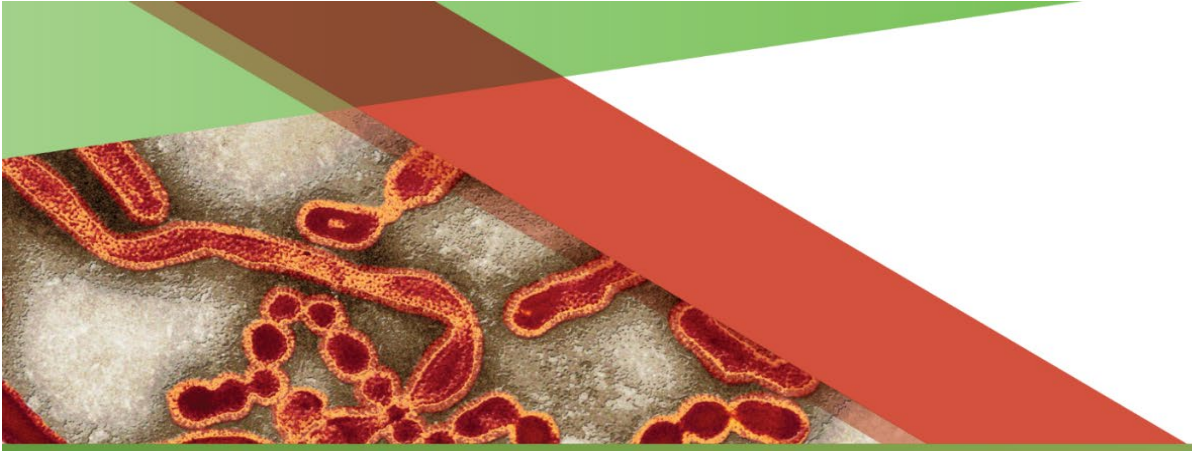


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2022

Summary

This is the fourth report for the 2021–2022 influenza season. As of week 08/2022, 44 665 influenza detections across the WHO European Region were reported to TESSy, an increase of over 41 000 since week 47/2021 with most being reported from week 49/2021 onwards. Of these 44 665 detections, 97% were type A viruses, with A(H3N2) (93%) dominating over A(H1N1)pdm09 (7%), and 3% type B, with only 19 having been ascribed to a lineage, all of which were B/Victoria. This represents a large increase (43 953, 6273%) in detections compared to the 2020–2021 season, on the back of a large increase (1 274 874, 383%) in the number of samples tested. However, while there have been clear indications of an influenza epidemic in 2021–2022, with the epidemic threshold of 10% positivity within sentinel specimens having been crossed for a number of weeks (unlike 2020–2021), detection numbers are significantly reduced compared to earlier seasons (e.g. 65% reduced compared to 2019–2020). The increased testing but reduced number of influenza detections is undoubtedly related to the emergence of SARS-CoV-2 and measures introduced to combat it.

Since the December 2021 characterisation report[1], 17 shipments from EU/EEA countries have been received at the London World Health Organization (WHO) Collaborating Centre, the Francis Crick Worldwide Influenza Centre (WIC) and many of the samples in these shipments have yet to be fully characterised. This report therefore focuses on viruses with collection dates after 31 August 2021 for which HA gene sequences were available in GISAID as of 8 February 2022, together with sequences generated and antigenic data determined at the WIC.

On a global scale, relatively few A(H1N1)pdm09 viruses have been detected in the course of the 2021–2022 season. The subgroups 6B.1A.5a.1 and 6B.1A.5a.2 are equally represented, with subgroup dominance varying between countries. The subgroups are antigenically different and while 6B.1A.5a.1 viruses have been most widespread in Europe, an emergent genetic group within this subgroup has been detected, defined by HA1 P137S and G155E amino acid substitutions and showing antigenic drift. At the February 2022 WHO influenza vaccine composition meeting (VCM) the recommendation was to retain A/Victoria/2570/2019-like viruses (6B.1A.5a.2) as the vaccine component for the northern hemisphere 2022–2023 influenza season.

In Europe and across the world A(H3N2) viruses have been dominant with the vast majority of recently detected viruses falling in subgroup 3C.2a1b.2a being 'Bangladesh-like'. While small clusters of viruses showing antigenic drift have emerged within this subgroup, the vast majority of viruses retained good recognition by post-infection ferret antisera raised against A/Darwin/9/2021-like and A/Darwin/6/2021-like (3C.2a1b.2a.2) viruses, which were recommended for egg- and cell-based vaccines to be used in the 2022 southern hemisphere season. At the February 2022 WHO VCM the recommendation was to change the A(H3N2) vaccine component for the northern hemisphere 2022–2023 influenza season to match those to be used in the 2022 southern hemisphere season.

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, December 2021. Stockholm: ECDC; 2020. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/Influenza-characterisation-report-Dec-2021.pdf

This report was prepared by Rod Daniels, Burcu Ermetal, Aine Rattigan and John McCauley (Crick Worldwide Influenza Centre) for the European Centre for Disease Prevention and Control under an ECDC framework contract.

Suggested citation: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, February 2022. Stockholm: ECDC; 2022.

In Europe and across the world, few B/Victoria-lineage viruses have been detected during the 2021–2022 influenza season. All have lost encoding of a three amino acid triplet (HA1 residues 162-164) placing them in subclade V.1A.3 represented by B/Washington/02/2019, the vaccine virus recommended for inclusion in influenza vaccines for the 2021–2022 northern hemisphere season. The majority of HA sequences from recently detected viruses in geographically dispersed countries have fallen in the V1A.3a group, defined by a series of HA1 amino acid substitutions including N150K. Most of these fall within the V1A.3a.2 subgroup with defining HA1 A127T, P144L and K203R amino acid substitutions. Viruses in subgroup V1A.3a.2 are not recognised well by post-infection ferret antisera raised against B/Washington/02/2019-like viruses and B/Austria/1359417/2021-like (V.1A.3a.2) viruses were recommended for use in the southern hemisphere 2022 influenza season. At the February 2022 WHO VCM, the recommendation was to change the B/Victoria-lineage vaccine component for the northern hemisphere 2022–2023 influenza season to match those to be used in the 2022 southern hemisphere season.

No cases of infection with circulating B/Yamagata-lineage viruses have been confirmed since March of 2020. All HA gene sequences from the 77 viruses detected in 2020, inclusive of 12 from EU/EEA countries, belong to genetic clade 3 (Y3) and carry three HA1 amino acid substitutions (L172Q, D229N and M251V) compared to B/Phuket/3073/2013-like viruses which are still recommended for use in quadrivalent influenza vaccines. The antigenic effects of these amino acid substitutions have been minimal, as assessed in earlier reports.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to The European Surveillance System (TESSy) database during the 2021–2022 season (weeks 40/2021–8/2022), compared to the same period in the 2020–2021 season. There has been a vast increase in the number of samples from patients fulfilling Influenza-Like Illness (ILI) and/or Acute Respiratory Infection (ARI) criteria being tested (1 274 874, 383%), even when compared with a more 'normal' season, 2019–2020 (1 173 775, 313%: results not shown), which led into the COVID-19 pandemic. This increased testing has led to a rise in the number of influenza-positive samples (43 953, 6273%), although there was a reduction against the same period in 2019–2020 (82 456, 65%: results not shown). These data probably relate to a number of factors:

- significant numbers of samples taken from patients fulfilling ILI and/or ARI criteria being infected with other agents, possibly SARS-CoV-2, the virus responsible for the COVID-19 pandemic;
- restrictions on travel and social/work place gatherings, imposed to help curtail the spread of SARS-CoV-2, also impeding the spread of influenza viruses;
- increased use of personal protective equipment (e.g. face masks) and hygiene measures (e.g. hand-washing and surface disinfection);
- viral interference, with SARS-CoV-2 infection impeding infection by influenza viruses.

With these caveats, and being mindful of the low number of detections during the 2020–2021 season, the ratio of type A to type B detections has increased compared to the 2020–2021 season (1:1 to 28:1), with a greater dominance of A(H3N2) over A(H1N1)pdm09 viruses. While the number of influenza B virus detections has increased from 349 to 1 520 (436%), only small numbers were ascribed to a lineage in both time periods (Table 1). However, based on sequences available in GISAID, B/Yamagata lineage viruses with collection dates after March 2020 have not been characterised genetically. At present, it appears that measures introduced relating to the COVID-19 pandemic are still having an effect but there has been a clear indication of an influenza season in the Region during 2021–2022, with the rate of influenza positivity having been above 10%, the epidemic threshold set for the Region, for five weeks (weeks 49/2021 to 1/2022) with A(H3N2) viruses dominating.

Table 1. Influenza virus detections in the WHO European Region since the start of reporting for the 2021–22 season (weeks 40/2021–8/2022)[a]

Virus type/subtype/lineage	Cumulative number of detections for weeks 40/2021-08/2022			Totals*		Cumulative number of detections for weeks 40/2020-08/2021			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**2512**	**40633**	**43145**	**96.6**	**28:1**	**20**	**343**	**363**	**51.0**	**1:1**
A(H1N1)pdm09	144	942	1086	6.8		13	28	41	48.8	
A(H3N2)	1662	13313	14975	93.2	14:1	6	37	43	51.2	1:1
A not subtyped	706	26378	27084			1	278	279		
Influenza B	**34**	**1486**	**1520**	**3.4**		**13**	**336**	**349**	**49.0**	
Victoria lineage	6	13	19	100.0		2	6	8	80.0	4:1
Yamagata lineage	0	0	0			0	2	2	20.0	
Lineage not ascribed	28	1473	1501			11	328	339		
Total detections (total tested)	**2 546 (36 483)**	**42 119 (>1 688 538)**	**44 665 (>1 725 021)**			**33 (25 606)**	**679 (>424 541)**	**712 (>450 147)**		

[a] Numbers taken from Flu News Europe to week 08/2022 and week 08/2021 reports for the two influenza seasons

* Percentages are shown for total detections (types A & B [in bold type], and for viruses ascribed to influenza A subtype and influenza B lineage). Ratios are given for type A:B [in bold type], A(H3N2):A(H1N1)pdm09 and Victoria:Yamagata lineages.

Genetic and antigenic characterisation data generated at the WIC for viruses with collection dates after 31 August 2020 until 31 January 2021, up to a report deadline of 15 February 2021, contributed to the WIC virus characterisation report presented at the WHO influenza vaccine composition meeting (VCM) in February 2021 when recommendations were made for the northern hemisphere 2021–2022 season [1]. Data generated on viruses with collection dates after 31 January 2021 until 31 August 2021 informed the September 2021 VCM when recommendations were made for the 2022 southern hemisphere season [2]. Data presented here for viruses with collection dates after 31 August 2021 until 31 January 2022 contributed to the recent VCM (21–24 February) where recommendations were made for the 2022–2023 northern hemisphere influenza seasons [3]. For the 2022–2023 northern hemisphere season a recommendation was made to change the A(H3N2) and B/Victoria-lineage components of influenza vaccines to match those to be used in 2022 southern hemisphere vaccination campaigns.

Due to the relatively low number of influenza-positive specimens detected until recently and available to share with WIC, this and recent influenza characterisation reports have mainly been based on phylogenetic analyses of complete HA gene sequences submitted to the EpiFlu™ database of the Global Initiative on Sharing All Influenza Data (GISAID). This includes sequences generated at the WIC, with those from EU/EEA countries highlighted. For A(H1N1)pdm09, A(H3N2) and B/Victoria-lineage viruses separate trees are presented, for viruses with collection dates after 31 August 2021, for representative non-WIC generated sequences available in GISAID (Figures 1a, 2a and 3a) and all sequences generated at the WIC (Figures 1b, 2b and 3b). These six phylogenies were presented in the February 2022 VCM report prepared by WIC and, for the GISAID figures, these relate to sequences available as of 8 February 2022, together with 114 B/Victoria-lineage HA sequences provided by the WHO Collaborating Centre, China. Table 2 shows the numbers of HA sequences, derived from viruses with collection dates after 31 August 2021, available and used in the respective phylogenies.

Table 2. Summary of the numbers of HA gene sequences available and used to generate the phylogenies presented in this report

Virus subtype/lineage	Number of HA sequences from viruses collected in the 2021-2022 season		
	GISAID (non-WIC) total[1]	GISAID representatvive set[2]	WIC total
A(H1N1)pdm09	132	71	99
A(H3N2)	2886	109	394
B/Victoria	228	95	59

[1] For B/Victoria lineage the total includes 114 shared by WHO CC China

[2] For B/Victoria lineage the number includes 42 shared by WHO CC China

Since week 40/2021, 31 shipments of specimens (virus isolates and/or clinical specimens) were received at the WIC from a total of 16 EU/EEA countries and the UK (Table 3). Of the 445 samples received, 428 (96%) are type A viruses and 17 (4%) are type B viruses. Seventeen of the shipments were received in 2022, hence characterisation of many samples is 'in process'.

Table 3. Summary of seasonal influenza clinical samples and virus isolates* with collection dates after week 39/2021 contained in packages received from EU/EEA Member States

MONTH / Country	TOTAL RECEIVED Seasonal viruses	A Number received	A Number propagated[1]	H1N1pdm09 Number received	H1N1pdm09 Number propagated[1]	H3N2 Number received	H3N2 Number propagated[2]		B Number received	B Number propagated[1]	B Victoria lineage Number received	B Victoria lineage Number propagated[1]	B Yamagata lineage Number received	B Yamagata lineage Number propagated[1]
2021														
September														
Belgium	1					1	1							
Croatia	3					3	2	0						
Denmark	5					5	5							
France	11			1	0	10	9	0						
Italy	1					1	1	0						
Netherlands	13					12	in process				1	1		
Spain	1					1	in process							
Sweden	2			1	1	1	1							
UK (England)	2					2	2							
October														
Denmark	3			1	1	2	1	0						
Estonia	1					1	0	0						
France	12			9	8	3	3							
Germany	2					2	in process							
Ireland	1					1	1							
Italy	5			3	3	2	2							
Netherlands	37					37	in process							
Norway	7					7	in process							
Portugal	3					2	0		1	0				
Spain	3					3	in process							
Sweden	2					2	2							
UK (England)	8					8	8							
UK (Scotland)	5										1		4	
November														
Belgium	2					2	2							
Croatia	1			1	1									
Estonia	1					1	0	0						
France	28			18	13	10	in process							
Germany	5					4	in process				1	1		
Ireland	3					2	0				1	1		
Ireland	1					1								
Italy	5					5	5							
Netherlands	23					23	in process							
Norway	8					8	in process							
Romania	1										1	1		
Spain	35			1	1	32	in process		1	0	1	0		
Sweden	5					5	5							
UK (Scotland)	2					2								
UK (N. Ireland)	3					2			1					
December														
Belgium	15	1	in process	7	in process	7	in process							
Croatia	7			1	1	6	in process							
Estonia	7					7	in process							
France	1					1	1							
Germany	10					10	in process							
Hungary	2					2	2							
Ireland	4			1	0	3	3							
Ireland	1					1								
Latvia	5					5	5							
Netherlands	26			5	5	21	in process							
Norway	1					1	1							
Portugal	17	1	0			13	in process		1	0	2	1		
Romania	5					5	5							
Spain	50					49	in process				1	0		
2022														
January														
Belgium	16			7	in process	9	in process							
Estonia	4					4	4							
Germany	3					3	3							
Hungary	2					2	2							
Ireland	2					2	in process							
Ireland	2			1		1								
Latvia	1					1	1							
Norway	9			1	in process	8	4	0						
Romania	4			1	1	3	3							
	445	2	0	59	35	367	84	0	4	0	9	5	4	0
17 Countries		0.45%		13.3%		82.5%			0.9%		2.0%		0.9%	
		96.2%							3.8%					

*** Note: Where clinical sample and a virus isolate from the same patient were received, this is counted as one in the Total Received and following columns.**

1. Propagated to sufficient titre to perform HI assay (the totalled number does not include any from batches that are in process)
2. Propagated to sufficient titre to perform HI assay in the presence of 20nM oseltamivir (the totalled number does not include any from batches that are in process)
Numbers in red indicate viruses recovered but with insufficient HA titre to permit HI assay (H3N2 only)
Samples provided in lysis buffer, so genetic characterisation only possible

As of 2022-02-28

A total of 143 viruses from EU/EEA countries, 41 A(H1N1)pdm09, 100 A(H3N2) and two B/Victoria-lineage, have been characterised antigenically since the December 2021 report (Tables 3 to 5 respectively).

