Influenza virus characterization

Summary report, Europe, May 2022

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Summary

This is the sixth report for the 2021-2022 influenza season. The March 2022 characterization report[1], gave a breakdown of influenza detections across the World Health Organization (WHO) European Region reported to TESSy up to week 13/2022. As of week 20/2022, 133 099 detections had been reported (a rise of over 42 000 since week 13/2022) resulting from extended late season influenza activity. Of these 133 099 detections, 98% were type A viruses, with A(H3N2) (92%) dominating over A(H1N1)pdm09 (8%), and 2% type B of which only 111 were ascribed to a lineage, with all but four being B/Victoria. This represents a large increase (132 190, 146-fold) in detections compared to the 2020-2021 season, on the back of a great increase (1 724 858, 194%) 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 17 weeks as of week 20/2022 (unlike in 2020-2021), numbers of detections are reduced compared to earlier seasons (e.g., 19% 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.

Fifteen shipments from countries and areas within the WHO European Region were received at the London WHO Collaborating Centre, the Francis Crick Worldwide Influenza Centre (WIC) after February 2022. This report focuses on viruses with collection dates after 31 December 2021 for which HA gene sequences were submitted to, and released in, the EpiFlu™ database of the Global Initiative on Sharing All Influenza Data (GISAID) after 31 March 2022 for influenza type A viruses and 31 December 2021 for influenza type B viruses, together with sequences generated and antigenic data determined at the WIC.

Globally relatively few A(H1N1)pdm09 viruses have been detected in the course of the 2021-2022 season with 6B.1A.5a.1 and 6B.1A.5a.2 subgroups being most commonly detected, but with dominance of a particular subgroup varying between countries. The subgroups are clearly antigenically different as shown by viruses from Albania (6B.1A.5a.2) and Germany/Spain (6B.1A.5a.1) characterized here. In Europe, 6B.1A.1A.5a.1 viruses have been most numerous but 6B.1A.5a.2 viruses are currently dominant in some southern hemisphere countries, notably Australia. An emergent 6B.1A.5a.1 genetic group showing antigenic drift, defined by HA1 P137S and G155E amino acid substitutions, has been detected. 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 the ‘Bangladesh-like’ (3C.2a1b.2a.2) subgroup. While small clusters of viruses showing antigenic drift have emerged among the ‘Bangladesh-like’ viruses, the great majority of these 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. Antisera raised against viruses in two of the emergent antigenically drifted clusters gave poorer recognition of 3C.2a1b.2a.2 viruses than the antisera raised against the Darwin vaccine viruses. At the February 2022 WHO VCM the recommendation was to change the A(H3N2) vaccine components for the northern hemisphere 2022-2023 influenza season to match those to be used in the 2022 southern hemisphere season.

In Europe and across the world few B/Victoria-lineage viruses have been detected during the 2021-2022 influenza season. All fall within 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. Most HA sequences from recently detected viruses, in geographically dispersed countries and areas, have fallen in the V1A.3a group defined by a series of HA1 amino acid substitutions including N150K, with most falling in the V1A.3a.2 subgroup with defining HA1 A127T, P144L and K203R amino acid substitutions. However, at least three virus genetic clusters have emerged among B/Washington/02/2019-like (V.1A.3) viruses, one of which has recently been detected in the Netherlands. 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 and the northern hemisphere 2022-2023 influenza seasons.

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 16 from the WHO European Region, belong to genetic clade Y3 and carry three HA1 amino acid substitutions (L172Q,

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, March 2022. Stockholm: ECDC; 2020 (https://www.ecdc.europa.eu/en/publications-data/influenza-virus-characterisation-summary-europe-march-2022, accessed 13 September 2022).

D229N and M251V) compared to B/Phuket/3073/2013-like viruses which are still recommended for use in quadrivalent influenza vaccines. **There is need to share all B/Yamagata-lineage viruses detected recently for detailed characterization to determine if there are any in circulation that are not related to Live Attenuated Influenza Vaccines.**

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 40/2021-20/2022), 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 (1 724 858, 194%), even when compared with a more 'normal' season, 2019-2020 (1 703 745, 187%: results not shown), which led into the COVID-19 pandemic. With this increased testing there has been a rise in the number of influenza-positive samples (132 190, 146-fold), though there was a reduction compared to the same period in 2019-2020 (31 769, 19%: results not shown). These data probably relate to a number of factors: (i) 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; (ii) 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; (iii) increased use of personal protective equipment (e.g. face masks) and hygiene measures (e.g. hand-washing and surface disinfection), and; (iv) 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 of the 2020-2021 season, the ratio of type A to type B detections has increased compared to the 2020-2021 season (1.1:1 to 57:1), with a greater dominance of A(H3N2) over A(H1N1)pdm09 viruses. While the number of influenza B virus detections has increased from 441 to 2 302 (522%), only small numbers were ascribed to a lineage in both time periods (Table 1) though, based on sequences available in GISAID, B/Yamagata lineage viruses with collection dates after March 2020 have not been characterized genetically. Currently, it appears that measures introduced relating to the COVID-19 pandemic are still having an effect but there has been clear indication of an influenza season in the Region during 2021-2022 with the rate of influenza positivity in sentinel samples having been at or above 10%, the epidemic threshold set for the Region, for 17 weeks during a bi-phasic season (weeks 49/2021 to 1/2022 and weeks 8-19/2022) with A(H3N2) viruses dominating (Figure 1).

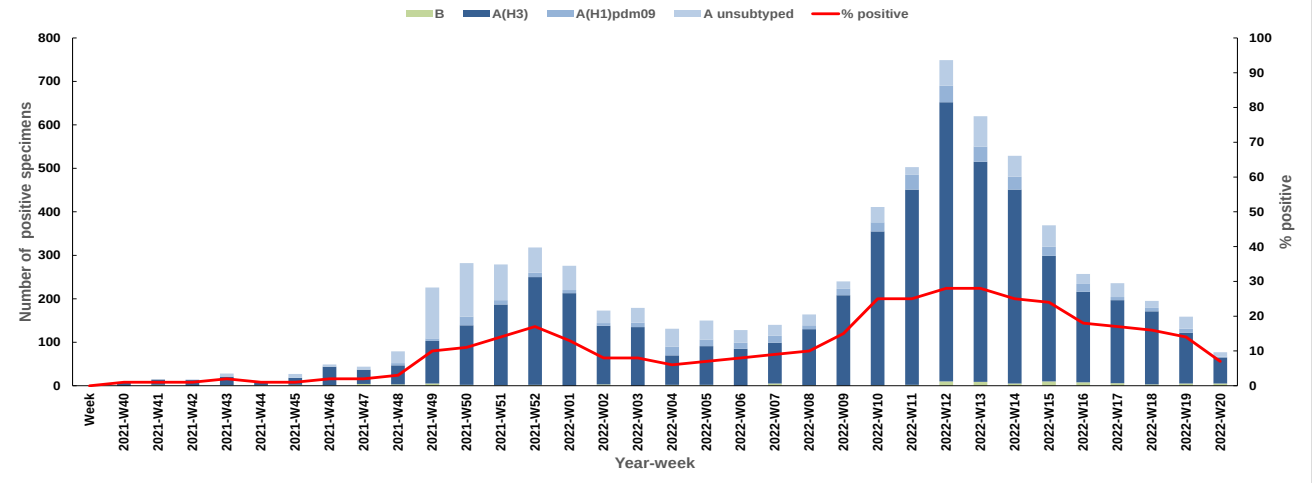
Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2021-22 season (weeks 40/2021-20/2022)[a]

Virus type/subtype/lineage	Cumulative number of detections for weeks 40/2021-20/2022			Totals*		Cumulative number of detections for weeks 40/2020-20/2021			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**6962**	**123835**	**130797**	**98.3**	**57:1**	**30**	**438**	**468**	**51.5**	**1.1:1**
A(H1N1)pdm09	388	2465	2853	8.0		13	28	41	40.6	
A(H3N2)	5449	27297	32746	92.0	11.5:1	9	51	60	59.4	1.5:1
A not subtyped	1125	94073	95198			8	359	367		
Influenza B	**101**	**2201**	**2302**	**1.7**		**16**	**425**	**441**	**48.5**	
Victoria lineage	15	92	107	96.4	27:1	2	11	13	81.3	4.3:1
Yamagata lineage	0	4	4	3.6		0	3	3	9.7	
Lineage not ascribed	86	2105	2191			14	411	425		
Total detections (total tested)	**7 063 (59 814)**	**126 036 (>2 554 328)**	**133 099 (>2 614 142)**			**46 (43 474)**	**863 (>845 810)**	**909 (>889 284)**		

[a] Numbers taken from Flu News Europe to week 20/2022 and week 20/2021 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.

Figure 1. Influenza positivity in sentinel-source specimens by week (2021-2022) – WHO/Europe[a]



[a] Figure adapted from FluNewsEurope week 20/2022 (https://flunewseurope.org/Archives)

Genetic and antigenic characterization 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 characterization report that was 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 in the February report for viruses with collection dates after 31 August 2021 until 31 January 2022 contributed to the most 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 it was recommended 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 thereby available for sharing with WIC, this and recent influenza characterization reports (https://www.ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/influenza-virus-characterisation) have been based mainly on phylogenetic analyses of complete HA gene sequences submitted to the EpiFlu™ database GISAID inclusive of sequences generated at the WIC. Here A(H1N1)pdm09, A(H3N2) and B/Victoria-lineage HA gene phylogenies for viruses with collection dates after 31 August 2021, for representative non-WIC generated sequences available in GISAID, generated for the March report are presented (Figures 2a, 3a and 4a). Additional phylogenies are presented for HA sequences derived from more recently collected viruses (Figures 2b, 3b and 4b). Table 2 shows the numbers of HA sequences, derived from viruses with collection dates after 31 December 2021, available and used in the new representative phylogenies generated for this May report.

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

Virus subtype/lineage	Global HA sequences available for viruses collected in the 2021-2022 season as of 2022-05-29				
	Virus collection date (from)	Sequence submission date (from)	Number Downloaded	Number de-duplicated and aligned	Number used in phylogenies*
A(H1N1)pdm09	2022-01-01	2022-04-01	359	356	114
A(H3N2)	2022-01-01	2022-04-01	2939	2733	217
B/Victoria	2022-01-01	2022-01-01	109	108	108
B/Yamagata	2022-01-01	2022-01-01	0	0	0

*** Inclusive of sequences generated recently at the WIC, but not including sequences from reference and vaccine viruses**

Sixty shipments of specimens (virus isolates and/or clinical specimens) were received at the WIC from WHO Global Influenza Surveillance and Response System (GISRS) recognised National Influenza Centres (NICs) in a total of 35 WHO European Region Member States and areas (Table 3). Of the 1 137 samples received 1 115 (98.1%) were type A viruses and 22 (1.9%) were type B viruses. Fifteen of the shipments were received after February and contained samples from the second phase of the epidemic (Figure 1) many of which are still in the virus characterization process (Table 3).

A total of 194 viruses from the WHO European Region, six A(H1N1)pdm09, 187 A(H3N2) and one B/Victoria-lineage, have been characterized antigenically since the March report (Tables 4, 5 and 6 respectively).

Table 3. Summary of seasonal influenza clinical samples and virus isolates* with collection dates after 2021-08-31 contained in packages received from WHO European Region Member States and areas

Table 3. Summary of clinical samples and virus isolates received, with collection dates after 2021-08-31, by country*

MONTH	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country/area	Seasonal viruses	Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	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						
Israel	2					2	2							
Italy	1					1	1	0						
Netherlands	13					12	12				1	1		
Spain	1					1	0	0						
Sweden	2			1	1	1	1							
the United Kingdom (England)	2					2	2							
October														
Denmark	2			1	1	1	1	0						
Estonia	1					1	0	0						
France	12			9	8	3	3							
Germany	2					2	2							
Ireland	1					1	1							
Italy	5			3	3	2	2							
Kyrgyzstan	28					28	0	0						
Netherlands	36					36	17	0						
Norway	7					7	7							
Portugal	3					2	0	0	1	0				
Russian Federation	3					3	3							
Spain	4					4	3	0						
Sweden	2					2	2							
Tajikistan	7	6	0			1	1							
the United Kingdom (England)	8					8	8							
the United Kingdom (Scotland)	5										1		4	
November														
Armenia	2					2	0	0						
Belgium	2					2	2							
Croatia	1			1	1									
Estonia	1					1	0	0						
France	28			18	13	10	8	0						
Germany	5					4	4				1	1		
Ireland	3					2	0	0			1	1		
Ireland	1					1								
Israel	10					10	6	0						
Italy	5					5	5							
Kyrgyzstan	22					22	0	0						
Netherlands	23					23	19	0						
Norway	8					8	5	0						
Romania	1										1	1		
Russian Federation	36					36	35							
Spain	36			1	1	33	10	0	1	0	1	0		
Slovenia	2					2	1	0						
Sweden	5					5	5							
Switzerland	4					2	2				2	2		
Tajikistan	8	7	0	1	0									
the United Kingdom (Scotland)	2					2								
the United Kingdom (N. Ireland)	3					2			1					
Kosovo[$]	2					2	1	0						
December														
Albania	39	1	0	3	3	35	10	0						
Armenia	21					21	10	0						
Belgium	15	1	0	7	6	7	2	0						
Bosnia and Herzegovina	3					3	0	0						
Croatia	7			1	1	6	5	0						
Estonia	7					7	1	0						
France	1					1	1							
Germany	10					10	10							
Georgia	11			1	0	9	4	0			1	0		
Hungary	2					2	2							
Ireland	4			1	0	3	3							
Ireland	1					1								
Israel	30					30	5	0						
Latvia	5					5	5							
Montenegro	6					6	1	0						
Netherlands	26			5	5	21	20	1						
Norway	1					1	1							
Portugal	17	1	0			13	3	0	1	0	2	1		
Romania	5					5	5							
Russian Federation	5					5	5							
Serbia	7			5	0	2	1	0						
Slovenia	1					1	1							
Spain	53					52	10	0			1	0		
Switzerland	10	1	0			9	6	0						
Ukraine	13					13	1	0						
Kosovo[$]	56	3	0	5	0	48	7	0						

