaccine (A/Wisconsin/588/2019|6B1.A-5A2) used in HI assays and the most similar vaccine (A/California/07/2009).

Relative to HI

site	A/Wisconsin/588/2019	A/swine/Kansas/A0263 6184/2021	annotations
35	D	E	
71	S	F	Cb
74	R	S	Cb
120	T	A	
126	H	Y	
127	D	E	
128	S	T	
129	D	S	
130	N	R	
134	A	S	RBS
138	H	Y	
142	K	N	Ca2
146	K	R	
156	K	N	Sb
161	I	L	
162	N	S	Sa
163	Q	K	Sa
164	T	S	Sa
168	D	N	
170	G	E	Ca1
183	P	S	
185	I	S	
186	A	T	
203	T	S	
205	R	K	
222	D	N	Ca2, RBS
224	E	A	RBS
239	K	T	
250	A	V	
256	T	A	
258	E	K	

Relative to most similar vaccine

site	A/California/07/2009	A/swine/Kansas/A0263 6184/2021	annotations
35	D	E	
71	S	F	Cb
83	P	S	
84	S	N	
97	D	N	
120	T	A	
126	H	Y	
127	D	E	
128	S	T	
129	N	S	
130	K	R	
134	A	S	RBS
138	H	Y	
142	K	N	Ca2
146	K	R	
168	D	N	
170	G	E	Ca1
186	A	T	
205	R	K	
216	I	T	
222	D	N	Ca2, RBS
224	E	A	RBS
239	K	T	
258	E	K	
260	N	G	
261	A	S	
271	P	S	
278	T	N	
298	I	V	
302	K	E	
310	T	K	

260	D	G	
261	A	S	
271	P	S	
278	T	N	
283	E	K	
295	V	I	
298	I	V	
302	K	E	
310	T	K	
314	L	M	
321	V	I	
<b>aadiff</b>		<b>42</b>	

314	L	M	
<b>aadiff</b>		<b>32</b>	

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

# 1B human-like lineage

★ H1v candidate vaccine virus

■ A/Brisbane/59/2007

Previous seasonal H1N1 vaccine

Reported H1v cases

+ New variant(s)

# HI tested viruses

Requested/pending HI

▲ Consensus sequence

# H1 1B swine genetic clades

● 1B.2.1 (n=21)

● 1B.2.2.2 (n=16)

● 1B.2.2.1 (n=8)

● 1B.1.2.2 (n=19)

● 1B.1.2.1 (n=7)

● 1B.1.1 (n=14)

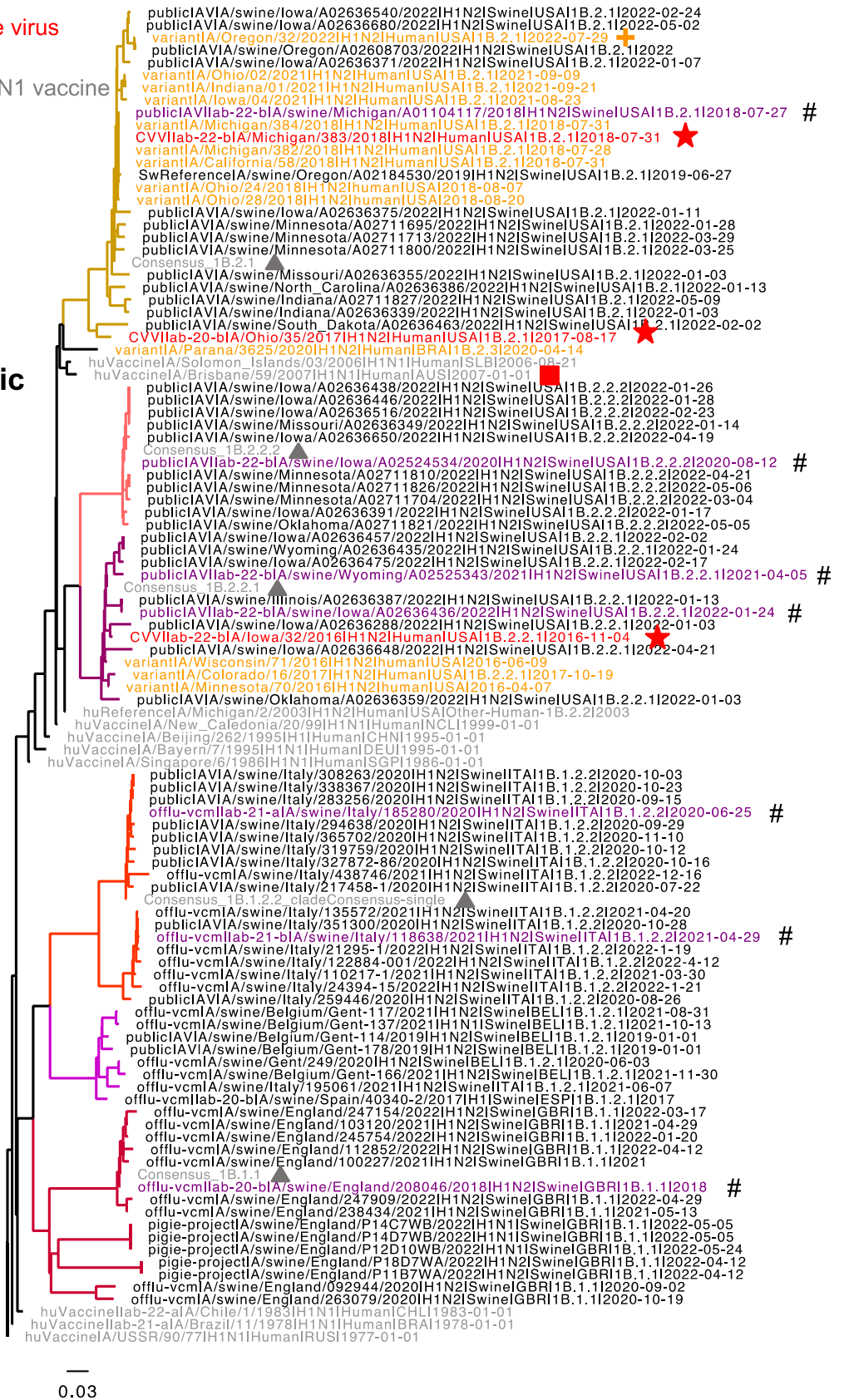


Figure 8. Swine H1 HA genes of the 1B lineage (tree was proportionally down sampled to 66 swine HA genes, excluding references). Number of detections of each clade from data deposited between January 1, 2022 - June 30, 2022 are presented adjacent to the clade name in the figure key.

## 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	rg-A/swine/Brazil/274-18/2018 #21	rg-A/swine/Brazil/274-18/2018 #22
A/Michigan/383/2018 RG58A	1B.2.1	delta-2	80	<10	<10	<10	40	80
A/swine/Michigan/A01104117/2018*	1B.2.1	delta-2	80	<10	<10	<10	40	80
A/Iowa/32/2016	1B.2.2.1	delta-1a	<10	160	40	20	10	10
<b>A/swine/Iowa/A02636436/2022*</b>	1B.2.2.1	delta-1a	40	20	20	10	40	80
A/swine/Wyoming/A02525343/2021**	1B.2.2.1	delta-1a	<10	20	160	160	10	10
A/swine/Iowa/A02524534/2020*	1B.2.2.2	delta-1b	<10	10	<10	<10	10	10
rg-A/swine/Brazil/274-18/2018	1B.2.3		640	20	20	10	1280	2560

Reference CVV in red, new swine strains in bold. Homologous titers highlighted grey. \*Previously tested in report 2021a; \*\*Previously tested in report 2021b; rg- annotation is a synthetic HA/NA on PR8 backbone.

- The contemporary swine 1B.2.1 (delta-2) was 100% identical in the HA1 to the within-clade CVV A/Michigan/383/2018 and there was no loss in cross-reactivity.
- Two contemporary swine 1B.2.2.1 (delta-1a) representing diverging clades were tested. Both A/swine/Iowa/A02636436/2022 and A/swine/Wyoming/A02525343/2021 had a 8-fold reduction from the within clade CVV A/Iowa/32/2016 and demonstrated loss in cross-reactivity to each other.
- The contemporary swine 1B.2.2.2 (delta-1b) does not have a CVV contained within clade and had a significant greater than 8-fold decrease from CVV A/Iowa/32/2016.
- The Brazil 1B.2.3 clade has no within clade CVV, and the representative strain had a significant 8-fold loss in cross reactivity to the 1B.2.2.1 A/Iowa/32/2016 CVV but retained reactivity with the 1B.2.1 A/Michigan/383/2018 CVV.

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

Global Clade		A/Michigan/383/2018 RG58A	A/Chile/1/1983
A/Michigan/383/2018 RG58A	1B.2.1 d2	160	1280
A/Chile/1/1983	H1 seasonal	160	1280
<b>A/swine/England/208046/2018</b>	1B.1.1	nt	80
<b>A/swine/Italy/118638/2021</b>	1B.1.2.2	20	40
<b>A/swine/Italy/185280/2020</b>	1B.1.2.2	nt	40

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

Reference CVV in red, seasonal vaccine strains in dark red, new swine strains in bold. Homologous titers highlighted in gray.

