Influenza virus characterization

Summary report, Europe, June 2022

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Acknowledgments

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Summary

This is the seventh report for the 2021-2022 influenza season. The May 2022 characterization report[1], gave a breakdown of influenza detections across the World Health Organization (WHO) European Region reported to TESSy up to week 20/2022. As of week 25/2022, 138 352 detections had been reported (a rise of over 5 000 since week 20/2022) resulting from extended late season influenza activity. Of these 138 352 detections, 98% were type A viruses, with A(H3N2) (92%) dominating over A(H1N1)pdm09 (8%), and 2% type B of which only 125 were ascribed to a lineage, with all but two being B/Victoria. This represents a large increase (137 418, 148-fold) in detections compared to the 2020-2021 season, on the back of a great increase (1 900 146, 200%) 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 25/2022 (unlike in 2020-2021), numbers of detections are reduced compared to earlier seasons (e.g., 16% 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.

Eleven shipments from countries within the WHO European Region were received at the London WHO Collaborating Centre, the Francis Crick Worldwide Influenza Centre (WIC) since the May report. 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 April 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. 6B.1A.5a.1 and 6B.1A.5a.2 genetic subgroups have been detected which are clearly antigenically different, as shown by viruses from seven WHO Region countries (6B.1A.5a.1) and Austria/Norway (6B.1A.5a.2) characterized here. 6B.1A.5a.1 viruses have been most numerous in Europe but 6B.1A.5a.2 viruses are currently dominant in some southern hemisphere countries, notably Australia, and greater numbers have recently been detected in Europe. 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, except in China where 3C.2a1b.2a.1 viruses are circulating. 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 being 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 V1A.3 represented by B/Washington/02/2019 the vaccine virus recommended for inclusion in influenza vaccines for the 2021-2022 northern hemisphere season. A large majority of HA sequences from recently detected viruses, in geographically dispersed countries, have fallen in the V1A.3a group defined by a series of HA1 amino acid substitutions including N150K, 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 (V1A.3) viruses, one of which was recently been detected in the Netherlands but has not yet undergone detailed antigenic analysis. Post-infection ferret antisera raised against B/Washington/02/2019-like viruses do not recognise V1A.3a.2 viruses well and B/Austria/1359417/2021-like (V1A.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, belonged to genetic clade Y3 and had three HA1 amino acid substitutions (L172Q, D229N and M251V) compared to B/Phuket/3073/2013-like viruses which are still recommended for use in

[1] Influenza virus characterization: summary report, Europe, May 2022. Copenhagen: World Health Organization Regional Office for Europe and European Centre for Disease Prevention and Control; Copenhagen and Stockholm; 2022 (https://apps.who.int/iris/handle/10665/363369, accessed 05 October 2022).

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 40/2021-25/2022), 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 (1 900 146, 200%), even when compared with a more 'normal' season, 2019-2020 (1 920 481, 207%: 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 (137 418, 148-fold), though there was a reduction compared to the same period in 2019-2020 (26 531, 16%: 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 to 55:1), with a greater dominance of A(H3N2) over A(H1N1)pdm09 viruses. While the number of influenza B virus detections has increased from 456 to 2 458 (539%), 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).

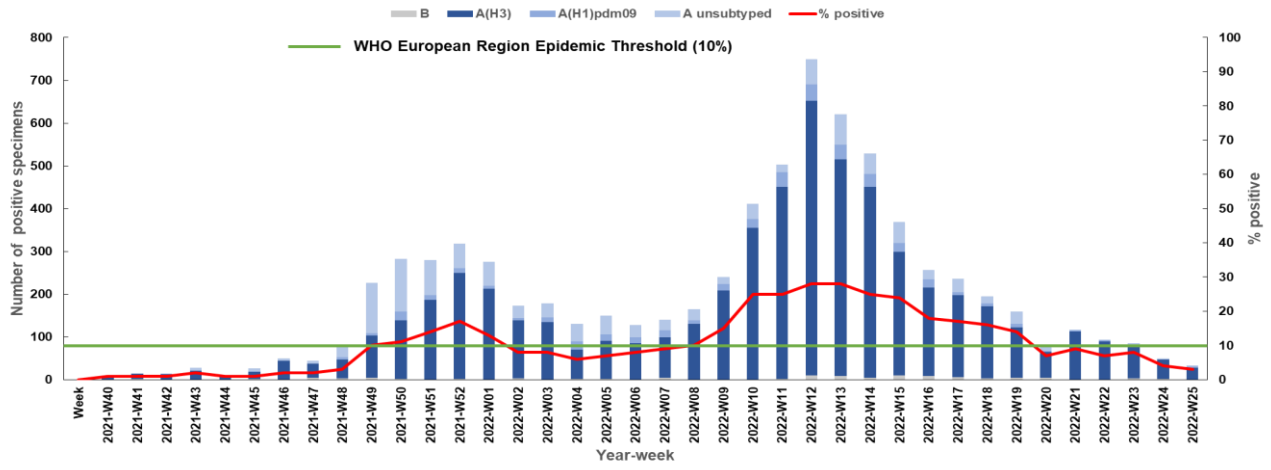
Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2021-2022 season (weeks 40/2021-25/2022)[a]

Virus type/subtype/lineage	Cumulative number of detections for weeks 40/2021-25/2022			Totals*		Cumulative number of detections for weeks 40/2020-24/2021			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**7514**	**128380**	**135894**	**98.2**	**55:1**	**30**	**448**	**478**	**51.2**	**1:1**
A(H1N1)pdm09	395	2563	2958	7.9		14	28	42	41.6	
A(H3N2)	5993	28629	34622	92.1	11.7:1	8	51	59	58.4	1.4:1
A not subtyped	1126	97188	98314			8	369	377		
Influenza B	**107**	**2351**	**2458**	**1.8**		**17**	**439**	**456**	**48.8**	
Victoria lineage	19	104	123	98.4	62:1	2	11	13	81.3	4.3:1
Yamagata lineage	0	2	2	1.6		0	3	3	9.7	
Lineage not ascribed	88	2245	2333			15	425	440		
Total detections (total tested)	**7 621 (67 452)**	**130 731 (>2 779 488)**	**138 352 (>2 846 940)**			**47 (43 238)**	**887 (>903 556)**	**934 (>946 794)**		

[a] **Numbers taken from Flu News Europe to week 25/2022, week 24/2021 and week 25/2020 reports for the three 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 25/2022 (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 GISAID's EpiFlu™ database, 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 December 2021, for representative non-WIC generated sequences available in GISAID, generated for the March report are presented (Figures 2a, 3a and 4a). Additional phylogenies (Figures 2b, 3b and 4b) are presented for HA sequences derived from viruses collected after 31 December 2021 (28 February 2022 for A(H3N2)) and submitted to GISAID during the time periods indicated (Table 2). The numbers of HA sequences, downloaded from GISAID, numbers remaining after de-duplication and the numbers used in the new representative phylogenies generated for this June report are shown.

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 2022-06-30				
	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	2022-05-29	150	137	137
A(H3N2)	2022-03-01	2022-05-01	3487	1865[$]	264
B/Victoria	2022-01-01	2022-01-01	142	130	130
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**

[$] Removal of sequences downloaded for the May report as well

Seventy-one 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 39 WHO European Region Member States (Table 3). Of the 1 708 samples received 1 639 (96%) were type A viruses and 69 (4%) were type B viruses. Eleven of the shipments were received in June 2022 and contained samples from the second phase of the epidemic (Figure 1) many of which are still in the virus characterization process (Table 3). NICs were requested to send clinical specimens with real-time RTPCR Ct values of ≤30 and/or virus isolates, all those available for A(H1N1)pdm09 and influenza type B (as relatively few have been detected), and a representative selection of A(H3N2) samples.

A total of 185 viruses from the WHO European Region, 34 A(H1N1)pdm09, 133 A(H3N2) and 18 B/Victoria-lineage, have been characterized antigenically since the May 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

MONTH / Country/area	TOTAL RECEIVED Seasonal viruses	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
		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							
Kazakhstan	13					13	0	0						
Kyrgyzstan	22					22	0	0						
Netherlands	23					23	19	0						
Norway	8					8	5	0						
Romania	1										1	1		
Russian Federation	36					36	35	0						
Slovenia	2					2	1	0						
Spain	36			1	1	33	10	0	1	0	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[$]	2					2	1	0						
December														
Albania	39	1	0	3	3	35	10	0						
Armenia	21					21	10	0						
Belgium	15	1	0	7	6	7	2	0						
Bosnia and Herzegovina	3					3	0	0						
Croatia	7			1	1	6	5	0						
Estonia	7					7	1	0						
France	1					1	1							
Georgia	11			1	0	9	4	0			1	0		
Germany	10					10	10							
Hungary	2					2	2							
Ireland	4			1	0	3	3							
Ireland	1					1								
Israel	30					30	5	0						
Kazakhstan	17					17	2	0						
Latvia	5					5	5							
Montenegro	6					6	1	0						
Netherlands	26			5	5	21	20	1						
Norway	1					1	1							
Portugal	18	1	0			14	in process		1	0	2	1		
Romania	5					5	5							
Russian Federation	5					5	5							
Serbia	7			5	0	2	1	0						
Slovenia	1					1	1							
Spain	53					52	10	0			1	0		
Switzerland	10	1	0			9	6	0						
Ukraine	13					13	1	0						
Kosovo[$]	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

As of 2022-07-04

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	8							
Estonia	4					4	4							
Georgia	4					4	2	0						
Germany	11					11	11							
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							
Portugal	7					7	in process							
Romania	4			1	1	3	3							
Serbia	21					21	in process							
Slovenia	2					2	1	0						
Spain	3					3	3							
Switzerland	7			1	1	6	4	0						
Ukraine	15					15	6	0						
Kosovo[$]	2	1	0			1	0	0						
FEBRUARY														
Austria	3			1	1	2	in process							
Bulgaria	4					4	4							
Denmark	1					1	1							
Germany	12			1	1	11	11							
Hungary	3					3	in process							
Moldova	1					1	in process							
Norway	2					2	in process							
Poland	1					1	1							
Portugal	32			1	in process	31	in process							
Slovakia	1					1	in process							
Slovenia	12					12	12							
Spain	10					10	10							
Sweden	2										2	in process		
Switzerland	4			4	3									
MARCH														
Austria	27			4	4	23	in process							
Bosnia and Herzegovina	2					2	in process							
Bulgaria	16					16	16							
Denmark	12			1	1	11	11							
Germany	8			1	1	7	7							
Hungary	4					4	in process							
Iceland	4					4	in process							
Ireland	39					39	in process							
Kyrgyzstan	6								6	in process				
Lithuania	1					1	in process							
Moldova	7			2	in process	5	in process							
Montenegro	19					19	in process							
Norway	20			2	1	16	in process				2	2		
Poland	19	2	0			17	14	0						
Portugal	10					10	in process							
Serbia	13			4	in process	9	in process							
Slovakia	2					2	in process							
Slovenia	43					43	in process							
Spain	4			2	2	2	2							
Sweden	7					4	4				3	3		
Switzerland	20			6	6	14	in process							
the United Kingdom (N. Ireland)	3					3								
APRIL														
Austria	23			1	in process	22	in process							
Bosnia and Herzegovina	5					5	in process							
Bulgaria	3					3	in process							
Denmark	2					2	2							
Germany	8			2	2	6	6							
Hungary	2					2	in process							
Iceland	27			2	0	25	in process							
Ireland	11			1	1	10	in process							
Kyrgyzstan	6								6	in process				
Latvia	15			2	2	12	12				1	0		
Lithuania	46					46	in process							
Moldova	7			1	in process	6	in process							
Montenegro	6					6	in process							
Norway	38			10	10	25	in process				3	1		
Poland	30	3	0			15	13		2	0	10	5		
Portugal	10					10	in process							
Serbia	11			5	in process	4	in process		1	in process	1	in process		
Slovakia	7					7	in process							
Slovenia	11					11	11							
Spain	43			2	in process	40	in process				1	in process		
Sweden	9			1	in process	7	7				1	1		
Switzerland	14			2	0	12	in process							
the United Kingdom (N. Ireland)	24					24								
MAY														
Austria	2					2	in process							
Bosnia and Herzegovina	2	1	in process			1	in process							
Germany	11			1	1	8	8				2	2		
Iceland	18					18	in process							
Lithuania	2					2	in process							
Norway	3										3	3		
Portugal	7			3	in process	4	4							
Serbia	5								5	in process				
Spain	16					16	in process							
Sweden	1					1	1							
39 Countries/areas	1708	29	0	137	87	1473	512	1	24	0	41	24	4	0
		1.7%		8.0%		86.3%			1.4%		2.4%		0.2%	
		96.0%							4.0%					

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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
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As of 2022-07-04

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**).