Influenza A(H1N1)pdm09 virus analyses

All recently circulating viruses have fallen into clade **6B.1A**, defined by the amino acid substitutions **S74R**, **S84N**, **S162N** (introducing a potential N-linked glycosylation site), **S164T** (which alters the glycosylation motif at residues 162 to 164), **I216T** and **I295V** in **HA1**. Within clade **6B.1A**, clusters of viruses (genetic groups) encoding a range of **HA** amino acid substitutions have emerged, with the most recently circulating viruses carrying the substitution **S183P** in **HA1**, although this is not retained in all genetic groups. Figures 1a and 1b are annotated with **HA1 S183P** substitution groups assigned for the February 2019 WHO VCM, updated for the September 2020 WHO VCM, and with a new nomenclature introduced at the September 2021 WHO VCM (**6B.1A.1 to 6B.1A.7**). The recommended vaccine viruses for the northern hemisphere 2021–2022 and 2022–2023, and southern hemisphere 2022 (egg-based A/Victoria/5270/2019-like and cell-based A/Wisconsin/588/2019-like) influenza seasons are shown in red [1, 3, 2]. The seven subclades are defined by the following HA amino acid substitutions:

1. Subclade **6B.1A.1** viruses, represented by the 2019-2020 vaccine virus **A/Brisbane/02/2018**, carry an HA gene mutation encoding **HA1 S183P** amino acid substitution.
2. Subclade **6B.1A.2** viruses, represented by **A/Denmark/2728/2019**, carry HA gene mutations encoding **HA1 S183P** and **L233I** with **HA2 V193A** amino acid substitutions – a group within this subclade has emerged with additional **HA1** amino acid substitutions of **N129D, K130N, P137S, N156K** and **K211R** (e.g. **A/Hong Kong/110/2019**).
3. Subclade **6B.1A.3** viruses, represented by **A/Norway/3737/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions.
4. Subclade **6B.1A.4** represented by **A/Hungary/20/2018** carries HA gene mutations encoding **HA1 N129D, A144E** and **S183P** amino acid substitutions.
5. Subclade **6B.1A.5** viruses carry HA gene mutations encoding **HA1 S183P** and **N260D** amino acid substitutions and splits into two groups designated **6B.1A.5a** represented by **A/Norway/3433/2018** with additional **HA1** amino acid substitutions of **N129D** and **T185A**, and **6B.1A.5b** represented by **A/Switzerland/3330/2017** with additional amino acid substitutions of **HA1 E235D** and **HA2 V193A**. Two subgroups within the **6B.1A.5a** group have been defined based on **HA1** amino acid substitutions of **D187V/A** and **Q189E** (**6B.1A.5a.1**) or **K130N**, **N156K**, **L161I** and **V250A** (**6B.1A.5a.2**).
6. Subclade **6B.1A.6** viruses, represented by **A/Ireland/84630/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions, like subclade **6B.1A.3** viruses, but fall within a separate phylogenetic branch which is closer to subclade **6B.1A.5** viruses.
7. Subclade **6B.1A.7** viruses, represented by **A/Slovenia/1489/2019**, carry HA gene mutations encoding **HA1 K302T** and **HA2 I77M, N169S** and **E179D** amino acid substitutions sometimes with additional **HA1** substitutions of **E68D, S121N** and **L161I** (e.g. **A/Moscow/193/2019**). Note: a group within this subclade has emerged with **P183S** (reversion)**, T185I, I240V** and **I286L** substitutions in **HA1** (e.g. **A/Estonia/120012/2019**).

Relatively few (132: Table 2) A(H1N1)pdm09 HA sequences from viruses with collection dates after 31 August 2021 were available in GISAID for phylogenetic analysis. The representative set chosen for phylogenetic analysis shows an apparent dominance of subgroup **6B.1A.5a.2** viruses over **6B.1A.5a.1** viruses, but the **6B.1A.5a.2** set is dominated by viruses from Bangladesh with collection dates in September through November (Figure 1a). Viruses from EU/EEA countries fell within both subgroups, with a preponderance of those from the Netherlands falling in the **6B.1A.5a.1** subgroup.

For viruses shared with and characterised by WIC a preponderance of **6B.1A.5a.1** subgroup viruses was observed, with large numbers being detected in African countries (Cameroon, Senegal and South Africa) and France where co-dominance of A(H1N1)pdm09 and A(H3N2) viruses has been reported to TESSy (Figure 1b). The smaller number of **6B.1A.5a.2** subgroup viruses received were shared by South Africa, Middle Eastern countries and EU/EEA countries (Denmark, France, Italy, Romania and Sweden).

Of the 41 A(H1N1)pdm09) viruses from EU/EEA countries characterised antigenically since the December report, 35 were **6B.1A.5a.1** subgroup, five were **6B.1A.5a.2** subgroup and one was not sequenced (Tables 3-1 to 3-3). The five **6B.1A.5a.2** subgroup viruses were recognised well, all within two-fold of the respective homologous titres, only by post-infection ferret antisera raised against **6B.1A.5a.2** viruses (cell culture-propagated A/Denmark/3280/2019 and A/Sydney/5/2021, and the vaccine virus IVR-215 [egg-cultured A/Victoria/2570/2019]). This indicates that additional **HA1** amino acid substitutions in these viruses (notably **K54Q**, **K130N**, **A186T**, **Q189E**, **E224A**, **R259K** and **K308R**), compared to A/Victoria/2570/2019, had little/no effect on the antigenicity of the test viruses. The virus for which sequence was not obtained, A/Ancona/01/2021, gave a reactivity profile with the panel of antisera typical of a virus with a **6B.1A.5a.2** HA.

HI results for **6B.1A.5a.1** subgroup test viruses are summarised in Table 3-4. The 35 test viruses were generally recognised well by eight of the antisera, notably those raised against the cell culture- and egg-propagated cultivars of A/Guangdong-Maonan/SWL1536/2019, the vaccine viruses for the northern hemisphere 2020–2021 influenza season. However, they were not well recognised by the three raised against **6B.1A.5a.2** subgroup viruses. Nevertheless, a phylogenetic cluster of **6B.1A.5a.1** viruses has emerged with **HA1 P137S** and **G155E** substitutions that showed significantly reduced HI titres with the eight antisera, notably that raised against the egg-propagated cultivar of A/Guangdong-Maonan/SWL1536/2019. Viruses from Belgium, France, the Netherlands and Spain have fallen in this cluster (Tables 3-1 to 3-3).

The great majority of A(H1N1)pdm09 viruses characterised antigenically by the WIC in the course of the 2019–2020 influenza season, with the exception of those in subgroup **6B.1A.5a.2**, were antigenically similar to A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like viruses (**6B.1A.5a.1** with **HA1 D187A** and **Q189E** amino acid substitutions), recommended for use in the northern hemisphere 2020–2021 influenza season, as assessed by haemagglutination inhibition (HI) assays with a panel of post-infection ferret antisera raised against vaccine and reference viruses. Very few A(H1N1)pdm09 viruses were available for characterisation during the 2020–2021 season due to the low number of viruses detected. Results of HI assays for viruses detected in EU/EEA countries can be seen in previous influenza characterisation reports[2].

At the recent WHO VCM, held in Geneva 21–24 February 2022, A/Victoria/2570/2019-like viruses were recommended for use in the northern hemisphere 2022–2023 influenza season [3]. This decision was largely based on the fact that antisera induced by **6B.1A.5a.1** subgroup viruses, in ferrets and humans, gave poor recognition of **6B.1A.5a.2** subgroup viruses and most of the human population are unlikely to have been exposed to **6B.1A.5a.2** subgroup viruses, given their low level circulation during the COVID-19 pandemic.

[2] https://www.ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/influenza-virus-characterisation [accessed 3 March 2022].

Figure 1a. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID, February 2022)

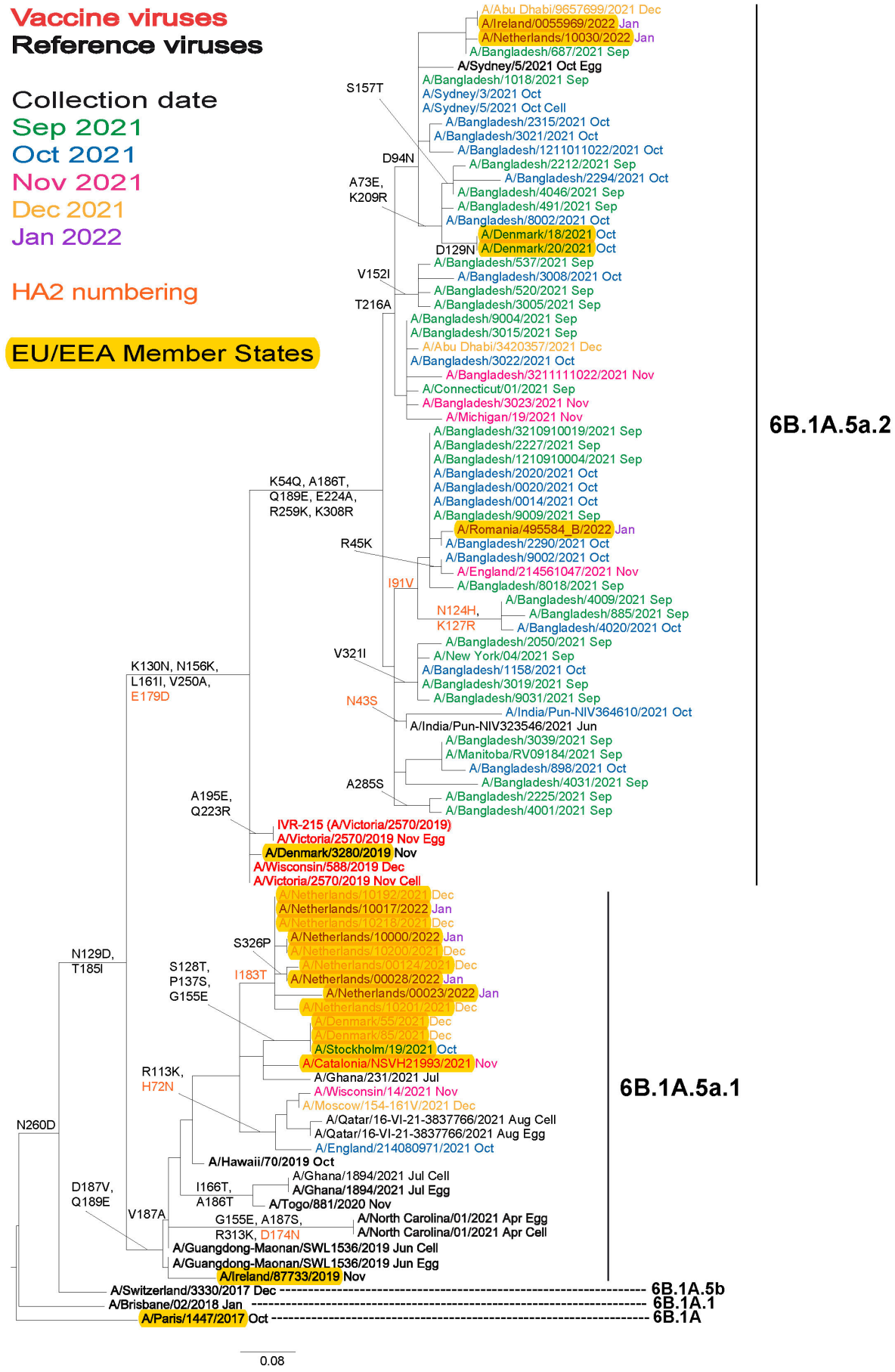


Figure 1b. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (WIC, February 2022)