- The swine 1B.1.1 was poorly cross-reactive with A/Chile/1/1983 with the 1B.2.1.d2 CVV.
- The contemporary swine 1B.1.2.2 representing strains circulating in Italy and had a significant decrease in cross reactivity against both the 1B.2.1 d2 CVV and against the human seasonal strain reference. There are no within-clade CVVs for 1B lineages from Europe.

Table 10. Amino acid substitutions between representative swine 1B.2.1 strain compared to the within-clade CVV (A/Michigan/383/2018 RG58A). Within-clade H1N2v detected within this reporting period are presented in orange.

No amino acid substitutions were detected.



Table 11. Amino acid substitutions between representative swine 1B.2.2.1 and 1B.2.2.2 strains compared to the most similar CVV (A/Iowa/32/2016 1B.2.2.1).

site	A/Iowa/32/2016	A/swine/Iowa/A02524534/2020	A/swine/Wyoming/A02525343/2021	A/swine/Iowa/A02636436/2022	annotations
2	T	M			
19	L	V	V	V	
50	L	I			
68	E			D	
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	A	
104	Q			H	
106	S		N		
119	R	K			
129	V	T			
130	T		D		
132	K		T	V	RBS
141	E			K	
142	G			S	Ca2
149	I	V			
153	V	E			Sb
157	L		R		Sa
163	K			M	Sa
168	E	N	D	D	
170	G	E			Ca1
175	I		V		
176	L	I			

179	V			I	
183	S	P			
184	N	D			
186	G	E			
187	D	N			RBS
193	H	R			Sb, RBS
194	T	K		A	RBS
202	M	A			
208	R	E	K		
215	T		A		
222	D	N	N	N	Ca2, RBS
228	N	K			
236	P	A			
241	I		V		
244	T	A			
249	I	V			
256	A	T			
269	K	N			
271	P	S			
273	D	N			
274	E	K			
277	A	T			
283	K	Q			
287	N		T		
289	N	S		S	
310	T	A	R		
314	M	L			
<b>aadiff</b>		<b>38</b>	<b>16</b>	<b>15</b>	

Reference CVV in red, HI strains in purple.

Table 12. Amino acid substitutions between representative swine 1B.1.X strains compared to the most similar human seasonal vaccine A/Chile/1/1983 used in HI assays.

site	A/Chile/1/1983	A/swine/Italy/185280/2020 1B.1.2.2	A/swine/Italy/118638/2021 1B.1.2.2	A/swine/England/208046/2018 1B.1.1	annotations
19	V			I	
35	D	N		N	
36	N	S		S	
44	L			M	
47	I	V	V		
54	K		R		
70	L			S	Cb
71	F		L		Cb
73	K			R	Cb
82	T	P	A		
85	S	A	A	P	
89	T	L	L	I	
94	Y		H		
96	A	S	S	S	
109	S	A			
111	F		I	V	
116	I			M	
124	P	S			Sa
127	N	S	S		
128	V		I		
129	T	-	-		
130	K	-	-	R	
132	V	S	A	K	RBS
134	A			V	RBS
135	A	S	S	S	RBS
137	S	P			Ca2
138	H	K	K		
139	K	Q	Q	N	

141	K		R		
142	S		R		Ca2
146	R	T	T	K	
155	N			D	Sa
157	S			L	Sa
161	L			I	
162	S	T	T		Sa
163	K	M	M	N	Sa
164	S			H	Sa
166	V	M	M		Ca1
168	N	D	D		
170	E		K		Ca1
171	K	R	R		
176	L			I	
181	H			N	
184	N		S		
185	I	M		M	
187	D			N	RBS
189	K	R	R	R	Sb, RBS
190	T	A	A	A	Sb, RBS
196	N	T	T	T	
202	V	M	T		
205	H	Q			
208	R		K		
209	R		K		
211	T	A			
215	A			E	
220	V	I	I	I	RBS
222	N		D		Ca2, RBS
235	E	D			
237	G	R	S		Ca1
238	D			E	
241	I	T			
248	L			F	
249	I	V			
258	S	K	N		
261	F			L	
262	G	E	E	R	
267	T	V	V	I	
268	S			T	
270	A		V		
276	D		N		

277	A			T	
278	K		T	E	
283	Q		R		
288	S	N	N	N	
295	V		I		
298	V		I		
299	T			A	
307	V			I	
308	R	K	K	K	
310	T	A			
311	K			R	
313	R	K	K		
315	V	A	A		
<b>aadiff</b>		<b>43</b>	<b>49</b>	<b>44</b>	

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

# 1C Eurasian avian lineage

- ★ H1v candidate vaccine virus
- Reported H1v cases
- + New variant(s)
- # HI tested viruses
- Requested/pending HI
- ▲ Consensus sequences

## H1 1C swine genetic clades

- 1C.2.4 (n=27)
- 1C.2.2 (n=18)
- 1C.2.3 (n=13)
- 1C.2.5 (n=3)
- 1C.2.1 (n=12)

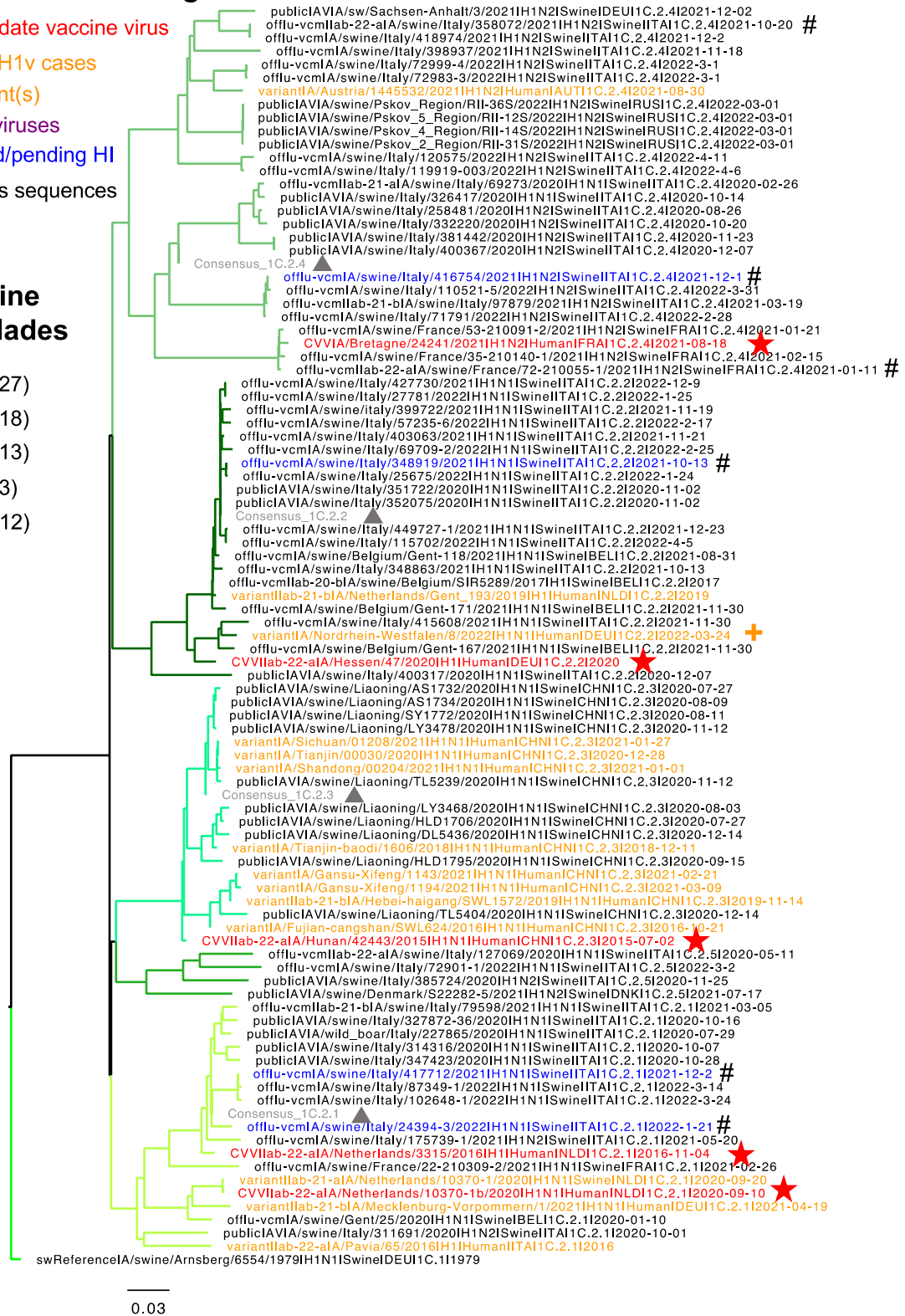


Figure 9. Swine H1 HA genes of the 1C lineage (tree was proportionally down sampled to 64 swine HA genes, excluding references). Number of detections of each clade from data deposited between January 1, 2022 - June 30, 2022 are presented adjacent to the clade name in the figure key.

## Antigenic analysis: Swine 1C Lineage

Table 13. UK & EU Data: Hemagglutination inhibition of CVV vaccine ferret antisera against contemporary swine 1C lineage strains selected to represent clade consensus.