*** 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.**

[$] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

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 only genetic characterisation possible

Some samples are RNA, so only genetic characterisation possible

Some samples not cultured because Ct value high (>30), failed sequence, identical sequence, mixed sequence or SARS-COV-2 positive

MONTH Country/area	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]
2022														
January														
Armenia	2					2	1	0						
Belgium	16			7	6	9	2	0						
Bosnia and Herzegovina	5					5	0	0						
Bulgaria	8			8	in process									
Estonia	4					4	4							
Germany	11					11	11							
Georgia	4					4	2	0						
Hungary	2					2	2							
Ireland	2					2	0	0						
Ireland	2			1		1								
Israel	9					9	0	0						
Latvia	1					1	1							
Montenegro	8	2	0			6	1	0						
Norway	10			1	0	9	in process							
Romania	4			1	1	3	3							
Serbia	17					17	8	0						
Slovenia	2					2	1	0						
Spain	3					3	3							
Switzerland	7			1	in process	6	4	0						
Ukraine	15					15	6	0						
Kosovo[$]	2	1	0			1	0	0						
FEBRUARY														
Bulgaria	4			4	in process									
Denmark	1			1	1									
Germany	12			1	1	11	11							
Norway	2					2	in process							
Poland	1					1	1							
Slovenia	12					12	12							
Spain	10					10	10							
Switzerland	4			4	in process									
MARCH														
Bulgaria	16			16	in process									
Denmark	12			1	in process	11	11							
Germany	8			1	in process	7	in process							
Iceland	4					4	in process							
Ireland	39					39	in process							
Lithuania	1					1	in process							
Norway	20			2	in process	16	in process				2	in process		
Poland	19	2	0			17	14	0						
Slovenia	78					78	in process							
Spain	4			2	2	2	2							
Switzerland	20			7	in process	13	in process							
the United Kingdom (N. Ireland)	3					3								
APRIL														
Bulgaria	3			3	in process									
Denmark	2					2	2							
Germany	8			2	in process	6	in process							
Iceland	27			2	in process	25	in process							
Ireland	11			1	in process	10	in process							
Latvia	15			2	in process	12	in process				1	in process		
Lithuania	46					46	in process							
Norway	38			10	in process	25	in process				3	in process		
Poland	30	3	0			15	13		2	0	10	in process		
Slovenia	22					22	in process							
Switzerland	14			2	0	12	in process							
the United Kingdom (N. Ireland)	24					24								
MAY														
Germany	11			1	in process	8	in process				2	in process		
Iceland	18					18	in process							
Lithuania	2					2	in process							
Norway	3										3	in process		
	1137	25	0	122	54	968	417	1	4	0	14	7	4	0
35 Countries/areas		2.2%		10.7%		85.1%			0.4%		1.2%		0.4%	
		98.1%							1.9%					

*** 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.**

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Numbers in red indicate viruses recovered but with insufficient HA titre to permit HI assay (H3N2 only)

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As of 2022-05-31

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 most recently circulating viruses carrying the substitution **S183P** in **HA1**, although this is not retained in all genetic groups. Figures 2a and 2b 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 time of 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 split 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**).

During March 2022 a total of 166 A(H1N1)pdm09 HA sequences from viruses with collection dates after 31 August 2021 became available from GISAID and WIC. These were composed of: a set of **6B.1A.5a** viruses from Zambia with collection dates in 2021 together with one from Mozambique collected in January 2022; a large number of **6B.1A.5a.1** subgroup viruses detected in African countries (Cameroon, Cote d'Ivoire, Ghana, Niger and Togo), South America (Argentina) and the countries/areas of the WHO European Region (Belgium, Croatia, France, the Netherlands, the United Kingdom (England), and Kosovo[2]); and a smaller number of **6B.1A.5a.2** subgroup viruses detected in India, Oman, USA and the WHO European Region (Albania, the Netherlands and the United Kingdom (England)) (Figure 2a). The great majority of HA gene sequences from viruses with collection dates in 2022 fell in the **6B.1A.5a.1** subgroup.

The phylogeny prepared for this report was based on a representative set of HA sequences derived from viruses with collection dates after 31 December 2021 that had been submitted to GISAID after 31 March 2022 (Table 2). Viruses of subgroup **6B.1A.5a.1** have clearly continued to dominate in the WHO European Region but with the Netherlands and Romania having detected a few viruses belonging to subgroup **6B.1A.5a.2** (Figure 2b). Strikingly, viruses of subgroup **6B.1A.5a.2** are dominating in Australia, where the influenza season has started earlier than usual, as is the case in Pakistan, while a single virus in this subgroup from Morocco has been identified.

A set of three A(H1N1)pdm09) viruses from Albania, with collection dates in December 2021, characterized antigenically since the March report all fell in subgroup **6B.1A.5a.2** (Figure 2a and Table 4-1). These three viruses were recognised well (all within twofold of respective homologous titres) in HI by the three antisera raised against subgroup **6B.1A.5a.2** viruses which included the current vaccine virus, A/Victoria/2570/2019 (IVR-215), but poorly by antisera raised against five subgroup **6B.1A.5a.1** viruses. Conversely, three viruses falling in subgroup **6B.1A.5a.1** (one from Germany and two from Spain) were recognised well (all within twofold of respective homologous titres) in HI by the five antisera raised against subgroup **6B.1A.5a.1** viruses which included the previous (2020-2021 northern hemisphere season) vaccine virus, A/Guangdong-Maonan/SWL1536/2019, but poorly by antisera raised against three subgroup **6B.1A.5a.2** viruses (Figure 2b and Table 4-2).

At the most 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 antisera induced by **6B.1A.5a.1** subgroup viruses in ferrets and humans yielding poor recognition of **6B.1A.5a.2** subgroup viruses and most of the human population unlikely to have been exposed to **6B.1A.5a.2** subgroup viruses given their low-level circulation during the COVID-19 pandemic.

[2] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Figure 2a. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID/WIC, March 2022)

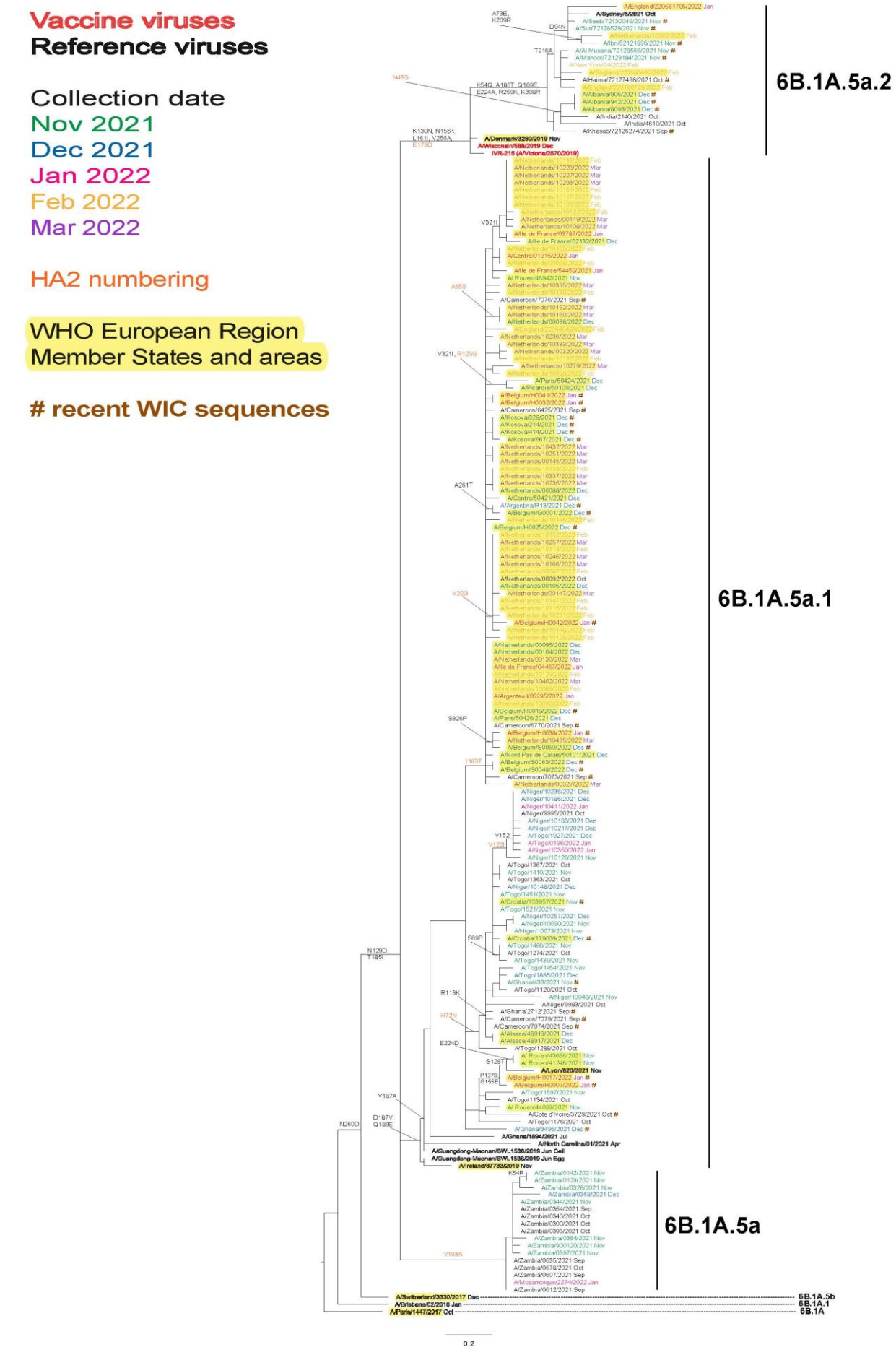


Figure 2b. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID/WIC, May 2022)