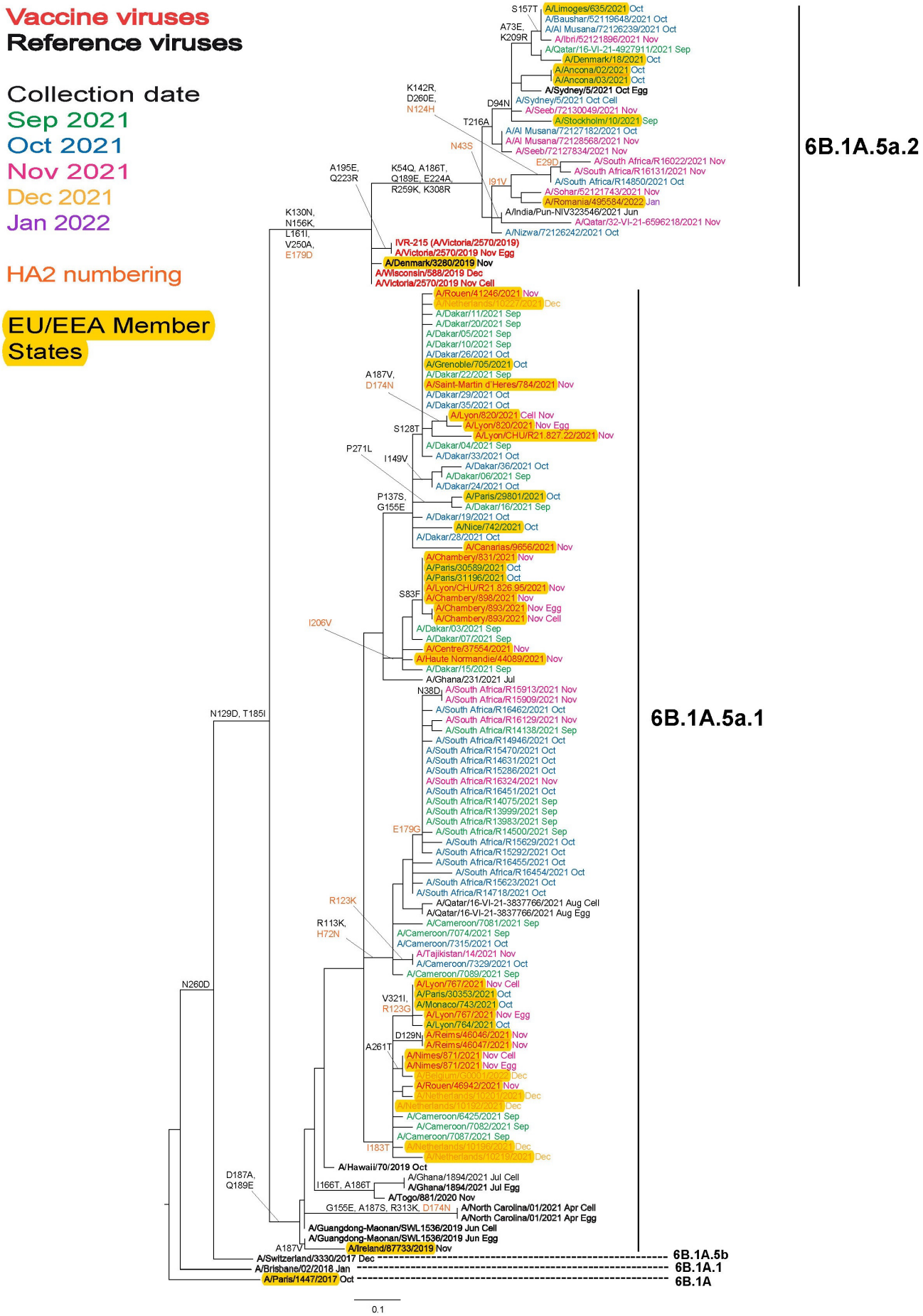


Table 3-1. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre							
					Post-infection fereret antisera							
	Substitutions in HA1 additional to clade defining substitutions	Passage history			A/Paris 1447/17* MDCK	A/Bris 02/18 Egg	A/Swit 3330/17 Egg	A/Ire 87733/19 Egg	A/G-M SWL1536/19 Egg	A/G-M SWL1536/19 MDCK	A/Denmark 3280/19 MDCK	IVR-215 A/Vic/2570/19 Egg
		Ferret number			F03/18*2	F09/19*1	F23/18*1	St Jude's F18/20*1	F12/20*1	F09/20*1	F08/20*1	F37/21*1
		Genetic group			6B.1A	6B.1A.1	6B.1A.5b	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.2	6B.1A.5a.2
REFERENCE VIRUSES												
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	1280	640	640	640	1280	1280	<	40
A/Brisbane/02/2018		6B.1A.1	2018-01-04	E3/E2	2560	1280	1280	1280	2560	2560	<	160
A/Switzerland/3330/2017	clone 35	6B.1A.5b	2017-12-20	E6/E2	640	640	1280	640	1280	1280	<	80
A/Ireland/87733/2019		6B.1A.5a.1	2019-11-03	E4	1280	640	1280	1280	2560	2560	<	160
A/Guangdong-Maonan/SWL1536/2019		6B.1A.5a.1	2019-06-17	E3/E2	1280	640	640	640	2560	2560	<	160
A/Guangdong-Maonan/SWL1536/2019		6B.1A.5a.1	2019-06-17	C2/MDCK1	1280	640	640	1280	2560	2560	<	160
A/Denmark/3280/2019		6B.1A.5a.2	2019-11-10	MDCK4/MDCK5	80	40	80	80	160	160	1280	2560
IVR-215 (A/Victoria/2570/2019)		6B.1A.5a.2	2018-11-22	E4/D7/E2	<	40	40	80	80	160	1280	2560
TEST VIRUSES												
A/Limoges/635/2021	A73E, D94N, S157T, K209R, T216A	6B.1A.5a.2	2021-10-06	MDCK2/MDCK1	<	<	<	<	<	40	640	1280
A/Stockholm/10/2021	D94N, T216A	6B.1A.5a.2	2021-09-13	SIAT1/MDCK1	<	<	40	40	40	40	1280	2560
A/Paris/30589/2021	S83F, T164X(-CHO)	6B.1A.5a.1	2021-10-18	MDCK2/MDCK1	1280	640	640	1280	2560	2560	<	160
A/Paris/31196/2021	S83F	6B.1A.5a.1	2021-10-19	MDCK2/MDCK1	2560	640	640	640	2560	2560	<	80
A/Monaco/743/2021	V321I	6B.1A.5a.1	2021-10-26	MDCK2/MDCK1	1280	640	640	640	2560	1280	40	80
A/Lyon/764/2021	V321I	6B.1A.5a.1	2021-10-27	MDCK2/MDCK1	1280	320	320	640	1280	1280	<	80
A/Lyon/767/2021	A187X, V321I	6B.1A.5a.1	2021-11-01	MDCK2/MDCK1	1280	320	640	640	1280	1280	<	80
A/Chambery/831/2021	S83F	6B.1A.5a.1	2021-11-16	MDCK2/MDCK1	1280	320	640	640	1280	1280	<	80
A/Chambery/898/2021	S83F	6B.1A.5a.1	2021-11-19	MDCK2/MDCK1	1280	640	640	1280	2560	1280	<	80
A/Nimes/871/2021	A261T	6B.1A.5a.1	2021-11-19	MDCK3/MDCK1	1280	320	320	640	1280	1280	<	80
A/Reims/46047/2021	D129N	6B.1A.5a.1	2021-11-28	MDCK1/MDCK1	1280	640	640	640	2560	1280	<	80
A/Centre/37554/2021	D35N	6B.1A.5a.1	2021-11-02	MDCK2/MDCK1	640	640	640	640	1280	1280	<	160
A/Lyon/CHU/R21.826.95/2021	S83F	6B.1A.5a.1	2021-11-19	MDCK2/MDCK1	640	320	320	640	1280	1280	<	80
A/Reims/46046/2021	D129N	6B.1A.5a.1	2021-11-21	MDCK2/MDCK1	640	320	640	320	1280	1280	<	40
A/Chambery/893/2021	S83F	6B.1A.5a.1	2021-11-23	MDCK2/MDCK1	640	320	320	320	1280	1280	<	80
A/Grenoble/705/2021	D127X, S128T, P137S, G155E	6B.1A.5a.1	2021-10-23	MDCK2/MDCK1	320	160	160	320	320	640	<	80
A/Nice/742/2021	P137S, G155E, T164X(-CHO), K308E	6B.1A.5a.1	2021-10-24	MDCK2/MDCK1	160	80	80	160	320	640	<	80
A/Saint-Martin d'Heres/784/2021	D127X, S128T, P137S, G155E	6B.1A.5a.1	2021-11-02	MDCK2/MDCK1	160	160	160	160	160	640	<	80
A/Canarias/9656/2021	R113K, P137S, G155E, I298V, L314M	6B.1A.5a.1	2021-11-08	SIAT1/MDCK1	160	80	80	160	160	320	<	80
A/Rouen/41246/2021	S128T, P137S, G155E, E224D	6B.1A.5a.1	2021-11-15	MDCK2/MDCK1	160	80	160	160	160	320	<	80
A/Lyon/820/2021	S128T, P137S, G155E, N162X(-CHO), A187X	6B.1A.5a.1	2021-11-16	MDCK2/MDCK1	160	80	80	160	160	640	<	80
A/Lyon/CHU/R21.827.22/2021	S128T, D129G, P137S, G155E	6B.1A.5a.1	2021-11-20	MDCK2/MDCK1	160	80	80	160	160	320	<	40
A/Paris/29801/2021	P137S, G155E, T216K, P271L	6B.1A.5a.1	2021-10-10	MDCK1/MDCK1	80	80	80	80	160	320	<	40
						Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22 SH 2022 NH 2022-23

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80; ND = Not Done

Table 3-2. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Substitutions in HA1 additional to clade defining substitutions	Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection fereret antisera										NEW
		Passage history			A/Paris	A/Bris	A/Swit	A/Ire	A/G-M	A/G-M	A/Ghana	A/Denmark	IVR-215	A/Sydney
					1447/17	02/18	3330/17	87733/19	SWL1536/19	SWL1536/19	1894/21	3280/19	A/Vic/2570/19	5/21
					MDCK	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	Egg	Egg
		Ferret number			F03/18*2	F09/19*1	F23/18*1	St Jude's F18/20*1	F12/20*1	F09/20*1	F02/22*1	F08/20*1	F37/21*1	F04/22*1
		Genetic group			6B.1A	6B.1A.1	6B.1A.5b	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.2	6B.1A.5a.2	6B.1A.5a.2
REFERENCE VIRUSES															
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	2560	1280	640	640	2560	1280	640	<	80	40
A/Brisbane/02/2018		6B.1A.1	2018-01-04	E3/E2	2560	1280	640	1280	2560	2560	1280	40	160	80
A/Switzerland/3330/2017	clone 35	6B.1A.5b	2017-12-20	E6/E2	1280	640	640	640	1280	1280	640	<	80	80
A/Ireland/87733/2019		6B.1A.5a.1	2019-11-03	E4	2560	1280	640	1280	2560	2560	1280	<	160	80
A/Guangdong-Maonan/SWL1536/2019		6B.1A.5a.1	2019-06-17	E3/E2	2560	640	640	1280	2560	2560	1280	<	160	80
A/Guangdong-Maonan/SWL1536/2019		6B.1A.5a.1	2019-06-17	C2/MDCK1	1280	640	320	640	2560	1280	1280	<	80	80
A/Ghana/1894/2021		6B.1A.5a.1	2021-07-21	E2	2560	1280	640	1280	>5120	>5120	>5120	40	320	160
A/Denmark/3280/2019		6B.1A.5a.2	2019-11-10	MDCK4/MDCK5	160	80	40	80	80	160	40	2560	2560	2560
IVR-215 (A/Victoria/2570/2019)		6B.1A.5a.2	2018-11-22	E4/D7/E2	80	80	40	80	160	160	40	1280	2560	2560
A/Sydney/5/2021		6B.1A.5a.2	2021-10-16	E3/E1	80	40	40	40	80	80	80	640	1280	1280
TEST VIRUSES															
A/Ancona/01/2021		no sequence	2021-10-19	MDCK3/MDCK1	<	<	<	<	<	<	<	640	1280	640
A/Ancona/02/2021	D94N, T216A, E268X	6B.1A.5a.2	2021-10-24	MDCK3/MDCK1	40	40	40	<	80	80	80	1280	2560	2560
A/Ancona/03/2021	D94N, T216A, E268X	6B.1A.5a.2	2021-10-26	MDCK3/MDCK1	40	40	40	40	40	40	<	1280	2560	2560
A/Romania/495584/2022		6B.1A.5a.2	2022-01-04	SIAT1/MDCK1	40	40	40	80	80	80	40	2560	>5120	>5120
A/Nimes/871/2021	A261T	6B.1A.5a.1	2021-11-19	E1/E1	1280	640	640	1280	2560	1280	1280	<	160	80
A/Chambery/893/2021	S93F	6B.1A.5a.1	2021-11-23	E1/E1	1280	640	640	1280	2560	2560	2560	80	320	160
A/Netherlands/10192/2021	Y7X	6B.1A.5a.1	2021-12-19	MDCK-MIX2/MDCK1	2560	640	640	1280	2560	2560	2560	<	80	160
A/Netherlands/10196/2021	P218X	6B.1A.5a.1	2021-12-20	MDCK-MIX2/MDCK1	2560	1280	1280	1280	2560	2560	2560	<	160	80
A/Netherlands/10201/2021		6B.1A.5a.1	2021-12-26	MDCK-MIX2/MDCK1	2560	1280	1280	1280	2560	2560	2560	80	160	80
A/Netherlands/10219/2021	F200X, S326P	6B.1A.5a.1	2021-12-29	MDCK-MIX2/MDCK1	2560	1280	1280	2560	>5120	>5120	2560	40	160	160
A/Lyon/767/2021	A187X, V321I	6B.1A.5a.1	2021-11-01	E2/E1	640	320	320	640	1280	1280	640	<	80	80
A/Netherlands/10227/2021	D127X, S128T, P137S, G155E	6B.1A.5a.1	2021-12-30	MDCK-MIX2/MDCK1	320	160	160	160	320	640	640	<	80	80
A/Lyon/820/2021	S128T, P137S, G155E, N162X(-CHO), A187X	6B.1A.5a.1	2021-11-16	E1/E1	160	160	160	160	320	640	320	<	80	80
						Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21				Vaccine SH 2021 NH 2021-22 SH 2022 NH 2022-23		

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80; ND = Not Done

Table 3-3. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection fereret antisera											
	Substitutions in HA1 additional to clade defining substitutions		Passage history	A/Paris 1447/17 MDCK	A/Bris 02/18 Egg	A/Swit 3330/17 Egg	A/Ire 87733/19 Egg St Jude's	A/G-M SWL1536/19 Egg	A/G-M SWL1536/19 MDCK	A/Ghana 1894/21 Egg	A/N Carolina 01/21 Cell CDC	A/Denmark 3280/19 MDCK	IVR-215 A/Vic/2570/19 Egg	A/Sydney 5/21 Egg
			Ferret number	F03/18[*2]	F09/19[*1]	F23/18[*1]	F18/20[*1]	F12/20[*1]	F09/20[*1]	F02/22[*1]	F2021-105	F08/20[*1]	F37/21[*1]	F04/22[*1]
			Genetic group	6B.1A	6B.1A.1	6B.1A.5b	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.2	6B.1A.5a.2	6B.1A.5a.2
REFERENCE VIRUSES															
A/Paris/1447/2017		2017-10-20	MDCK1/MDCK3	2560	1280	640	640	2560	1280	640	80	<	80	40
A/Brisbane/02/2018		2018-01-04	E3/E2	2560	1280	640	1280	2560	2560	1280	80	40	160	80
A/Switzerland/3330/2017	clone 35	2017-12-20	E6/E2	1280	640	1280	640	1280	1280	640	80	<	80	40
A/Ireland/87733/2019		2019-11-03	E4	2560	1280	640	640	2560	2560	640	160	<	160	40
A/Guangdong-Maonan/SWL1536/2019		2019-06-17	E3/E2	2560	640	640	1280	1280	2560	640	160	<	160	40
A/Guangdong-Maonan/SWL1536/2019		2019-06-17	C2/MDCK1	1280	640	320	640	2560	1280	1280	160	<	80	80
A/Ghana/1894/2021		2021-07-21	E2	2560	1280	1280	1280	>5120	>5120	2560	1280	ND	ND	160
A/North Carolina/01/2021			SIAT3/MDCK1	160	80	80	80	160	640	640	640	<	<	40
A/Denmark/3280/2019		2019-11-10	MDCK4/MDCK6	160	80	40	80	80	160	40	40	2560	2560	2560
IVR-215 (A/Victoria/2570/2019)		2018-11-22	E4/D7/E2	80	80	40	80	160	160	80	160	1280	2560	1280
A/Sydney/5/2021		2021-10-16	E3/E1	80	40	40	40	80	80	40	80	1280	2560	2560
TEST VIRUSES														
A/Belgium/S0063/2022		2021-12-07	MDCK1	1280	320	640	640	1280	1280	1280	320	<	80	80
A/Belgium/G0001/2022	A261T	2021-12-17	MDCK1	1280	320	320	640	1280	1280	1280	640	<	40	80
A/Belgium/H0007/2022	P137S, G155E, T164I(-CHO)	2022-01-11	MDCK1	160	80	80	160	160	640	640	640	<	40	40
A/Belgium/H0038/2022	S326P	2022-01-17	MDCK1	640	320	320	640	1280	1280	640	320	<	40	40
A/Belgium/H0042/2022	D86N, V234L	2022-01-20	MDCK1	1280	320	640	640	1280	1280	1280	640	<	80	80
					Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21					Vaccine SH 2021 NH 2021-22 SH 2022 NH 2022-23	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80; ND = Not Done