Of the 356 A(H1N1)pdm09 HA sequences from viruses with collection dates after 31 December 2021 that became available in April and May, 114 were used to generated the representative phylogeny in the May report (Figure 2a). Viruses of subgroup **6B.1A.5a.1** 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**. Strikingly, viruses of subgroup **6B.1A.5a.2** were dominating in Australia, where the influenza season had started earlier than usual, as was the case in Pakistan, while a single virus in this subgroup from Morocco had been identified.

The phylogeny prepared for this report was based on HA sequences derived from viruses with collection dates after 31 December 2021 that had been submitted to GISAID after 29 May 2022 (Table 2). Viruses of subgroup **6B.1A.5a.1** continued to dominate in the WHO European Region with a few detections reported by Canada and the USA (Figure 2b). For viruses with the most recent collection dates, subgroup **6B.1A.5a.2** continued to dominate in Australia and a significant number were also detected in England, together with a single detection in Canada.

The panel of post-infection ferret antisera used give clear discrimination of test viruses in subgroups **6B.1A.5a.1** and **6B.1A.5a.2** viruses (Table 4). Of the 23 **6B.1A.5a.1** test viruses, detected across seven countries, all but one was well inhibited by antisera raised against five different **6B.1A.5a.1** reference viruses, which included the vaccine virus (A/Guangdong-Maonan/SWL1536/2019) for the 2020-2021 northern hemisphere season. A/Switzerland/36111/2022 was recognised less well and fell within a cluster of viruses defined by HA1 substitutions P137S and G155E (Figure 2b and Table 4). Poor recognition of viruses in this cluster has been mentioned in previous reports. Of the 11 **6B.1A.5a.2** viruses, detected in Austria and Norway, all were recognised well by antisera raised against four different **6B.1A.5a.2** reference viruses, which included the vaccine virus (IVR-215: A/Victoria/2570/2019) for the 2021-2022 northern hemisphere season.

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.

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

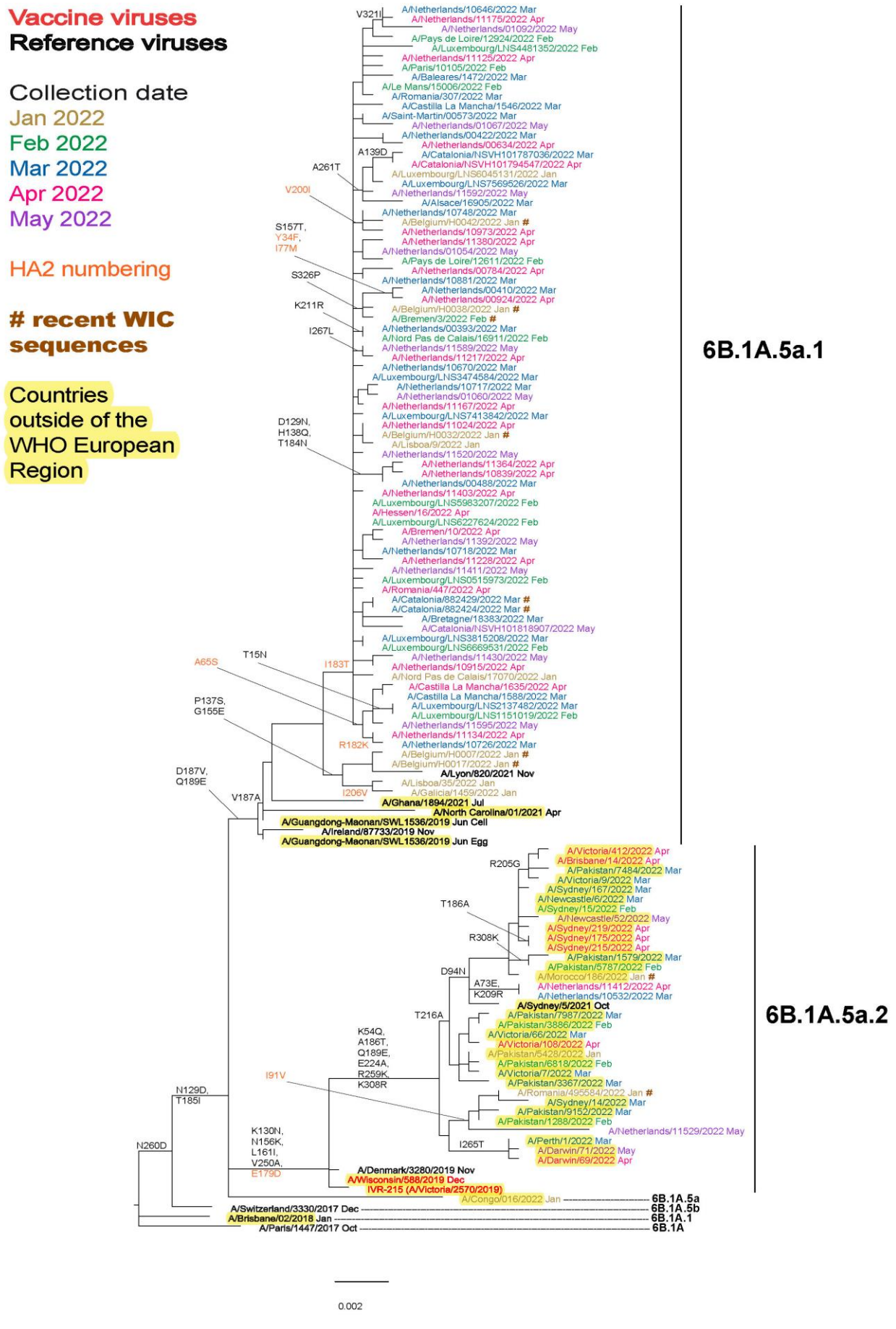


Figure 2b. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID/WIC, June 2022)