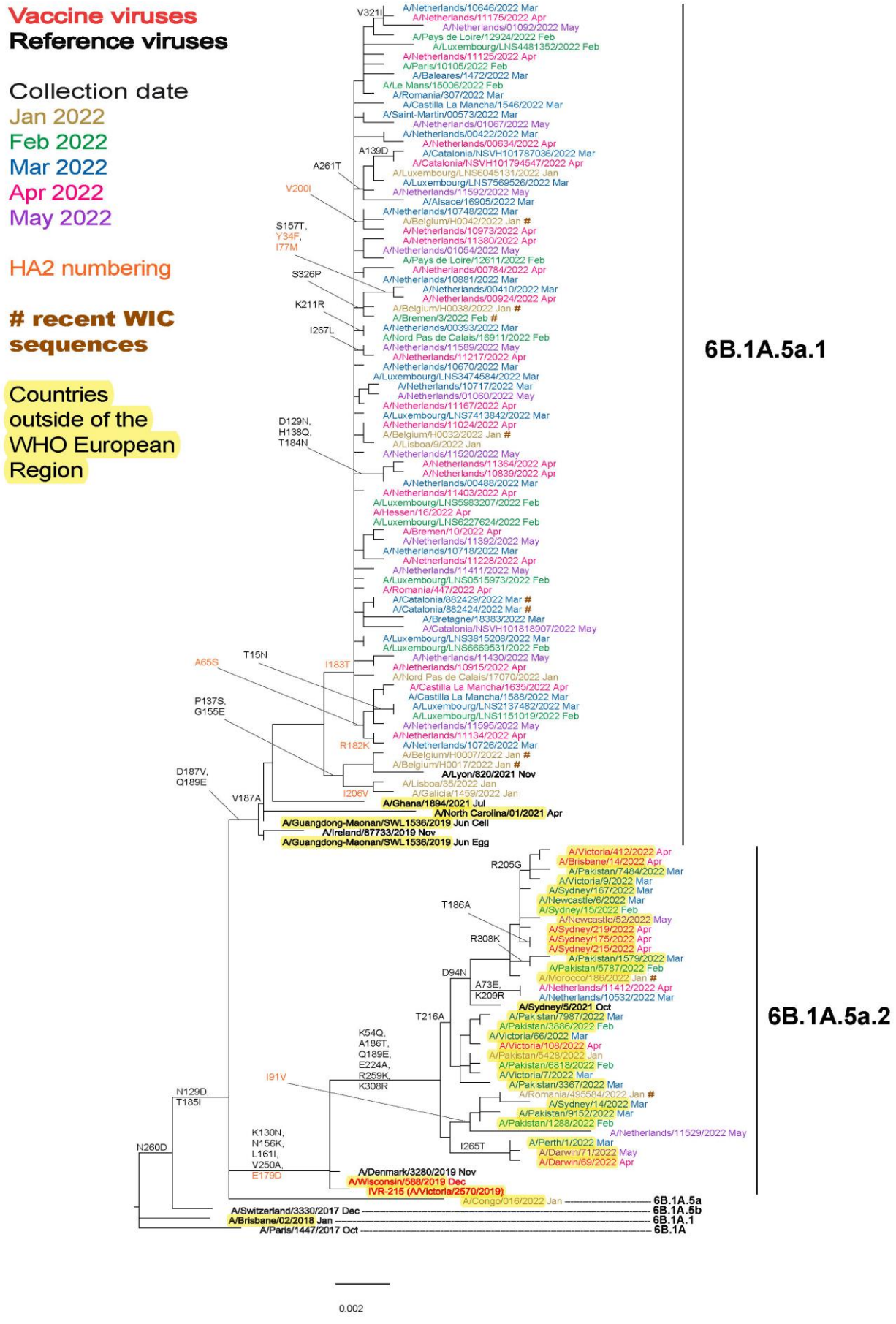


Table 4-1. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
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 MDCK	A/G-M SWL1536/19 Egg	A/Ghana 1894/21 Egg	A/Lyon 820/21 Egg	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	St Jude's F18/20*1	F09/20*1	F12/20*1	F02/22*1	F06/22*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.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	1280	640	1280	2560	640	80	<	80	40
A/Brisbane/02/2018	6B.1A.1	2018-01-04	E3/E2	2560	2560	1280	1280	2560	2560	1280	160	80	160	80
A/Switzerland/3330/2017	6B.1A.5b	2017-12-20	E6/E2	1280	640	1280	640	1280	1280	640	160	<	80	40
A/Ireland/87733/2019	6B.1A.5a.1	2019-11-03	E4	2560	1280	640	1280	2560	2560	1280	640	40	160	80
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	C2/MDCK1	2560	1280	640	640	2560	2560	1280	640	<	80	40
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	E3/E2	1280	640	640	640	1280	1280	640	320	<	80	40
A/Ghana/1894/2021	6B.1A.5a.1	2021-07-21	E3	1280	1280	640	640	2560	2560	1280	320	<	160	80
A/Lyon/820/2021	6B.1A.5a.1	2021-11-16	E1/E2	320	160	80	160	640	320	320	640	<	80	80
A/Denmark/3280/2019	6B.1A.5a.2	2019-11-10	MDCK4/MDCK6	80	40	<	40	80	80	<	80	1280	2560	2560
IVR-215 (A/Victoria/2570/2019)	6B.1A.5a.2	2018-11-22	E4/D7/E2	80	80	<	40	160	80	40	80	640	2560	1280
A/Sydney/5/2021	6B.1A.5a.2	2021-10-16	E3/E1	<	40	<	40	80	160	40	80	1280	2560	2560
TEST VIRUSES														
A/Albania/8093/2021	6B.1A.5a.2	2021-12-10	MDCK1	<	40	<	40	80	40	80	40	1280	5120	2560
A/Albania/942/2021	6B.1A.5a.2	2021-12-21	MDCK1	<	<	<	<	40	40	40	40	640	2560	1280
A/Albania/905/2021	6B.1A.5a.2	2021-12-21	MDCK1	<	<	<	<	40	<	<	40	1280	2560	1280
					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 4-2. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection fereret antisera								
Passage history				A/Ire 87733/19 Egg	A/G-M SWL1536/19 MDCK	A/G-M SWL1536/19 Egg	A/Ghana 1894/21 Egg	A/Lyon 820/21 Egg	A/Denmark 3280/19 MDCK	IVR-215 A/Vic/2570/19 Egg	A/Sydney 5/21 Egg
Ferret number				St Jude's F18/20[*1]	F09/20[*1]	F12/20[*1]	F02/22[*1]	F06/22[*1]	F08/20[*1]	F37/21[*1]	F04/22[*1]
Genetic group				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/Ireland/87733/2019	6B.1A.5a.1	2019-11-03	E4	640	2560	2560	1280	640	40	160	80
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	C2/MDCK1	1280	2560	2560	1280	640	<	80	80
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	E3/E2	640	2560	1280	1280	320	<	80	40
A/Ghana/1894/2021	6B.1A.5a.1	2021-07-21	E3	1280	1280	2560	2560	320	<	80	80
A/Lyon/820/2021	6B.1A.5a.1	2021-11-16	E1/E2	80	32	320	160	640	<	40	40
A/Denmark/3280/2019	6B.1A.5a.2	2019-11-10	MDCK4/MDCK6	40	80	80	40	80	2560	2560	2560
IVR-215 (A/Victoria/2570/2019)	6B.1A.5a.2	2018-11-22	E4/D7/E2	80	320	160	80	160	1280	2560	2560
A/Sydney/5/2021	6B.1A.5a.2		E3/E1	40	80	80	80	80	1280	2560	2560
TEST VIRUSES											
A/Bremen/3/2022	6B.1A.5a.1	2022-02-23	C1/MDCK1	640	2560	2560	1280	320	<	80	40
A/Catalonia/882424/2022	6B.1A.5a.1	2022-03-17	MDCK1	640	1280	1280	1280	320	<	<	40
A/Catalonia/882429/2022	6B.1A.5a.1	2022-03-17	MDCK1	640	1280	2560	1280	320	<	80	40
					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

Influenza A(H3N2) virus analyses

The first A(H3N2) HA phylogeny was generated using a representative set of sequences available in GISAID and generated at the WIC, as of 31 March 2022, for viruses with collection dates in the 2021-2022 influenza season (Figure 3a). The second phylogeny is based on representative A(H3N2) HA sequences made available in GISAID and generated at the WIC since 31 March 2022 for viruses with collection dates after 31 December 2021 (Figure 3b).

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 had 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 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 geographic 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 3a, for samples shared by many countries and areas and based on a representative set of sequences derived from those released in GISAID and those generated by WIC after 8 February 2022 until 31 March 2022, indicates small numbers of **3C.2a1b.1b** and **3C.2a1b.1a** viruses (notably in Africa with a small number detected in the WHO European Region) to have been detected and characterized 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** (gain a glycosylation site) 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. Just two viruses from Timor-Leste collected in January 2022 were 'Cambodia-like' (**3C.2a1b.2a.1** with **HA1** substitutions of **K171N**, **G186S** and **S198P**).

The second phylogeny, based on a representative set of HA sequences derived from viruses with collection dates after 31 December 2021 that had been submitted to GISAID after 31 March 2022 (Table 2), shows a very similar profile (Figure 3b). No recent 'Cambodia-like' (**3C.2a1b.2a.1**) viruses were reported, as was the case for **3C.2a1b.1b** viruses, while there were few **3C.2a1b.1a** viruses detected. The vast majority of recently collected viruses were 'Bangladesh-like' (**3C.2a1b.2a.2**) with notable expansion of subgroup (iv) viruses with HA1 D53G, D104G and K276R substitutions (Figure 3b). In both phylogenies sequences derived from samples collected in the WHO European Region are dispersed throughout the trees with the

'Bangladesh-like' (**3C.2a1b.2a.2**) viruses falling into multiple virus clusters defined by specific amino acid substitutions (Figures 3a and 3b).

'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 3a and 3b).

As described in many previous reports[3], influenza A(H3N2) viruses had been difficult to characterize 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 is now much alleviated 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 a single A(H3N2) virus from the Netherlands failed to yield a sufficient HA titre with guinea pig RBCs to allow HI analysis (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 187 A(H3N2) viruses characterized antigenically since the March report, 170 were 'Bangladesh-like' **3C.2a1b.2a.2** viruses, one was a **3C.2a1b.1a** virus and for 16 viruses sequencing is pending (Tables 5-1 to 5-7). The single **3C.2a1b.1a** virus, A/Netherlands/10206/2021, was recognised well, within fourfold of the respective homologous titres, by antisera raised against eight of the reference viruses; only that raised against A/England/214191723/2021 gave poor recognition (Table 5-4). Results for the 170 'Bangladesh-like' **3C.2a1b.2a.2** test viruses are summarised in Table 5-8. These viruses were recognised well only by post-infection ferret antisera raised against viruses with **3C.2a1b.2a.2** HAs. Antisera raised against cell culture-propagated A/Bangladesh/4005/2020, A/Stockholm/5/2021 and A/England/214191723/2021 recognised 157 (92%), 169 (99%) and 169 (99%) of the test viruses at titres within fourfold of the homologous titres, respectively. The antiserum raised against egg-propagated A/Darwin/9/2021 recognised 163 (96%) of the test viruses at titres within fourfold of the homologous titres. Antisera raised against the egg-propagated **3C.2a1b.2a.2** viruses A/Florida/01/2021 (**D53N**, commonly with **N96S** (gain a glycosylation site) and **I192F subgroup)** and A/Wyoming/01/2021 (**D53G**, **D104G** and **K276R** subgroup) recognised **3C.2a1b.2a.2** test viruses less well, only 11/27 (41%) and 1/27 (4%) respectively.

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 characterization 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 (https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf. Accessed on 15 September 2022)

[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2014. Stockholm: ECDC; 2014 (https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf. Accessed 15 September 2022)

Figure 3a. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID/WIC, March 2022)

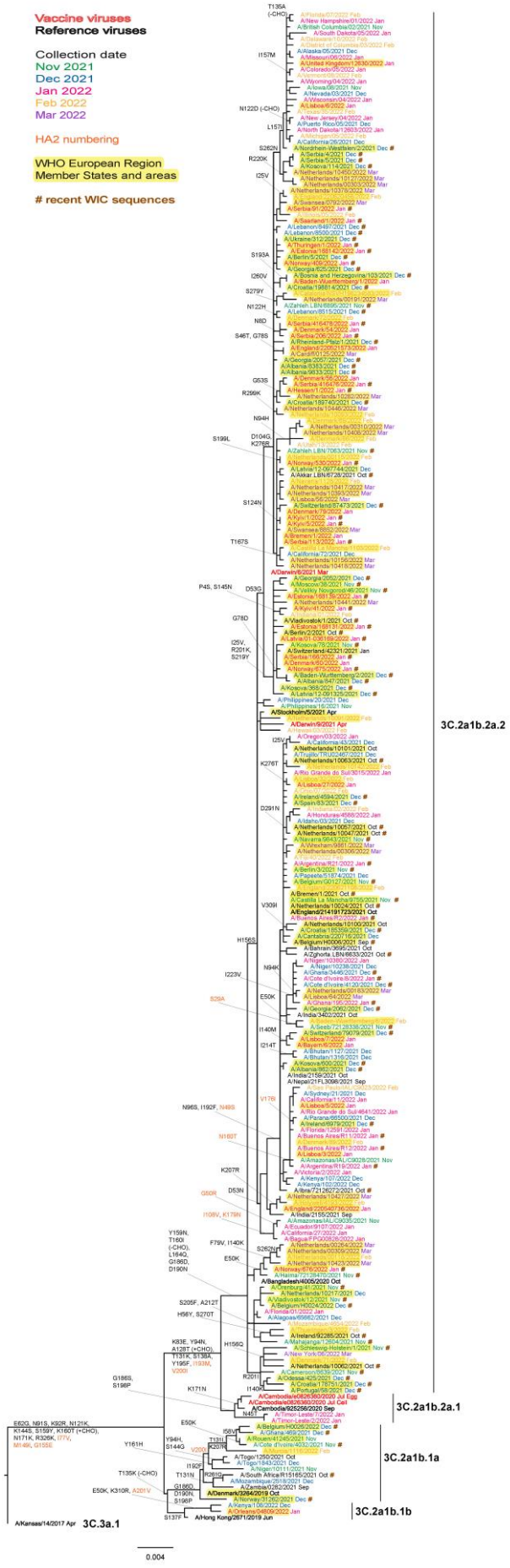


Figure 3b. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID/WIC, May 2022)