Table 3-4. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI: Summary for 6B.1A.5a.1 viruses

Viruses		Haemagglutination inhibition titre										
		Post-infection fereret antisera										
	A/Paris 1447/17	A/Bris 02/18	A/Swit 3330/17	A/Ire 87733/19	A/G-M SWL1536/19	A/G-M SWL1536/19	A/Ghana 1894/21	A/N Carolina 01/21	A/Denmark 3280/19	IVR-215 A/Vic/2570/19	A/Sydney 5/21
Passage history	MDCK	Egg	Egg	Egg	Egg	MDCK	Egg	Cell	MDCK	Egg	Egg
Ferret number	F03/18*2	F09/19*1	F23/18*1	St Jude's F-18/20*1	F12/20*1	F09/20*1	F02/22*1	CDC F2021-105	F08/20*1	F37/21*1	F04/22*1
Genetic group	6B.1A	6B.1A.1	6B.1A.5b	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.1	6B.1A.5a.2	6B.1A.5a.2	6B.1A.5a.2
REFERENCE VIRUSES											
A/Paris/1447/2017	6B.1A	2560	1280	640	640	2560	1280	640	80	<	80	40
A/Brisbane/02/2018	6B.1A.1	2560	1280	640	1280	2560	2560	1280	80	40	160	80
A/Switzerland/3330/2017	6B.1A.5b	1280	640	1280	640	1280	1280	640	80	<	80	40
A/Ireland/87733/2019	6B.1A.5a.1	2560	1280	640	640	2560	2560	640	160	<	160	40
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2560	640	640	1280	1280	2560	640	160	<	160	40
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	1280	640	320	640	2560	1280	1280	160	<	80	80
A/Ghana/1894/2021	6B.1A.5a.1	2560	1280	1280	1280	>5120	2560	640	1280	ND	ND	160
A/North Carolina/01/2021	6B.1A.5a.1	160	80	80	80	160	640	640	40	<	<	40
A/Denmark/3280/2019	6B.1A.5a.2	160	80	40	80	80	160	40	40	2560	2560	2560
IVR-215 (A/Victoria/2570/2019)	6B.1A.5a.2	80	80	40	80	160	160	80	160	1280	2560	1280
A/Sydney/5/2021	6B.1A.5a.2	80	40	40	40	80	80	40	80	1280	2560	2560
TEST VIRUSES												
Number tested	6B.1A.5a.1	35	35	35	35	35	35	14	5	35	35	14
No with titre reduction ≤2-fold		22	12	18	22	23	27	8	5			
%		*62.9*	*34.3*	*51.4*	*62.9*	*65.7*	*77.2*	*57.2*	*100*			
No with titre reduction =4-fold		3	12	8	4	1	4	3				
%		*8.5*	*34.3*	*22.9*	*11.4*	*2.9*	*11.4*	*21.4*				
No with titre reduction ≥8-fold		10	11	9	9	11	4	3		35	35	14
%		*28.6*	*31.4*	*25.7*	*25.7*	*31.4*	*11.4*	*21.4*		*100*	*100*	*100*
		Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21					Vaccine SH 2021 NH 2021-22 SH 2022 NH 2022-23		

Reference virus results are taken from an individual table as an example. Summaries for each antiserum are based on fold-reductions observed on the days that HI

Influenza A(H3N2) virus analyses

The first A(H3N2) HA phylogeny was generated using a representative set of non-WIC generated HA gene sequences released in GISAID, as of 8 February 2022, for viruses with collection dates in the 2021−2022 influenza season (Figure 2a). The second phylogeny is based on A(H3N2) HA sequences generated at the WIC for viruses with collection dates during the 2021−2022 influenza season (Figure 2b).

Viruses in clade **3C.2a** have been dominant since the 2014-15 influenza season, with group **3C.2a1b** viruses predominating over the course of the 2019−2020 season in most WHO-defined Regions of the world, but for the European Region where there was equivalence of clade **3C.3a** viruses. The HA gene sequences of viruses in both clades **3C.2a** and **3C.3a** continue to diverge. Notably, clade **3C.3a.1** viruses have evolved to carry **HA1** amino acid substitutions of **L3I, S91N**, **N144K** (loss of a N-linked glycosylation motif at residues 144-146), **F193S** and **K326R**, and **D160N** in **HA2**, compared with cell culture-propagated A/Stockholm/6/2014. Greater variation has been observed among clade **3C.2a** viruses, resulting in the designation of new subclades/groups/subgroups. Amino acid substitutions that define these subclades/groups/subgroups are:

- Subclade **3C.2a1**: those in clade **3C.2a** plus **N171K** in **HA1** and **I77V** and **G155E** in **HA2**, most also carry **N121K** in **HA1**, e.g. **A/Singapore/INFIMH-16-0019/2016** (a former vaccine virus).
- Group **3C.2a1a**: those in subclade **3C.2a1** plus **T135K** in **HA1**, resulting in the loss of a potential glycosylation site, and **G150E** in **HA2**, e.g. **A/Greece/4/2017.**
- Group **3C.2a1b**: those in subclade **3C.2a1** plus **E62G, R142G** and **H311Q** in **HA1**, often with additional amino acid substitutions – notably **HA1 T135K** (resulting in the loss of a potential glycosylation site) commonly with **T128A** (resulting in the loss of a potential glycosylation site), the **3C.2a1b.1** subgroup (e.g. **A/La Rioja/2202/2018**) or **HA1 T131K** and **HA2 V200I**, the **3C.2a1b.2** subgroup (e.g. **A/South Australia/34/2019**). Distinct clusters of viruses within both of these subgroups have emerged, defined by specific **HA1** and/or **HA2** amino acid substitutions: **3C.2a1b.1a** with additional amino acid substitutions of **HA1 A138S**, **F193S** and **S198P**, many also with **G186D** and **D190N** (e.g. **A/Denmark/3284/2019**); **3C.2a1b.1b** with additional amino acid substitutions of **HA1 S137F, A138S** and **F193S** (e.g. **A/Hong Kong/2671/2019**); **3C.2a1b.2a** with additional amino acid substitutions of **HA1 K83E** and **Y94N** with **HA2 I193M** (e.g. **A/Slovenia/1637/2020**); **3C.2a1b.2b** with **HA2 V18M** substitution, often with additional **HA1** substitutions (e.g. **A/Bretagne/1323/2020**).
- Clade **3C.3a**: represented by a former vaccine virus, **A/Switzerland/9715293/2013**, with recently circulating clade **3C.3a.1** viruses carrying additional substitutions of **S91N, N144K** (resulting in the loss of a potential glycosylation site)**, and F193S** in **HA1** and **D160N** in **HA2** (e.g. **A/England/538/2018** and **A/Kansas/14/2017**, the A(H3N2) vaccine virus for the 2019−2020 northern hemisphere influenza season.

The significant geographical spread of viruses in the antigenically distinct **3C.2a1b.1b** cluster influenced the selection of an A/Hong Kong/2671/2019-like or an A/Hong Kong/45/2019-like virus as the A(H3N2) component of vaccines for the 2020−2021 northern hemisphere and 2021 southern hemisphere influenza seasons.

Figure 2a indicates a single **3C.3a.1** virus and small numbers of **3C.2a1b.1b** and **3C.2a1b.1a** (notably in Africa) viruses to have been detected and characterised during the 2021−2022 influenza season. The great majority of viruses with collection dates after 31 August 2021 were 'Bangladesh-like' (**3C.2a1b.2a.2** with **HA1** substitutions of **Y159N**, **T160I** (loss of a glycosylation site), **L164Q**, **G186D**, **D190N** and **Y195F**). The latter viruses were split into four subgroups defined by specific **HA1** amino acid substitutions: (i) **S205F** and **A212T**; (ii) **H56Y** and **S270T**; (iii) **D53N**, commonly with **N96S** and **I192F**; (iv) **D53G** often with **I25V**, **R201K** and **S219Y** or **D104G** and **K276R**. Subgroups (iii) and (iv) also share **HA1 H156S** amino acid substitution.

The second phylogeny, based on WIC generated sequences from samples shared by many countries, shows a very similar profile with the vast majority of sequences being derived from 'Bangladesh-like' (**3C.2a1b.2a.2**) viruses (Figure 2b). Small numbers of viruses were 'Cambodia-like' (**3C.2a1b.2a.1** with **HA1** substitutions of **K171N**, **G186S** and **S198P**) – one from Estonia and two from Italy. Similarly, small numbers of **3C.2a1b.1a** viruses were shared by countries in the WHO African (Algeria and South Africa), European (Belgium, France, Italy, Sweden and Switzerland) and Middle Eastern (Lebanon and Oman) Regions and **3C.2a1b.1b** viruses were received from Africa (Madagascar and South Africa) and Europe (Armenia and France [and French overseas territories]). In both phylogenies sequences derived from samples collected in EU/EEA countries are dispersed throughout the trees.

'Bangladesh-like' **3C.2a1b.2a.2** viruses, A/Darwin/9/2021 and A/Darwin/6/2021 for egg- and cell-based vaccines respectively, were recently recommended for use in the southern hemisphere 2022 and northern hemisphere 2022−2023 influenza seasons [2,3].

The locations of HA sequences for egg- and cell culture-propagated cultivars of A/Cambodia/e0826360/2020 (**3C.2a1b.2a.1**) recommended for use in northern hemisphere 2021−2022 vaccines [1], are indicated on the phylogenies, as are egg- and cell-culture based vaccines to be used in the 2022 southern hemisphere and northern hemisphere seasons, A/Darwin/9/2021 and A/Darwin/6/2021 (**3C.2a1b.2a.2**) respectively [2,3] (Figures 2a and 2b).

As described in many previous reports[3], influenza A(H3N2) viruses had been difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells (RBCs) from guinea pigs, turkeys, and humans, often with the loss of ability to agglutinate any of these RBCs. As was highlighted first in the November 2014 report[4], this was a significant problem for most viruses that fell in genetic clade **3C.2a**, although there was some alleviation of this during 2019−2020, with continuation into the 2020−2021 influenza season. This issue has now significantly improved for 'Bangladesh-like' **3C.2a1b.2a.2** viruses which agglutinate guinea pig RBCs well, allowing HI assays to be performed. At the time of writing this report no A(H3N2) viruses recovered failed to agglutinate guinea pig RBCs (Table 3).

While the number of detections of seasonal influenza viruses was low from April 2020 to July 2021 compared to previous years, the WHO Collaborating Centres for Influenza have shown viruses in these emerged virus clusters to be antigenically distinguishable from one another and other A(H3N2) virus subgroups.

Of the 100 A(H3N2) viruses characterised antigenically since the December report, 92 were 'Bangladesh-like' **3C.2a1b.2a.2** viruses, two were 'Cambodia-like' **3C.2a1b.2a.1**, three were **3C.2a1b.1b**, two were **3C.2a1b.1a** viruses and one virus was not sequenced (Tables 4-1 to 4-5). The **3C.2a1b.1a** viruses were recognised well, within four-fold of the respective homologous titres, for antisera raised against cell culture-propagated viruses A/Denmark/3264/2019 (1a), A/Hong Kong/2671/2019 (1b), A/Cambodia/925256/2020 (2a.1) and A/Bangladesh/4005/2020 (2a.2); **3C.2a1b.1b** viruses by antisera raised against cell culture-propagated A/Denmark/3264/2019 (1a), A/Hong Kong/2671/2019 (1b) and A/Cambodia/925256/2020 (2a.1); **3C.2a1b.2a.1** viruses showed somewhat broader reactivity with at least one of two viruses showing good reactivity with seven of the antisera – reactivity was poor with the antiserum raised against egg-propagated A/Darwin/9/2021 (2a.2), but yielded HI titres of 320 with both test viruses.

A summary of the HI results for the 92 'Bangladesh-like' **3C.2a1b.2a.2** test viruses is given in Table 4-6. These viruses were only recognised well by post-infection ferret antisera raised against viruses with 3C.2a1b.2a.2 HAs. Antisera raised against cell culture-propagated A/Bangladesh/4005/2020 and A/Stockholm/5/2021 recognised 81 (88%) and 80 (87%) of the test viruses at titres within four-fold of the homologous titres, respectively. The antiserum raised against egg-propagated A/Darwin/9/2021 recognised 67 (73%) of the test viruses at titres within four-fold of the homologous titres. The virus for which sequence was not obtained, A/Baleares/9868/2021, gave a reactivity profile with the panel of antisera typical of a virus with a 3C.2a1b.2a.2 HA.

Results of HI assays with panels of post-infection ferret antisera raised against A(H3N2) vaccine and reference viruses for viruses detected in EU/EEA countries can be seen in previous influenza characterisation reports on ECDC's website. Overall, these data show strong clade/subclade-specific recognition of test viruses by post-infection ferret antisera raised against cell culture-propagated reference viruses, with limited cross-clade/subclade recognition and further reductions in recognition of cell culture-propagated recently circulating viruses by antisera raised against A(H3N2) egg-propagated vaccine viruses.