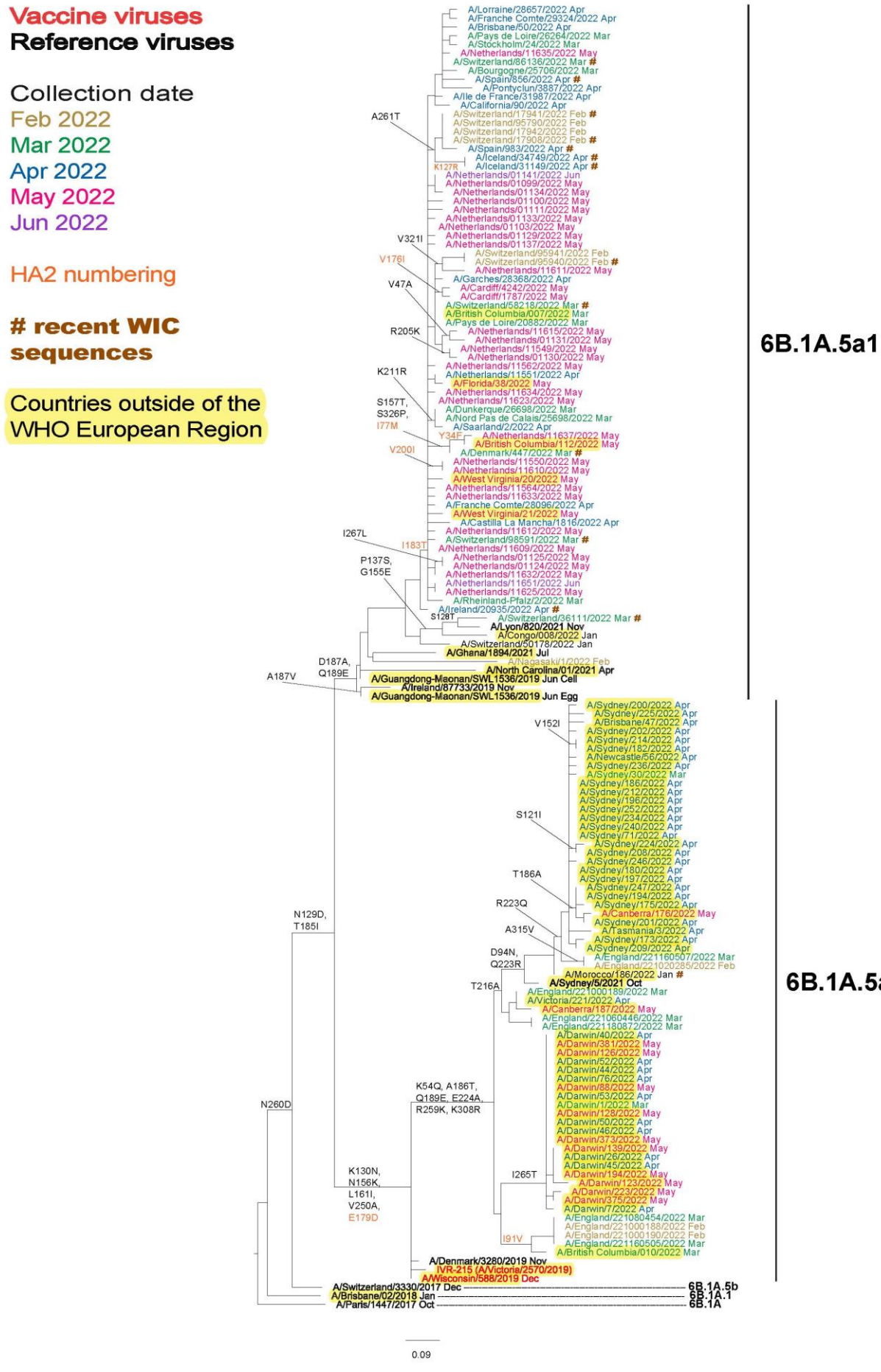


Table 4. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection fereret antisera							NEW		
	Passage history			A/Ire 87733/19 Egg St Jude's F-18/20*1	A/G-M SWL1536/19 MDCK F09/20*1	A/G-M SWL1536/19 Egg F12/20*1	A/Ghana 1894/21 Egg F02/22*1	A/Lyon 820/21 Egg F06/22*1	A/Denmark 3280/19 MDCK F08/20*1	A/Stock 10/21 MDCK F22/22*1	IVR-215 A/Vic/2570/19 Egg F37/21*1	A/Sydney 5/21 Egg F04/22*1
	Ferret number											
	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	6B.1A.5a.2
REFERENCE VIRUSES												
A/Ireland/87733/2019	6B.1A.5a.1	2019-11-03	E4	320	1280	1280	320	160	<	<	40	<
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	C2/MDCK1	640	1280	1280	640	320	<	40	80	40
A/Guangdong-Maonan/SWL1536/2019	6B.1A.5a.1	2019-06-17	E3/E2	640	1280	1280	640	160	<	<	40	<
A/Ghana/1894/2021	6B.1A.5a.1	2021-07-21	E2/E1	640	1280	1280	640	160	<	<	80	40
A/Lyon/820/2021	6B.1A.5a.1	2021-11-16	E1/E2	80	320	320	160	320	<	<	40	40
A/Denmark/3280/2019	6B.1A.5a.2	2019-11-10	MDCK4/MDCK6	<	40	80	40	80	640	640	1280	640
A/Stockholm/10/2021	6B.1A.5a.2	2021-09-13	SIAT1/MDCK1	40	40	40	<	<	1280	1280	2560	2560
IVR-215 (A/Victoria/2570/2019)	6B.1A.5a.2	2018-11-22	E4/D7/E2	40	80	40	40	80	640	640	1280	1280
A/Sydney/5/2021	6B.1A.5a.2	2021-10-16	E3/E1	<	80	40	40	40	640	640	1280	1280
TEST VIRUSES												
A/Switzerland/50178/2022	6B.1A.5a.1	2022-01-25	MDCK1	640	1280	1280	320	320	<	<	40	40
A/Switzerland/95789/2022	6B.1A.5a.1	2022-02-14	MDCK1	320	1280	1280	640	320	<	40	40	40
A/Switzerland/17908/2022	6B.1A.5a.1	2022-02-17	MDCK1	320	1280	1280	640	160	<	<	40	40
A/Switzerland/17941/2022	6B.1A.5a.1	2022-02-17	MDCK1	320	1280	1280	640	160	<	<	40	40
A/Austria/1495794/2022	6B.1A.5a.1	2022-02-24	Cx/MDCK1	640	1280	1280	640	160	<	<	40	40
A/Denmark/447/2022	6B.1A.5a.1	2022-03-06	MDCK4/MDCK1	320	1280	1280	640	160	<	ND	80	40
A/Rheinland-Pfalz/2/2022	6B.1A.5a.1	2022-03-08	P1/MDCK1	640	1280	1280	640	320	<	<	40	40
A/Switzerland/36111/2022	6B.1A.5a.1	2022-03-10	MDCK1	80	640	160	320	320	<	<	40	40
A/Austria/1500599/2022	6B.1A.5a.1	2022-03-14	Cx/MDCK1	160	640	640	640	160	<	<	40	40
A/Switzerland/86136/2022	6B.1A.5a.1	2022-03-15	MDCK1	640	1280	2560	1280	320	<	40	80	40
A/Switzerland/98591/2022	6B.1A.5a.1	2022-03-16	MDCK1	640	1280	1280	1280	320	<	<	40	40
A/Switzerland/46339/2022	6B.1A.5a.1	2022-03-18	MDCK1	640	1280	1280	1280	320	<	40	40	40
A/Switzerland/46068/2022	6B.1A.5a.1	2022-03-22	MDCK1	640	2560	2560	1280	320	<	40	80	40
A/Switzerland/58218/2022	6B.1A.5a.1	2022-03-22	MDCK2	320	1280	1280	640	160	<	<	40	<
A/Austria/1504570/2022	6B.1A.5a.1	2022-03-28	Cx/MDCK1	640	1280	1280	640	160	<	<	40	40
A/Norway/18189/2022	6B.1A.5a.1	2022-04-02	MDCK1	640	1280	1280	640	160	<	<	40	40
A/Bremen/10/2022	6B.1A.5a.1	2022-04-04	P1/MDCK1	640	1280	1280	1280	160	<	<	40	40
A/Ireland/20935/2022	6B.1A.5a.1	2022-04-10	MDCK2	320	640	1280	640	160	<	<	40	<
A/Norway/20048/2022	6B.1A.5a.1	2022-04-11	MDCK2	320	640	1280	640	320	<	<	40	<
A/Hessen/16/2022	6B.1A.5a.1	2022-04-11	P2/MDCK1	640	1280	1280	640	320	<	<	40	40
A/Latvia/04-67712/2022	6B.1A.5a.1	2022-04-20	P1/MDCK1	160	1280	640	320	80	<	<	<	<
A/Latvia/04-67670/2022	6B.1A.5a.1	2022-04-20	P1/MDCK1	320	640	640	320	160	<	<	40	<
A/Niedersachsen/12/2022	6B.1A.5a.1	2022-05-04	P1/MDCK1	640	1280	1280	1280	160	<	<	40	40
A/Austria/1502441/2022	6B.1A.5a.2	2022-03-21	Cx/MDCK1	<	<	<	<	<	640	320	640	640
A/Norway/17569/2022	6B.1A.5a.2	2022-03-22	MDCK2	<	40	40	<	<	640	640	640	640
A/Austria/1505769/2022	6B.1A.5a.2	2022-03-31	Cx/MDCK1	<	<	<	<	<	640	640	1280	640
A/Norway/21029/2022	6B.1A.5a.2	2022-04-02	MDCK2	<	<	<	<	<	640	640	1280	640
A/Norway/18421/2022	6B.1A.5a.2	2022-04-03	MDCK1	<	<	40	<	<	640	1280	2560	1280
A/Norway/21030/2022	6B.1A.5a.2	2022-04-04	MDCK1	<	<	<	<	<	320	320	640	640
A/Norway/18428/2022	6B.1A.5a.2	2022-04-05	MDCK2	<	<	40	<	<	1280	1280	1280	1280
A/Norway/20702/2022	6B.1A.5a.2	2022-04-07	MDCK1	<	<	<	<	<	320	320	640	320
A/Norway/19418/2022	6B.1A.5a.2	2022-04-08	MDCK1	<	40	40	<	<	640	640	1280	640
A/Norway/20045/2022	6B.1A.5a.2	2022-04-11	MDCK1	<	<	<	<	<	640	640	1280	640
A/Norway/20652/2022	6B.1A.5a.2	2022-04-12	MDCK1	<	<	40	<	<	640	640	1280	1280

Vaccine
NH 2020-21
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 29 May 2022, for viruses with collection dates after 31 December 2021 (Figure 3a). The second phylogeny is based on representative A(H3N2) HA sequences made available in GISAID and generated at the WIC since 01 May 2022 for viruses with collection dates after 28 February 2022 (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 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. A small number of **3C.2a1b.1a** viruses from the WHO European Region, Australia and the USA had been reported on. The great majority of viruses with collection dates after 31 December 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 five subgroups defined by specific **HA1** amino acid substitutions: (i) **S205F** and **A212T**; (ii) **H56Y** and **S270T**; (iii) **E50K**; (iv) **D53N**, commonly with **N96S** (gain a glycosylation site) and **I192F**; (v) **D53G** often with **I25V**, **R201K** and **S219Y** or **D104G** and **K276R**. Subgroups (iv) and (v) also share **HA1 H156S** amino acid substitution. No recent 'Cambodia-like' (**3C.2a1b.2a.1**) viruses were reported.

The second phylogeny, based on a representative set of HA sequences derived from viruses with collection dates after 28 February 2022 that had been submitted to GISAID after 30 April 2022 (Table 2), shows a very similar profile (Figure 3b). The vast majority of recently collected viruses were 'Bangladesh-like' (**3C.2a1b.2a.2**), falling in the five subgroups identified in the preceding paragraph, with notable expansion of viruses in subgroups (iv; HA1 substitutions of **D53N**, **N96S** and **I192F**) and (v; HA1 substitutions of **D53G**, **D104G** and **K276R**). Small numbers of **3C.2a1b.2a.1** (from China) and **3C.2a1b.1a** (from Sweden) were reported on. 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[2], 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[3], 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 with a single A(H3N2) virus from the Netherlands failing 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 133 A(H3N2) viruses characterized antigenically since the May report, 118 were 'Bangladesh-like' **3C.2a1b.2a.2** viruses, two were **3C.2a1b.1a** viruses and for 13 viruses sequencing is pending, though their HI reactivity profiles are indicative of **3C.2a1b.2a.2** viruses (Tables 5-1 to 5-3). The two **3C.2a1b.1a** viruses, detected in Sweden, were recognised well, within fourfold of the respective homologous titres, by antisera raised against six of the reference viruses inclusive of that raised against the northern hemisphere 2021-2022 vaccine virus; while the antiserum raised against the 2022-2023 vaccine virus had a high homologous titre (1280) it still recognised the **3C.2a1b.1a** viruses at titres of 160 (Table 5-3). Results for the 118 'Bangladesh-like' **3C.2a1b.2a.2** test viruses are summarised in Table 5-4. 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, A/England/214191723/2021, A/Slovenia/8720/2022 and A/Norway/24873/2021 recognised 99-100% of the test viruses at titres within fourfold of the respective homologous titres. The antiserum raised against egg-propagated A/Darwin/9/2021, the northern hemisphere 2022-2023 vaccine virus, recognised 113 (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/Norway/24873/2021 (**D53N**, commonly with **N96S** (gain a glycosylation site) and **I192F subgroup)** and A/Norway/29511/2021 (**E50K**, **F79V** and **I140K** subgroup) both recognised **3C.2a1b.2a.2** test viruses slightly less well, only 14/15 (93%) all at fourfold-reduced compared to homologous titres.

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.

[2] For example, the September 2013 report: Influenza virus characterisation, summary Europe, September 2013. Stockholm: European Centre for Disease Prevention and Control; 2013 (https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf, accessed 18 October 2022).

[3] Influenza virus characterisation, summary Europe, November 2014. Stockholm: European Centre for Disease Prevention and Control; 2014 https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf, accessed 18 October 2022).

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

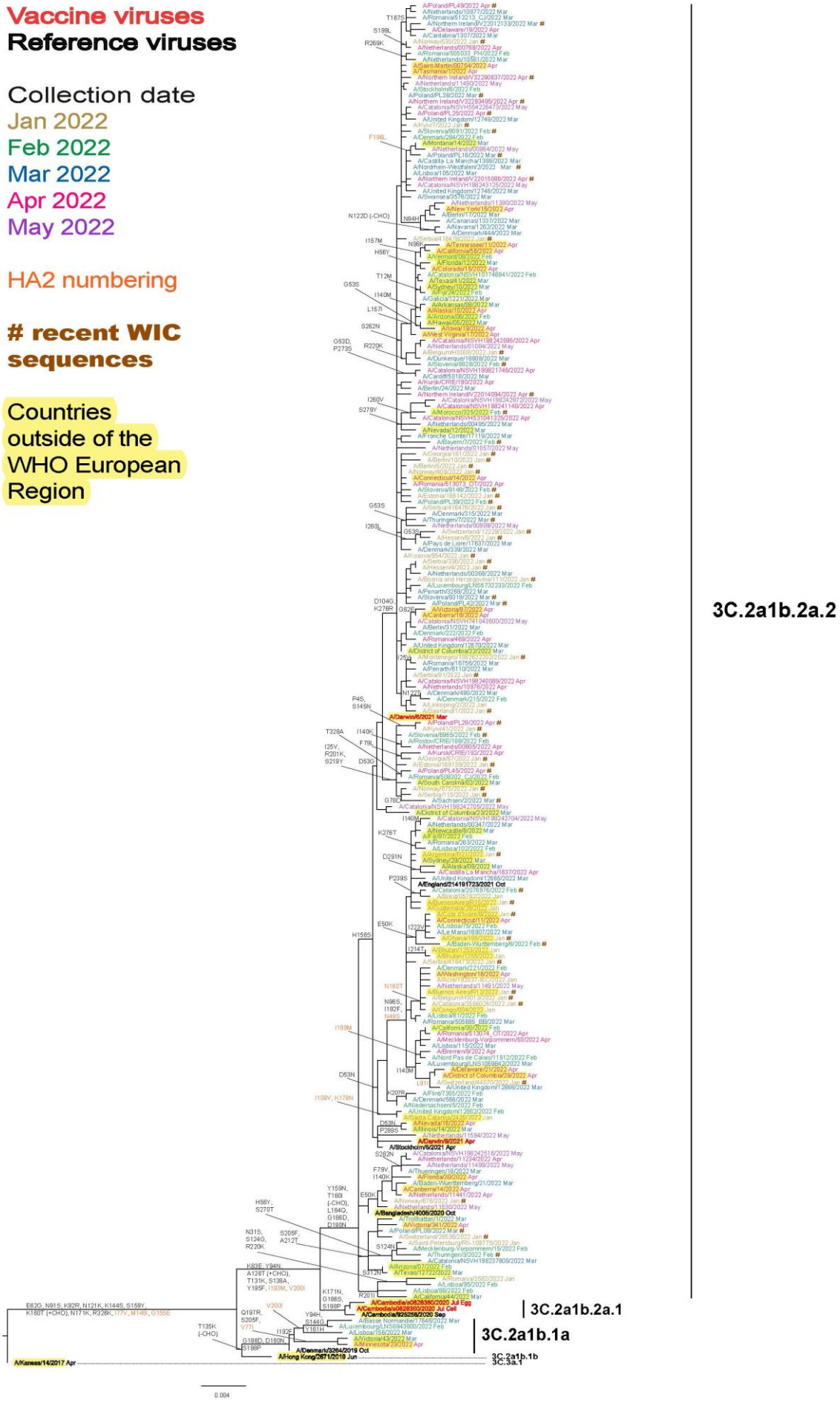


Figure 3b. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID/WIC, June 2022)