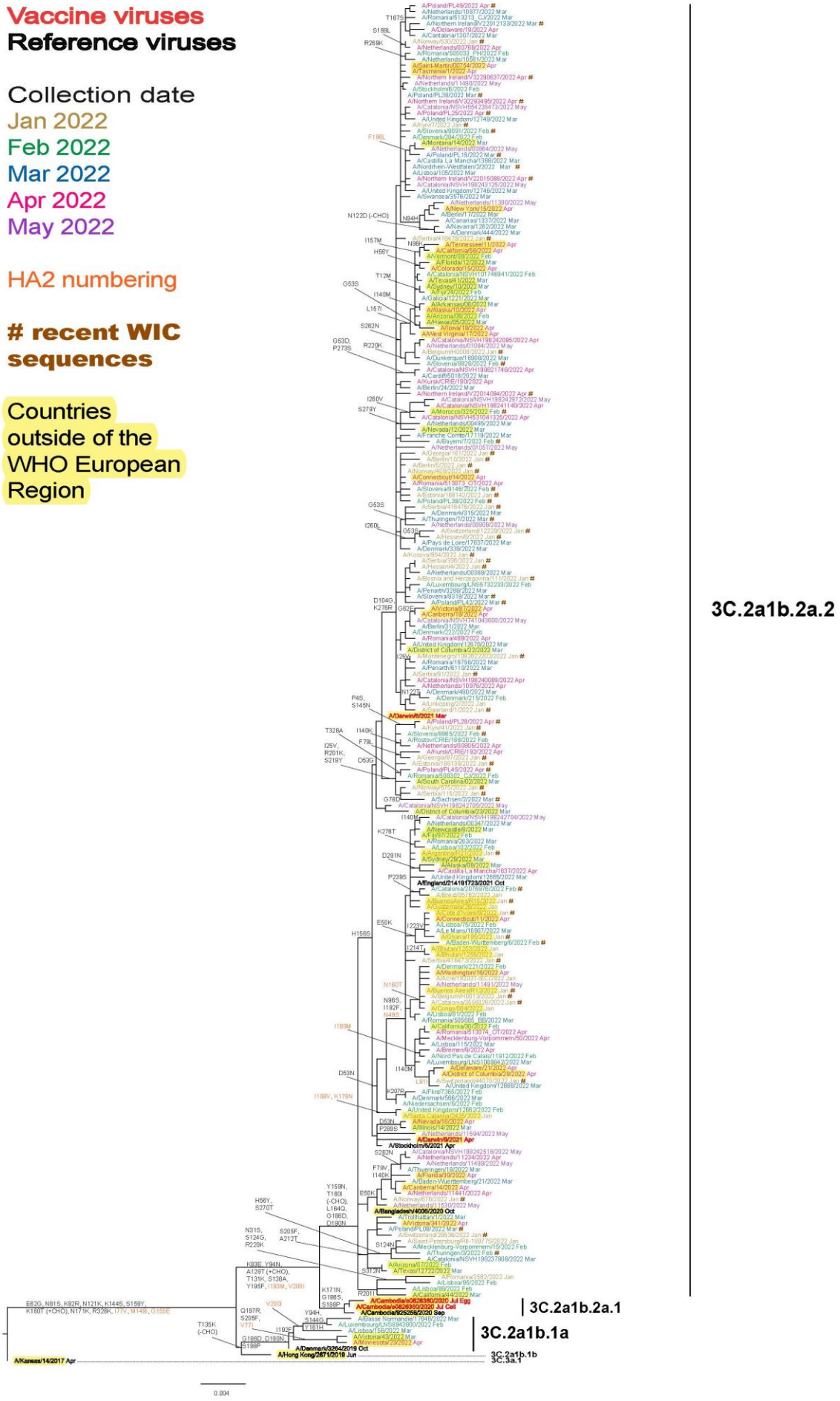


Table 5-1. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
	Passage history			A/Denmark 3264/19 SIAT	A/HK 2671/19 Cell	A/Camb 925256/20 SIAT	A/Camb e0826360/20 Egg	A/Bang 4005/20 SIAT	A/Stock 5/21 SIAT	A/Eng 214191723/21 SIAT	A/Darwin 9/21 Egg	A/Kansas 14/17 SIAT
	Ferret number			F19/20*1	St Judes F21/20*1	F03/21*1	F10/21*1	F07/21*1	F35/21*1	F07/22*1	F38/21*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.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	320	640	160	160	160	40	320	80
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	640	160	160	160	40	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT6	160	160	640	160	160	160	<	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	320	1280	320	320	320	640	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	160	320	320	640	640	640	1280	320
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	160	<	80	160	320	640	320	1280	80
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	80	<	80	80	160	320	640	1280	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	40	80	640	320	640	640	2560	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	40	80	80	40	80	80	160	640
TEST VIRUSES												
A/Israel/R-9278/2021	3C.2a1b.2a.2	2021-12-15	SIAT1	80	<	40	80	160	320	320	1280	40
A/Israel/R-9337/2021	3C.2a1b.2a.2	2021-12-17	SIAT1	40	<	40	80	160	320	320	640	40
A/Israel/R-9526/2021	3C.2a1b.2a.2	2021-12-21	SIAT1	320	40	160	320	320	640	320	1280	160
A/Israel/R-9603/2021	3C.2a1b.2a.2	2021-12-22	SIAT1	80	<	40	80	160	320	320	1280	40
A/Montenegro/596841121102/2021	3C.2a1b.2a.2	2021-12-28	SIAT1	80	<	40	160	160	640	320	1280	40
A/Israel/R-9997/2021	3C.2a1b.2a.2	2021-12-28	SIAT1	40	<	40	80	160	160	640	640	40
A/Montenegro/108262202/2022	3C.2a1b.2a.2	2022-01-10	SIAT1	80	<	40	160	160	640	320	1280	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 5-2. 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	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Darwin	A/Kansas
				3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	214191723/21	9/21	14/17
	Passage history			SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			F19/20*1	St Judes F21/20*1	F03/21*1	F10/21*1	F07/21*1	F35/21*1	F07/22*1	F38/21*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.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	640	640	640	320	160	320	80	640	320
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	640	160	160	160	40	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT4	160	160	640	160	160	160	40	160	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	80	<	80	1280	80	320	160	320	80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	160	160	320	640	320	1280	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	80	<	80	160	160	640	320	1280	40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	40	<	40	440	80	320	320	640	<
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	80	320	160	640	640	2560	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<	40	40	40	80	40	160	320
TEST VIRUSES												
A/Netherlands/10018/2021	3C.2a1b.2a.2		MDCK-MIX2/SIAT1	40	<	40	80	80	160	640	640	40
A/Netherlands/10011/2021	3C.2a1b.2a.2	2021-09-20	MDCK-MIX2/SIAT1	40	<	40	40	80	160	320	640	<
A/Netherlands/10012/2021	3C.2a1b.2a.2	2021-09-30	MDCK-MIX1/SIAT1	40	<	40	80	80	320	640	1280	<
A/Bremen/1/2021	3C.2a1b.2a.2	2021-10-11	P1/SIAT2	40	160	80	80	80	320	640	640	40
A/Netherlands/10062/2021	3C.2a1b.2a.2	2021-10-21	MDCK-MIX2/SIAT1	160	<	80	160	160	320	320	640	80
A/Netherlands/10057/2021	3C.2a1b.2a.2	2021-10-22	MDCK-MIX2/SIAT2	40	<	40	80	80	320	640	640	<
A/Netherlands/10063/2021	3C.2a1b.2a.2	2021-10-23	MDCK-MIX2/SIAT1	40	<	40	40	40	160	320	320	<
A/Berlin/2/2021	3C.2a1b.2a.2	2021-10-25	P1/SIAT1	80	160	80	160	160	320	640	1280	80
A/Schleswig-Holstein/1/2021	3C.2a1b.2a.2	2021-11-15	P1/SIAT1	160	160	80	320	160	320	160	640	80
A/Berlin/3/2021	3C.2a1b.2a.2	2021-11-16	P1/SIAT1	40	160	40	80	80	320	640	640	<
A/Hessen/1/2021	3C.2a1b.2a.2	2021-11-22	P1/SIAT1	40	160	<	40	80	320	320	1280	<
A/Baden-Wurttemberg/1/2021	3C.2a1b.2a.2	2021-11-26	P1/SIAT1	40	160	<	40	80	160	160	640	<
A/Slovenia/19583/2021	3C.2a1b.2a.2	2021-11-27	MDCKx/SIAT1	160	<	80	160	320	640	640	1280	80
A/Kyiv/393/2021	3C.2a1b.2a.2	2021-12-13	SIAT1	40	160	40	80	160	320	640	640	40
A/Rheinland-Pfalz/1/2021	3C.2a1b.2a.2	2021-12-16	P1/SIAT1	40	160	<	40	80	320	320	640	40
A/Slovenia/679/2022	3C.2a1b.2a.2	2021-12-30	MDCKx/SIAT1	160	<	80	160	160	640	640	1280	80
A/Slovenia/1054/2022	3C.2a1b.2a.2	2022-01-05	MDCKx/SIAT1	160	<	80	320	320	640	640	1280	80
A/Slovenia/8821/2022	3C.2a1b.2a.2	2022-02-02	SIAT1/SIAT1	<	<	40	80	160	320	320	1280	<
A/Slovenia/8830/2022	3C.2a1b.2a.2	2022-02-03	MDCK1/SIAT1	<	<	40	80	160	320	320	640	40
A/Slovenia/8828/2022	3C.2a1b.2a.2	2022-02-03	SIAT1/SIAT1	<	<	40	80	80	160	320	640	<
A/Slovenia/8720/2022	3C.2a1b.2a.2	2022-02-10	SIAT1/MDCK1/SIAT1	<	<	<	40	80	320	320	640	<
A/Slovenia/8723/2022	3C.2a1b.2a.2	2022-02-11	MDCK1/SIAT1	<	<	<	40	80	320	320	640	<
A/Slovenia/8799/2022	3C.2a1b.2a.2	2022-02-15	SIAT1/SIAT1	<	<	40	40	160	320	320	1280	<
A/Slovenia/8965/2022	3C.2a1b.2a.2	2022-02-21	MDCK1/SIAT3	80	<	40	160	160	320	320	640	<
A/Slovenia/9091/2022	3C.2a1b.2a.2	2022-02-22	MDCKx/SIAT1	<	<	<	<	80	160	160	640	<
A/Slovenia/9090/2022	3C.2a1b.2a.2	2022-02-22	MDCKx/SIAT1	<	<	<	40	160	320	320	1280	<
A/Slovenia/9146/2022	3C.2a1b.2a.2	2022-02-23	SIAT1/SIAT1	<	<	<	40	160	320	320	640	<
A/Slovenia/9216/2022	3C.2a1b.2a.2	2022-02-24	MDCKx/SIAT1	<	<	40	80	160	320	320	640	<
A/Slovenia/9302/2022	3C.2a1b.2a.2	2022-02-28	MDCKx/SIAT1	<	<	40	160	320	640	640	1280	80
A/Slovenia/9318/2022	3C.2a1b.2a.2	2022-03-02	SIATx/SIAT1	<	<	40	40	160	320	320	1280	<
A/Slovenia/9356/2022	3C.2a1b.2a.2	2022-03-03	SIATx/SIAT1	40	160	40	40	80	320	320	1280	<
							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 5-3. 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	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Darwin	A/Kansas
	Passage history			3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	21419172 3/21	9/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			F19/20 $^{+1}$	St Judes F21/20 $^{+1}$	F03/21 $^{+1}$	F10/21 $^{+1}$	F07/21 $^{+1}$	F35/21 $^{+1}$	F07/22 $^{+1}$	F38/21 $^{+1}$	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.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	320	640	160	160	160	40	320	80
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	640	160	160	160	40	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT6	160	160	320	160	160	160	<	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	320	1280	320	320	320	640	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	160	320	320	640	640	640	1280	320
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	160	<	80	160	320	640	320	1280	80
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	80	<	80	80	160	320	640	1280	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	40	80	640	320	640	640	2560	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	40	80	80	40	80	80	160	640
TEST VIRUSES												
A/Serbia/5/2021	3C.2a1b.2a.2	2021-12-31	SIAT1	80	<	40	160	160	320	320	1280	<
A/Serbia/91/2022	3C.2a1b.2a.2	2022-01-06	SIAT1	40	<	40	40	160	320	320	1280	<
A/Serbia/112/2022	3C.2a1b.2a.2	2022-01-06	SIAT1	80	<	40	80	160	320	320	1280	<
A/Serbia/199/2022	3C.2a1b.2a.2	2022-01-10	SIAT1	80	<	40	80	160	320	320	1280	<
						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 5-4. 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	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Darwin	A/Kansas
					3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	214191723/21	9/21	14/17
		Passage history			SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
		Ferret number			F19/20*1	St Judes F21/20*1	F03/21*1	F10/21*1	F07/21*1	F35/21*1	F07/22*1	F38/21*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.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES													
A/Denmark/3264/2019		3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	160	320	160	160	160	<	320	80
A/Hong Kong/2671/2019		3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	160	320	640	160	160	160	<	160	160
A/Cambodia/925256/2020		3C.2a1b.2a.1	2020-09-25	SIAT5	80	160	640	160	160	160	<	320	160
A/Cambodia/e0826360/2020		3C.2a1b.2a.1	2020-07-16	E5/E2	80	<	160	1280	320	160	320	320	80
A/Bangladesh/4005/2020		3C.2a1b.2a.2	2020-10-04	SIAT3	160	80	320	320	640	640	640	1280	160
A/Stockholm/5/2021		3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	80	<	80	160	320	640	320	1280	40
A/England/214191723/2021		3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	80	<	80	80	160	320	640	640	<
A/Darwin/9/2021		3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	160	640	640	640	640	2560	80
A/Kansas/14/2017		3C.3a.1	2017-12-14	SIAT3/SIAT2	40	40	80	80	80	80	80	160	320
TEST VIRUSES													
A/Netherlands/10066/2021		3C.2a1b.2a.2	2021-10-20	MDCK-MIX2/SIAT1	<	<	40	40	80	80	320	320	<
A/Netherlands/10067/2021		3C.2a1b.2a.2	2021-10-21	MDCK-MIX2/SIAT2	40	<	80	80	160	320	640	640	<
A/Netherlands/10122/2021		3C.2a1b.2a.2	2021-10-26	MDCK-MIX2/SIAT2	80	<	40	160	160	160	640	640	40
A/Netherlands/10065/2021		3C.2a1b.2a.2	2021-10-29	MDCK-MIX2/SIAT1	40	<	80	80	160	160	640	640	<
A/Netherlands/10121/2021		3C.2a1b.2a.2	2021-10-31	MDCK-MIX2/SIAT2	40	<	40	80	160	160	640	640	<
A/Netherlands/10109/2021		3C.2a1b.2a.2	2021-10-31	MDCK-MIX2/SIAT1	<	<	40	80	80	160	320	320	<
A/Netherlands/10108/2021		3C.2a1b.2a.2	2021-11-07	MDCK-MIX2/SIAT2	40	<	80	80	160	320	640	640	<
A/Netherlands/10128/2021		3C.2a1b.2a.2	2021-11-08	MDCK-MIX2/SIAT1	<	<	40	40	80	160	640	640	<
A/Netherlands/10119/2021		3C.2a1b.2a.2	2021-11-09	MDCK-MIX2/SIAT1	<	<	40	40	80	160	320	640	<
A/Netherlands/10114/2021		3C.2a1b.2a.2	2021-11-09	MDCK-MIX2/SIAT1	40	<	40	80	160	320	640	1280	<
A/Netherlands/10129/2021		3C.2a1b.2a.2	2021-11-10	MDCK-MIX2/SIAT1	40	<	80	160	160	320	640	1280	40
A/Netherlands/10138/2021		3C.2a1b.2a.2	2021-11-15	MDCK-MIX2/SIAT1	80	<	40	80	80	160	640	640	<
A/Netherlands/10137/2021		3C.2a1b.2a.2	2021-11-16	MDCK-MIX2/SIAT1	40	<	40	80	160	160	640	640	<
A/Netherlands/10132/2021		3C.2a1b.2a.2	2021-11-16	MDCK-MIX2/SIAT1	40	<	40	80	160	160	640	640	<
A/Netherlands/10145/2021		3C.2a1b.2a.2	2021-11-17	MDCK-MIX2/SIAT1	40	<	80	80	160	160	640	640	40
A/Netherlands/10144/2021		3C.2a1b.2a.2	2021-11-17	MDCK-MIX2/SIAT1	40	<	80	80	160	160	640	640	<
A/Netherlands/10140/2021		3C.2a1b.2a.2	2021-11-17	MDCK-MIX2/SIAT1	40	<	<	80	160	160	640	640	<
A/Netherlands/10148/2021		3C.2a1b.2a.2	2021-11-18	MDCK-MIX2/SIAT1	40	<	80	80	160	320	640	640	<
A/Netherlands/10147/2021		3C.2a1b.2a.2	2021-11-20	MDCK-MIX2/SIAT2	40	<	80	160	320	320	1280	1280	40
A/Netherlands/10150/2021		3C.2a1b.2a.2	2021-11-23	MDCK-MIX2/SIAT1	40	<	80	80	160	160	640	640	<
A/Netherlands/10151/2021		3C.2a1b.2a.2	2021-11-24	MDCK-MIX2/SIAT1	40	40	80	80	160	160	640	640	<
A/Netherlands/10154/2021		3C.2a1b.2a.2	2021-11-25	MDCK-MIX2/SIAT1	<	<	40	80	160	160	640	640	<
A/Kosova/78/2021		3C.2a1b.2a.2	2021-11-29	SIAT1	160	<	80	320	320	640	640	1280	80
A/Netherlands/10180/2021		3C.2a1b.2a.2	2021-12-02	MDCK-MIX2/SIAT1	<	<	<	40	160	160	640	640	<
A/Netherlands/10182/2021		3C.2a1b.2a.2	2021-12-03	MDCK-MIX2/SIAT1	80	<	80	320	160	320	320	640	40
A/Kosova/114/2021		3C.2a1b.2a.2	2021-12-03	SIAT1	80	<	40	160	160	320	320	640	40
A/Netherlands/10202/2021		3C.2a1b.2a.2	2021-12-06	MDCK-MIX2/SIAT1	<	<	40	80	160	160	320	640	<
A/Netherlands/10184/2021		3C.2a1b.2a.2	2021-12-08	MDCK-MIX2/SIAT1	80	<	80	160	160	640	320	640	40
A/Albania/8441/2021		3C.2a1b.2a.2	2021-12-10	SIAT1	<	<	40	80	80	160	320	640	<
A/Albania/8322/2021		3C.2a1b.2a.2	2021-12-10	SIAT1	80	<	80	320	320	640	640	1280	40
A/Netherlands/10203/2021		3C.2a1b.2a.2	2021-12-11	MDCK-MIX2/SIAT1	80	<	40	80	160	320	320	1280	<
A/Albania/8614/2021		3C.2a1b.2a.2	2021-12-11	SIAT1	80	<	80	320	320	640	640	1280	40
A/Kosova/368/2021		3C.2a1b.2a.2	2021-12-14	SIAT1	40	<	40	40	160	320	320	640	<
A/Netherlands/10206/2021		3C.2a1b.1a	2021-12-15	MDCK-MIX2/SIAT1	160	160	320	320	320	320	40	640	80
A/Netherlands/10193/2021		3C.2a1b.2a.2	2021-12-16	MDCK-MIX2/SIAT1	160	<	80	320	320	320	320	640	80
A/Albania/9833/2021		3C.2a1b.2a.2	2021-12-16	SIAT1	40	<	40	40	160	320	320	640	<
A/Albania/9725/2021		3C.2a1b.2a.2	2021-12-16	SIAT1	160	<	80	320	320	640	640	1280	80
A/Albania/78/2021		3C.2a1b.2a.2	2021-12-17	SIAT1	80	<	40	160	320	640	640	1280	40
A/Albania/31/2021		3C.2a1b.2a.2	2021-12-17	SIAT1	160	<	160	320	320	640	640	2560	80
A/Netherlands/10204/2021		3C.2a1b.2a.2	2021-12-18	MDCK-MIX2/SIAT1	40	<	40	40	160	160	320	640	<
A/Netherlands/10205/2021		3C.2a1b.2a.2	2021-12-19	MDCK-MIX2/SIAT1	160	<	80	160	640	320	320	640	80
A/Netherlands/10194/2021		3C.2a1b.2a.2	2021-12-19	MDCK-MIX2/SIAT1	40	<	40	40	80	160	1280	640	<
A/Netherlands/10197/2021		3C.2a1b.2a.2	2021-12-20	MDCK-MIX2/SIAT1	40	<	<	80	160	320	320	640	<