[3] For example, the September 2013 report: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2013. Stockholm: ECDC; 2013. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf

[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2014. Stockholm: ECDC; 2014. Available from: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf

Figure 2a. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID, February 2022)

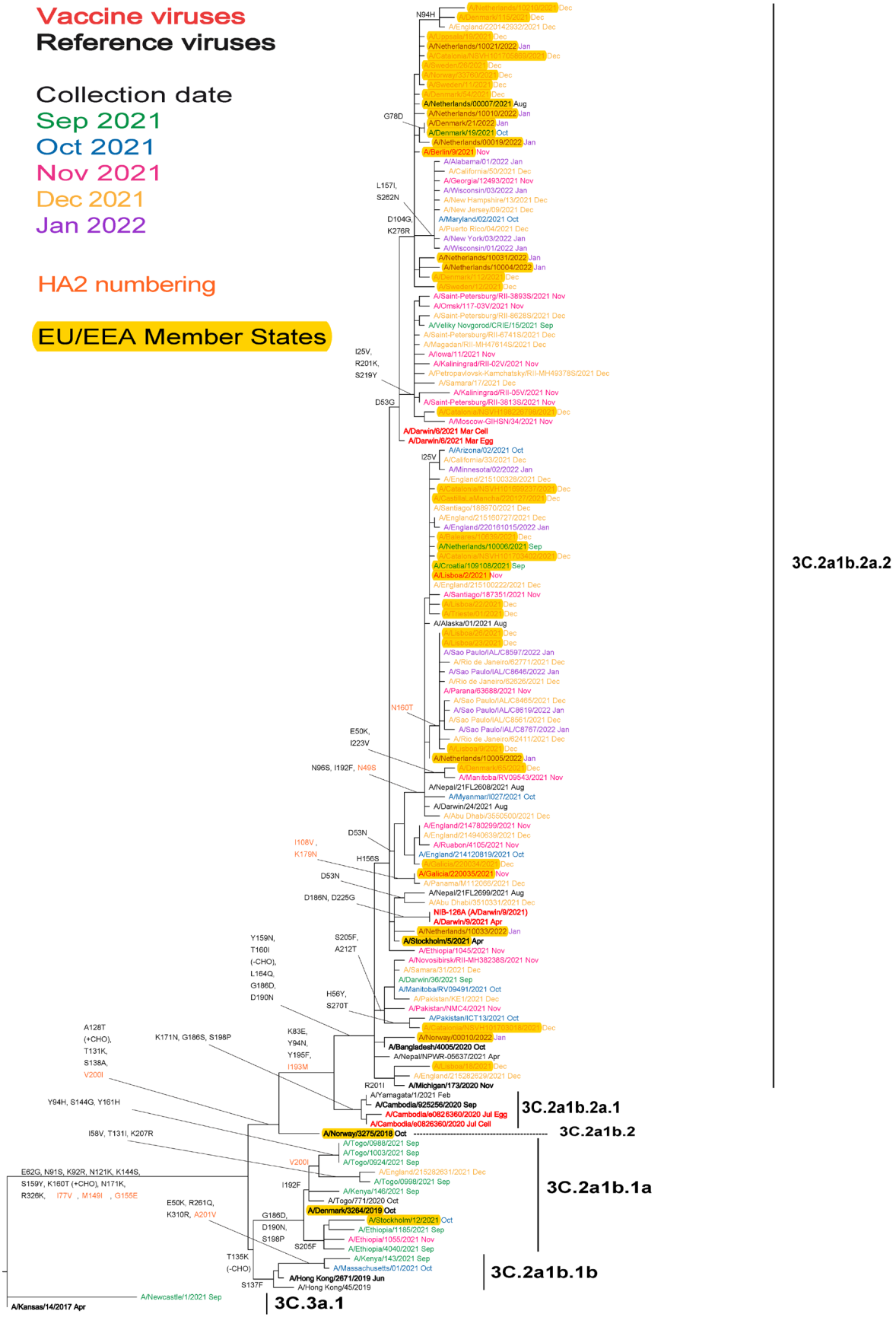


Figure 2b. Phylogenetic comparison of influenza A(H3N2) HA genes (WIC, February 2022)

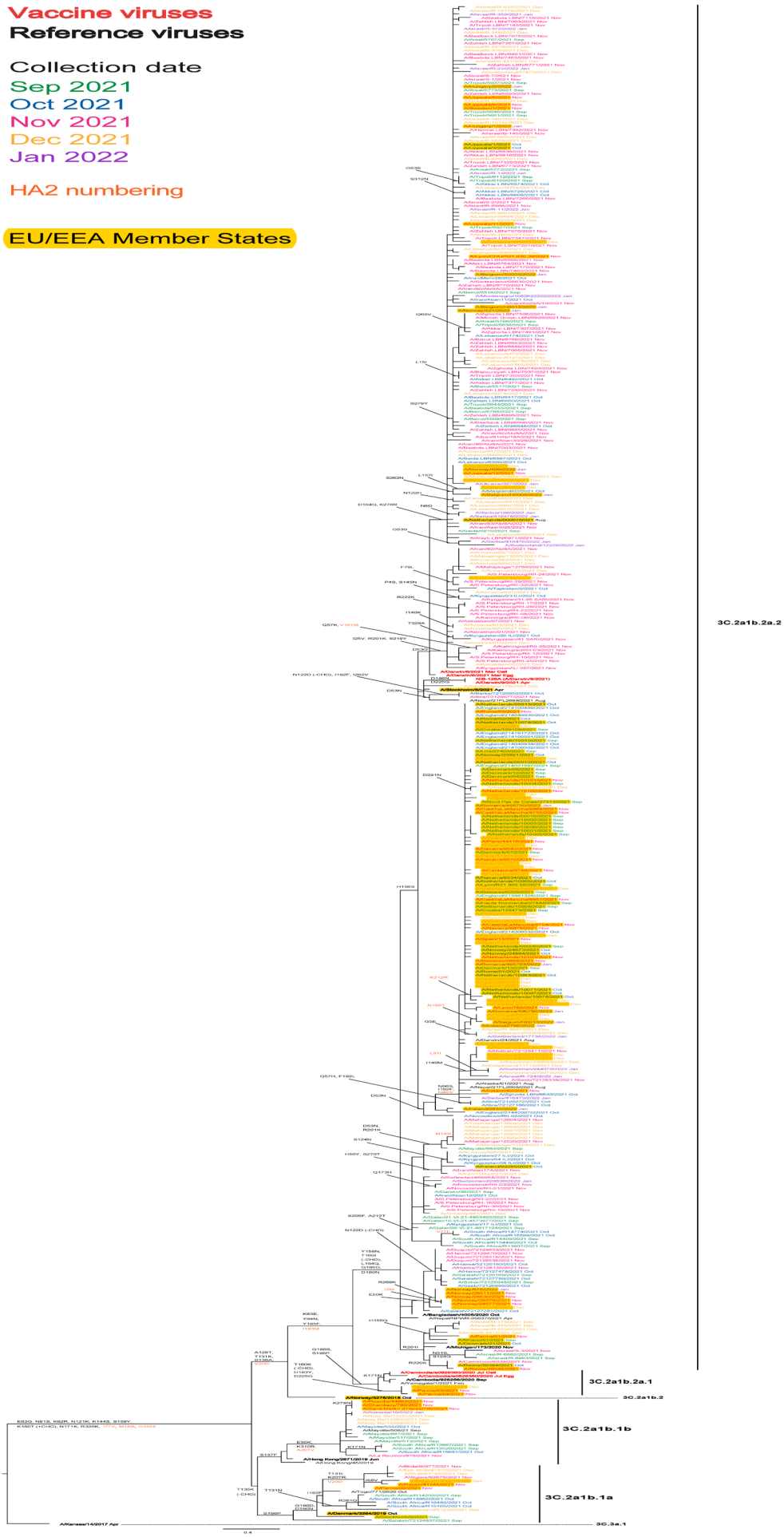


Table 4-1. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre							
					Post-infection ferret antisera							
		Passage history			A/Denmark 3264/19	A/HK 2671/19	A/Camb e0826360/20	A/Camb 925256/20	A/Bang 4005/20	A/Darwin 9/21	A/Stock 5/21	A/Kansas 14/17
					SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT
		Ferret number			F19/20*1	St Judes F21/20*1	F10/21*1	F03/21*1	F07/21*1	F38/21*1	F35/21*1	F17/19*1
		Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019		3C.2a1b.1a	2019-10-25	SIAT5	640	640	160	640	320	320	160	160
A/Hong Kong/2671/2019		3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	640	640	160	640	320	320	160	160
A/Cambodia/e0826360/2020		3C.2a1b.2a.1	2020-07-16	E5/E2	320	<	2560	160	320	320	320	80
A/Cambodia/925256/2020		3C.2a1b.2a.1	2020-09-25	SIAT4	160	160	160	640	320	320	160	80
A/Bangladesh/4005/2020		3C.2a1b.2a.2	2020-10-04	SIAT3	320	80	320	160	640	640	640	320
A/Darwin/9/2021		3C.2a1b.2a.2	2021-04-17	E3/E2	320	40	320	80	640	2560	640	80
A/Stockholm/5/2021		3C.2a1b.2a.2	2021-04-16	S0/S3	160	40	80	80	320	1280	640	40
A/Kansas/14/2017		3C.3a.1	2017-12-14	SIAT3/SIAT2	80	40	40	80	80	160	160	640
TEST VIRUSES												
A/Chambery/760/2021		3C.2a1b.1b	2021-11-01	MDCK2/SIAT1	640	320	<	320	40	80	<	<
A/Saint-Martin d'Heres/785/2021		3C.2a1b.1b	2021-11-03	MDCK2/SIAT1	160	320	<	160	40	<	<	<
A/Picardie/44663/2021		3C.2a1b.1b	2021-11-24	MDCK1/SIAT1	160	160	<	320	40	40	<	<
A/Baleares/9868/2021		no sequence	2021-11-26	SIAT1/SIAT1	40	<	40	40	160	640	320	<
A/Nord Pas de Calais/27313/2021		3C.2a1b.2a.2	2021-09-09	MDCK1/SIAT1	40	<	40	40	160	640	320	<
A/Haute Normandie/27444/2021		3C.2a1b.2a.2	2021-09-11	MDCK1/SIAT1	80	<	80	40	160	640	320	<
A/Lille/27403/2021		3C.2a1b.2a.2	2021-09-13	MDCK1/SIAT1	80	<	80	80	160	1280	320	<
A/Lyon/R21.800.58/2021		3C.2a1b.2a.2	2021-09-16	MDCK2/SIAT1	40	<	40	40	160	320	160	<
A/Reims/30384/2021		3C.2a1b.2a.2	2021-10-08	MDCK2/SIAT2	640	40	640	160	1280	1280	1280	320
A/Norway/23621/2021		3C.2a1b.2a.2	2021-10-13	SIAT1	40	<	40	40	160	640	320	<
A/Navarra/9534/2021		3C.2a1b.2a.2	2021-10-16	SIAT1/SIAT1	80	<	80	40	160	640	320	<
A/Norway/24873/2021		3C.2a1b.2a.2	2021-10-24	SIAT1	40	<	40	80	160	640	320	<
A/Norway/24864/2021		3C.2a1b.2a.2	2021-10-26	SIAT1	40	<	40	40	160	640	320	<
A/Netherlands/10071/2021		3C.2a1b.2a.2	2021-10-26	MDCK-MIX2/SIAT1	<	<	40	40	160	640	160	<
A/Netherlands/10074/2021		3C.2a1b.2a.2	2021-10-28	MDCK-MIX2/SIAT1	<	<	40	40	80	640	160	<
A/Netherlands/10087/2021		3C.2a1b.2a.2	2021-10-31	MDCK-MIX2/SIAT1	40	<	40	40	160	640	160	<
A/Lyon/782/2021		3C.2a1b.2a.2	2021-11-06	MDCK2/SIAT1	40	<	40	40	160	320	160	<
A/Navarra/9643/2021		3C.2a1b.2a.2	2021-11-06	SIAT1/SIAT1	40	<	40	40	160	640	160	<
A/Cantabria/9788/2021		3C.2a1b.2a.2	2021-11-15	SIAT1/SIAT1	40	<	40	40	160	640	320	<
A/Castilla La Mancha/9869/2021		3C.2a1b.2a.2	2021-11-16	SIAT1/SIAT1	40	<	40	40	80	640	160	<
A/Norway/28578/2021		3C.2a1b.2a.2	2021-11-19	SIAT1	320	40	160	160	640	640	640	160
A/Norway/28830/2021		3C.2a1b.2a.2	2021-11-21	SIAT1	320	40	160	160	640	640	1280	160
A/Norway/28577/2021		3C.2a1b.2a.2	2021-11-21	SIAT1	320	80	160	160	1280	1280	1280	160
A/Lyon/CHU- R21.830.39/2021		3C.2a1b.2a.2	2021-11-22	MDCK2/SIAT1	80	<	40	40	160	1280	640	<
A/Norway/29511/2021		3C.2a1b.2a.2	2021-11-25	SIAT1	320	80	160	160	640	1280	640	160
A/Reims/46045/2021		3C.2a1b.2a.2	2021-11-30	MDCK1/SIAT1	160	40	320	80	640	640	320	160
A/Paris/47350/2021		3C.2a1b.2a.2	2021-12-02	MDCK1/SIAT1	40	<	40	80	160	640	320	<
							Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40, ND = Not Done

Table 4-2. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre							
					Post-infection ferret antisera							
					A/Denmark 3264/19	A/HK 2671/19	A/Camb e0826360/20	A/Camb 925256/20	A/Bang 4005/20	A/Darwin 9/21	A/Stock 5/21	A/Kansas 14/17
		Passage history			SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT
		Ferret number			F19/20[*1]	St Judes F21/20[*1]	F10/21[*1]	F03/21[*1]	F07/21[*1]	F38/21[*1]	F35/21[*1]	F17/19[*1]
		Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019		3C.2a1b.1a	2019-10-25	SIAT5	640	640	320	640	320	320	320	160
A/Hong Kong/2671/2019		3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	640	160	640	160	320	160	160
A/Cambodia/e0826360/2020		3C.2a1b.2a.1	2020-07-16	E5/E2	320	<	2560	160	320	320	320	80
A/Cambodia/925256/2020		3C.2a1b.2a.1	2020-09-25	SIAT4	160	160	160	640	320	320	160	160
A/Bangladesh/4005/2020		3C.2a1b.2a.2	2020-10-04	SIAT3	320	80	320	320	640	640	640	320
A/Darwin/9/2021		3C.2a1b.2a.2	2021-04-17	E3/E2	320	40	320	80	640	2560	640	80
A/Stockholm/5/2021		3C.2a1b.2a.2	2021-04-16	S0/S3	160	40	80	80	320	1280	640	40
A/Kansas/14/2017		3C.3a.1	2017-12-14	SIAT3/SIAT2	80	40	40	80	80	160	160	640
TEST VIRUSES												
A/Stockholm/9/2021		3C.2a1b.1a	2021-09-06	SIAT1/SIAT1	320	160	160	640	160	160	80	80
A/Stockholm/8/2021		3C.2a1b.2a.2	2021-08-10	SIAT1/SIAT1	80	<	80	80	160	1280	320	40
A/Orebro/1/2021		3C.2a1b.2a.2	2021-08-21	SIAT1/SIAT1	80	<	80	40	160	640	320	40
A/Uppsala/1/2021		3C.2a1b.2a.2	2021-10-21	SIAT1/SIAT1	80	<	80	80	160	640	320	40
A/Netherlands/10068/2021		3C.2a1b.2a.2	2021-10-24	MDCK-MIX2/SIAT2	40	<	40	40	40	320	160	40
A/Uppsala/3/2021		3C.2a1b.2a.2	2021-10-26	SIAT1/SIAT1	80	<	80	80	160	640	320	40
A/Netherlands/10083/2021		3C.2a1b.2a.2	2021-10-28	MDCK-MIX2/SIAT2	40	<	80	40	160	320	160	40
A/England/214420670/2021		3C.2a1b.2a.2	2021-10-28	MDCK1/SIAT1	80	<	80	80	160	640	320	40
A/Netherlands/10078/2021		3C.2a1b.2a.2	2021-10-29	MDCK-MIX2/SIAT2	40	<	80	80	160	640	320	40
A/Uppsala/6/2021		3C.2a1b.2a.2	2021-11-01	SIAT1/SIAT1	80	<	80	80	160	1280	320	40
A/Sweden/1/2021		3C.2a1b.2a.2	2021-11-03	SIAT1/SIAT1	80	<	80	80	320	1280	640	40
A/Uppsala/8/2021		3C.2a1b.2a.2	2021-11-03	SIAT1/SIAT1	80	<	80	80	320	2560	640	40
A/Uppsala/11/2021		3C.2a1b.2a.2	2021-11-09	SIAT1/SIAT1	80	<	80	80	160	640	320	80
A/Uppsala/12/2021		3C.2a1b.2a.2	2021-11-10	SIAT1/SIAT1	80	<	80	40	160	640	320	40
A/Navarra/9870/2021		3C.2a1b.2a.2	2021-11-24	SIAT1/SIAT2	40	<	80	40	160	320	160	40
A/Netherlands/10162/2021		3C.2a1b.2a.2	2021-11-26	MDCK-MIX2/SIAT1	40	<	40	80	80	320	160	40
A/Netherlands/10161/2021		3C.2a1b.2a.2	2021-11-28	MDCK-MIX2/SIAT1	40	<	80	80	80	320	160	40
A/Netherlands/10163/2021		3C.2a1b.2a.2	2021-11-30	MDCK-MIX2/SIAT1	40	<	80	40	80	320	160	40
A/Netherlands/10174/2021		3C.2a1b.2a.2	2021-12-01	MDCK-MIX2/SIAT1	40	<	80	80	80	320	320	40
A/Netherlands/10168/2021		3C.2a1b.2a.2	2021-12-01	MDCK-MIX2/SIAT1	40	<	80	40	80	320	160	40
A/Netherlands/10177/2021		3C.2a1b.2a.2	2021-12-02	MDCK-MIX2/SIAT1	40	<	80	80	160	320	320	40
							Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40, ND = Not Done