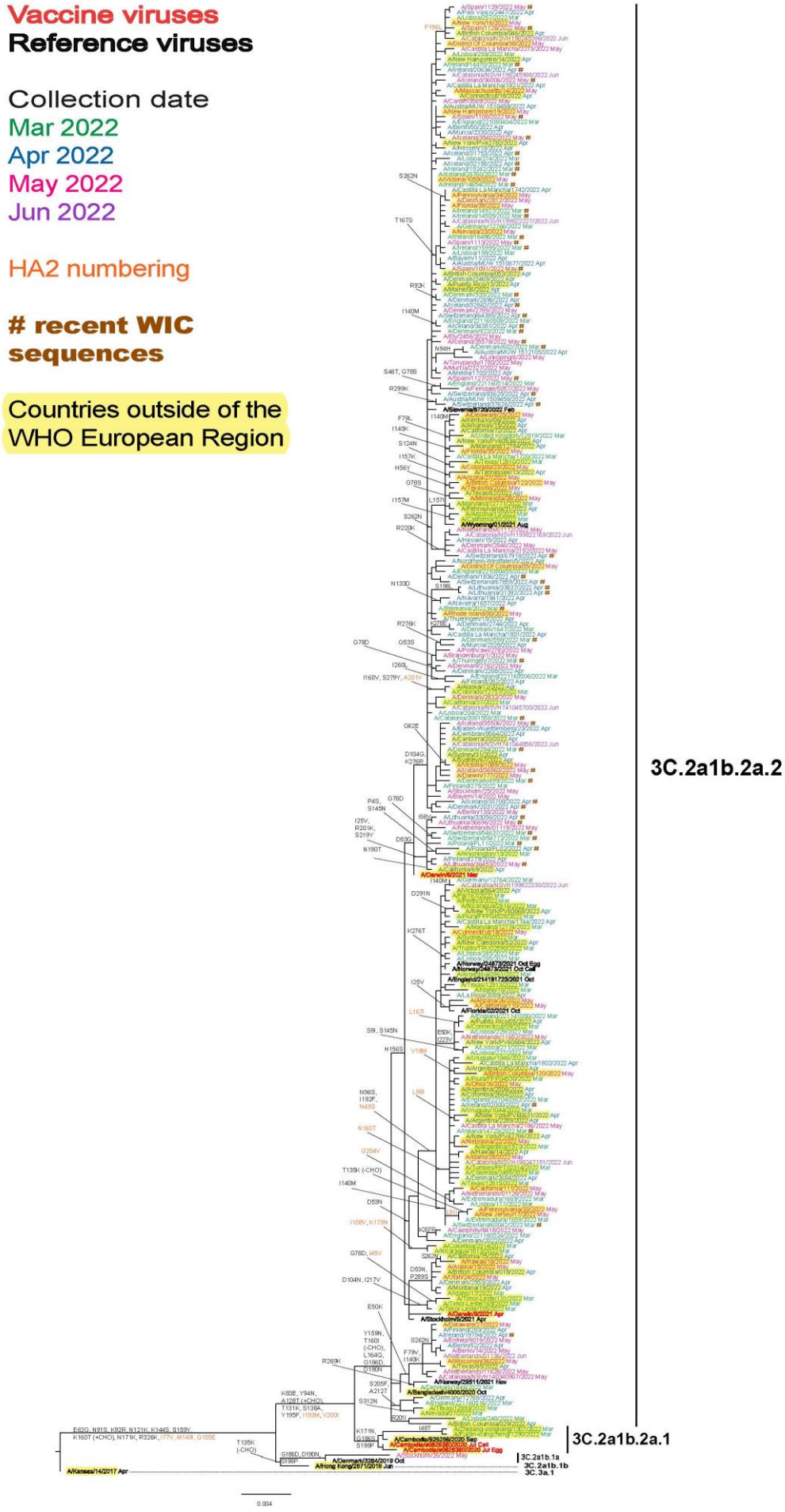


Table 5-1. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre															
				Post-infection ferret antisera															
											NEW		NEW		NEW		NEW		
				A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Slov	A/Norway	A/Norway	A/Norway	A/Darwin	A/Norway	A/Kansas
				3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	214191723/21	8720/2022	24873/21	24873/21	24873/21	9/21	29511/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	SIAT	SIAT	Egg	Egg	Egg	Egg	SIAT
	Passage history			F19/20[-1]	St Judes F21/20[-1]	F03/21[-1]	F10/21[-1]	F07/21[-1]	F35/21[-1]	F07/22[-1]	F24/22[-1]	F10/22[-1]	F11/22[-1]		F38/21[-1]	F12/22[-1]	F17/19[-1]
	Ferret number			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.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
	Genetic group																
REFERENCE VIRUSES																	
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	160	320	160	160	160	<	ND	ND	ND	320	ND	80	
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	640	1280	320	320	320	40	<	160	80	320	40	320	
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	80	160	640	160	160	160	<	ND	ND	ND	320	ND	160	
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<	160	2560	320	160	320	320	80	160	320	320	160	
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	320	160	320	640	1280	640	1280	1280	320	640	2560	640	160	
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	160	40	160	320	640	1280	640	1280	160	320	1280	320	80	
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT3	80	<	80	160	320	640	1280	640	320	640	1280	80	40	
A/Slovenia/8720/2022	3C.2a1b.2a.2	2022-02-10	SIAT1/MDCK1/SIAT2	160	<	80	160	320	1280	640	1280	160	320	1280	160	40	
A/Norway/2487/2021	3C.2a1b.2a.2	2021-10-24	SIAT2	80	<	80	160	320	640	1280	640	320	640	1280	160	40	
A/Norway/2487/2021	3C.2a1b.2a.2	2021-10-24	E4 (Am2A/2)	160	<	160	640	640	1280	1280	1280	320	1280	2560	320	160	
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E4	160	<	160	640	640	640	640	1280	160	320	2560	320	80	
A/Norway/29511/2021	3C.2a1b.2a.2	2021-11-25	E4 (Am2A/2)	ND	ND	160	ND	640	320	640	640	160	160	1280	640	ND	
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	80	40	160	160	80	80	80	80	<	<	160	80	640	
TEST VIRUSES																	
A/Bulgaria/193/2022	3C.2a1b.2a.2	2022-01-16	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/142/2022	3C.2a1b.2a.2	2022-01-16	SIAT2/SIAT1	160	<	80	160	320	640	640	640	ND	ND	1280	ND	40	
A/Bulgaria/104/2022	3C.2a1b.2a.2	2022-01-16	SIAT2/SIAT1	160	<	80	160	320	640	640	640	ND	ND	1280	ND	40	
A/Bulgaria/75/2022	3C.2a1b.2a.2	2022-01-16	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/404/2022	3C.2a1b.2a.2	2022-01-18	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/648/2022	3C.2a1b.2a.2	2022-01-30	SIAT2/SIAT1	160	<	160	160	320	640	640	640	ND	ND	1280	ND	80	
A/Bulgaria/646/2022	3C.2a1b.2a.2	2022-01-30	SIAT2/SIAT1	160	40	160	160	320	640	640	1280	ND	ND	1280	ND	80	
A/Bulgaria/644/2022	3C.2a1b.2a.2	2022-01-30	SIAT2/SIAT1	160	<	160	320	320	640	640	640	ND	ND	1280	ND	80	
A/Bulgaria/1057/2022	3C.2a1b.2a.2	2022-02-11	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/1127/2022	3C.2a1b.2a.2	2022-02-16	SIAT2/SIAT1	160	<	80	160	320	640	640	640	ND	ND	1280	ND	40	
A/Bulgaria/1195/2022	3C.2a1b.2a.2	2022-02-21	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/1273/2022	3C.2a1b.2a.2	2022-02-25	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	320	1280	160	40	
A/Bulgaria/1473/2022	3C.2a1b.2a.2	2022-03-10	SIAT2/SIAT1	80	<	40	160	320	640	320	640	80	160	1280	80	40	
A/Bulgaria/1616/2022	3C.2a1b.2a.2	2022-03-17	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/1611/2022	3C.2a1b.2a.2	2022-03-17	SIAT2/SIAT1	160	<	80	160	320	640	320	1280	ND	ND	1280	ND	40	
A/Bulgaria/1537/2022	3C.2a1b.2a.2	2022-03-18	SIAT2/SIAT1	160	40	160	160	320	640	640	1280	ND	ND	1280	ND	80	
A/Bulgaria/1536/2022	3C.2a1b.2a.2	2022-03-18	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	160	320	1280	160	40	
A/Bulgaria/1582/2022	3C.2a1b.2a.2	2022-03-21	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Bulgaria/1581/2022	3C.2a1b.2a.2	2022-03-21	SIAT2/SIAT1	160	<	80	320	320	640	640	1280	ND	ND	1280	ND	80	
A/Bulgaria/1579/2022	3C.2a1b.2a.2	2022-03-21	SIAT2/SIAT1	160	<	80	160	320	640	320	1280	ND	ND	1280	ND	40	
A/Bulgaria/1588/2022	3C.2a1b.2a.2	2022-03-22	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1666/2022	3C.2a1b.2a.2	2022-03-23	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1665/2022	3C.2a1b.2a.2	2022-03-23	SIAT2/SIAT1	80	<	40	160	320	640	640	640	80	320	1280	160	40	
A/Bulgaria/1660/2022	3C.2a1b.2a.2	2022-03-23	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1659/2022	3C.2a1b.2a.2	2022-03-23	SIAT2/SIAT1	80	<	80	160	320	640	640	640	80	320	1280	160	40	
A/Bulgaria/1646/2022	3C.2a1b.2a.2	2022-03-23	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1763/2022	3C.2a1b.2a.2	2022-03-28	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1726/2022	3C.2a1b.2a.2	2022-03-28	SIAT2/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1813/2022	3C.2a1b.2a.2	2022-04-04	SIAT2/SIAT1	80	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Bulgaria/1827/2022	3C.2a1b.2a.2	2022-04-07	SIAT2/SIAT1	80	<	80	160	320	640	640	640	80	320	1280	160	40	
A/Slovenia/9891/2022	3C.2a1b.2a.2	2022-04-11	MDCKx/SIAT1	80	<	40	160	320	640	640	1280	ND	ND	1280	ND	40	
A/Slovenia/9967/2022	3C.2a1b.2a.2	2022-04-20	MDCKx/SIAT1	160	<	80	160	320	640	640	1280	80	320	1280	160	40	
A/Slovenia/9905/2022	3C.2a1b.2a.2	2022-04-12	MDCKx/SIAT1	640	40	160	640	640	1280	640	1280	ND	ND	1280	ND	160	
A/Slovenia/10081/2022	3C.2a1b.2a.2	2022-04-21	MDCKx/SIAT1	160	<	80	160	320	640	640	1280	160	320	1280	160	40	
							Vaccine NH 2021-22							Vaccine SH 2022 NH 2022-23			