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

	Global Clade	A/Netherlands/3315/2016 CVV (Crick or APHA)	A/Hebei-Haigang/1572/2019	A/Hessen/47/2020-like CVV	A/Netherlands/10370-1b/2020 CVV	A/Mecklenburg-Vorpommern/1/2021	A/Bretagne/24241/2021 CVV
A/Netherlands/3315/2016 CVV (Crick or APHA)	1C.2.1 H1N1v	2560	320	320	160	160	160
A/Hebei-Haigang/1572/2019	1C.2.3	640	20480	2560	640	320	80
A/Hessen/47/2020-like CVV	1C.2.2 H1v	80	2560	10240	320	320	40
A/Netherlands/10370-1b/2020 CVV	1C.2.1	80	320	160	640	160	20
A/Mecklenburg-Vorpommern/1/2021	1C.2.1	160	640	320	160	640	80
A/Bretagne/24241/2021 CVV	1C.2.4	40	40	160	20	80	10240
<b>A/Swine/France/56-180424/2018</b>	1C.2.4	80	80	160	40	1280	40
<b>A/swine/Italy/127069/2020</b>	1C.2.5	1280	640	640	160	320	160
<b>A/Swine/France/72-210055-1/2021</b>	1C.2.4	20	80	160	40	160	5120
<b>A/swine/Italy/358072/2021</b>	1C.2.4	40	80	160	40	320	20
<b>A/swine/Italy/416754/2021</b>	<b>1C.2.4</b>	160	320	80	160	320	80
A/swine/Italy/348919/2021	1C.2.2	80	1280	1280	160	160	40
<b>A/swine/Italy/417712/2021</b>	<b>1C.2.1</b>	1280	640	80	80	160	20
<b>A/swine/Italy/24394-3/2022</b>	<b>1C.2.1</b>	640	320	160	80	160	0

Reference CVV in red, seasonal vaccine strains in gray, new swine strains in bold, variant in orange. Homologous titers highlighted in gray.

- 1C.2.1, 1C.2.4 and 1C.2.5: The selected contemporary viruses represented the diverse 1C.2.1, 1C.2.4 - with multiple deletion patterns and 1C.2.5 groups. In general, they were poorly recognised by all 1C antisera except by A/Mecklenburg-Vorpommern/1/2021 – a 1C.2.1 variant virus.
- The new designated 1C.2.4 CVV A/Bretagne/24241/2021 recognized well the swine virus closely associated with the variant infection but poorly recognized any of the other 1C.2.4 viruses and also the 1C.2.1, 1C.2.2 and 1C.2.5 viruses.

Table 14. Amino acid substitutions between representative swine 1C.2.1 strains compared to the within-clade CVV (A/Netherlands/10370-1b/2020 CVV); the additional within-clade CVV (A/Netherlands/3315/2016 CVV) is included.

site	A/Netherlands/10370-1b/2020	A/Netherlands/3315/2016	A/swine/Italy/417712/2021	A/swine/Italy/24394-3/2022	annotations
20	M		L	L	
31	D	N	N	N	
44	M	L	L	L	
48	A		P		
71	L	I	T	I	Cb
74	K	N	N	N	Cb
83	P	S	S	S	
89	A		T		
97	N	D	D	D	
120	A	E			
132	T	S	S	S	RBS
137	P	S	S	S	Ca2
141	A	I	V	D	
142	N	K	K	K	Ca2
155	G	E	D	E	Sa
161	L	I	I	I	
163	K	T	T	M	Sa
175	V	I		I	
199	I	V	V	V	
202	E	G	G	G	
208	Q	K	K	R	
209	R			K	
215	A	V		V	
227	M		I		
236	Q			P	
253	H	Y	Y	Y	
258	D	N	N	N	
267	I	M	M	M	



271	H	N	N	N	
308	K			R	
311	R	Q	Q	Q	
321	I	T			
324	I	V	V	V	
326	S		T		
<b>aadiff</b>		<b>26</b>	<b>27</b>	<b>28</b>	

Reference CVV in red, pending/requested HI swine strains in blue.

Table 15. Amino acid substitutions between a representative swine 1C.2.2 strain compared to the within-clade CVV (A/Hessen/47/2020 CVV).

site	A/Hessen/47/2020	A/swine/Italy/348919/2021	A/Nordrhein-Westfalen/8/2022	annotations
3	I	L		
53	K	R		
66	E	D		
84	D	N		
97	D	N	N	
118	P	S		
120	A	S		
125	N	D		Sa
127	D		E	
130	R		K	
155	G		R	Sa
161	L	I		
163	N	K	K	Sa
175	V	I	I	
185	D	E		
214	T	I	I	
235	D	N	K	
239	T		S	
253	Y	H		
267	M	I	R	
269	N	D		
270	A		V	
271	R		Q	
288	S		I	
289	N		D	
302	E	K	K	
<b>aadiff</b>		<b>18</b>	<b>15</b>	

Reference CVV in red, pending/requested HI swine strain in blue, recent variant strain in orange.

Table 16. Amino acid substitutions between representative swine 1C.2.4 strains compared to the within-clade CVV (A/Bretagne/24241/2021 CVV).

site	A/Bretagne/24241/2021	A/swine/Italy/416754/2021	annotations
20	M	L	
36	N	S	
51	Q	N	
56	D	N	
69	L	P	
71	V	L	Cb
84	N	D	
112	E	K	
119	K	E	
120	-	A	
121	N	T	
124	P	S	Sa
125	S	N	Sa
128	-	T	
129	E	T	
130	A	G	
134	V	A	RBS
138	K	H	
142	N	S	Ca2
149	L	S	
153	S	K	Sb
156	K	S	Sb
157	P	S	Sa
159	S	P	Sa
163	K	R	Sa
166	K	T	Ca1
169	K	Q	
170	G	E	Ca1
185	Y	D	
186	S	R	
189	Q	L	Sb, RBS
195	N	D	Sb, RBS

202	V	A	
205	K	T	
208	Q	K	
216	P	T	
219	E	K	RBS
222	E	D	Ca2, RBS
224	R	A	RBS
237	E	G	Ca1
252	R	K	
253	Y	H	
258	E	S	
262	N	I	
271	H	N	
289	D	N	
<b>aadiff</b>		<b>46</b>	

Reference CVV in red, swine strains in black, pending/requested HI swine strains in blue.

### H3 swine lineage

- ★ H3v candidate vaccine virus
- A/Darwin/6/2021
- ◆ A/Cambodia/e826360/2020
- Previous H3N2 seasonal vaccines
- Reported H3N2v cases
- + New variant(s)
- # HI tested viruses
- Requested/pending HI
- ▲ Consensus sequences

### H3 swine genetic clades

- 3.2010.2 (n=5)
- 3.2010.1 (n=52)
- 3.1990.6 (n=1)
- 3.1990.4.a (n=43)
- 3.1990.4.i (n=2)
- 3.1990.4 (n=2)
- 3.1990.7 (n=2)
- 3.1970.1 (n=7)
- Human vaccine or seasonal