A/Netherlands/10195/2021		3C.2a1b.2a.2	2021-12-20	MDCK-MIX2/SIAT2	160	<	80	160	640	640	640	1280	80
A/Albania/622/2021		3C.2a1b.2a.2	2021-12-20	SIAT1	160	<	80	320	320	640	640	1280	80
A/Kosova/587/2021		3C.2a1b.2a.2	2021-12-21	SIAT1	80	<	80	320	320	640	640	1280	40
A/Albania/890/2021		3C.2a1b.2a.2	2021-12-21	SIAT1	40	<	40	40	160	320	320	640	<
A/Albania/862/2021		3C.2a1b.2a.2	2021-12-21	SIAT1	40	<	40	80	160	320	640	640	<
A/Kosova/607/2021		3C.2a1b.2a.2	2021-12-22	SIAT1	80	<	40	160	160	320	640	1280	40
A/Kosova/618/2021		3C.2a1b.2a.2	2021-12-22	SIAT1	<	<	40	80	80	160	640	640	<
A/Netherlands/10215/2021		3C.2a1b.2a.2	2021-12-23	MDCK-MIX1/SIAT1	80	<	80	320	320	320	320	640	80
A/Netherlands/10210/2021		3C.2a1b.2a.2	2021-12-23	MDCK-MIX2/SIAT1	160	<	40	320	320	640	640	640	40
A/Netherlands/10208/2021		3C.2a1b.2a.2	2021-12-26	MDCK-MIX2/SIAT1	40	<	40	40	80	160	320	320	<
A/Kosova/701/2021		3C.2a1b.2a.2	2021-12-27	SIAT1	80	<	40	160	160	320	320	1280	40
A/Kosova/710/2021		3C.2a1b.2a.2	2021-12-27	SIAT1	80	<	40	320	320	320	640	1280	40
A/Netherlands/10231/2021		3C.2a1b.2a.2	2021-12-28	MDCK-MIX1/SIAT1	160	<	80	320	320	320	160	640	80
A/Netherlands/10230/2021		3C.2a1b.2a.2	2021-12-28	MDCK-MIX1/SIAT1	160	<	80	320	320	320	160	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 5-5. 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	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Darwin	A/Kansas
	Passage history			3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	21419172 3/21	9/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			F19/20 -1	St Judes F21/20 -1	F03/21 -1	F10/21 -1	F07/21 -1	F35/21 -1	F07/22 -1	F38/21 -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.2a1b.2a.2	3C.3a1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	160	640	160	320	160	40	320	160
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	160	160	640	160	160	80	40	320	80
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT4	160	160	640	160	320	160	40	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	160	1280	320	160	320	640	80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	320	320	640	640	640	1280	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	160	<	80	160	320	640	640	1280	40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	40	<	80	80	160	320	640	640	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	80	640	320	640	640	2560	80
A/Kansas/14/2017	3C.3a1	2017-12-14	SIAT3/SIAT2	80	40	80	80	80	160	80	160	640
TEST VIRUSES												
A/Georgia/2048/2021	3C.2a1b.2a.2	2021-12-16	SIAT1	160	<	160	320	320	640	640	1280	80
A/Georgia/2052/2021	3C.2a1b.2a.2	2021-12-17	SIAT1	160	40	80	320	320	640	640	1280	80
A/Georgia/2060/2021	3C.2a1b.2a.2	2021-12-18	SIAT2	<	<	40	40	80	160	640	640	<
A/Georgia/2063/2021	3C.2a1b.2a.2	2021-12-19	SIAT1	320	40	80	640	320	320	640	1280	80
A/Georgia/87/2022	3C.2a1b.2a.2	2022-01-12	SIAT1	160	<	160	320	320	640	640	2560	80
A/Georgia/132/2022	3C.2a1b.2a.2	2022-01-18	SIAT1	80	<	80	80	160	640	640	1280	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 5-6. 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/326/4/19	A/HK/2671/19	A/Camb/925256/20	A/Camb/e0826360/20	A/Bang/400/5/20	A/Stock/5/21	A/Eng/214191723/21	A/Darwin/9/21	A/Kansas/14/17
Passage history				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
Ferret number				F19/20^{-1}	St Judes F21/20^{-1}	F03/21^{-1}	F10/21^{-1}	F07/21^{-1}	F35/21^{-1}	F07/22^{-1}	F38/21^{-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.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	640	320	640	320	320	320	80	320	320
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	1280	160	160	160	80	320	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT4	160	160	1280	320	320	160	40	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	80	<	80	1280	160	160	160	160	40
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT5	320	80	320	320	640	640	640	1280	320
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	160	<	80	160	320	640	640	1280	40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	80	<	80	80	320	640	1280	640	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	160	640	320	640	640	1280	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	40	80	40	80	80	80	80	320
TEST VIRUSES												
A/Catalonia/800505/2021	3C.2a1b.2a.2	2021-10-25	C0/SIAT1	80	<	80	80	160	320	640	640	40
A/Catalonia/3551005/2021	3C.2a1b.2a.2	2021-12-07	C0/SIAT1	80	<	80	80	320	640	640	640	40
A/Thuringen/2/2022	3C.2a1b.2a.2	2022-01-04	C2/SIAT1	80	<	40	40	160	320	320	640	<
A/Catalonia/3556026/2022	3C.2a1b.2a.2	2022-01-06	C0/SIAT1	40	<	40	80	160	320	640	640	40
A/Berlin/5/2022	3C.2a1b.2a.2	2022-01-10	C1/SIAT1	40	<	40	80	160	320	320	640	<
A/Catalonia/13522/2022	3C.2a1b.2a.2	2022-01-17	C0/SIAT1	40	<	80	80	160	320	640	640	40
A/Catalonia/13520/2022	3C.2a1b.2a.2	2022-01-17	C0/SIAT1	80	<	80	80	160	320	1280	640	40
A/Baden-Wurttemberg/8/2022	3C.2a1b.2a.2	2022-01-24	C1/SIAT1	160	<	80	320	320	640	640	1280	80
A/Sachsen/1/2022	3C.2a1b.2a.2	2022-01-24	C1/SIAT1	40	<	40	40	160	320	320	640	<
A/Hessen/4/2022	3C.2a1b.2a.2	2022-01-24	C1/SIAT1	80	<	40	80	160	320	320	640	<
A/Berlin/10/2022	3C.2a1b.2a.2	2022-01-31	C1/SIAT1	80	<	80	40	160	320	320	1280	<
A/Bremen/1/2022	3C.2a1b.2a.2	2022-01-31	C1/SIAT1	160	40	80	160	320	1280	640	1280	40
A/Hessen/6/2022	3C.2a1b.2a.2	2022-01-31	C1/SIAT1	80	<	80	80	160	640	640	1280	40
A/Thuringen/3/2022	3C.2a1b.2a.2	2022-02-01	C1/SIAT1	320	80	160	640	1280	1280	1280	1280	160
A/Catalonia/13692/2022	pending	2022-02-02	C0/SIAT1	40	<	40	80	160	320	640	640	40
A/Bayern/4/2022	3C.2a1b.2a.2	2022-02-02	C1/SIAT1	80	<	40	40	160	320	320	640	<
A/Baden-Wurttemberg/5/2022	3C.2a1b.2a.2	2022-02-04	C1/SIAT1	160	<	160	320	320	1280	640	1280	80
A/Hessen/8/2022	3C.2a1b.2a.2	2022-02-07	C1/SIAT1	160	40	80	320	320	640	640	1280	80
A/Baden-Wurttemberg/6/2022	3C.2a1b.2a.2	2022-02-08	C1/SIAT1	40	<	40	80	160	320	1280	640	<
A/Catalonia/13731/2022	3C.2a1b.2a.2	2022-02-09	C0/SIAT1	40	<	80	80	160	320	640	640	40
A/Catalonia/13738/2022	3C.2a1b.2a.2	2022-02-10	C0/SIAT1	80	<	80	160	320	640	1280	640	80
A/Catalonia/13737/2022	3C.2a1b.2a.2	2022-02-10	C0/SIAT1	40	<	40	<	40	160	640	640	40
A/Niedersachsen/8/2022	3C.2a1b.2a.2	2022-02-11	C1/SIAT1	80	<	40	80	160	320	320	640	<
A/Thuringen/4/2022	3C.2a1b.2a.2	2022-02-14	C1/SIAT1	40	<	40	40	160	320	320	640	<
A/Catalonia/13758/2022	3C.2a1b.2a.2	2022-02-16	C0/SIAT1	<	<	40	40	80	160	320	320	<
A/Catalonia/13756/2022	3C.2a1b.2a.2	2022-02-16	C0/SIAT1	80	<	80	80	160	640	320	640	40
A/Catalonia/13755/2022	3C.2a1b.2a.2	2022-02-16	C0/SIAT1	80	<	80	80	160	320	320	640	<
A/Bremen/2/2022	3C.2a1b.2a.2	2022-02-18	C1/SIAT1	160	<	80	320	320	640	640	1280	80
A/Catalonia/2076976/2022	3C.2a1b.2a.2	2022-02-23	C0/SIAT1	40	<	80	80	160	320	320	640	<
A/Catalonia/13775/2022	3C.2a1b.2a.2	2022-02-23	C0/SIAT1	40	<	80	80	160	320	320	640	40
A/Catalonia/13766/2022	3C.2a1b.2a.2	2022-02-23	C0/SIAT1	80	<	80	160	320	640	1280	640	80
A/Bayern/7/2022	3C.2a1b.2a.2	2022-02-24	C1/SIAT1	40	<	40	40	160	320	160	640	<
A/Rheinland-Pfalz/1/2022	3C.2a1b.2a.2	2022-02-25	C1/SIAT1	80	80	80	80	320	640	640	1280	40
A/Thuringen/6/2022	3C.2a1b.2a.2	2022-02-28	C1/SIAT1	80	<	40	80	160	320	320	640	<
A/Denmark/267/2022	pending	2022-02-28	SIAT2/SIAT1	80	<	80	80	160	320	640	1280	<
A/Catalonia/2081558/2022	3C.2a1b.2a.2	2022-03-01	C0/SIAT1	80	<	40	80	160	320	640	1280	40
A/Denmark/294/2022	pending	2022-03-01	SIAT2/SIAT1	80	<	80	80	160	640	640	1280	<
A/Denmark/333/2022	pending	2022-03-02	SIAT2/SIAT1	80	<	40	80	160	320	320	640	<
A/Denmark/320/2022	pending	2022-03-02	SIAT2/SIAT2	80	<	80	80	160	640	320	1280	<
A/Denmark/335/2022	pending	2022-03-03	SIAT2/SIAT1	80	<	40	80	160	320	320	1280	<
A/Thuringen/7/2022	3C.2a1b.2a.2	2022-03-06	C1/SIAT1	160	40	160	160	320	640	1280	1280	40
A/Bremen/4/2022	3C.2a1b.2a.2	2022-03-07	C2/SIAT2	80	<	40	40	160	320	320	640	<
A/Denmark/499/2022	pending	2022-03-07	SIAT2/SIAT1	80	<	40	40	160	320	320	640	<
A/Catalonia/3565654/2022	3C.2a1b.2a.2	2022-03-08	C0/SIAT1	80	<	40	80	160	640	640	1280	40
A/Denmark/558/2022	pending	2022-03-09	SIAT2/SIAT1	80	<	80	80	160	320	640	1280	40
A/Nordrhein-Westfalen/2/2022	3C.2a1b.2a.2	2022-03-10	C1/SIAT1	320	80	320	640	640	1280	1280	5120	80
A/Denmark/1098/2022	pending	2022-03-10	SIAT2/SIAT1	80	<	80	80	160	320	320	640	<
A/Denmark/602/2022	pending	2022-03-10	SIAT2/SIAT1	80	<	40	40	160	320	320	640	40
A/Denmark/612/2022	pending	2022-03-11	SIAT2/SIAT1	80	<	40	80	320	320	320	1280	<
A/Sachsen/2/2022	3C.2a1b.2a.2	2022-03-14	C1/SIAT1	160	<	80	320	320	640	640	640	80
A/Denmark/922/2022	pending	2022-03-16	SIAT2/SIAT1	80	<	40	40	160	320	320	640	<
A/Denmark/1253/2022	pending	2022-03-18	SIAT2/SIAT1	80	<	40	80	160	320	320	640	<
A/Denmark/2031/2022	pending	2022-04-05	SIAT2/SIAT1	80	<	40	80	320	320	320	1280	40
A/Denmark/1836/2022	pending	2022-04-05	SIAT2/SIAT1	80	<	40	80	160	320	320	1280	<
							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 5-7. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera								NEW	NEW		
	Passage history			A/Denmark/3264/19	A/HK/2671/19 Cell	A/Camb/925256/20 SIAT	A/Camb/e08263360/20 Egg	A/Bang/4005/20 SIAT	A/Stock/5/21 SIAT	A/Eng/214191723/21 SIAT	A/Darwin/9/21 Egg	A/Flor/02/21 Egg	A/Wyom/01/21 Egg	A/Kansas/14/17 SIAT
	Ferret number			F19/20[-1]	F21/20[-1] St Judes	F03/21[-1]	F10/21[-1]	F07/21[-1]	F35/21[-1]	F07/22[-1]	F38/21[-1]	F19/22[-1]	F20/22[-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.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	320	640	160	320	320	40	320	80	<	160
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	160	320	320	160	160	160	40	160	80	<	80
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	80	640	160	160	160	40	320	40	<	80
A/Cambodia/e08263360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	160	1280	320	160	160	320	80	40	80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	160	160	640	640	160	640	160	40	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	80	<	80	80	320	640	160	1280	320	160	40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	40	<	40	80	160	320	160	640	320	80	<
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	160	<	80	640	320	640	160	2560	320	640	80
A/Florida/02/2021	3C.2a1b.2a.2	2021-10-20	E4 (Am2AL2)	80	<	80	320	320	640	320	1280	1280	320	80
A/Wyoming/01/2021	3C.2a1b.2a.2	2021-08-27	E4 (Am2AL2)	160	<	80	320	320	640	160	1280	320	2560	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<	80	40	80	80	40	80	40	<	320
TEST VIRUSES														
A/Poland/PL39/2022	3C.2a1b.2a.2	2022-02-18	SIAT2	40	<	40	40	160	320	160	640	160	320	<
A/Poland/PL16/2022	3C.2a1b.2a.2	2022-03-13	SIAT1	80	<	40	40	160	640	320	1280	320	640	<
A/Poland/PL40/2022	3C.2a1b.2a.2	2022-03-14	SIAT2	40	<	40	40	160	320	320	640	160	320	<
A/Poland/PL15/2022	3C.2a1b.2a.2	2022-03-22	SIAT1	80	<	40	40	160	320	320	640	160	320	<
A/Poland/PL14/2022	3C.2a1b.2a.2	2022-03-26	SIAT1	40	<	40	80	160	320	320	640	160	320	40
A/Poland/PL13/2022	3C.2a1b.2a.2	2022-03-26	SIAT1	40	<	40	80	160	640	320	640	160	160	40
A/Poland/PL12/2022	3C.2a1b.2a.2	2022-03-28	SIAT1	160	<	80	320	320	640	640	640	320	160	40
A/Poland/PL10/2022	3C.2a1b.2a.2	2022-03-29	SIAT1	40	<	40	80	160	320	320	640	160	160	40
A/Poland/PL09/2022	3C.2a1b.2a.2	2022-03-29	SIAT1	80	<	80	160	320	640	640	1280	320	320	40
A/Poland/PL11/2022	pending	2022-03-29	SIAT1	160	<	80	160	160	640	320	640	160	160	40
A/Poland/PL42/2022	3C.2a1b.2a.2	2022-03-30	SIAT2	80	<	40	40	160	320	320	640	160	320	<
A/Poland/PL38/2022	3C.2a1b.2a.2	2022-03-30	SIAT1	80	<	40	40	160	320	320	640	160	320	<
A/Poland/PL19/2022	3C.2a1b.2a.2	2022-03-30	SIAT1	40	<	40	40	160	320	160	320	160	320	<
A/Poland/PL08/2022	3C.2a1b.2a.2	2022-03-30	SIAT1	160	<	80	320	320	320	160	320	80	<	80
A/Poland/PL07/2022	3C.2a1b.2a.2	2022-03-31	SIAT1	80	<	40	80	320	640	640	640	320	320	40
A/Poland/PL06/2022	3C.2a1b.2a.2	2022-04-02	SIAT1	40	<	40	160	160	640	320	1280	320	320	40
A/Poland/PL04/2022	3C.2a1b.2a.2	2022-04-03	SIAT1	80	<	40	80	160	320	320	640	160	320	<
A/Poland/PL03/2022	3C.2a1b.2a.2	2022-04-03	SIAT1	40	<	<	80	160	640	320	640	160	160	40
A/Poland/PL21/2022	3C.2a1b.2a.2	2022-04-04	SIAT1	40	<	40	80	320	640	320	640	320	160	40
A/Poland/PL24/2022	3C.2a1b.2a.2	2022-04-05	SIAT1	40	<	80	80	320	640	320	640	320	160	40
A/Poland/PL23/2022	3C.2a1b.2a.2	2022-04-05	SIAT1	80	<	40	160	160	640	320	640	320	160	40
A/Poland/PL22/2022	3C.2a1b.2a.2	2022-04-05	SIAT1	80	<	40	160	320	640	640	640	320	320	40
A/Poland/PL25/2022	3C.2a1b.2a.2	2022-04-07	SIAT1	80	<	40	40	160	320	160	640	160	320	<
A/Poland/PL27/2022	3C.2a1b.2a.2	2022-04-09	SIAT1	40	<	40	40	160	320	160	640	160	320	<
A/Poland/PL28/2022	3C.2a1b.2a.2	2022-04-11	SIAT1	80	<	40	160	320	640	320	640	320	320	40
A/Poland/PL44/2022	3C.2a1b.2a.2	2022-04-13	SIAT1	80	<	40	40	160	320	320	640	160	320	<
A/Poland/PL45/2022	3C.2a1b.2a.2	2022-04-14	SIAT1	160	<	80	320	320	640	640	1280	320	320	80
A/Poland/PL49/2022	3C.2a1b.2a.2	2022-04-19	SIAT1	80	<	40	40	160	320	320	640	160	320	<
							Vaccine NH 2021				Vaccine NH 2022 NH 2022-23			