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

1 < = <40, ND = Not Done

Table 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								
	Passage history			A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	AStock	A/Eng	A/Darwin	A/Kansas
	Ferret number			326419	2671/19	92525/20	e0826360/20	4005/20	5/21	2141917232/21	9/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
				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/32642/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	160	640	160	160	160	40	320	80
A/Hong Kong/29712/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	320	640	160	160	160	40	160	160
A/Cambodia/9252566/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	160	640	320	160	160	40	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	80	<	160	1280	160	160	320	320	80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	320	320	640	640	640	640	320
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	160	<	160	160	320	640	320	1280	40
A/England/2141917232/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT3	80	<	80	80	320	320	640	640	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E4	160	<	160	640	640	1280	640	2560	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<	80	80	40	80	40	80	320
TEST VIRUSES												
A/Kazakhstan/5832/2021	3C.2a1b.2a.2	2021-12-06	SIAT1	160	40	160	320	640	320	640	640	160
A/Kazakhstan/5862/2021	3C.2a1b.2a.2	2021-12-09	SIAT1	160	<	160	320	320	320	320	640	160
A/Switzerland/185592/2022	3C.2a1b.2a.2	2022-03-08	SIAT1	160	<	80	320	320	640	640	1280	80
A/Switzerland/40042/2022	3C.2a1b.2a.2	2022-03-10	SIAT1	40	<	40	80	160	160	640	640	<
A/Switzerland/129812/2022	3C.2a1b.2a.2	2022-03-14	SIAT1	40	<	40	80	160	320	320	640	<
A/Switzerland/730280/2022	3C.2a1b.2a.2	2022-03-16	SIAT1	40	<	40	80	160	160	320	640	<
A/Switzerland/34074/2022	3C.2a1b.2a.2	2022-03-18	SIAT1	40	<	40	80	160	320	320	640	<
A/Switzerland/457842/2022	3C.2a1b.2a.2	2022-03-21	SIAT1	40	<	40	80	160	320	640	640	<
A/Switzerland/108712/2022	3C.2a1b.2a.2	2022-03-28	SIAT1	80	<	80	160	320	640	640	640	40
A/Switzerland/180162/2022	3C.2a1b.2a.2	2022-03-28	SIAT1	80	<	40	160	160	320	320	320	40
A/Switzerland/191300/2022	3C.2a1b.2a.2	2022-03-28	SIAT1	40	<	40	80	320	320	320	640	<
A/Switzerland/096832/2022	3C.2a1b.2a.2	2022-03-30	MDCK0/SIAT2	320	<	80	640	320	640	640	1280	160
A/Switzerland/546372/2022	3C.2a1b.2a.2	2022-03-30	SIAT1	320	40	320	640	640	1280	640	1280	160
A/Mecklenburg-Vorpommern/482/2022	3C.2a1b.2a.2	2022-03-30	P1/SIAT1	40	<	40	80	160	320	320	640	<
A/Switzerland/763932/2022	3C.2a1b.2a.2	2022-03-31	SIAT1	80	<	40	80	160	320	320	640	<
A/Switzerland/899032/2022	3C.2a1b.2a.2	2022-03-31	SIAT1	160	<	160	320	320	1280	640	1280	80
A/Hessen/1/2022	3C.2a1b.2a.2	2022-03-31	P1/SIAT1	40	<	40	80	160	320	320	640	<
A/Berlin/4/2022	3C.2a1b.2a.2	2022-04-01	P2/SIAT1	80	<	40	160	320	640	320	1280	40
A/Thuringen/1/2022	3C.2a1b.2a.2	2022-04-01	P1/SIAT1	160	<	80	160	320	640	320	640	80
A/Niedersachsen/9/2022	3C.2a1b.2a.2	2022-04-04	P1/SIAT1	40	<	40	80	160	320	320	1280	<
A/Slovenia/9860/2022	3C.2a1b.2a.2	2022-04-06	MDCK1/SIAT2	160	40	160	320	640	320	320	640	160
A/Norway/185750/2022	3C.2a1b.2a.2	2022-04-06	SIAT1	40	<	40	80	160	320	320	640	<
A/Sachsen/4/2022	3C.2a1b.2a.2	2022-04-07	P1/SIAT1	40	<	40	80	160	320	320	640	<
A/Norway/188962/2022	3C.2a1b.2a.2	2022-04-08	SIAT2	160	<	80	320	320	320	640	640	160
A/Norway/188942/2022	3C.2a1b.2a.2	2022-04-08	SIAT2	40	<	80	160	320	640	640	1280	40
A/Norway/188932/2022	3C.2a1b.2a.2	2022-04-08	SIAT1	40	<	40	80	160	320	320	640	<
A/Norway/194192/2022	3C.2a1b.2a.2	2022-04-09	SIAT1	160	<	80	320	320	640	640	1280	80
A/Slovenia/9904/2022	3C.2a1b.2a.2	2022-04-12	MDCK0/SIAT2	160	<	80	320	640	640	640	640	80
A/Norway/19253/2022	3C.2a1b.2a.2	2022-04-13	SIAT1	40	<	40	80	160	320	320	640	<
A/Norway/190532/2022	3C.2a1b.2a.2	2022-04-13	SIAT1	40	<	40	80	160	320	320	640	<
A/Norway/198652/2022	3C.2a1b.2a.2	2022-04-14	SIAT1	40	<	40	40	160	320	320	640	<
A/Norway/198592/2022	3C.2a1b.2a.2	2022-04-15	SIAT1	40	<	40	80	160	320	320	640	<
A/Norway/192592/2022	3C.2a1b.2a.2	2022-04-15	SIAT1	40	<	40	80	160	320	320	320	<
A/Norway/200472/2022	3C.2a1b.2a.2	2022-04-17	SIAT1	160	<	80	320	320	320	320	320	80
A/Latvia/04-589752/2022	3C.2a1b.2a.2	2022-04-18	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-585972/2022	3C.2a1b.2a.2	2022-04-19	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Nordrhein-Westfalen/52/2022	3C.2a1b.2a.2	2022-04-19	P1/SIAT1	40	<	40	40	160	320	320	640	<
A/Latvia/04-784142/2022	3C.2a1b.2a.2	2022-04-22	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-784082/2022	3C.2a1b.2a.2	2022-04-23	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-783852/2022	3C.2a1b.2a.2	2022-04-23	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-783812/2022	3C.2a1b.2a.2	2022-04-23	P2/SIAT1	40	<	40	80	160	320	320	320	<
A/Latvia/04-826372/2022	3C.2a1b.2a.2	2022-04-24	P2/SIAT1	80	<	40	80	320	320	320	640	<
A/Latvia/04-826612/2022	3C.2a1b.2a.2	2022-04-25	P2/SIAT1	40	<	40	40	160	320	320	640	<
A/Hessen/182/2022	3C.2a1b.2a.2	2022-04-25	P1/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-862992/2022	3C.2a1b.2a.2	2022-04-26	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Latvia/04-862612/2022	3C.2a1b.2a.2	2022-04-26	P2/SIAT1	80	<	40	80	160	320	320	640	<
A/Latvia/04-902212/2022	3C.2a1b.2a.2	2022-04-28	P2/SIAT1	80	<	40	80	320	320	320	640	<
A/Latvia/04-901452/2022	3C.2a1b.2a.2	2022-04-28	P2/SIAT1	40	<	40	80	160	320	320	640	<
A/Mecklenburg-Vorpommern/59/2022	3C.2a1b.2a.2	2022-05-02	P1/SIAT1	80	<	40	40	160	640	320	1280	<
A/Bayern/16/2022	3C.2a1b.2a.2	2022-05-03	P1/SIAT1	80	<	40	80	160	640	320	1280	<
A/Baden-Wurttemberg/27/2022	3C.2a1b.2a.2	2022-05-04	P1/SIAT1	80	<	40	80	160	640	320	640	<
A/Brandenburg/2/2022	3C.2a1b.2a.2	2022-05-05	P1/SIAT1	80	<	40	160	320	320	320	640	80
A/Berlin/87/2022	3C.2a1b.2a.2	2022-05-06	P1/SIAT1	80	<	40	80	320	320	320	1280	<
A/Bremen/172/2022	3C.2a1b.2a.2	2022-05-06	P1/SIAT1	80	<	40	80	160	320	320	1280	<
A/Sachsen/112/2022	3C.2a1b.2a.2	2022-05-06	P1/SIAT1	80	<	40	80	320	160	320	640	<
A/Rheinland-Pfalz/80/2022	3C.2a1b.2a.2	2022-05-09	P1/SIAT1	40	<	40	80	160	320	320	640	<
							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									
	Passage history			A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	A/Stock	A/Eng	A/Darwin	A/Kansas
	Ferret number			326/419	2671/19	925256/20	e0826360/20	4005/20	5/21	21419723/21	9/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
				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.1a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES												
A/Denmark/326419/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	320	320	640	160	320	160	80	320	160
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	160	320	640	160	160	80	40	160	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	160	640	160	320	160	40	320	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	ES/E2	80	<	80	640	160	80	160	160	40
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	160	320	640	640	640	640	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	80	<	80	160	320	640	320	640	80
A/England/21419723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT3	40	<	80	80	160	320	640	640	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E4	160	<	80	320	320	640	640	1280	80
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<	80	80	80	80	80	80	640
TEST VIRUSES												
A/Halmstad/4/2022	3C.2a1b.1a	2022-04-11	SIAT1/SIAT1	160	160	320	320	320	160	40	160	80
A/Eskilstuna/3/2022	3C.2a1b.1a	2022-05-01	SIAT1/SIAT1	160	160	320	320	320	160	40	160	80
A/Linkoping/3/2022	3C.2a1b.2a.2	2022-03-12	SIAT1/SIAT1	80	<	40	80	320	640	320	640	40
A/Stockholm/9/2022	3C.2a1b.2a.2	2022-03-15	SIAT1/SIAT1	40	<	40	80	160	320	320	640	40
A/Stockholm/10/2022	3C.2a1b.2a.2	2022-03-21	SIAT1/SIAT1	80	<	40	80	320	640	320	640	40
A/Bayern/9/2022	3C.2a1b.2a.2	2022-03-29	P1/SIAT1	160	<	160	320	320	640	640	640	80
A/Austria/1506342/2022	3C.2a1b.2a.2	2022-03-29	Cx/SIAT1	160	<	80	640	640	1280	640	1280	160
A/Austria/1504947/2022	3C.2a1b.2a.2	2022-03-29	Cx/SIAT1	160	<	80	640	320	640	640	640	160
A/Austria/1504943/2022	pending	2022-03-29	Cx/SIAT1	160	<	80	160	640	320	320	640	160
A/Austria/1504938/2022	3C.2a1b.2a.2	2022-03-29	Cx/SIAT1	80	<	40	160	160	640	320	640	40
A/Austria/1506788/2022	3C.2a1b.2a.2	2022-03-31	Cx/SIAT1	80	<	40	80	160	320	320	640	40
A/Austria/1505762/2022	3C.2a1b.2a.2	2022-03-31	Cx/SIAT1	80	<	40	80	160	320	320	640	40
A/Slovenia/97682/2022	pending	2022-04-01	MDCK1/SIAT1	80	<	40	160	320	320	320	640	40
A/Slovenia/98542/2022	pending	2022-04-01	MDCK1/SIAT1	80	<	40	80	320	640	320	640	40
A/Austria/1506181/2022	3C.2a1b.2a.2	2022-04-01	Cx/SIAT1	40	<	40	80	160	320	320	640	40
A/Stockholm/12/2022	3C.2a1b.2a.2	2022-04-03	SIAT1/SIAT1	160	<	40	320	320	320	320	640	80
A/Slovenia/98062/2022	pending	2022-04-04	SIAT1/SIAT1	40	<	40	80	160	320	320	640	40
A/Austria/1507395/2022	3C.2a1b.2a.2	2022-04-04	Cx/SIAT1	40	<	40	80	160	320	320	640	40
A/Austria/1507013/2022	3C.2a1b.2a.2	2022-04-04	Cx/SIAT1	80	<	40	80	320	160	320	320	80
A/Austria/1506583/2022	3C.2a1b.2a.2	2022-04-04	Cx/SIAT1	80	<	40	160	320	160	320	320	80
A/Austria/1506576/2022	3C.2a1b.2a.2	2022-04-04	Cx/SIAT1	160	<	40	160	320	320	320	320	80
A/Slovenia/98452/2022	pending	2022-04-05	MDCK1/SIAT1	40	<	40	80	160	320	320	640	40
A/Slovenia/98631/2022	pending	2022-04-06	SIAT1/SIAT1	160	<	160	320	640	640	640	640	160
A/Stockholm/19/2022	3C.2a1b.2a.2	2022-04-06	SIAT1/SIAT1	80	<	40	160	160	320	320	640	40
A/Austria/1507884/2022	3C.2a1b.2a.2	2022-04-07	Cx/SIAT1	80	<	40	80	160	320	320	640	40
A/Sweden/3/2022	3C.2a1b.2a.2	2022-04-11	SIAT1/SIAT1	40	<	<	80	80	160	320	320	40
A/Eskilstuna/1/2022	3C.2a1b.2a.2	2022-04-16	SIAT1/SIAT1	80	<	40	80	160	160	320	320	40
A/Portugal/211329/2022	pending	2022-04-19	SIAT1/SIAT1	80	<	40	80	160	320	320	640	40
A/Portugal/211330/2022	pending	2022-04-19	SIAT1/SIAT1	80	<	40	80	320	320	640	320	40
A/Portugal/211338/2022	pending	2022-04-19	SIAT1/SIAT1	160	<	80	160	320	640	1280	640	80
A/Linkoping/5/2022	3C.2a1b.2a.2	2022-04-19	SIAT1/SIAT1	80	<	40	160	160	320	320	640	40
A/Stockholm/21/2022	3C.2a1b.2a.2	2022-04-19	SIAT1/SIAT1	40	<	40	160	160	320	640	320	40
A/Portugal/211316/2022	pending	2022-04-23	SIAT1/SIAT1	<	<	<	80	320	320	640	640	40
A/Portugal/211317/2022	pending	2022-04-24	SIAT1/SIAT1	80	<	40	160	160	320	320	640	40
A/Portugal/211412/2022	pending	2022-04-28	SIAT1/SIAT1	40	<	40	80	160	320	320	640	40
A/Portugal/211439/2022	3C.2a1b.2a.2	2022-05-04	SIAT1/SIAT1	40	<	40	80	160	320	320	320	40
A/Portugal/211442/2022	3C.2a1b.2a.2	2022-05-04	SIAT2/SIAT1	40	<	40	80	160	320	320	640	40
A/Portugal/211459/2022	3C.2a1b.2a.2	2022-05-05	SIAT2/SIAT1	80	<	40	80	160	640	320	640	40
A/Portugal/211462/2022	3C.2a1b.2a.2	2022-05-05	SIAT1/SIAT1	<	<	40	80	160	320	320	640	40
A/Portugal/211456/2022	3C.2a1b.2a.2	unknown	SIAT2/SIAT1	80	<	40	160	320	640	320	640	80
A/Portugal/211458/2022	3C.2a1b.2a.2	unknown	SIAT2/SIAT1	40	<	40	80	160	320	320	640	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 5-4. Antigenic analysis of influenza A(H3N2) 3C.2a1b.2a.2 viruses by HI - Summary