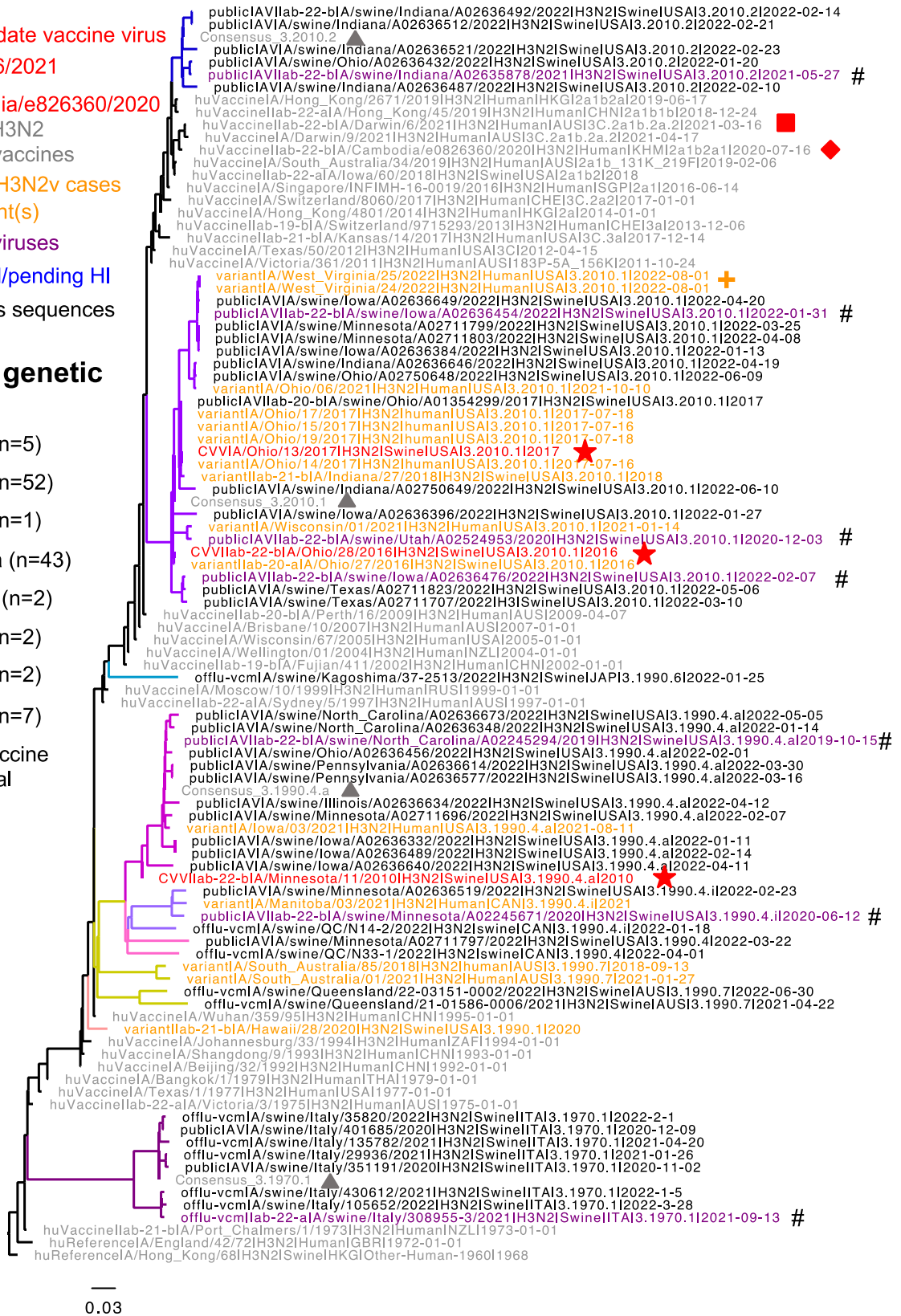


Figure 10. Swine H3 HA genes. Number of detections of each clade from data deposited between January 1, 2022 - June 30, 2022 are presented adjacent to the clade name in the figure key. Clades within the tree were proportionally down sampled to 45 swine HA genes (excluding references); tree includes clade consensus sequences, and human vaccine strains.

### Antigenic analysis: Swine H3

Table 17. 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/Minnesota/11/2010 x 203	A/swine/North Carolina/A02245294/2019 (H3N2) #32	A/swine/North Carolina/A02245294/2019 (H3N2) #18	IDCDC-RG55C A/Ohio/28/2016-like CVV	IDCDC-RG60A A/Ohio/13/2017 CVV	Indiana/27/2018	A/swine/Utah/A02524953/2020 (H3N2) #19	A/swine/Utah/A02524953/2020 (H3N2) #20	rg-A/Cambodia/e826360/2020 (H3N2)-like #1	rg-A/Cambodia/e826360/2020 (H3N2)-like #25	rg-A/Darwin/6/2021 (H3N2)-like #5	rg-A/Darwin/6/2021 (H3N2)-like #6
A/Minnesota/11/2010 x 203	1990.4.a	1280	80	160	20	nt	20	40	80	<10	<10	80	10
A/swine/North Carolina/A02245294/2019*	1990.4.a	80	2560	1280	10	nt	40	20	40	20	40	40	10
A/swine/Minnesota/A02245671/2020*	1990.4.i	10	20	20	<10	nt	20	10	20	<10	20	10	<10
ID40CDC-RG55C A/Ohio/28/2016-like CVV	2010.1	20	40	40	5120	320	40	160	320	40	40	40	20
IDCDC-RG60A A/Ohio/13/2017 CVV	2010.1	nt	nt	nt	80	640	nt	160	160	nt	nt	nt	nt
A/Indiana/27/2018	2010.1	20	nt	nt	40	40	640	10	10	nt	nt	nt	nt
A/swine/Iowa/A02636476/2022*	2010.1	10	40	80	160	160	80	640	640	10	40	40	10
A/swine/Iowa/A02636454/2022*	2010.1	10	20	40	40	160	40	320	320	10	20	40	<10
A/swine/Utah/A02524953/2020	2010.1	10	40	40	40	160	40	640	640	<10	10	20	10
A/swine/Indiana/A02635878/2021	2010.2	20	20	20	10	nt	nt	20	40	10	20	20	<10
rg-A/Cambodia/e826360/2020-like	3C.2a1b.2a.1	<10	<10	<10	<10	nt	nt	10	10	160	160	40	80
rg-A/Darwin/6/2021-like	3C.2a1b.2a.2	<10	<10	10	10	nt	nt	20	20	20	40	640	1280

Reference CVV in red, seasonal vaccine strains in gray, new swine strains in bold, variant in orange. Homologous titers highlighted in gray. \*Previously tested in report 2021a; rg is a synthetic HA/NA on PR8 backbone.

- The contemporary swine 1990.4.a demonstrated a significant 8-fold decrease from CVV A/Minnesota/11/2010 x 203.
- The contemporary swine 1990.4.i does not have a CVV contained within clade and demonstrated a significant 32-fold decrease from CVV A/Minnesota/11/2010 x 203.
- The contemporary swine 2010.1 representative strains had a significant decrease to CVV IDCDC-RG55C A/Ohio/28/2016-like, whereas CVV A/Ohio/13/2017 had greater cross-reactivity to recent swine strains.
- The contemporary swine 2010.2 representative strain does not have a CVV contained within clade but reacted to A/Iowa/60/2018 and an 8-fold decrease to A/Hong Kong/45/2019.

Table 18. 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/Victoria/3/1975	IDCDC-RG55C A/Ohio/28/2016-like CVV	A/Sydney/5/97
A/Victoria/3/1975	Human seasonal	1280	40	160
IDCDC-RG55C A/Ohio/28/2016-like CVV	2010.1	160	1280	160
A/Sydney/5/97	Human seasonal	320	80	2560
<b>A/swine/Italy/308955-3/2021</b>	1970.1	640	320	320

Reference CVV in red, seasonal vaccine strains in dark red, new swine strains in bold. Homologous titers highlighted in gray. ND=not done.

- The contemporary swine 3 A/swine/Italy/308955-3/2021 demonstrated good reactivity with A/Victoria/3/1975 and poor cross reactivity to the 2010.1 CVV and another antiserum raised to a human seasonal strain.

Table 19. Amino acid substitutions between a representative swine 1990.4.X strain compared to the within-clade CVV (A/Minnesota/11/2010 x 203) used in the HI assay.

site	A/Minnesota/11/2010	A/swine/North_Carolina/A022452 94/2019 1990.4.a	A/swine/Minnesota/A02245671/2 020 1990.4.i	annotations
5	G			
6	S			
8	N		K	
9	S		N	
10	M		T	
12	T		M	
31	D			
45	S		X	
46	S			
49	G		D	
50	R		K	
53	N			Site C
57	Q		K	
58	I		V	
62	K		G	
80	Q		E	
91	S			
96	N	S	D	
101	Y			
107	T		S	
114	S			
117	N		T	
119	E	K		
121	T		N	
122	Q		L	Site A
124	S	I	N	
126	N			
128	T			
131	A	T	D	



133	D			Site A
135	S			
137	Y		F	Site A
138	A	S	S	
140	R		K	
142	G		N	
155	Y		H	Site B
156	N	H	Q	
159	Y		H	
163	E		A	
164	Q		L	
173	K			
182	V			
186	G			Site B
188	D			Site B
189	K		M	Site B
192	T			
193	N		S	Site B
197	Q			
198	A		E	
201	R			Site D
202	V			
203	I		T	
207	K	R		Site D
208	R			Site D
214	I			
223	V			
226	V			
229	I			
238	K			
242	I			
260	I		M	
261	Q		R	
262	S		I	
264	K			
268	M			
269	R		K	
273	H		L	
275	D		G	Site C
276	E		N	
289	P	S		
299	K		R	

323	V	I		
<b>aadiff</b>		<b>9</b>	<b>39</b>	

Reference CVV in red, HI swine strains in purple, recent variant detection in orange.

Table 20. Amino acid substitutions between a representative swine 2010.1 strain compared to the within-clade CVV (A/Ohio/28/2016 IDCDC-RG55C) used in the HI assay. A second within-clade CVV (A/Ohio/13/2017) is presented.

site	A/Ohio/28/2016	A/Ohio/13/2017	A/Indiana/27/2018	A/swine/Iowa/A02636454/2022	A/swine/Utah/A02524953/2020	A/swine/Iowa/A02636476/2022	A/West_Virginia/25/2022	A/West_Virginia/24/2022	annotations
3	L					F			
25	I						M	M	
31	N			D			D	D	
45	S			N			N	N	
56	H	Y	Y	Y			Y	Y	
62	E			G			G	G	
88	V				I				
91	S					N			
92	K				R				
96	N			D			D	D	
106	A			V					
112	V				A				
122	N			K			K	K	Site A
138	A	S	S	S	S	S	S	S	
142	R		G						
144	S				T				Site A
145	K	N	N	N	N	N	N	N	Site A
156	H		R		Q				
158	N		D						
167	T				A				
188	D					E			Site B
189	K		T						Site B
198	A					T			
202	I			T			T	T	
209	S	N	N	N	G		N	N	
212	A			T			T	T	
223	V			I			I	I	
238	R			K			K	K	
264	K			R			R	R	

280	A					E			
312	N				K				
323	I					L			
<b>aadiff</b>		<b>4</b>	<b>8</b>	<b>15</b>	<b>10</b>	<b>8</b>	<b>15</b>	<b>15</b>	

Reference CVV in red, HI swine strains in purple, new variant detection in orange.