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

Table 5-8. Antigenic analysis of influenza A(H3N2) 3C.2a1b.2a.2 viruses by HI - Summary

Viruses	Haemagglutination inhibition titre														
	Post-infection ferret antisera														
											NEW		NEW		
	A/Denmark/3264/2019		A/HK/2671/19	A/Camb/925256/20	A/Camb/e0826360/20	A/Bang/4005/20	A/Stock/5/21	A/Eng/21419172 3/21	A/Darwin/9/21		A/Flor/02/21		A/Wyom/01/21		A/Kansas/14/17
Passage history	SIAT		Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg		Egg		Egg		SIAT
Ferret number	F19/20[*1]		St Judes F21/20[*1]	F03/21[*1]	F10/21[*1]	F07/21[*1]	F35/21[*1]	F07/22[*1]	F38/21[*1]		F19/22[*1]		F20/22[*1]		F-17/19[*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.2a1b.2a.2		3C.2a1b.2a.2		3C.2a1b.2a.2		3C.3a.1
REFERENCE VIRUSES															
A/Denmark/3264/2019	3C.2a1b.1a	320	320	640	160	320	320	40	320		80		<		160
A/Hong Kong/2671/2019	3C.2a1b.1b	160	320	320	160	160	160	40	160		80		<		80
A/Cambodia/925256/2020	3C.2a1b.2a.1	160	80	640	160	160	160	40	320		40		<		80
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	160	<	160	1280	320	160	160	320		80		40		80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	160	40	160	160	640	640	160	640		160		40		160
A/Stockholm/5/2021	3C.2a1b.2a.2	80	<	80	80	320	640	160	1280		320		160		40
A/England/214191723/2021	3C.2a1b.2a.2	40	<	40	80	160	320	160	640		320		80		<
A/Darwin/9/2021	3C.2a1b.2a.2	160	<	80	640	320	640	160	2560		320		640		80
A/Florida/02/2021	3C.2a1b.2a.2	80	<	80	320	320	640	320	1280		1280		320		80
A/Wyoming/01/2021	3C.2a1b.2a.2	160	<	80	320	320	640	160	1280		320		2560		80
A/Kansas/14/2017	3C.3a.1	40	<	80	40	80	80	40	80		40		<		320
TEST VIRUSES															
Number tested	3C.2a1b.2a.2	170	170	170	170	170	170	170	170		27		27		170
No with titre reduction ≤2-fold		20	9	0	3	60	137	154	84		0		0		1
%		*11.8*	*5.3*		*1.7*	*35.3*	*80.6*	*90.6*	*49.4*						*0.6*
No with titre reduction =4-fold		47	5	5	28	97	32	15	79		11		1		28
%		*27.6*	*2.9*	*2.9*	*16.5*	*57.1*	*18.8*	*8.8*	*46.5*		*40.7*		*3.7*		*16.5*
No with titre reduction ≥8-fold		103	156	165	139	13	1	1	7		16		26		141
%		*60.6*	*91.8*	*97.1*	*81.8*	*7.6*	*0.6*	*0.6*	*4.1*		*59.3*		*96.3*		*82.9*
					Vaccine NH 2021				Vaccine NH 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 characterization report[5] and earlier ones), 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 geographic 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 geographic 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 the March report, based on sequences becoming available in GISAID and generated at the WIC during March 2022, shows all recent viruses to fall in the **V1A.3** subclade with small numbers of viruses being related to **B/Washington/02/2019** but with viruses from Honduras having additional **HA1** substitutions of **T73I** and **N233K** (resulting in loss of a glycosylation site), those from Kenya having **HA1 K75E**, **E128K**, **T155A** and **G230N** substitutions and those from Madagascar having **HA1 E128K** and **T170I** substitutions (Figure 4a). The great majority of viruses fell in the **V1A.3a** group characterized 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** (characterized by **HA1 V220M** and **P241Q** substitutions, detected predominantly in China) and **V1A.3a.2** (characterized 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). Viruses from the WHO European Region all fell in the dominant **V1A.3a.2** subgroup.