Haemagglutination inhibition titre

Viruses		Post-infection ferret antisera														
									NEW		NEW			NEW		
	A/Denmark/3264/19	3264/19	2671/19	925256/20	e0826360/20	4005/20	5/21	21419723/21	8720/2022	24873/21	24873/21	9/21	29511/21	A/Kansas/14/17
Passage history	SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	SIAT	SIAT	Egg	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	F24/22-1	F10/22-1	F11/22-1	F38/21-1	F12/22-1	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.2a1b.2a.2	3C.2a1b.2a.2	3C.3a.1
REFERENCE VIRUSES														
A/Denmark/3264/2019	3C.2a1b.1a	320	160	320	160	160	160	<	ND	ND	ND	320	ND	80
A/Hong Kong/2671/2019	3C.2a1b.1b	320	640	1280	320	320	320	40	<	160	80	320	40	320
A/Cambodia/925256/2020	3C.2a1b.2a.1	80	160	640	160	160	160	<	ND	ND	ND	320	ND	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	160	<	160	2560	320	160	320	320	80	160	320	320	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	320	160	320	640	1280	640	1280	1280	320	640	2560	640	160
A/Stockholm/5/2021	3C.2a1b.2a.2	160	40	160	320	640	1280	640	1280	160	320	1280	320	80
A/England/214191723/2021	3C.2a1b.2a.2	80	<	80	160	320	640	1280	640	320	640	1280	80	40
A/Slovenia/8720/2022	3C.2a1b.2a.2	160	<	80	160	320	1280	640	1280	160	320	640	1280	160	40
A/Norway/24873/2021	3C.2a1b.2a.2	80	<	80	160	320	640	1280	1280	320	320	640	1280	160	40
A/Norway/24873/2021	3C.2a1b.2a.2	160	<	160	640	640	1280	1280	1280	320	320	1280	2560	320	160
A/Darwin/9/2021	3C.2a1b.2a.2	160	<	160	640	640	640	640	1280	160	160	320	2560	320	80
A/Norway/29511/2021	3C.2a1b.2a.2	ND	ND	160	ND	640	320	640	640	160	160	320	1280	640	ND
A/Kansas/14/2017	3C.3a.1	80	40	160	160	80	80	80	80	<	<	<	160	80	640
TEST VIRUSES															
Number tested	3C.2a1b.2a.2	118	118	118	118	118	118	118	34	15	15	15	118	15	118
No with titre reduction ≤2-fold		45	0	2	6	33	111	115	34	2	0	0	66	0	6
%		*38.1*		*1.7*	*5.0*	*28.0*	*94.1*	*97.5*	*100.0*	*13.3*			*55.9*		*5.1*
No with titre reduction =4-fold		34	0	11	18	84	7	3	0	13	14	47	14	14	10
%		*28.8*		*9.3*	*15.3*	*71.2*	*5.9*	*2.5*		*86.7*	*93.3*	*39.8*	*93.3*	*93.3*	*8.5*
No with titre reduction ≥8-fold		39	118	105	94	1	0	0	0	0	1	5	1	1	102
%		*33.1*	*100*	*89.0*	*79.7*	*0.8*					*6.7*	*4.3*	*6.7*	*6.7*	*86.4*
					Vaccine NH 2021-22							Vaccine SH 2022 NH 2022-23			

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

Influenza B virus analyses

Influenza B/Victoria-lineage

All recently circulating B/Victoria-lineage viruses have fallen in genetic clade **V1A**, represented by **B/Brisbane/60/2008**, a former vaccine virus, but with additional **HA1** amino acid substitutions of **I117V** and **N129D** (e.g., **B/Ireland/3154/2016**). Viruses retaining full-length HAs 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 emerged. Viruses in these groups were/are antigenically distinct from B/Brisbane/60/2008 and each other (as noted in the September 2018 characterization report[4] 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**. No detections of viruses in this group have been reported recently.
- 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, represented by **B/Hong Kong/269/2017**. No detections of viruses in this group have been reported recently.
- 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 May report, based on sequences from viruses with collection dates after 31 December 2021 that were submitted to GISAID in April and May of 2022, showed detected viruses to fall in the **V1A.3** subclade represented by **B/Washington/02/2019**. 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 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). 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 4a). **V1A.3** viruses from Guatemala had **HA1 T73I** and **N233K** (resulting in loss of a glycosylation site) substitutions. Among the **V1A.3a.2** subgroup viruses a group of five viruses reported by Luxembourg appeared to have 'repaired' the three amino acid deletion at **HA1** residues **162** to **164** (Figure 4a), something that has not been confirmed at the WIC.

The phylogeny generated for this report is essentially the same with just 21 new sequences having become available in June 2022. Of these 21, three fell in subclade **V1A.3** (one in the 'Guatemala' cluster and two in the 'Netherlands' cluster) and 18 were dispersed in the **V1A.3a.2** subgroup (Figure 4b).

The WHO Collaborating Centres for Influenza Research and Response 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 18 subgroup **V1A.3a.2** viruses characterized antigenically since the May report (Tables 6-1 and 6-2). All test viruses were recognised well by post-infection ferret antisera raised against three cell culture-propagated subgroup V1A.3a.2 viruses and the egg-propagated **B/Austria/1359417/2021** virus carrying **HA1 G141**. In contrast, the **B/Austria/1359417/2021** vaccine virus, which has an 'egg-adaptation' **HA1 G141R** amino acid substitution induced a high titre (5120) antiserum and all test viruses showed a drop in recognition of at least eightfold compared to the homologous titre, but all test viruses reacted with a titre of at least 160, well above the threshold of 40 that has been determined as the cut-off for a protective effect.

[4] Influenza virus characterisation, summary Europe, September 2018. Stockholm: European Centre for Disease Prevention and Control; 2018. (https://ecdc.europa.eu/sites/portal/files/documents/ECDC-Flu-Characterisation-Report-Sep-2018.pdf, accessed 18 October 2022)

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, May 2022)

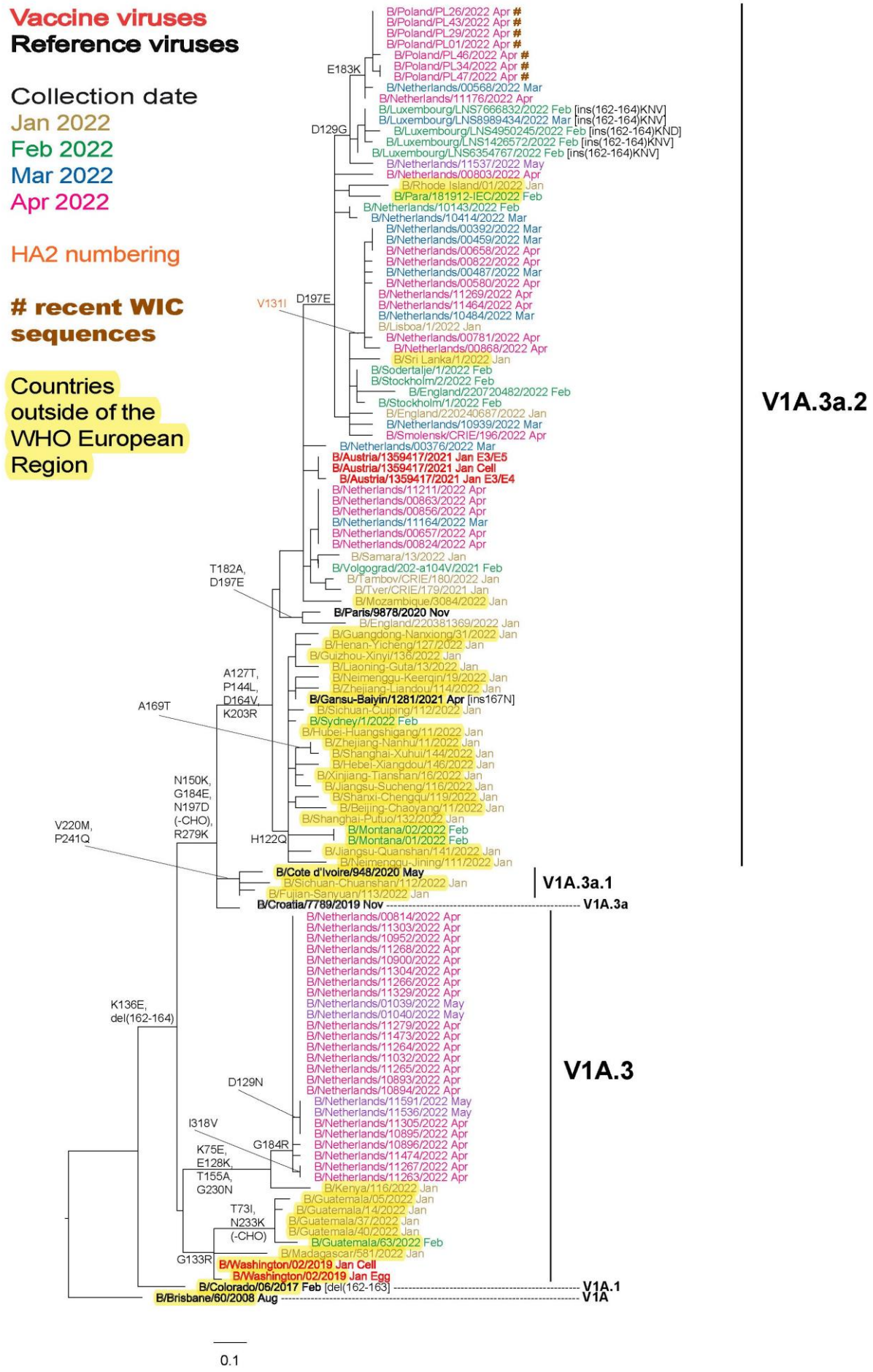


Figure 4b. Phylogenetic comparison of B/Victoria-lineage HA genes (GISAID/WIC, June 2022)