Table 21. Amino acid substitutions between a representative 2010.2 strain compared to the human seasonal vaccine (A/Cambodia/e0826360/2020 C.2a1b2a), and a second human seasonal vaccine (A/Darwin/6/2021 C.2a1b.2a).

site	A/Cambodia/e0826360/2020	A/Darwin/6/2021	A/swine/Indiana/A02635878/2021	annotations
9	S		G	
31	N		D	
53	D	G		Site C
58	I		V	
62	G		E	
83	E		Q	
94	N		Y	
106	A		I	
131	K		T	
135	T		I	
138	A		S	
144	S		N	Site A
156	H	S		
159	Y	N		
160	K	I		
164	L	Q		
167	T		I	
171	N	K		
186	R	D	G	Site B
189	K		N	Site B
190	D	N		
192	I		T	
195	F		Y	
197	Q		R	
198	P	S	S	
203	T		I	
291	D		N	
<b>aadiff</b>		<b>9</b>	<b>20</b>	

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

Table 22. Amino acid substitutions between a representative swine 1970.1 strain compared to the putative ancestral human seasonal H3 strain (H3 A/Port Chalmers/1/1973); the most similar human seasonal vaccine by amino acid similarity (A/Victoria/3/1975) is included.

site	A/Port_Chalmers/1/1973	A/Victoria/3/1975	A/swine/Italy/308955-3/2021	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		K	Site C
62	I		A	
67	I		V	
69	A		S	
83	T	K	K	
88	V		I	
92	K		R	
104	D		E	
106	A		T	
112	V		I	
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
242	I		T	
244	V		I	
260	M		I	
261	R		Q	
262	T		I	
267	I		V	
269	R		K	
278	I	S	D	Site C
299	K		R	
307	K		H	
309	V		I	
323	V		I	
<b>aadiff</b>		<b>11</b>	<b>48</b>	

Reference vaccine in gray, HI swine strain in purple.

## Summary and Risk Assessment

### Global Variant Cases:

During the reporting period (January 1, 2022 – June 30, 2022), 1 variant case was reported and included with the swine analyses:

- Germany: H1N1v (1C.2.2)

An additional 6 variant cases were reported July 1, 2022 – present but collected following the report window. When HA sequence were available, they were included in the phylogenetic trees:

- USA: H1N2v (1 1A.1.1; 1 1A.3.3.2; 1B.2.1 no sequence); H3N2v (3 2010.1)

### Europe Swine:

- The contemporary swine 1A.3.3.2 (pdm) with onward transmission in European swine were poorly recognized by the panel of human seasonal vaccine strains with the exception of two viruses, where there was good recognition.
- The swine 1B.1.1 was poorly cross-reactive with A/Chile/1/1983 with the 1B.2.1.d2 CVV.
- The contemporary swine 1B.1.2.2 representing strains circulating in Italy and had a significant decrease in cross reactivity against both the 1B.2.1 d2 CVV and against the human seasonal strain reference. There are no within-clade CVVs for 1B lineages from Europe.
- 1C.2.1, 1C.2.4 and 1C.2.5: The selected contemporary viruses represented the diverse 1C.2.1, 1C.2.4 - with multiple deletion patterns and 1C.2.5 groups. In general, they were poorly recognised by all 1C antisera except by A/Mechlenburg-Vorpommern/1/2021 – a 1C.2.1 variant virus.
- The new designated 1C.2.4 CVV A/Bretagne/24241/2021 recognized well the swine virus closely associated with the variant infection but poorly recognized any of the other 1C.2.4 viruses and also the 1C.2.1, 1C.2.2 and 1C.2.5 viruses.

### North America Swine:

- The contemporary swine 1A.1.1 (alpha-del) was not detected by the 1A.1.1 CVV A/Ohio/24/2017 ferret anti-sera.
- The 1A.2 swine strain was not significantly detected by any CVV or vaccine anti-sera.
- The contemporary swine 1A.3.3.2 (pdm) with onward transmission in swine had significant 16-fold decrease in cross-reactivity to the A/Wisconsin/588/2019 6B1.A-5a.2 vaccine strain, but maintained cross-reactivity to A/Hawaii/70/2019-like 6B.1A.5a.1 vaccine strain.
- The contemporary swine 1A.3.3.3 (gamma) clade 3 virus had a 16-fold decrease with the 1A.3.3.3-clade 1 CVV A/Ohio/09/2015. The contemporary swine 1A.3.3.3 (gamma) clade 1 virus had an 8-fold decrease with the within-clade 1A.3.3.3-clade 1 CVV A/Ohio/09/2015.
- The contemporary swine 1A.4 (gamma-2-beta-like) virus was not significantly detected by any CVV or vaccine anti-sera.
- The contemporary swine 1B.2.1 (delta-2) was 100% identical in the HA1 to the within-clade CVV A/Michigan/383/2018 and there was no loss in cross-reactivity.
- Two contemporary swine 1B.2.2.1 (delta-1a) representing diverging clades were tested. Both A/swine/Iowa/A024636436/2022 and A/swine/Wyoming/A02525343/2021 had a 8-fold reduction from the within clade CVV A/Iowa/32/2016 and demonstrated loss in cross-reactivity to each other.



- The contemporary swine 1B.2.2.2 (delta-1b) does not have a CVV contained within clade and had a significant greater than 8-fold decrease from CVV A/Iowa/32/2016.
- The Brazil 1B.2.3 clade has no within clade CVV, and the representative strain had a significant 8-fold loss in cross reactivity to the 1B.2.2.1 A/Iowa/32/2016 CVV but retained reactivity with the 1B.2.1 A/Michigan/383/2018 CVV.
- The contemporary swine 1990.4.a demonstrated a significant 8-fold decrease from CVV A/Minnesota/11/2010 x 203.
- The contemporary swine 1990.4.i does not have a CVV contained within clade and demonstrated a significant 32-fold decrease from CVV A/Minnesota/11/2010 x 203.
- The contemporary swine 2010.1 representative strains had a significant decrease to CVV IDCDC-RG55C A/Ohio/28/2016-like, whereas CVV A/Ohio/13/2017 had greater cross-reactivity to recent swine strains.
- The contemporary swine 2010.2 representative strain does not have a CVV contained within clade but reacted to A/Iowa/60/2018 and an 8-fold decrease to A/Hong Kong/45/2019.

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

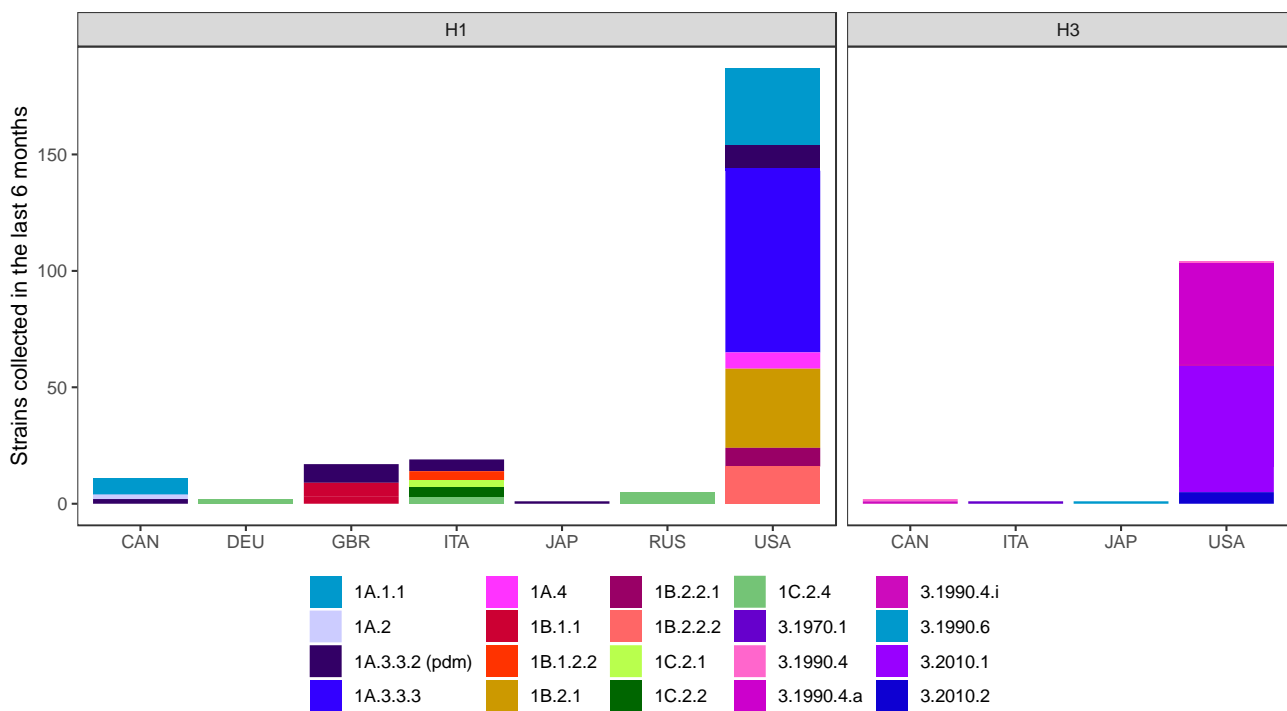


Figure A1. Summary of swine HA genes colored by phylogenetic clade for sequences deposited January 2022 – June 2022 and truncated to those collected within the last 6 months (n=350).