Table 4-3. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre							
					Post-infection ferret antisera							
					A/Denmark 3264/19	A/HK 2671/19	A/Camb e0826360/20	A/Camb 925256/20	A/Bang 4005/20	A/Darwin 9/21	A/Stock 5/21	A/Kansas 14/17
		Passage history			SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT
		Ferret number			F19/20*1	St Judes F21/20*1	F10/21*1	F03/21*1	F07/21*1	F38/21*1	F35/21*1	F17/19*1
		Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019		3C.2a1b.1a	2019-10-25	SIAT5	320	320	160	1280	320	320	320	160
A/Hong Kong/2671/2019		3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	160	320	160	640	160	160	160	160
A/Cambodia/e0826360/2020		3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	2560	160	320	320	320	160
A/Cambodia/925256/2020		3C.2a1b.2a.1	2020-09-25	SIAT5	160	80	320	640	320	320	320	160
A/Bangladesh/4005/2020		3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	160	320	640	640	640	160
A/Darwin/9/2021		3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	640	160	640	2560	1280	80
A/Stockholm/5/2021		3C.2a1b.2a.2	2021-04-16	S0/S3	80	<	80	80	320	640	1280	40
A/Kansas/14/2017		3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<	40	80	80	80	160	640
TEST VIRUSES												
A/Parma/02/2021		3C.2a1b.1a	2021-11-03	SIAT2/SIAT1	160	160	160	320	160	320	160	80
A/Parma/03/2021		3C.2a1b.2a.1	2021-11-14	SIAT2/SIAT1	320	80	640	320	320	320	320	160
A/Parma/04/2021		3C.2a1b.2a.1	2021-11-22	SIAT2/SIAT1	160	40	640	160	320	320	320	80
A/Milano/01/2021		3C.2a1b.2a.2	2021-09-26	SIAT3/SIAT1	160	<	320	160	320	640	640	160
A/Roma/01/2021		3C.2a1b.2a.2	2021-10-20	SIAT3/SIAT1	40	<	80	80	160	320	160	40
A/Roma/02/2021		3C.2a1b.2a.2	2021-10-27	SIAT3/SIAT1	40	<	80	80	160	320	160	40
A/Roma/03/2021		3C.2a1b.2a.2	2021-11-03	SIAT2/SIAT1	40	<	80	80	160	320	320	<
A/Parma/01/2021		3C.2a1b.2a.2	2021-11-17	SIAT4/SIAT1	320	80	320	160	640	640	640	160
A/Hungary/9/2021		3C.2a1b.2a.2	2021-12-07	MDCK1/SIAT1	40	<	40	40	160	320	160	40
A/Hungary/8/2021		3C.2a1b.2a.2	2021-12-07	MDCK1/SIAT1	40	<	80	40	160	320	160	40
A/Portugal/17/2021		3C.2a1b.2a.2	2021-12-15	SIAT1/SIAT1	<	<	40	40	160	320	160	<
A/Romania/493221/2021		3C.2a1b.2a.2	2021-12-15	SIAT2/SIAT1	40	<	80	40	160	320	320	40
A/Romania/493220/2021		3C.2a1b.2a.2	2021-12-15	SIAT2/SIAT1	40	<	80	40	160	320	320	40
A/Romania/493219/2021		3C.2a1b.2a.2	2021-12-16	SIAT2/SIAT1	40	<	80	80	160	640	320	40
A/Romania/495026/2021		3C.2a1b.2a.2	2021-12-29	SIAT2/SIAT1	80	<	80	40	160	640	320	<
A/Romania/495025/2021		3C.2a1b.2a.2	2021-12-29	SIAT2/SIAT1	40	<	<	<	160	640	320	<
A/Hungary/1/2022		3C.2a1b.2a.2	2022-01-03	MDCK1/SIAT1	40	<	40	40	160	640	320	<
A/Romania/495703/2022		3C.2a1b.2a.2	2022-01-07	SIAT1/SIAT1	<	<	40	40	160	320	160	<
A/Romania/495700/2022		3C.2a1b.2a.2	2022-01-07	SIAT1/SIAT1	40	<	80	40	160	320	160	<
A/Hungary/2/2022		3C.2a1b.2a.2	2022-01-11	MDCK1/SIAT1	80	<	80	40	160	640	320	40
A/Romania/496796/2022		3C.2a1b.2a.2	2022-01-13	SIAT1/SIAT1	40	<	40	40	160	320	160	40
							Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40, ND = Not Done

Table 4-4. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
	Passage history			A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	A/Darwin	A/Stock	A/Kansas
				3264/19	2671/19	e0826360/20	925256/20	4005/20	9/21	5/21	14/17
				SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT
	Ferret number			F19/20 [*1]	St Judes F21/20 [*1]	F10/21 [*1]	F03/21 [*1]	F07/21 [*1]	F38/21 [*1]	F35/21 [*1]	F17/19 [*1]
	Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES											
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT5	320	640	320	1280	320	640	320	160
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	640	320	1280	160	640	160	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	80	<	2560	160	160	320	160	80
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	160	160	1280	160	320	160	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	80	320	320	640	1280	640	320
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	40	640	160	320	2560	640	80
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	80	40	160	160	320	2560	1280	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	80	40	80	80	40	160	80	640
TEST VIRUSES											
A/Belgium/H0007/2021	3C.2a1b.2a.2	2021-08-06	P1/SIAT1	80	40	80	40	160	1280	640	40
A/Belgium/H0006/2021	3C.2a1b.2a.2	2021-09-04	P1/SIAT1	40	40	40	40	80	640	160	40
A/Belgium/H0010/2021	3C.2a1b.2a.2	2021-11-15	P1/SIAT1	80	40	160	80	160	1280	640	80
A/Belgium/G0127/2021	3C.2a1b.2a.2	2021-11-22	P1/SIAT1	40	<	80	80	160	640	160	40
A/Spain/89/2021	3C.2a1b.2a.2	2021-12-22	SIAT1	80	40	80	80	160	1280	320	40
A/Spain/87/2021	3C.2a1b.2a.2	2021-12-23	SIAT1	40	40	80	80	160	640	320	40
A/Spain/84/2021	3C.2a1b.2a.2	2021-12-25	SIAT1	40	<	80	80	160	640	320	40
A/Spain/83/2021	3C.2a1b.2a.2	2021-12-26	SIAT1	40	<	80	40	160	640	320	40
A/Spain/82/2021	3C.2a1b.2a.2	2021-12-27	SIAT1	<	<	80	80	160	1280	320	40
A/Spain/81/2021	3C.2a1b.2a.2	2021-12-28	SIAT1	<	40	80	80	80	640	160	40
A/Estonia/168139/2022	3C.2a1b.2a.2	2022-01-03	SIAT1/SIAT1	160	40	160	80	320	1280	640	80
A/Estonia/168142/2022	3C.2a1b.2a.2	2022-01-05	SIAT1/SIAT1	80	40	80	40	160	1280	320	40
A/Estonia/168141/2022	3C.2a1b.2a.2	2022-01-05	SIAT1/SIAT1	80	40	80	40	160	640	320	40
A/Estonia/168131/2022	3C.2a1b.2a.2	2022-01-06	MDCKx/SIAT1	80	40	160	80	160	640	320	80
						Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40, ND = Not Done

Table 4-5. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre							
				Post-infection ferret antisera							
	Passage history			A/Denmark 3264/19 SIAT	A/HK 2671/19 Cell	A/Camb e0826360/20 Egg	A/Camb 925256/20 SIAT	A/Bang 4005/20 SIAT	A/Darwin 9/21 Egg	A/Stock 5/21 SIAT	A/Kansas 14/17 SIAT
	Ferret number			F19/20*1	St Judes F21/20*1	F10/21*1	F03/21*1	F07/21*1	F38/21*1	F35/21*1	F17/19*1
	Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES											
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	640	320	1280	320	640	320	160
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	160	640	320	320	160	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	2560	160	320	640	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	160	160	1280	160	320	160	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	80	320	320	640	1280	640	320
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	40	320	160	640	>5120	1280	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	80	40	160	160	320	2560	1280	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	80	40	80	160	80	160	160	640
TEST VIRUSES											
A/Ireland/92285/2021	3C.2a1b.2a.2	2021-10-21	SIAT1	160	40	640	160	640	1280	640	320
A/Ireland/2707/2021	3C.2a1b.2a.2	2021-12-05	SIAT1	40	<	80	80	160	640	320	40
A/Berlin/4/2021	3C.2a1b.2a.2	2021-12-16	P2/SIAT1	160	<	80	80	320	1280	640	40
A/Ireland/6979/2021	3C.2a1b.2a.2	2021-12-20	SIAT1	80	<	80	80	160	1280	640	40
A/Nordrhein-Westfalen/1/2021	3C.2a1b.2a.2	2021-12-20	P1/SIAT1	1280	320	1280	320	640	2560	2560	320
A/Rheinland-Pfalz/2/2021	3C.2a1b.2a.2	2021-12-22	P1/SIAT1	160	<	80	80	320	1280	640	40
A/Nordrhein-Westfalen/2/2021	3C.2a1b.2a.2	2021-12-22	P1/SIAT1	80	<	80	40	160	640	160	40
A/Berlin/5/2021	3C.2a1b.2a.2	2021-12-23	P1/SIAT1	80	<	80	40	160	1280	320	40
A/Baden-Wurttemberg/2/2021	3C.2a1b.2a.2	2021-12-27	P1/SIAT1	160	80	160	160	320	1280	640	160
A/Nordrhein-Westfalen/3/2021	3C.2a1b.2a.2	2021-12-28	P1/SIAT1	80	<	80	80	160	1280	640	40
A/Berlin/7/2021	3C.2a1b.2a.2	2021-12-31	P1/SIAT1	160	40	80	80	320	1280	640	40
A/Saarland/1/2022	3C.2a1b.2a.2	2022-01-03	P1/SIAT1	80	<	80	80	160	1280	640	40
A/Thuringen/1/2022	3C.2a1b.2a.2	2022-01-03	P1/SIAT1	160	40	80	80	320	1280	640	40
A/Norway/409/2022	3C.2a1b.2a.2	2022-01-04	SIAT1	40	<	40	40	80	640	320	<
A/Hessen/1/2022	3C.2a1b.2a.2	2022-01-04	P1/SIAT1	80	<	80	80	160	1280	640	40
A/Norway/530/2022	3C.2a1b.2a.2	2022-01-06	SIAT1	80	<	80	40	160	1280	320	<
A/Norway/676/2022	3C.2a1b.2a.2	2022-01-11	SIAT1	320	160	320	160	640	1280	320	320
						Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40, ND = Not Done

Table 4-6. Antigenic analysis of influenza A(H3N2) viruses by HI: Summary for 3C.2a1b.2a.2 viruses

Viruses		Haemagglutination inhibition titre								
		Post-infection ferret antisera								
		A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	A/Darwin	A/Stock	A/Kansas
		3264/19	2671/19	e0826360/20	925256/20	4005/20	9/21	5/21	14/17
	Passage history	SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT
	Ferret number	F19/20 *1	St Judes F21/20 *1	F10/21 *1	F03/21 *1	F07/21 *1	F38/21 *1	F35/21 *1	F17/19 *1
	Genetic group	3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES									
A/Denmark/3264/2019	3C.2a1b.1a	320	640	320	1280	320	640	320	160
A/Hong Kong/2671/2019	3C.2a1b.1b	320	320	160	640	320	320	160	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	160	<	2560	160	320	640	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	160	160	160	1280	160	320	160	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	160	80	320	320	640	1280	640	320
A/Darwin/9/2021	3C.2a1b.2a.2	160	40	320	160	640	>5120	1280	160
A/Stockholm/5/2021	3C.2a1b.2a.2	80	40	160	160	320	2560	1280	80
A/Kansas/14/2017	3C.3a.1	80	40	80	160	80	160	160	640
TEST VIRUSES									
Number tested	3C.2a1b.2a.2	92	92	92	92	92	92	92	92
No with titre reduction ≤2-fold		16	2	1		19	16	45	4
%		*17.4*	*2.2*	*1.1*		*20.7*	*17.4*	*48.9*	*4.3*
No with titre reduction =4-fold		16	2	2	8	62	51	35	8
%		*17.4*	*2.2*	*2.2*	*8.7*	*67.4*	*55.4*	*38.0*	*8.7*
No with titre reduction ≥8-fold		60	88	89	84	11	25	12	80
%		*65.2*	*95.6*	*96.7*	*91.3*	*11.9*	*27.2*	*13.1*	*87.0*
				Vaccine NH 2021-22			Vaccine SH 2022 NH 2022-23		

Reference virus results are taken from an individual table as an example. Summaries for each antiserum are based on fold-reductions observed on the days that HI assays were performed.