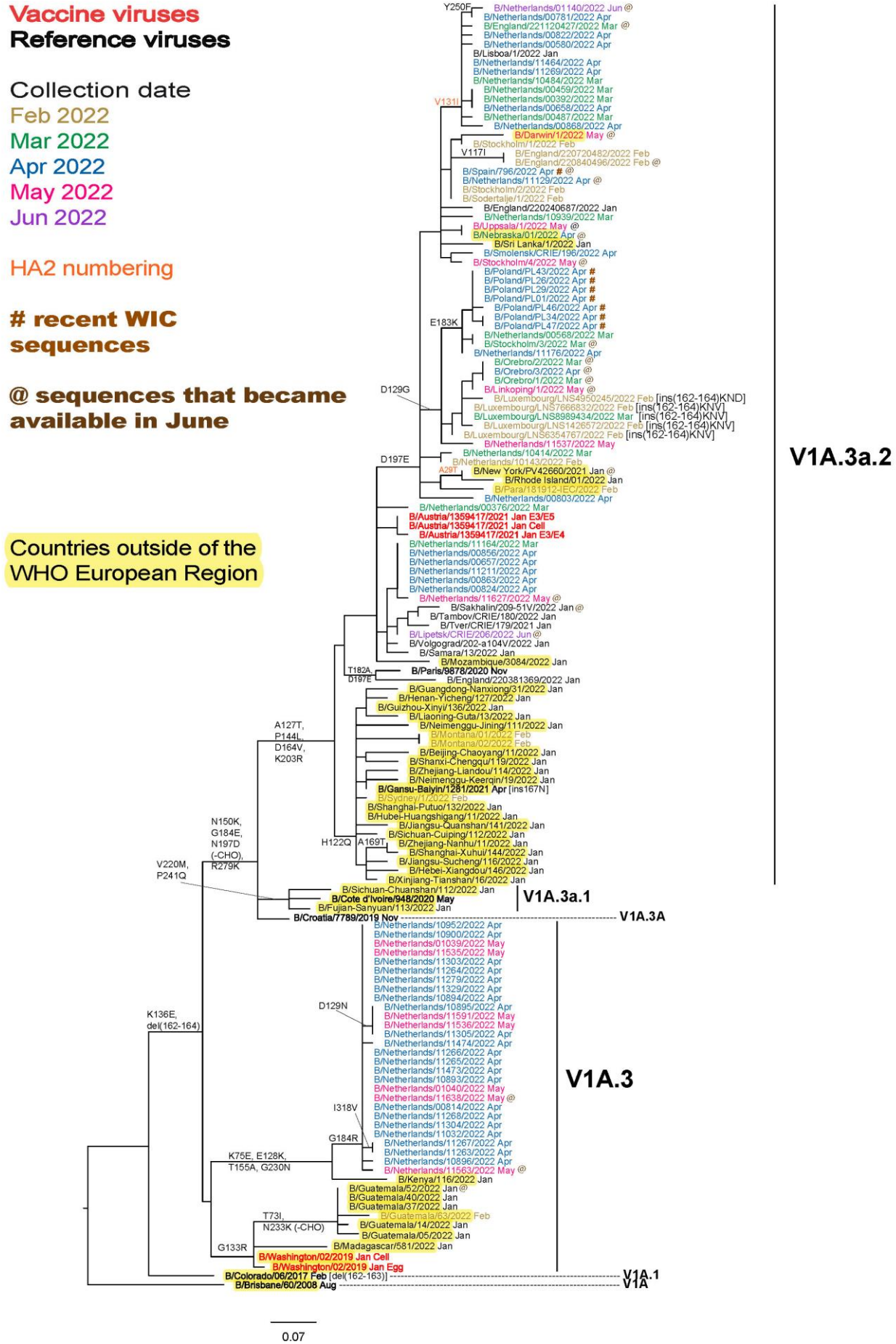


Table 6-1. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antiserum										NEW
	Passage history			B/Bris 60/08 Egg	B/Colorado 06/17 Egg	B/Washton 02/19 Egg	B/ClV 948/20 MDCK	B/Paris 9878/20 MDCK	B/G-Baiyin 1281/21 MDCK	B/Austria 1359417/21 MDCK	B/Austria 1359417/21 Egg G141	B/Austria 1359417/21 Egg G141R	CNIC-2204B Z-S/11203/21 Egg G141W	
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574 [*1,3]	F11/18 [*4]	F20/20 [*4]	F08/21 [*5]	F12/21 [*1]	F08/22 [*1]	NIB F01/21 [*1]	F15/21 [*1]	F44/21 [*1]	F16/22 [*1]	
	Genetic group			V1A	V1A.1	V1A.3	V1A.3a.1	V1A.3a.2	V1A.3a.2	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	1280	160	40	<	<	<	<	<	<	<	<
B/Colorado/06/2017	V1A.1	2017-02-05	E5/E2	1280	320	40	<	<	<	40	<	<	<	<
B/Washington/02/2019	V1A.3	2019-01-19	E3/E2	1280	320	80	40	<	<	40	<	<	<	<
B/Cote d'Ivoire/948/2020	V1A.3a.1	2020-05-28	MDCK4	320	40	40	320	<	40	160	<	80	80	80
B/Paris/9878/2020	V1A.3a.2	2020-11-20	MDCK2	640	160	<	160	320	320	1280	1280	640	ND	ND
B/Gansu-Baiyin/1281/2021	V1A.3a.2	2021-04-13	C1/C1/MDCK2	640	40	<	160	640	640	2560	1280	320	320	320
B/Austria/1359417/2021	V1A.3a.2	2021-01-09	SIAT1/MDCK4	640	40	<	160	320	320	2560	1280	320	320	320
B/Austria/1359417/2021 Isolate 2	G141 V1A.3a.2	2021-01-09	E3/E3	640	40	<	320	320	320	2560	1280	640	320	320
B/Austria/1359417/2021 Isolate 2	G141R V1A.3a.2	2021-01-09	E3/E5	320	20	<	320	320	320	1280	640	5120	1280	1280
CNIC-2204A (B/Zhejiang-Shangcheng/11203/2021)	G141W V1A.3a.2	2021-10-27	E2+2/E6/E1	80	10	<	40	40	40	320	160	160	320	320
TEST VIRUSES														
B/Poland/PL47/2022	V1A.3a.2	2022-04-15	MDCK1	320	40	<	80	160	80	320	320	160	40	40
B/Poland/PL46/2022	V1A.3a.2	2022-04-15	MDCK1	640	80	<	80	320	160	640	640	320	80	80
B/Poland/PL43/2022	V1A.3a.2	2022-04-12	MDCK1	640	80	<	160	320	320	1280	1280	640	80	80
B/Poland/PL29/2022	V1A.3a.2	2022-04-11	MDCK1	640	80	<	80	320	160	640	640	320	80	80
B/Poland/PL01/2022	V1A.3a.2	2022-04-04	MDCK1	320	80	<	80	320	160	640	640	160	40	40
						Vaccine SH 2020 NH 2020-21 SH 2021					Vaccine SH 2022 NH 2022-23			

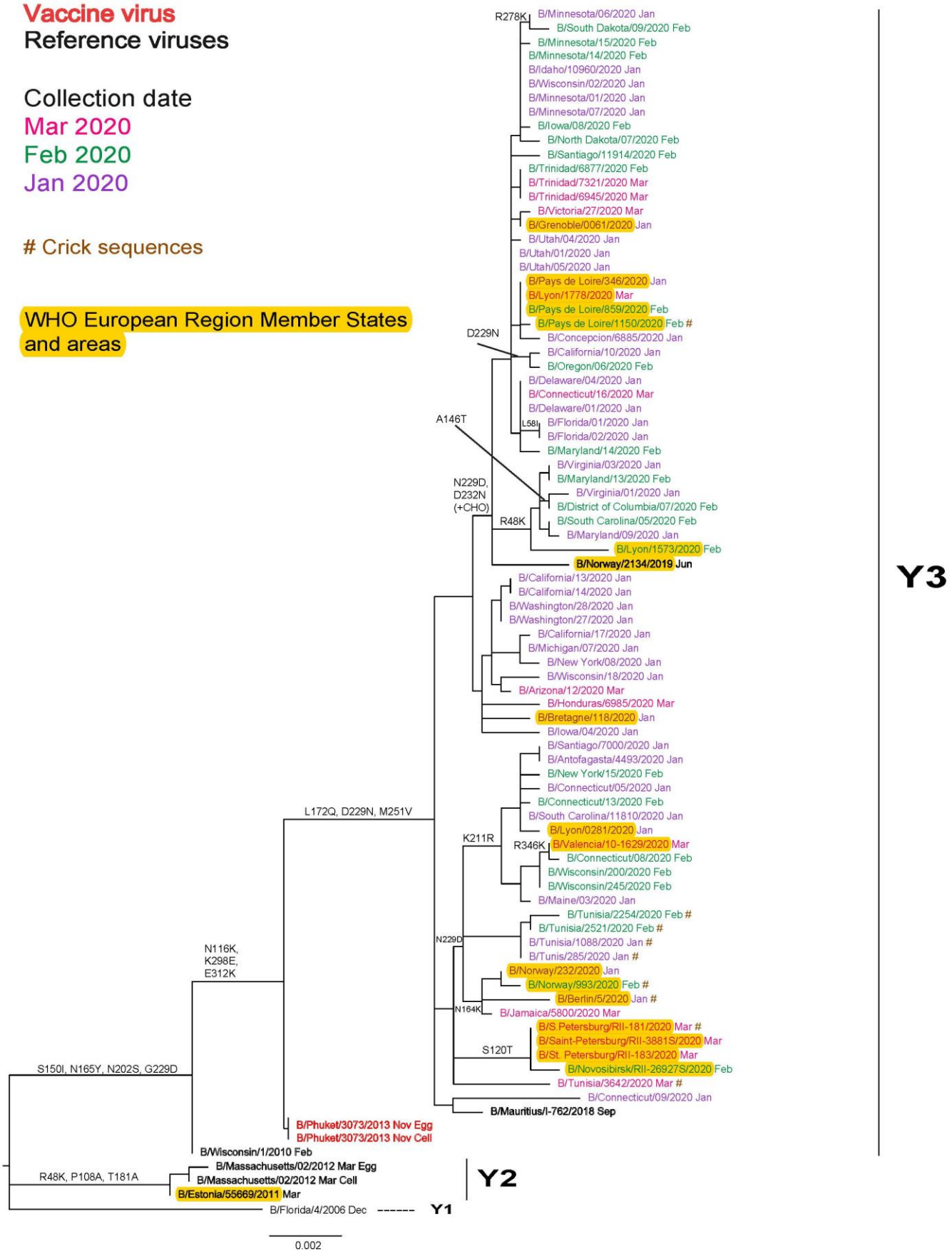
*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <20; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; [5] < = <80; ND = Not Done

Table 6-2. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antiserum								
				B/Bris 60/08	B/Colorado 06/17	B/Wash'ton 02/19	B/CIV 948/20	B/Paris 9878/20	B/G-Baiyin 1281/21	B/Austria 1359417/21	B/Austria 1359417/21	B/Austria 1359417/21
		Passage history		Egg	Egg	Egg	MDCK	MDCK	MDCK	MDCK	Egg G141	Egg G141R
		Ferret number		Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F11/18[*4]	F20/20[*4]	F08/21*[5]	F12/21[*1]	F08/22[*1]	NIB F01/21[*1]	F15/21[*1]	F44/21[*1]
		Genetic group		V1A	V1A.1	V1A.3	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	80	20	<	<	<	<	<	<
B/Colorado/06/2017		V1A.1	2017-02-05	E5/E2	1280	320	20	<	<	<	<	<	<
B/Washington/02/2019		V1A.3	2019-01-19	E3/E2	1280	80	80	<	<	<	<	<	<
B/Cote d'Ivoire/948/2020		V1A.3a.1	2020-05-28	MDCK4	160	20	<	320	<	<	80	40	80
B/Paris/9878/2020		V1A.3a.2	2020-11-20	MDCK2	640	80	<	80	320	320	640	640	320
B/Gansu-Baiyin/1281/2021		V1A.3a.2	2021-04-13	C1/C1/MDCK2	640	20	<	80	320	640	1280	1280	320
B/Austria/1359417/2021		V1A.3a.2	2021-01-09	SIAT1/MDCK4	640	40	<	80	320	320	1280	1280	320
B/Austria/1359417/2021 Isolate 2	G141	V1A.3a.2	2021-01-09	E3/E5	640	40	<	160	320	320	1280	1280	640
B/Austria/1359417/2021 Isolate 2	G141R	V1A.3a.2	2021-01-09	E3/E5	320	40	<	160	160	320	1280	640	5120
TEST VIRUSES													
B/Stockholm/2/2022		V1A.3a.2	2022-02-27	SIAT1/MDCK1	1280	80	<	160	320	320	1280	1280	320
B/Norway/14939/2022		V1A.3a.2	2022-03-15	MDCK1	1280	80	<	160	320	320	1280	1280	640
B/Stockholm/3/2022		V1A.3a.2	2022-03-22	SIAT1/MDCK1	1280	80	<	160	640	320	1280	1280	320
B/Norway/17464/2022		V1A.3a.2	2022-03-30	MDCK1	1280	80	<	160	320	320	1280	1280	320
B/Orebro/1/2022		V1A.3a.2	2022-03-30	SIAT1/MDCK1	640	80	<	160	320	320	1280	1280	320
B/Orebro/2/2022		V1A.3a.2	2022-03-31	SIAT1/MDCK1	1280	80	<	160	320	320	1280	1280	320
B/Norway/19688/2022		V1A.3a.2	2022-04-05	MDCK1	1280	80	<	80	320	320	1280	1280	320
B/Orebro/3/2022		V1A.3a.2	2022-04-08	SIAT1/MDCK1	640	80	<	80	320	320	640	1280	320
B/Norway/21604/2022		V1A.3a.2	2022-05-02	MDCK1	1280	80	<	80	320	320	1280	640	320
B/Berlin/1/2022		V1A.3a.2	2022-05-03	P1/MDCK1	2560	160	<	160	640	320	1280	1280	640
B/Norway/22070/2022		V1A.3a.2	2022-05-04	MDCK1	1280	80	<	80	320	320	1280	1280	320
B/Berlin/2/2022		V1A.3a.2	2022-05-04	P1/MDCK1	1280	40	<	160	320	320	2560	1280	320
B/Norway/22019/2022		V1A.3a.2	2022-05-09	MDCK1	640	80	<	80	320	320	640	640	320
							Vaccine SH 2020 NH 2020-21 SH 2021					Vaccine SH 2022 NH 2022-23	