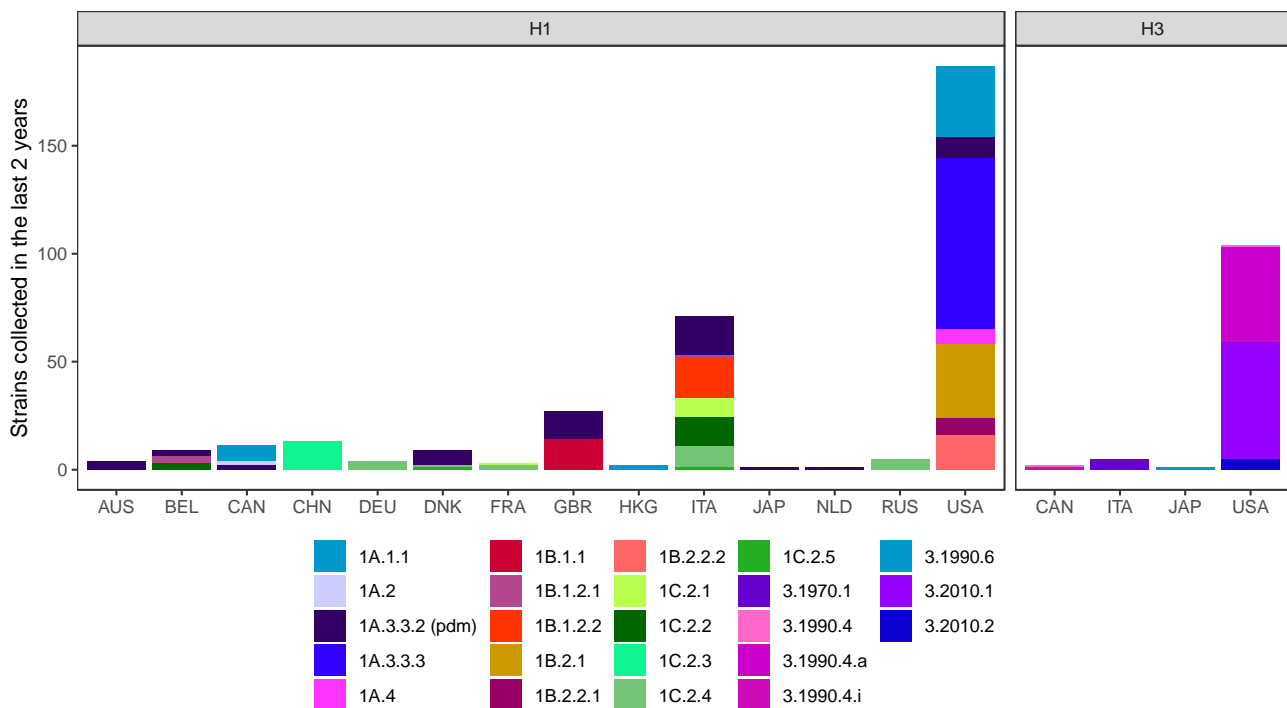


Figure A2. Summary of swine HA genes colored by phylogenetic clade for sequences deposited January 2022 - June 2022 and truncated to those collected within the last 24 months (n=459).

Table A1a. Summary of swine H1 clades by country collected in the past 6 months and deposited January 2022 – June 2022.

clade	country	count
1A.1.1	CAN	7
1A.2	CAN	2
1A.3.3.2	CAN	2
1C.2.4	DEU	2
1A.3.3.2	GBR	8
1B.1.1	GBR	9
1A.3.3.2	ITA	6
1B.1.2.2	ITA	4
1C.2.1	ITA	3
1C.2.2	ITA	6
1C.2.4	ITA	6
1C.2.5	ITA	1
1A.3.3.2	JAP	1
1A.5.1	JAP	1
1A.5.3	JAP	1
1C.2.4	RUS	5
1A.1.1	USA	33
1A.3.3.2	USA	10
1A.3.3.3	USA	79
1A.4	USA	7
1B.2.1	USA	34
1B.2.2.1	USA	8
1B.2.2.2	USA	16

Table A1b. Summary of swine H1 clades by country collected in the past 24 months and deposited January 2022 – June 2022.

clade	country	count
1A.3.3.2	AUS	4
1A.3.3.2	BEL	3
1B.1.2.1	BEL	3
1C.2.2	BEL	3
1A.1.1	CAN	7
1A.2	CAN	2
1A.3.3.2	CAN	2
1C.2.3	CHN	12
1C.2.4	DEU	4
1A.3.3.2	DNK	7
1C.2.4	DNK	1
1C.2.5	DNK	1
1C.2.1	FRA	1
1C.2.4	FRA	2
1A.3.3.2	GBR	13
1B.1.1	GBR	13
1A.1.1	HKG	2
1A.3.3.2	ITA	18
1B.1.2.1	ITA	1
1B.1.2.2	ITA	14

1C.2.1	ITA	6
1C.2.2	ITA	15
1C.2.4	ITA	12
1C.2.5	ITA	2
1A.3.3.2	JAP	1
1A.5.1	JAP	1
1A.5.3	JAP	1
1A.3.3.2	NLD	1
1C.2.4	RUS	5
1A.1.1	USA	33
1A.3.3.2	USA	10
1A.3.3.3	USA	79
1A.4	USA	7
1B.2.1	USA	34
1B.2.2.1	USA	8
1B.2.2.2	USA	16

Table A2a. Summary of swine H3 clades by country collected in the past 6 months and deposited January 2022 – June 2022.

<b>clade</b>	<b>country</b>	<b>count</b>
3.1990.7	AUS	1
3.1990.4	CAN	1
3.1990.4.i	CAN	1
3.1970.1	ITA	3
3.1990.6	JAP	1
3.1990.4	USA	1
3.1990.4.a	USA	43
3.1990.4.i	USA	1
3.2010.1	USA	54
3.2010.2	USA	5

Table A2b. Summary of swine H3 clades by country collected in the past 24 months and deposited January 2022 – June 2022.

<b>clade</b>	<b>country</b>	<b>count</b>
3.1990.7	AUS	2
3.1990.4	CAN	1
3.1990.4.i	CAN	1
3.1970.1	ITA	7
3.1990.6	JAP	1
3.1990.4	USA	1
3.1990.4.a	USA	43
3.1990.4.i	USA	1
3.2010.1	USA	54
3.2010.2	USA	5