Influenza B virus analyses

Influenza B/Victoria-lineage

All recently circulating B/Victoria-lineage viruses have fallen in genetic clade **V1A**, represented by **B/Brisbane/60/2008**, a former vaccine virus, but with additional **HA1** amino acid substitutions of **I117V** and **N129D** (e.g. **B/Ireland/3154/2016**). Viruses retaining full-length HAs had remained antigenically similar to B/Brisbane/60/2008. However, three genetic groups (described below with amino acid substitutions/deletions relative to B/Brisbane/60/2008 indicated) containing deletions of HA gene codons have emerged. Viruses in these groups are antigenically distinct from B/Brisbane/60/2008 and each other (as noted in the September 2018 characterisation report[5] and earlier reports), such that four antigenically distinguishable groups had been circulating:

- A group with double deletion of **HA1** residues **162** and **163** (subclade **V1A.1**) with amino acid substitutions of **D129G** and **I180V**, and **HA2 R151K** that spread worldwide and is represented by a previous vaccine virus, **B/Colorado/06/2017**.
- A group with triple deletion of **HA1** residues **162** to **164** (subclade **V1A.2**) first detected in Asia, with amino acid substitutions of **I180T** and **K209N** that showed limited geographical spread (with no detections having been made recently), represented by **B/Hong Kong/269/2017**.
- A group with triple deletion of **HA1** residues **162** to **164** (subclade **V1A.3**) first detected in Africa, with amino acid substitution **K136E** often with **G133R** that showed geographical spread and became dominant, represented by **B/Washington/02/2019** the vaccine virus recommended after the WHO VCM in February 2021 [1].

The phylogeny generated for non-WIC HA sequences available in GISAID shows all recent viruses falling in the **V1A.3** subclade, with small numbers of viruses being related to **B/Washington/02/2019**, but with viruses from the Americas having additional **HA1** substitutions of **T73I** and **N233K** (resulting in loss of a glycosylation site) and those from Kenya having **HA1 K75E**, **E128K**, **T155A** and **G230N** substitutions (Figure 3a). The great majority of viruses fall in the **V1A.3a** group, characterised by **HA1 N150K**, **G184E**, **N197D** (resulting in loss of a glycosylation site) and **R279K**, with this group splitting into two subgroups designated **V1A.3a.1** (characterised by **HA1 V220M** and **P241Q** substitutions, detected predominantly in China) and **V1A.3a.2** (characterised by **HA1 A127T**, **P144L** and **K203R**, often with additional substitutions, which has spread worldwide and is represented by the **B/Austria/1359417/2021** vaccine virus).

The second phylogeny, based on sequences generated at the WIC, shows a very similar profile but with an additional **B/Washington/02/2019**-like cluster of viruses from Madagascar characterised by **HA1 E128K** and **T170I** substitutions (Figure 3b).

Relatively few B/Victoria-lineage viruses have been detected in the WHO European Region (Table 1), but the WHO Collaborating Centres for Influenza have shown the **V.1A.3a** group viruses with additional HA1 substitutions to be antigenically distinct from one another. The two viruses from EU/EEA countries characterised at the WIC since the December 2021 report are subgroup **V1A.3a.2** viruses which were poorly recognised by post-infection ferret antiserum raised against **B/Washington/02/2019**, the current vaccine. However, they were well recognised (with HI titres of at least 320 with the antiserum raised against the egg-propagated variant with **HA1 G141R** substitution) by antisera raised against **B/Austria/1359417/2021**, the recommended vaccine virus for southern hemisphere 2022 and northern hemisphere 2022–2023 influenza seasons (Table 5: [2,3]).

Influenza B/Yamagata-lineage

It is assumed that no B/Yamagata-lineage viruses were detected after March 2020 as no sequences for such viruses with collection dates after this have been released by GISAID as of 28 February 2022. Figure 4 is repeated from the September report, with recently designated nomenclature indicated in bold/red type, and was generated based on the 77 HA sequences from viruses with collection dates after 31 December 2019 and until 31 March 2020, available in GISAID. All sequences fell in genetic clade **3** (**Y3**), the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade, within a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions compared to B/Phuket/3073/2013 which is recommended for inclusion in quadrivalent vaccines for the 2020–2021 and 2021–2022 northern hemisphere, 2021 and 2022 southern hemisphere seasons [1,2,3,4]. Some sub-clustering of sequences has occurred, defined by specific amino acid substitutions (e.g. **HA1 N164K, K211R, D229N** or **D232N** [introducing a potential N-linked glycosylation site] sometimes with **R48K**). As noted in previous characterisation reports, none of these amino acid substitutions have any obvious antigenic effects based on HI assays using post-infection ferret antisera raised against egg-propagated B/Phuket/3073/2013. Of the four samples recently shared with WIC by UK (Scotland: Table 3) only one yielded a good sequence which showed it to be associated with Live Attenuated Influenza Vaccine (LAIV).

[5] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2018. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/sites/portal/files/documents/ECDC-Flu-Characterisation-Report-Sep-2018.pdf

Figure 3a. Phylogenetic comparison of influenza B/Victoria-lineage HA genes (GISAID, February 2022)

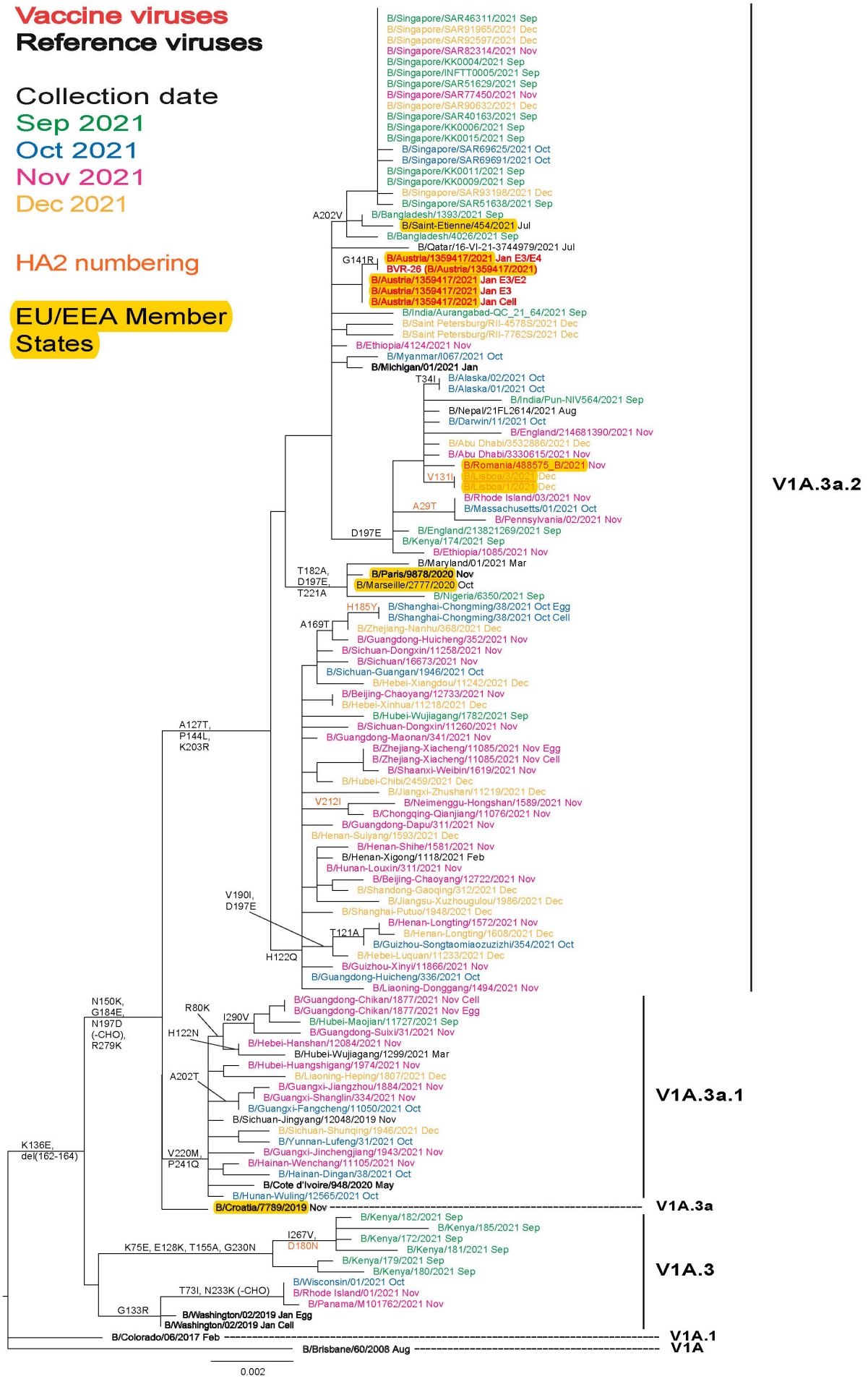


Figure 3b. Phylogenetic comparison of influenza B/Victoria-lineage HA genes (WIC, February 2022)