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <20; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; [5] < = <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

4 477 viruses detected over the course of the 2021-2022 season (weeks 40/2021-25/2022) were genetically characterized:

- Of 349 A(H1N1)pdm09 viruses, 321 belonged to clade 6B.1A.5a.1 (represented by A/Guangdong-Maonan/SWL1536/2019) and 27 belonged to clade 6B.1A.5a.2 (represented by A/Victoria/2570/2019). One was not attributed to a clade.
- Of 4 043 A(H3N2) viruses, 4 024 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 18 were attributed to clade 3C.2a1b.1a (represented by A/Denmark/3264/2019).
- Seventy-eight B/Victoria-lineage viruses, 28 belonging to clade V1A.3 (represented by B/Washington/02/2019) and 48 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. For weeks 21-25/2022 a further five viruses each were assessed for susceptibility to NAIs and baloxavir marboxil. 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, 606 influenza viruses detected within the WHO European Region during the 2021-2022 season have been assessed phenotypically against oseltamivir and zanamivir: 81 A(H1)pdm09, 491 A(H3) and 34 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 15 July 2022). The assessment published on 27 June 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 June 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 27 June 2022. Since the previous risk assessment on 13 May 2022, two human cases of infection with A(H5N6) avian influenza viruses were reported by China [6]. The first case was in a 49-year-old male with underlying medical conditions who had disease onset on 16 April 2022, was hospitalised with severe pneumonia and passed away on 24 April. The second case was in a 58-year-old male who had disease onset on 02 June 2022, was hospitalised with severe pneumonia and was still in a severe condition at the time of reporting. Both patients reported exposure to poultry at live poultry markets. The most recent confirmed case of human infection with an A(H5N1) virus was reported by 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 1 182 highly pathogenic avian influenza (HPAI) A(H5) detections between 16 March and 10 June 2022, 750 in poultry, 410 in wild birds and 22 in domestic birds [8]. Detections occurred in 28 EU/EEA countries and the United Kingdom. Of the poultry outbreaks 68% were reported by France and 24% by Hungary, while other affected countries accounted for less than 2% each. Majorities of wild bird detections were reported by Germany (n=158), the Netherlands (n=98), and the United Kingdom (n=48). 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. The risk of human infection was assessed as low for the general population in EU/EEA countries, and low to medium for occupationally exposed persons. According to reports compiled by the Food and Agricultural Organization of the United Nations (FAO) as of 22June 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 25 May 2022 a total of 770 HPAI outbreaks (13 H5Nx, 751 H5N1, and two each for H5N2, H5N5 and H5N8) and no low pathogenic avian influenza (LPAI) outbreaks had been reported [10].

Influenza A(H9N2) virus

Since the last risk assessment on 13 May 2022, China reported three cases of H9N2 infection in children (one, two and five years of age) all of whom had mild disease, were not hospitalized, and made full recoveries [6]. In one case poultry exposure was reported and investigations were taking place to identify sources of infection for the other two cases. 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 13 May 2022 an additional case of zoonotic infection with an avian A(H3N8) virus was reported by China involving a five-year-old boy who developed mild symptoms on 09 May 2022, did not require hospitalization and recovered. The boy had attended a live poultry market (without direct poultry contact) 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, but environmental samples from the poultry market were negative for A(H3) viruses.

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 15 July 2022).

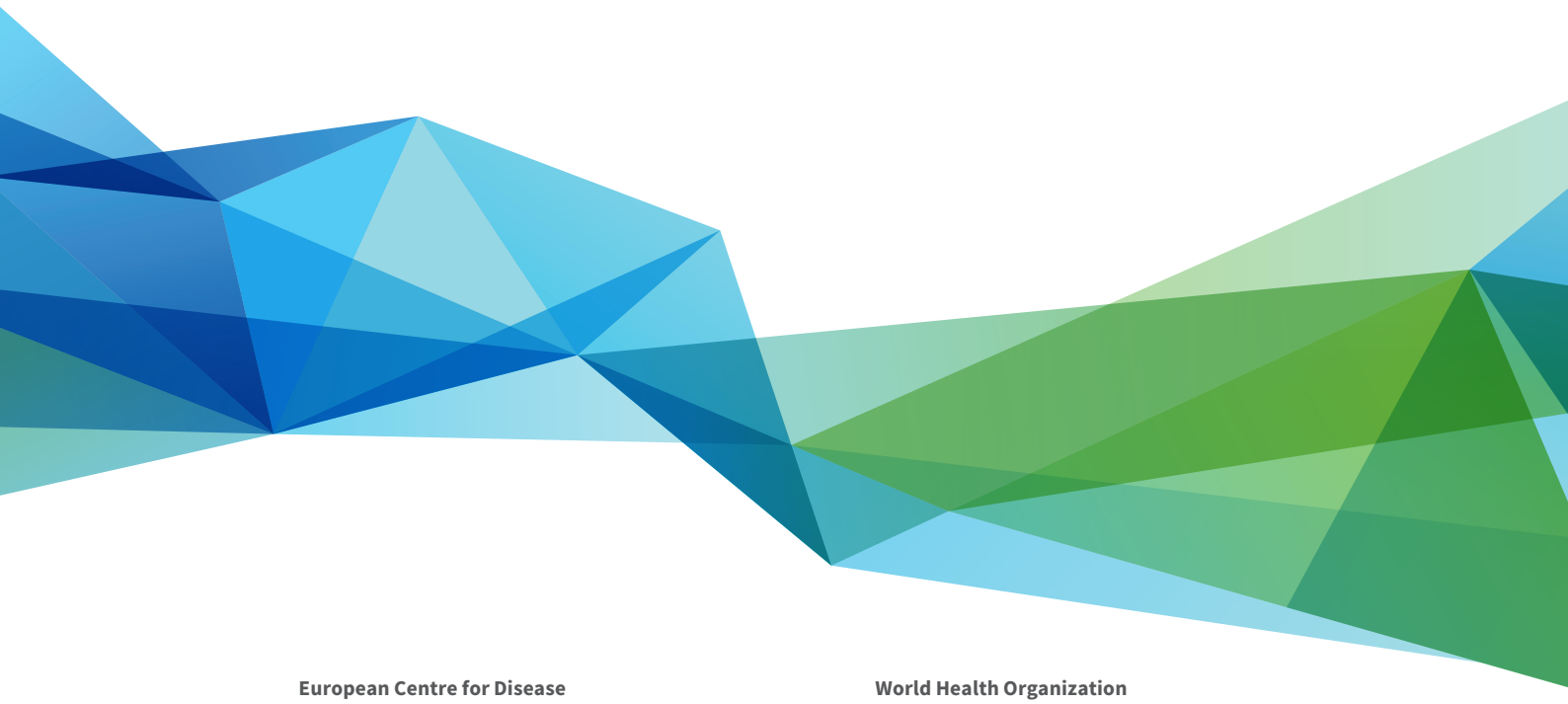
Note on the figures

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 non-WHO Europe countries were recovered from the GISAID EpiFlu™ database. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from the GISAID EpiFlu™ database, which were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website), along with all laboratories who submitted sequences directly to WHO CC London.

References[5]

1. Recommended composition of influenza virus vaccines for use in the 2021-2022 northern hemisphere influenza season. Weekly Epidemiological Record 19 March 2021, vol. 96, (11):77-88. Geneva: World Health Organization; 2021 (https://reliefweb.int/sites/reliefweb.int/files/resources/WER9611-eng-fre.pdf).
2. Recommended composition of influenza virus vaccines for use in the 2022 southern hemisphere influenza season. Weekly Epidemiological Record 22 October 2021, vol. 96(42):509-520. Geneva: World Health Organization; 2021 (https://reliefweb.int/sites/reliefweb.int/files/resources/WER9642-eng-fre.pdf).
3. Recommended composition of influenza virus vaccines for use in the 2022-2023 northern hemisphere influenza season. Weekly Epidemiological Record 25 March 2022, vol. 97(12):109-132. Geneva: World Health Organization; 2022 (https://reliefweb.int/sites/reliefweb.int/files/resources/WER9712-eng-fre.pdf).
4. Human infection with influenza A(H7N9) virus in China. 2013 – China, 1 April 2013 [website]. In: World Health Organization, disease outbreak news . Geneva: World Health Organization; 2013 (https://www.who.int/emergencies/disease-outbreak-news/item/2013_04_01-en).
5. Human infection with avian influenza A(H7N9) virus – China, 2017 – China, 26 October 2017 [website]. In: World Health Organization, disease outbreak news. Geneva: World Health Organization; 2017 (https://www.who.int/emergencies/disease-outbreak-news/item/26-october-2017-ah7n9-china-en).
6. World Health Organization. Influenza at the human-animal interface. Summary and assessment, from 14 May to 27 June 2022. Geneva: WHO; 2022 (https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza-at-the-human-animal-interface-summary-and-assessment--from-14-may-to-27-june-2022.pdf).
7. Influenza at the human–animal interface. Summary and assessment, 13 February to 9 April 2019. Geneva: World Health Organization; 2019 (https://cdn.who.int/media/docs/default-source/influenza/human-animal-interface-risk-assessments/influenza_summary_ira_ha_interface_09_04_2019.pdf).
8. European Centre for Disease Prevention and Control, European Food Safety Authority, European Union Reference Laboratory for Avian Influenza. Avian influenza overview March – June 2022. Parma and Stockholm: EFSA, ECDC; 2022 (https://www.ecdc.europa.eu/sites/default/files/documents/ON-7415-AI-report-final.pdf).
9. Oliver I, Roberts J, Brown CS, et al. A case of avian influenza A(H5N1) in England, January 2022. Euro Surveill. 2022;27(5): pii=2200061. https://doi.org/10.2807/1560-7917.ES.2022.27.5.2200061.
10. Global AIV with zoonotic potential situation update, 22 June 2022. Rome: Food and Agricultural Organization of the United Nations; 2022 (https://mcusercontent.com/dc0b96ca6646c8eedf16a2216/files/aec611eb-f56f-6280-a69b-422e3a4cc195/Global_update_zoonoticAIV_2022_06_22.pdf, accessed 15 July 2022).
11. Public Health England. Guidance, risk assessment of avian influenza A(H9N2) update, 9 August 2021. UK.gov: PHE; 2021 (https://www.gov.uk/government/publications/risk-assessment-of-avian-influenza-ah9n2/risk-assessment-of-avian-influenza-ah9n2).

[5] All references except reference 10 accessed 28 September 2022.



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