## Annex 2. Phylogenies of swine HA lineages with tree backbone annotated by inferred amino acid mutations.

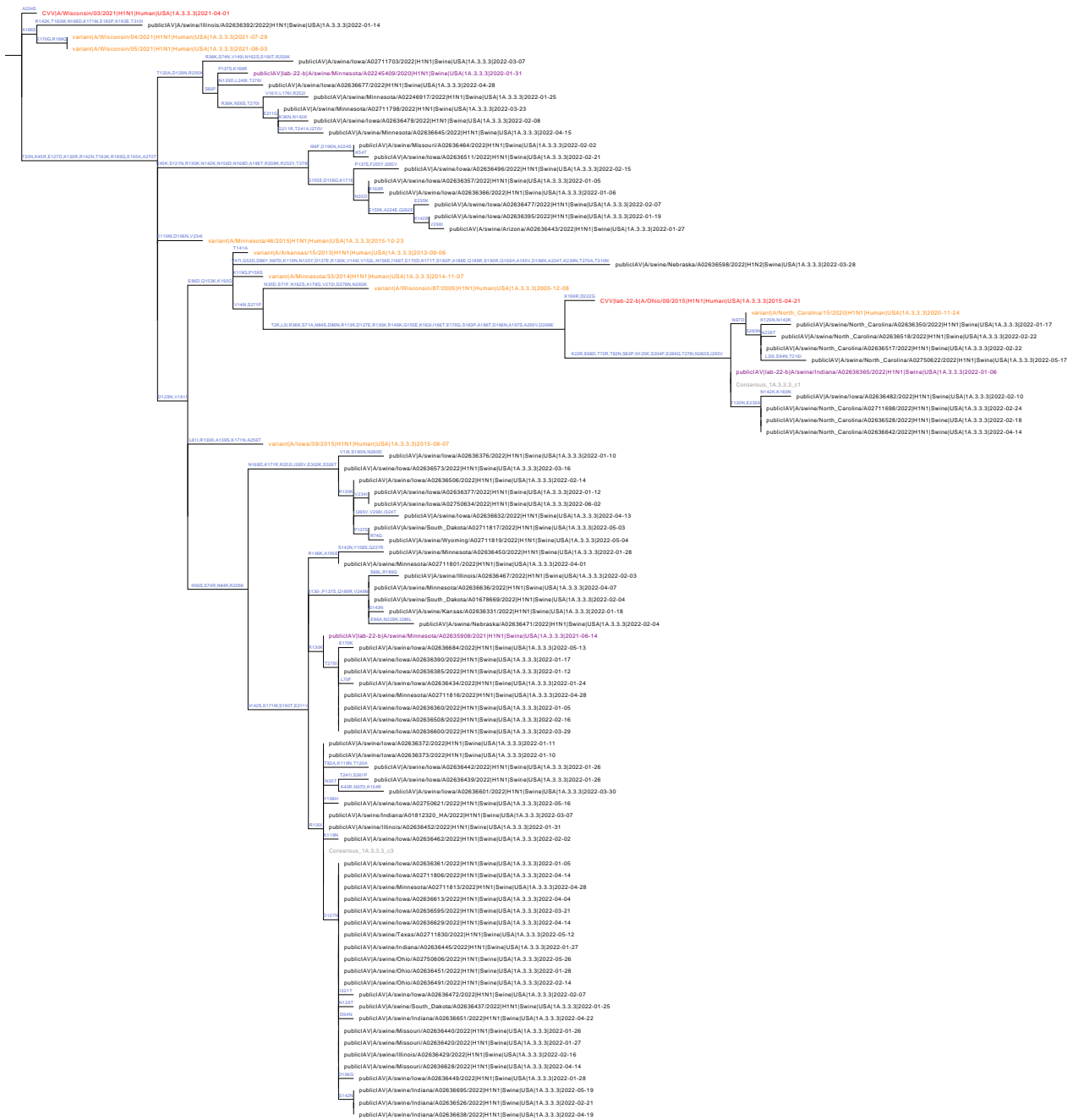


Figure A3. A phylogeny of the **1A.3.3.3** clade displaying sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022 (n=79) and 14 reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Wisconsin/03/2021) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 7.

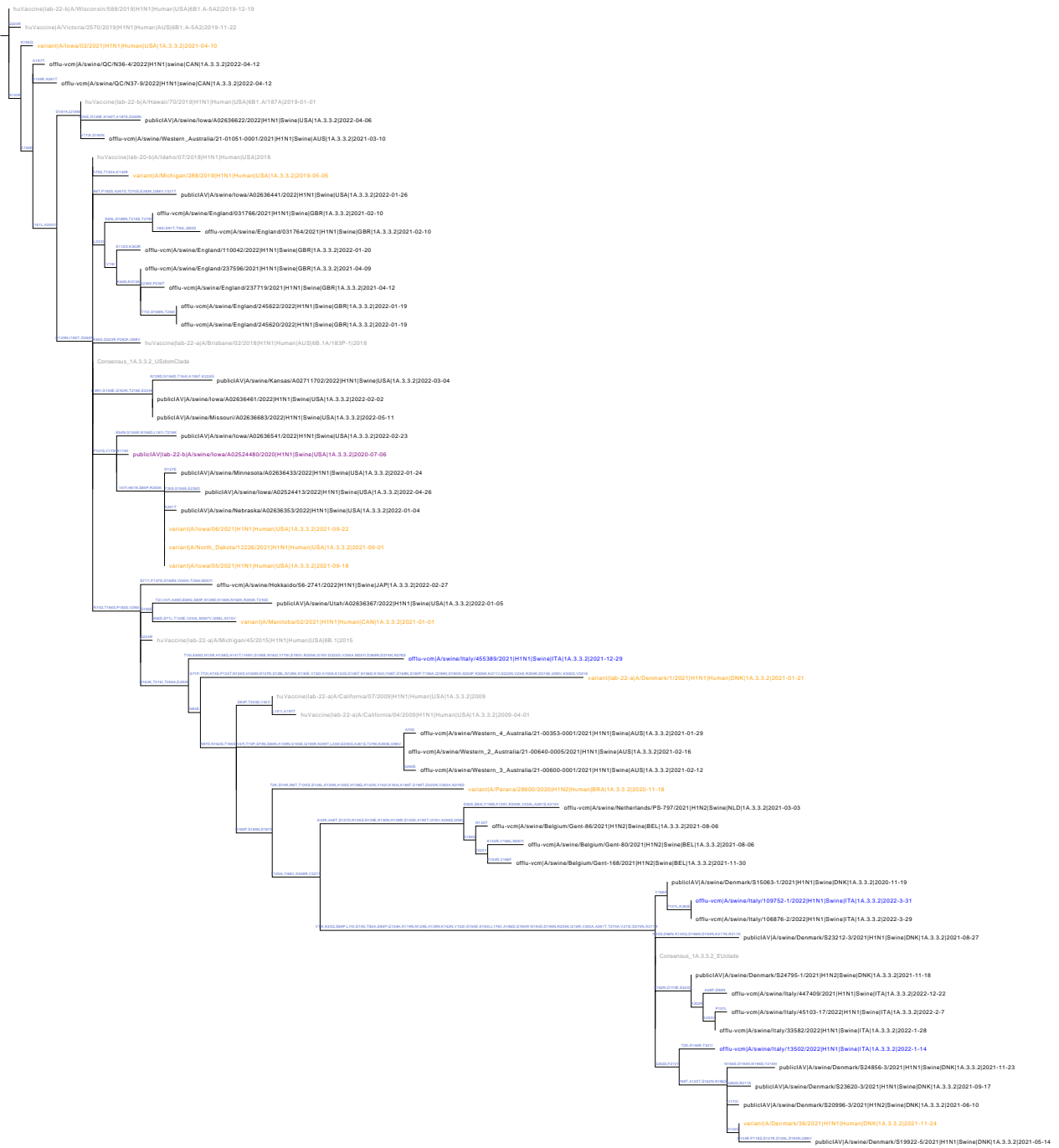


Figure A4. A phylogeny of the **1A.3.3.2 (pdm)** clade displaying n=42 sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and n=20 reference genes. The clade is rooted relative to the most recent human vaccine strain (A/Wisconsin/588/2019) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 7.



Figure A5. A phylogeny of the 1A.1.1 clade displaying n=40 sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and n=6 reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Ohio/24/2017) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 7.



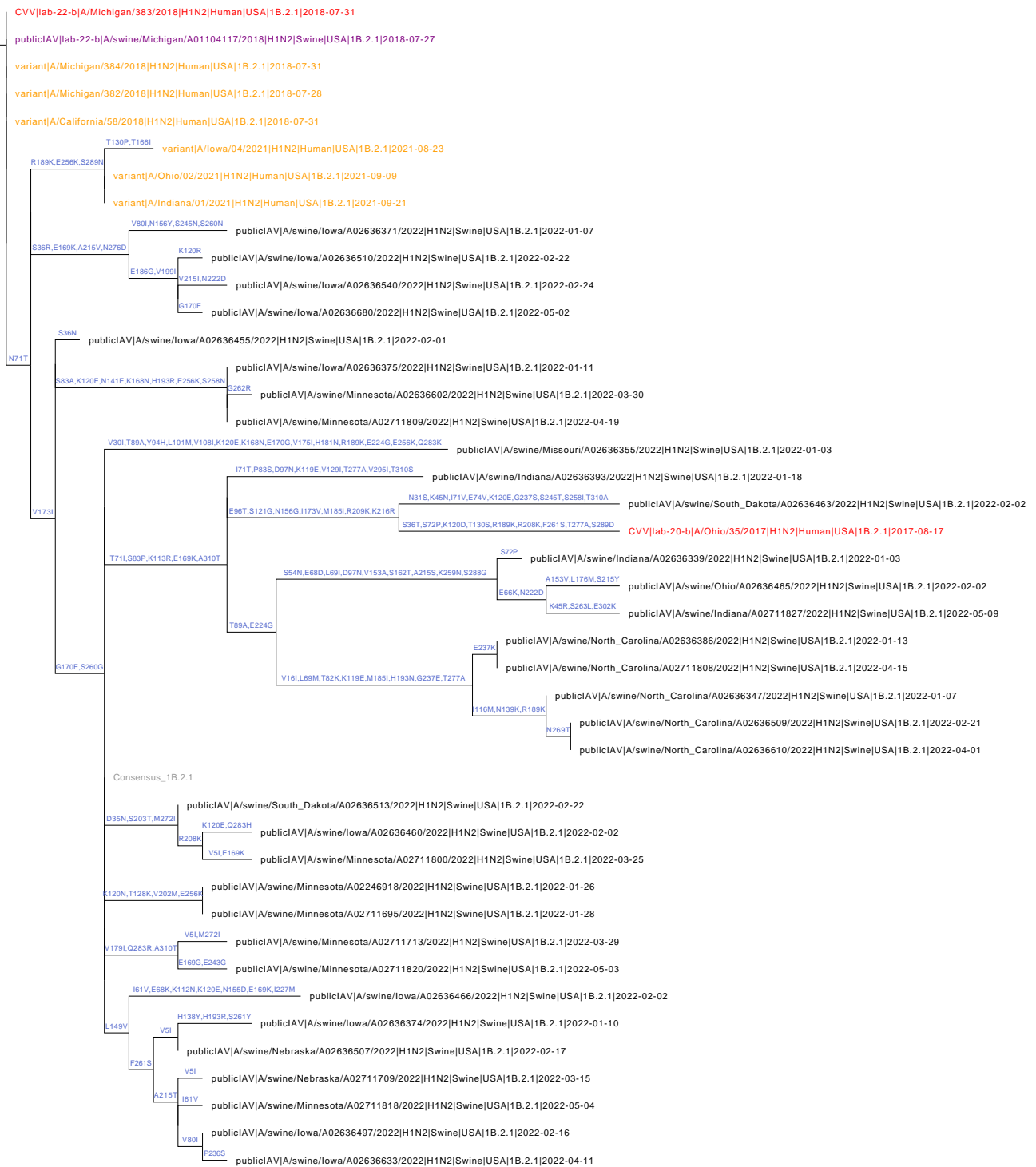


Figure A6. A phylogeny of the **1B.2.1** clade displaying  $n=33$  sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and  $n=10$  reference genes. The clade is rooted relative to the most recent in-clade CVV (A/Michigan/383/2018) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 8.