The phylogeny generated for this report shows a very similar profile with subgroup **V1A.3a.2** viruses dominating. Within this subgroup there are a group of five viruses reported by Luxembourg that appear to have 'repaired' the three amino acid deletion at **HA1** residues **162** to **164** (Figure 4b), something that has not been confirmed at the WIC. The large number of sequences submitted by the Netherlands split between the **V1A.3a.2** subgroup and subclade **V1A.3**, with the latter viruses being similar to those from Kenya having **HA1 K75E**, **E128K**, **T155A** and **G230N** substitutions, but with an additional **HA1 G184R** substitution sometimes with **D129N** (Figure 4b).

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. While relatively few B/Victoria-lineage viruses have been available for detailed antigenic characterization, those characterized earlier in the 2021-2022 season were subgroup **V1A.3a.2** viruses which were recognised poorly by post-infection ferret antiserum raised against **B/Washington/02/2019**, the 2021-2022 northern hemisphere vaccine virus [1]. However, the **V1A.3a.2** viruses were recognised well (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 [2, 3]. This was observed for the single subgroup **V1A.3a.2** virus, B/Slovenia/10026/2021, characterized antigenically since the March report (Table 6).

[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

Influenza B/Yamagata-lineage

It is assumed that no B/Yamagata-lineage viruses have been detected after March 2020 as no sequences for such viruses with collection dates after this had been released is GISAID as of 04 April 2022. Figure 5 is repeated from the September 2021 report. All sequences fell in genetic clade **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 2021-2022 northern, 2022 southern and 2022-2023 northern hemisphere seasons [1, 2, 3]. Some sub-clustering of sequences, defined by specific amino acid substitutions (e.g. **HA1 N164K, K211R, D229N** or **D232N** [introducing a potential N-linked glycosylation site] sometimes with **R48K**), had occurred. As noted in previous characterization 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 shared with WIC by the United Kingdom (Scotland: Table 3) only one yielded good sequence which showed it to be associated with Live Attenuated Influenza Vaccine (LAIV).

A concerted effort by all NICs of GISRS is required to identify B/Yamagata-lineage viruses for detailed characterization to determine if there are any in circulation that are non-LAIV-related.

Figure 4a. Phylogenetic comparison of B/Victoria-lineage HA genes (GISAID/WIC, March 2022)

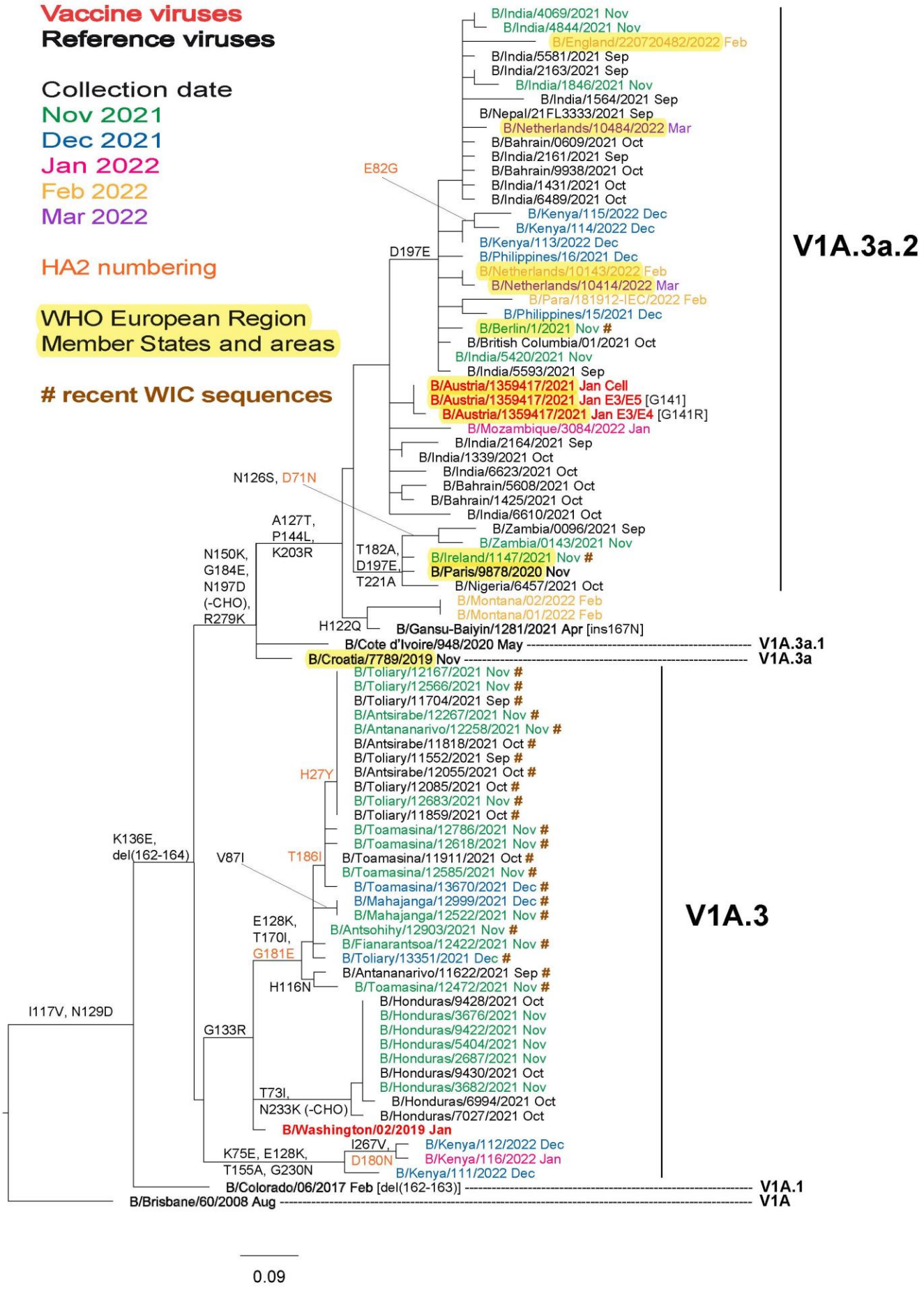


Figure 4b. Phylogenetic comparison of B/Victoria-lineage HA genes (GISAID/WIC, May 2022)