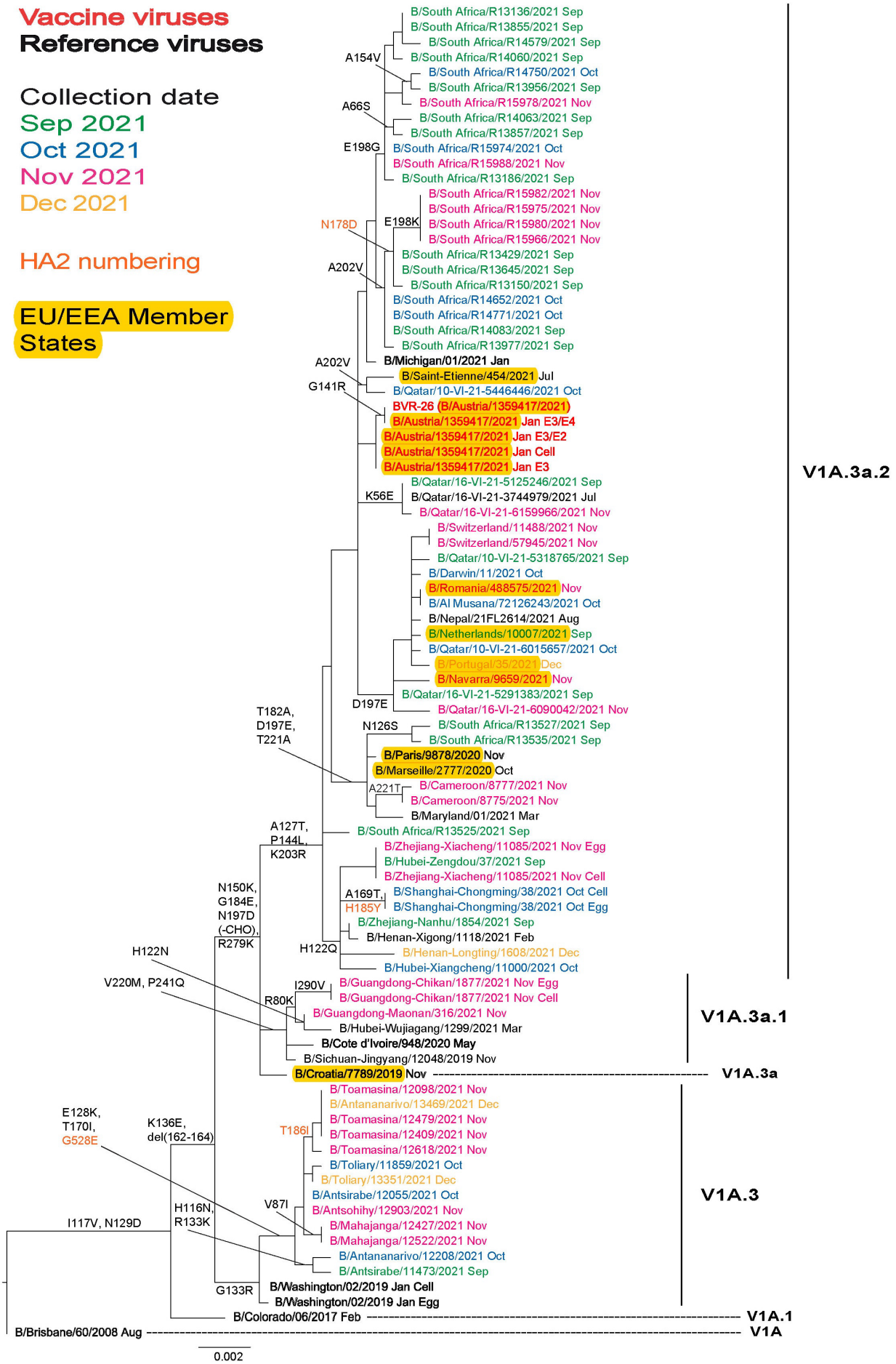


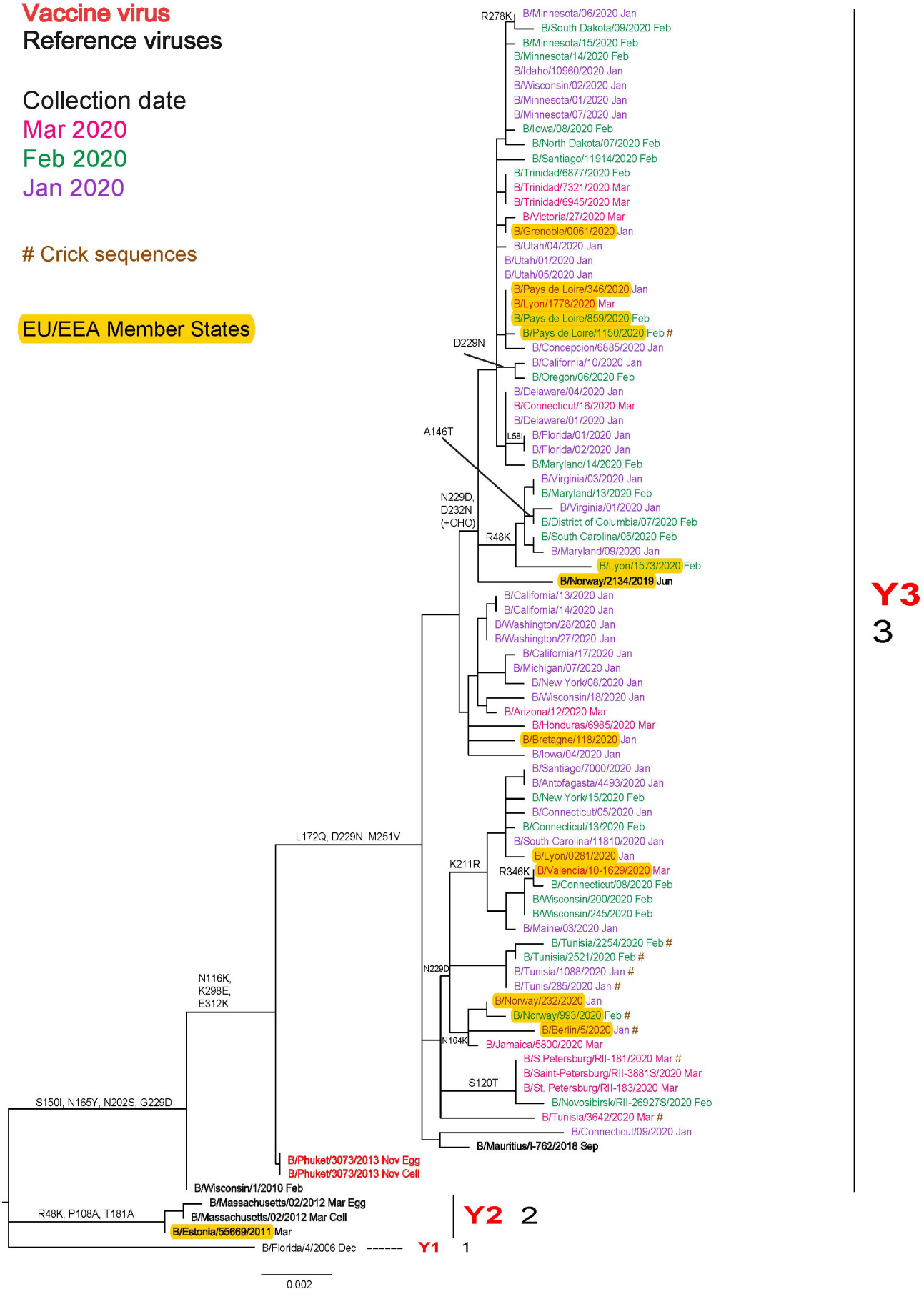
Table 5. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre								
					Post-infection ferret antisera								
					B/Bris	B/Colorado	B/Wash'ton	A/Croatia	B/CIV	B/Austria	B/Austria	B/Austria	B/Paris
					60/08	06/17	02/19	7889/19	948/20	1359417/21	1359417/21	1359417/21	9878/20
		Passage history			Egg	Egg	Egg	MDCK	MDCK	MDCK	Egg G141	Egg G141R	MDCK
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F11/18[*4]	F20/20[*2]	F19/21[*1]	F08/21[*5]	NIB F01/21[*1]	F15/21[*1]	F44/21[*1]	F12/21[*1]
		Genetic group			V1A	V1A.1	V1A.3	V1A.3a	V1A.3a.1	V1A.3a.2	V1A.3a.2	V1A.3a.2	V1A.3a.2
REFERENCE VIRUSES													
B/Brisbane/60/2008		V1A	2008-08-04	E4/E4	1280	80	40	80	<	<	<	<	<
B/Colorado/06/2017		V1A.1	2017-02-05	E5/E2	1280	640	80	80	<	<	<	<	<
B/Washington/02/2019		V1A.3	2019-01-19	E3/E2	1280	320	320	160	<	<	<	<	<
B/Croatia/7789/2019		V1A.3a	2019-11-11	MDCKx/MDCK3	640	160	160	640	160	160	160	40	<
B/Cote d'Ivoire/948/2020		V1A.3a.1	2020-05-28	MDCK2	320	40	80	640	640	160	160	160	<
B/Austria/1359417/2021		V1A.3a.2	2021-01-09	SIAT1/MDCK4	640	80	<	320	<	1280	1280	640	640
B/Austria/1359417/2021 Isolate 2	G141	V1A.3a.2	2021-01-09	E3	ND	ND	ND	320	160	2560	1280	640	320
B/Austria/1359417/2021 Isolate 2	G141R	V1A.3a.2	2021-01-09	E3/E4	320	40	<	320	160	1280	1280	>5120	640
B/Paris/9878/2020		V1A.3a.2	2020-11-20	MDCK2	640	160	<	320	<	1280	1280	640	640
TEST VIRUSES													
B/Romania/488575/2021		V1A.3a.2	2021-11-10	SIAT2/MDCK1	1280	320	<	320	160	1280	2560	320	640
B/Portugal/35/2021		V1A.3a.2	2021-12-15	MDCK3	640	160	<	80	80	640	640	320	320
						Vaccine SH 2019 NH 2019-20	Vaccine SH 2020 NH 2020-21 SH 2021 NH 2021-22				Vaccine SH 2022 NH 2022-23		

[*] Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; [5] < = <80; ND = Not Done

Figure 4. Phylogenetic comparison of influenza B/Yamagata-lineage HA genes (GISAID, September 2021)



Summaries of data submitted to TESSy

Genetic characterisation

In total, 934 viruses detected during the 2021−2022 season (weeks 40/2021-8/2022) were genetically characterised, as set out below.

- Of 63 A(H1N1)pdm09 viruses, 55 belonged to clade 6B.1A.5a.1 (represented by A/Guangdong-Maonan/SWL1536/2019) and eight belonged to clade 6B.1A.5a.1 (represented by A/Victoria/2570/2019).
- Of 864 A(H3N2) viruses, 858 belonged to the 'Bangladesh-like' clade (3C.2a1b.2a.2) represented by A/Bangladesh/4005/2020 and six were attributed to clade 3C.2a1b.1a (represented by A/Denmark/3264/2019).
- Seven B/Victoria-lineage viruses, one belonging to clade V1A.3 (represented by B/Washington/02/2019) and six to clade V1A.3a.2 (represented by B/Austria/1359417/2021).

Antiviral susceptibility

Up to week 8/2022, 902 viruses were assessed for susceptibility to neuraminidase inhibitors (NAIs): 577 A(H3), 34 A(H1)pdm09 and one B virus were assessed genotypically, and 277 A(H3), 10 A(H1)pdm09 and three B viruses were assessed phenotypically. Susceptibility to the PA inhibitor baloxavir marboxil was assessed genotypically for 422 viruses: 389 A(H3), 32 A(H1)pdm09 and one B virus. Phenotypically no viruses with reduced susceptibility were identified and genotypically no markers associated with reduced susceptibility were identified.

At the WIC, 154 influenza viruses detected within EU/EEA countries during the 2021−2022 season were assessed phenotypically against oseltamivir and zanamivir: 36 A(H1)pdm09, 114 A(H3) and four B/Victoria-lineage. All viruses showed normal inhibition (NI) by both NAIs and their PA gene sequences had no markers associated with reduced susceptibility to baloxavir marboxil.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization Global Alert and Response System [4] reported that the China Health and Family Planning Commission had notified WHO of three cases of human infection with influenza A(H7N9). Increased numbers of cases were reported over the course of the following seasons, and cases were reported in 2017, including the fifth (2016−17) and largest wave to date. This fifth wav included the emergence of highly pathogenic avian influenza (HPAI) strains that have caused some zoonoses, although few human cases were reported during the 2017−18 season [5]. WHO posted an analysis of information on A(H7N9) viruses on 10 February 2017 [6], and ECDC published a rapid risk assessment on the implications of A(H7N9) for public health on 3 July 2017 [7]. Current risk assessments can be found on WHO's website[6]. The assessment published on 21 January 2022 indicated that there had been no publicly available reports from animal health authorities in China or other countries on influenza A(H7N9) virus detections in animals in recent months [8]. The H7N9 situation update published by the Food and Agricultural Organization of the United Nations on 3 February 2021 indicated there had been 14 detections in chickens in Shandong province, China during October 2020, but the report published on 2 February 2022 indicated that there had been no additional detections since then [9], and an e-mailed notification on 2 March indicated there had been no reports of detections in the following month. The most recent human case was detected in mid-March 2019 [10]. The latest overview of avian influenza by ECDC, in collaboration with the European Food Safety Authority and the EU Reference Laboratory for Avian Influenza, was approved on 22 December 2021 and can be found on ECDC's website [11].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 21 January 2022. Since the previous risk assessment on 13 December 2021, ten human cases of infection with avian influenza A(H5) viruses have been reported: nine A(H5N6) and one A(H5N1) [8]. The A(H5N6) cases were reported by China with disease onset dates in December through January and the A(H5N1) case by the UK (England) in December with the patient being asymptomatic [8]. All cases reported exposure to poultry and, at the time of report publication, two A(H5N6)-infected cases were fatal (a 54-year-old female and a 75-year-old male) with the remaining seven being severe/critical. Prior to the case in the UK (England), the last confirmed case of human infection with an A(H5N1) virus was reported by India [12]. A full report has been published into the investigation of the case in England [13].

On 30 September 2020, ECDC published an alert related to outbreaks of avian influenza viruses in Europe [14]. The latest collaborative report from ECDC and the European Food Safety Authority (EFSA), reported 867 highly pathogenic avian influenza (HPAI) A(H5) detections between 16 September and 8 December 2021, 316 in poultry, 523 in wild birds and 28 in domestic birds [11]. Detections occurred in 27 EU/EEA countries and the UK. Of the poultry detections, 167 were reported by Italy and 35 each by Hungary and Poland. Countries reporting the majority of detections in wild birds were Germany (280), Netherlands (65) and the UK (53). Genetic analyses indicated that the circulating viruses belonged

[6] https://www.who.int/teams/global-influenza-programme/avian-influenza/monthly-risk-assessment-summary (accessed 1 March 2022).

to clade 2.3.4.4b, with such viruses having been circulating in Europe since October 2020. According to reports compiled by the Food and Agricultural Organization of the United Nations (FAO) as of 23 February 2022, various influenza A(H5Nx) subtypes continued to be detected in wild and/or domestic birds in Africa, Asia and Europe, and since 26 January 2022, a total of 935 HPAI (five not subtyped, 244 H5Nx, 676 H5N1, nine H5N5 and one H5N8) and one LPAI outbreaks had been reported, mentioning six A(H5N6) human infections in China [15].

Influenza A(H9N2) virus

Since the previous WHO update on 13 December 2021 five laboratory-confirmed human cases of influenza A(H9N2) virus infection, all in children, have been reported by China, with onset dates in November and December [8]. All cases reported mild severity and there were neither epidemiological links nor clusters of cases and A(H9) viruses detected in associated environmental samples. Public Health England has published and updated a risk assessment for avian influenza A(H9N2) [16]. Avian influenza A(H9N2) viruses are enzootic in poultry in Asia and increasingly being reported in poultry in Africa.

Other influenza zoonotic events

Since the previous WHO update on 13 December 2021, no A(H1)v or A(H3)v zoonotic events with swine-related variant influenza A viruses have been reported [8].

WHO Collaborating Centre reports

A description of results generated by the London WHO Collaborating Centre at the WIC and used at the September 2021 WHO VCM (held online: 13–23 September 2021 for seasonal influenza viruses) and reports from previous meetings can be found at https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports (accessed 2 March 2022). The report for the February 2022 VCM will be posted shortly.

Note on the figures

The phylogenetic trees were constructed using RAxML, drawn using FigTree, and annotated using Adobe Illustrator. The bars indicate the proportion of nucleotide changes between sequences. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the month(s) of sample collection. Isolates from WHO NICs in EU/EEA countries are highlighted in yellow. Sequences for many viruses from non-EU/EEA countries were recovered from the GISAID EpiFlu database. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from the GISAID EpiFlu database, which were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website), along with all laboratories who submitted sequences directly to WHO CC London.

References

1. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2021-2022 northern hemisphere influenza season. Wkly Epidemiol Rec. 2021 Mar 19;96(11):77-88. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/WER9611-eng-fre.pdf
2. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2022 southern hemisphere influenza season. Wkly Epidemiol Rec. 2021 Oct 22;96(42):509-520. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/WER9642-eng-fre.pdf
3. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2022-2023 northern hemisphere influenza season. Geneva: WHO; 2022 [accessed 3 March 2022]. Available from: https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2022-2023/202202_recommendation.pdf
4. World Health Organization (WHO). Human infection with influenza A(H7N9) virus in China. 1 April 2013. Geneva: WHO; 2013 [accessed 1 March 2022]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2013_04_01-en
5. World Health Organization (WHO). Human infection with avian influenza A(H7N9) virus – China. Geneva: WHO; 2017 [accessed 1 March 2022]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/26-october-2017-ah7n9-china-en
6. World Health Organization (WHO). Influenza at the human–animal interface. Summary and assessment, 26 January to 2 March 2018. Geneva: WHO; 2018. Available from: https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_02_03_2018.pdf
7. European Centre for Disease Prevention and Control (ECDC). Influenza A(H7N9) virus in China - implications for public health - 7th update, 3 July 2017. Stockholm: ECDC; 2017. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/2017-07-03-RRA-Disease-China_H7N9_0.pdf
8. World Health Organization (WHO). Influenza at the human-animal interface. Summary and assessment, from 14 December 2021 to 21 January 2022. Geneva: WHO; 2022. Available from: https://www.who.int/publications/m/item/influenza-at-the-human-animal-interface-summary-and-assessment-21-january-2022
9. Food and Agricultural Organization of the United Nations (FAO). H7N9 situation update, 2 February 2022. Rome: FAO; 2022 [accessed 2 March 2022]. Available from: https://www.fao.org/ag/againfo/programmes/en/empres/H7N9/Situation_update.html
10. World Health Organization (WHO). Influenza at the human–animal interface. Summary and assessment, 13 February to 9 April 2019. Geneva: WHO; 2019. Available from: https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_09_04_2019.pdf
11. European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA), European Union Reference Laboratory for Avian Influenza. Avian influenza overview September – December 2021. Parma and Stockholm: EFSA, ECDC; 2021. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/AI-Report-XVIII_draft_published.pdf
12. World Health Organization (WHO). Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003–2021. Geneva: WHO; 2021. Available from: https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/2021_oct_tableh5n1.pdf
13. Oliver I, Roberts J, Brown C, Byrne A, Mellon D, Hansen R, et al. A case of avian influenza A(H5N1) in England. Eurosurveillance. 3 Feb 2022. 27;5 [accessed 1 March 2022]. Available from: https://www.eurosurveillance.org/docserver/fulltext/eurosurveillance/27/5/eurosurv-27-5-1.pdf?expires=1646140238&id=id&accname=guest&checksum=5045AC487CE132037838BD69AAFFDC50
14. European Centre for Disease Prevention and Control (ECDC). Avian influenza: EU on alert for new outbreaks. 30 September 2020. Stockholm: ECDC; 2020 [accessed 1 March 2022]. Available from: https://www.ecdc.europa.eu/en/news-events/avian-influenza-eu-alert-new-outbreaks
15. Food and Agricultural Organization of the United Nations (FAO). Global AIV with zoonotic potential situation update, 23 February 2022. Rome: FAO; 2022 [accessed 1 March 2022]. Available from: https://mcusercontent.com/dc0b96ca6646c8eedf16a2216/files/bc782d4a-f1fd-5a03-c680-983b506e6749/Global_update_zoonoticAIV_2022_02_23.pdf
16. Public Health England. Guidance, risk assessment of avian influenza A(H9N2) update, 9 August 2021 [accessed 2 March 2022]. Available from: https://www.gov.uk/government/publications/risk-assessment-of-avian-influenza-ah9n2/risk-assessment-of-avian-influenza-ah9n2