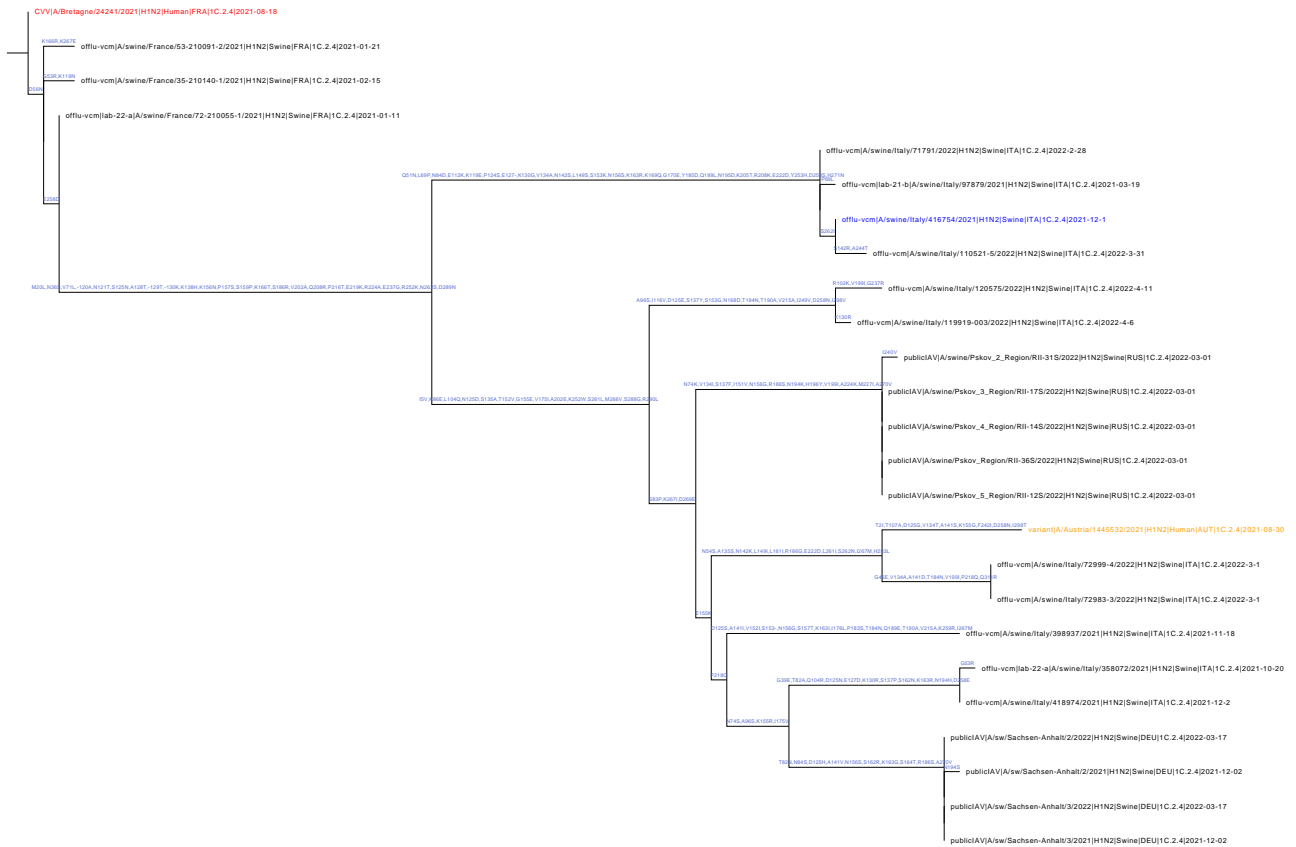


Figure A7. A phylogeny of the **1C.2.4** clade displaying n=20 sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and n=5 reference genes. The clade is rooted relative to the closest CVV (A/Britagne/24241/2021) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 9.



Figure A8. A phylogeny of the **3.2010.1** clade displaying n=54 sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and n=18 reference genes. The clade is rooted relative to the most representative in-clade CVV (A/Ohio/28/2016) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 10.

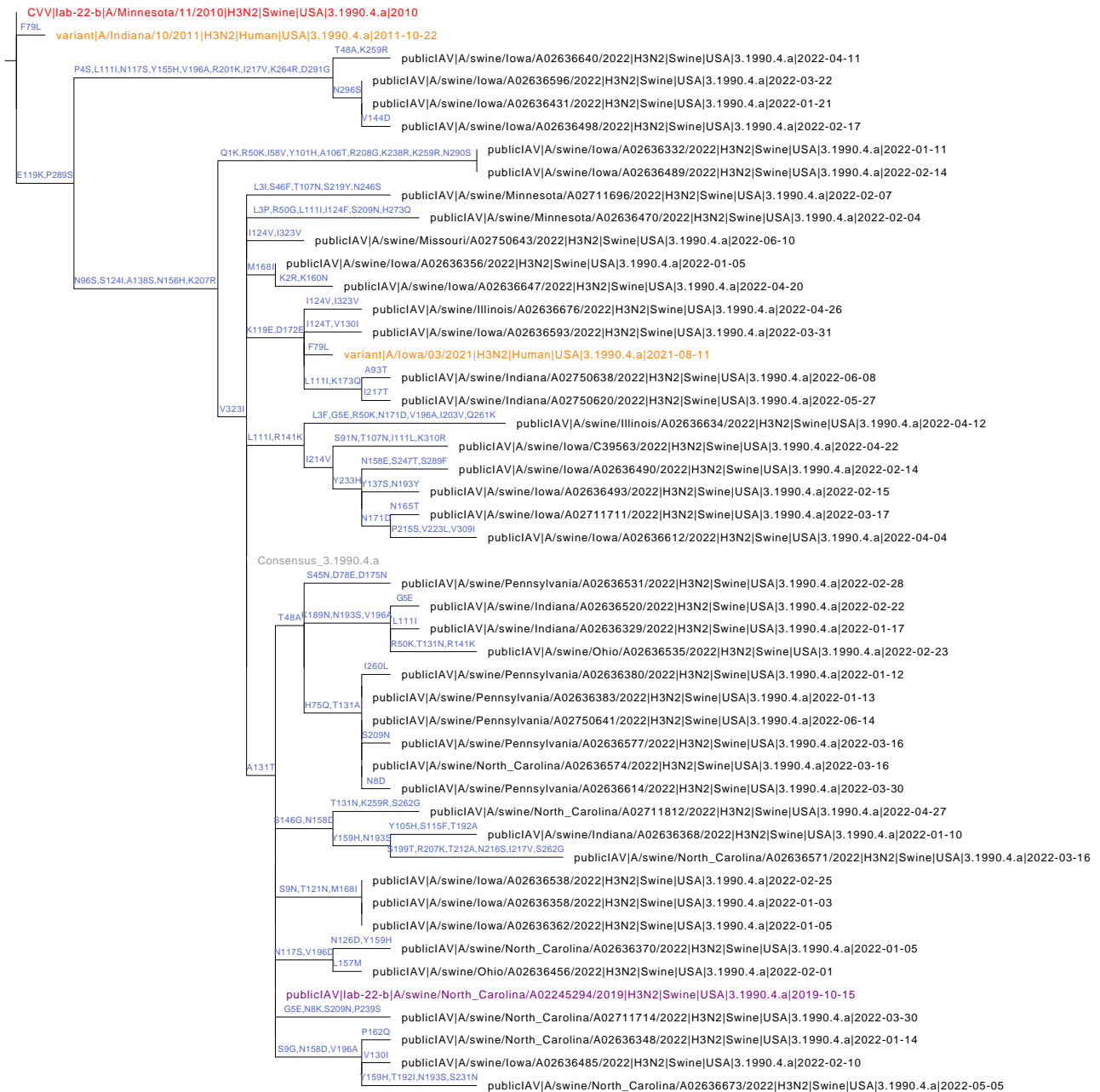


Figure A9. A phylogeny of the **3.1990.4.a** clade displaying n=43 swine sequences deposited January 1, 2022 - June 30, 2022 and collected in 2021-2022, and n=5 reference genes. The clade is rooted relative to the most representative in-clade CVV (A/Minnesota/11/2010) and all branches are annotated by the respective amino acid mutations in the HA1 region. The strains are colored in consistence with Figure 10.