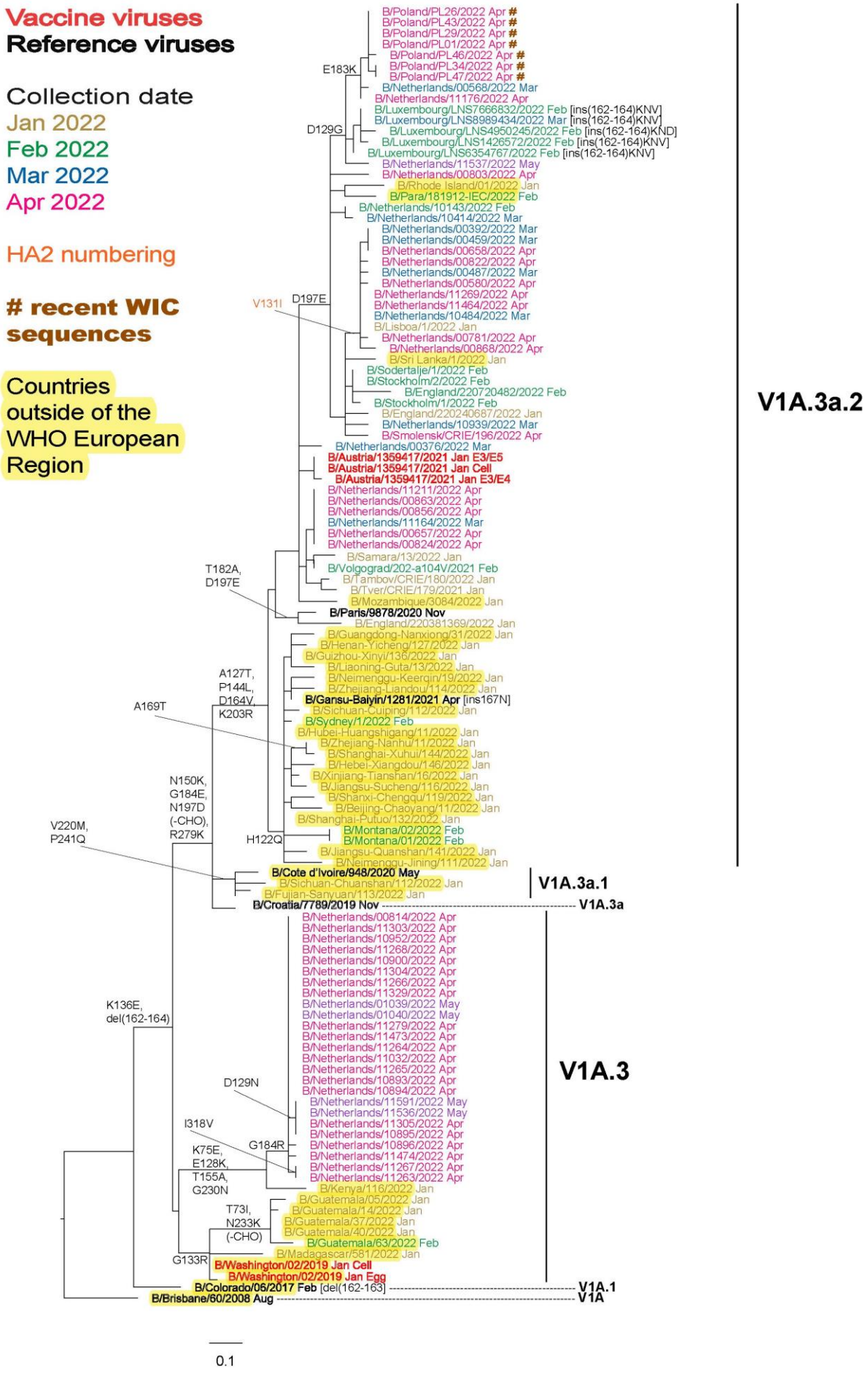


Table 6. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

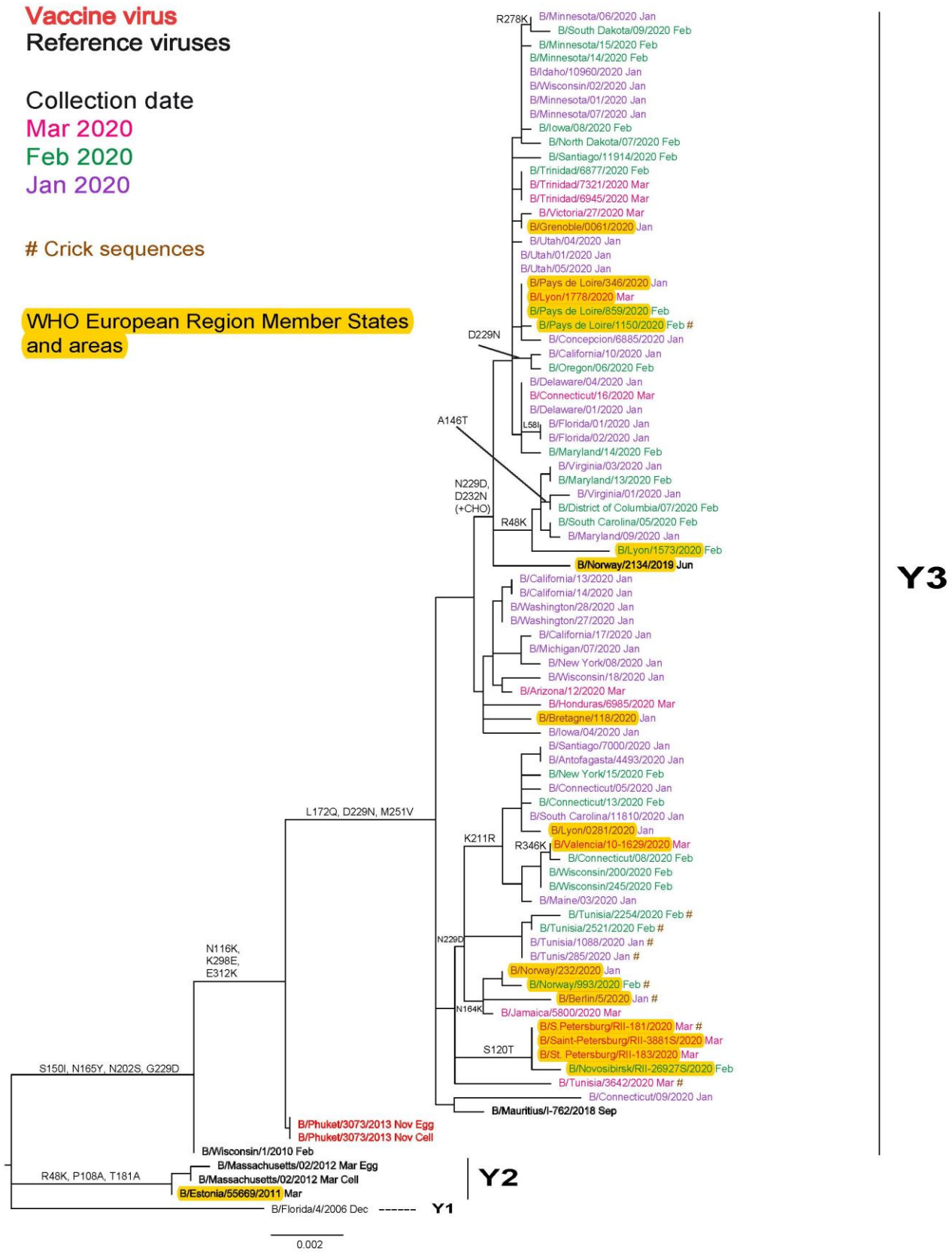
Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antiserum									NEW		
				B/Bris	B/Colorado	B/Wash'ton	A/Croatia	B/Civ	B/Austria	B/Paris	B/G-Baiyin	B/Austria	B/Austria		
			Passage history	60/08 Egg Sh 539, 540, 543, 544, 570, 571, 574 [1,2]	06/17 Egg	02/19 Egg	7789/19 MDCK	948/20 MDCK	1359417/21 MDCK	9878/20 MDCK	1281/21 MDCK	1359417/21 Egg G141	1359417/21 Egg G141R		
			Ferret number		F11/18 [*1]	F20/20 [*1]	F19/21 [*1]	F08/21 [*3]	NIB F01/21 [*1]	F12/21 [*1]	F08/22 [*1]	F15/21 [*1]	F44/21 [*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	V1A.3a.2		
REFERENCE VIRUSES															
B/Brisbane/60/2008		V1A	2008-08-04	E4/E4	2560	160	40	40	<	<	<	<	<		
B/Colorado/06/2017		V1A.1	2017-02-05	E5/E2	1280	640	40	<	<	40	<	<	<		
B/Washington/02/2019		V1A.3	2019-01-19	E3/E2	1280	320	160	80	40	40	<	<	<		
B/Croatia/7789/2019		V1A.3a	2019-11-11	MDCKx/MDCK3	640	160	80	640	320	160	<	40	80		
B/Cote d'Ivoire/948/2020		V1A.3a.1	2020-05-28	MDCK4	320	40	40	320	640	160	<	40	<	80	
B/Austria/1359417/2021		V1A.3a.2	2021-01-09	SIAT1/MDCK4	640	40	<	320	160	1280	320	320	1280	320	
B/Paris/9878/2020		V1A.3a.2	2020-11-20	MDCK5	640	160	<	320	160	1280	640	320	1280	640	
B/Gansu-Baiyin/1281/2021		V1A.3a.2	2021-04-13	C1/C1/MDCK2	640	40	<	320	160	2560	640	640	1280	320	
B/Austria/1359417/2021 Isolate 2	G141	V1A.3a.2	2021-01-09	E3/E5	640	40	<	320	320	2560	320	320	1280	640	
B/Austria/1359417/2021 Isolate 2	G141R	V1A.3a.2	2021-01-09	E3/E4	320	20	<	320	320	1280	320	320	640	2560	
TEST VIRUSES															
B/Slovenia/10026/2021		V1A.3a.2	2021-06-01	MDCK1/MDCK1	320	80	<	320	160	2560	320	320	1280	320	

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] < = <20; [2] hyperimmune sheep serum; [3] < = <80; ND = Not Done

Figure 5. Phylogenetic comparison of B/Yamagata-lineage HA genes (GISAID, September 2021)



Summaries of data submitted to TESSy

Genetic characterization

3 500 viruses detected over the course of the 2021-2022 season (weeks 40/2021-20/2022) were genetically characterized:

- Of 309 A(H1N1)pdm09 viruses, 282 belonged to clade 6B.1A.5a.1 (represented by A/Guangdong-Maonan/SWL1536/2019) and 24 belonged to clade 6B.1A.5a.1 (represented by A/Victoria/2570/2019). One was not attributed to a clade.
- Of 3 121 A(H3N2) viruses, 3 105 belonged to the 'Bangladesh-like' clade (3C.2a1b.2a.2) represented by A/Bangladesh/4005/2020, one to the 'Cambodia-like' clade (3C.2a1b.2a.1) and 15 were attributed to clade 3C.2a1b.1a (represented by A/Denmark/3264/2019).
- Sixty-three B/Victoria-lineage viruses, 24 belonging to clade V1A.3 (represented by B/Washington/02/2019) and 37 to clade V1A.3a.2 (represented by B/Austria/1359417/2021). Two were not attributed to a clade.
- Seven viruses were reported as B/Yamagata-lineage with four being B/Phuket/3073/2013-like. However, the possibility that these seven viruses were derived from live attenuated influenza vaccine (LAIV) could not be excluded.

Antiviral susceptibility

Up to week 20/2022, 2 547 viruses were assessed for susceptibility to neuraminidase inhibitors (NAIs): 1 715 A(H3), 258 A(H1)pdm09 and 54 B virus were assessed genotypically, and 476 A(H3), 31 A(H1)pdm09 and 13 B viruses were assessed phenotypically. Susceptibility to the PA inhibitor baloxavir marboxil was assessed genotypically for 1 792 viruses: 1 528 A(H3), 227 A(H1)pdm09 and 37 B viruses. Phenotypically no viruses with reduced susceptibility were identified and genotypically two A(H3) viruses showed PA amino acid substitutions potentially associated with reduced susceptibility to baloxavir marboxil and one A(H1)pdm09 virus with potential highly reduced inhibition by oseltamivir was identified.

At the WIC, 468 influenza viruses detected within the WHO European Region during the 2021-2022 season have been assessed phenotypically against oseltamivir and zanamivir: 54 A(H1)pdm09, 402 A(H3) and 12 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.

Animal influenza and zoonotic events

Influenza A(H7N9) virus

On 1 April 2013, the WHO 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, which 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]. Current risk assessments for influenza at the human-animal interface can be found on WHO's website https://www.who.int/teams/global-influenza-programme/avian-influenza/monthly-risk-assessment-summary (accessed 02 June 2022). The assessment published on 13 May 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 [6]. On 01 June 2022 the Food and Agricultural Organization of the United Nations announced that it was discontinuing monthly H7N9 updates as there had been no notifications of avian infections since October 2020. The most recent human case was detected in mid-March 2019 [7]. 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 30 March 2022 and can be found on ECDC's website [8].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 13 May 2022. Since the previous risk assessment on 07 April 2022, two human cases of infection with A(H5) avian influenza viruses were reported [6]. An A(H5N6) case was reported by China in a 56-year-old male who had disease onset on 31 March 2022, was hospitalised and was still in a severe condition at the time of reporting. He had been exposed to chickens and there was no evidence of onward human-to human

transmission. The second case was identified in a male 'poultry depopulation' worker in the USA and an A(H5N1) virus was detected. However, the patient reported no symptoms other than fatigue and made a full recovery. It is possible that detection of A(H5N1) in the specimen was a result of surface contamination in the nasal cavity. The most recent confirmed case of human infection with an A(H5N1) virus was reported by United Kingdom (England) and a full report into the investigation of this case has been published [9].

The latest collaborative report from ECDC and the European Food Safety Authority (EFSA), reported 2,653 highly pathogenic avian influenza (HPAI) A(H5) detections between 9 December 2021 and 15 March 2022, 1,030 in poultry, 1,489 in wild birds and 133 in domestic birds [8]. Detections occurred in 33 EU/EEA countries and the United Kingdom. Of the poultry detections 609 were reported by France, 131 by Italy, 73 by Hungary and 53 by Poland. Majorities of wild bird detections were reported by Germany (767), the Netherlands (293), Denmark (74) and the United Kingdom (118). Genetic analyses indicated that the circulating viruses belonged to clade 2.3.4.4b, with such viruses having been circulating in Europe since October 2020. Some of these viruses were also detected in wild mammal species in Finland, Ireland, the Netherlands and Slovenia, showing genetic markers of adaptation to replication in mammals. According to reports compiled by the Food and Agricultural Organization of the United Nations (FAO) as of 25 May 2022, various highly pathogenic avian influenza (HPAI) subtypes continued to be detected in wild and/or domestic birds in Africa, Americas, Asia and Europe, and since 27 April 2022 a total of 991 HPAI outbreaks (51 not subtyped, 25 H5Nx, 908 H5N1, four H5N5, two H5N8 and one H7N3) and no low pathogenic avian influenza (LPAI) outbreaks had been reported [10].

Influenza A(H9N2) virus

No mention of new human H9N2 infections were made in the latest WHO and FAO reports [6, 10]. Public Health England has published an updated risk assessment for avian influenza A(H9N2) [11]. Avian influenza A(H9N2) viruses are enzootic in poultry in Asia and increasingly reported in poultry in Africa.

Other influenza zoonotic events

Since the previous WHO update on 07 April 2022, one A(H1N1)v zoonotic event with a swine-related variant influenza A viruses was reported [8]. The case was reported by Germany in a 34-year-old patient who developed symptoms on 21 March 2022 but was not admitted to hospital and made a full recovery. The patient had contact with swine farmers and further epidemiologic investigations were taking place.

In addition, a case of zoonotic infection with an avian A(H3N8) virus was reported by China involving a four-year-old boy who developed symptoms on 05 April 2022 and was hospitalised on 10 April in a critical condition. The boy had been exposed to chickens prior to illness onset and clinical observation, with sampling, revealed no infections or symptoms of illness in the patient's close contacts. Avian influenza A(H3N8) viruses are commonly detected in domestic and wild birds globally.

WHO Collaborating Centre reports

A description of results generated by the London WHO Collaborating Centre at the WIC and used at the February 2022 WHO VCM (21-25 February 2022 for seasonal influenza viruses), and previous ones, can be found at https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports (accessed 01 June 2022).

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. Sequences for many viruses from countries outside the WHO European Region 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.

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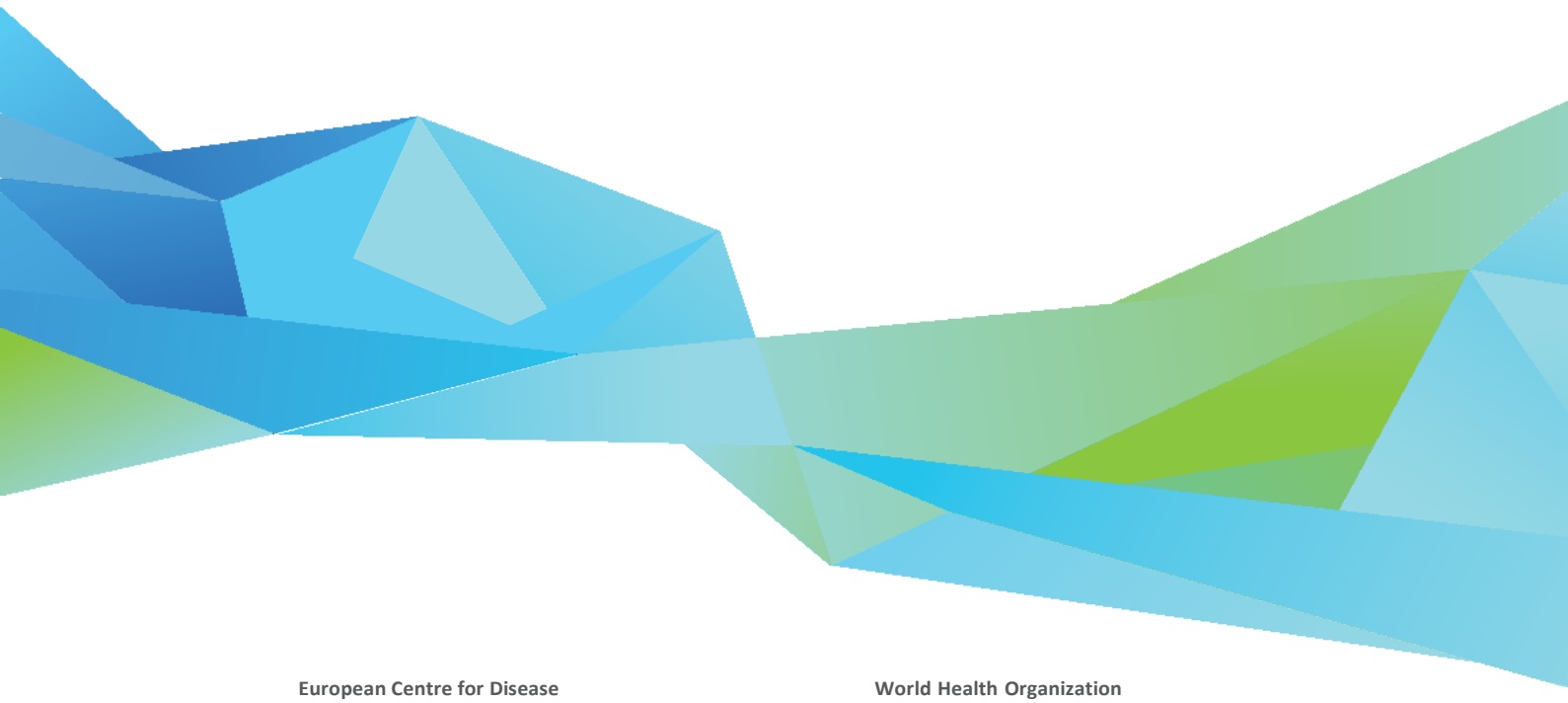

European Centre for Disease Prevention and Control (ECDC)

Gustav den III:s Boulevard 40, SE-169 73, Solna, Sweden

Tel. +46 858 60 1000
Fax +46 858 60 10 01
www.ecdc.europa.eu

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