Influenza virus characterization

Summary report, Europe, October 2022

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Summary

The September 2022 characterization report[1] gave a breakdown of influenza detections across the World Health Organization (WHO) European Region reported to TESSy up to week 39/2022 to complete the 2021–2022 season. This is the first report for the 2022-2023 influenza season. As of week 43/2022, 4 052 detections had been reported, resulting from extended late 2021-2022 season influenza activity. Of these detections, 87% were type A viruses, with A(H3N2) dominating (71%) over A(H1N1)pdm09 (29%), and 13% type B of which 105 were ascribed to a lineage, with all being B/Victoria. This represents a 7-fold increase in detections compared to the 2021-2022 season, despite only a modest increase (3%) in the number of samples tested. While there were 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, following an approximate two year period of low influenza virus circulation due to the COVID-19 pandemic, indications are that there will be an early start to the 2022-2023 season and a more intense epidemic than in 2021-2022.

Four 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 September report. This report focuses on viruses with collection dates within 2022 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 September 2022, together with sequences generated and antigenic data determined at the WIC.

Globally relatively few A(H1N1)pdm09 viruses were detected over the course of the 2021-2022 season and the first four weeks of the 2022-2023 season. While the 6B.1A.5a.1 genetic subgroup was dominant in the WHO European Region for most of the last season, 6B.1A.5a.2 viruses have dominated in the first weeks of the 2022-2023 season, coming in line with other WHO Regions. As a percentage of type A viruses detected in the WHO European Region there has been an increase to 29% from 4% in the same period in 2021. Clear antigenic discrimination of 6B.1A.5a.1 and 6B.1A.5a.2 viruses has been shown in many previous reports. A/Victoria/2570/2019-like viruses (6B.1A.5a.2) are being used in vaccines for the northern hemisphere 2022-2023 influenza season. At the September 2022 WHO influenza vaccine composition meeting (VCM) the recommendation was to change the southern hemisphere A(H1N1)pdm09 vaccine virus for the 2023 season to an A/Sydney/5/2021-like virus as recently circulating 6B.1A.5a.2 viruses carry HAI K54Q, A186T, Q189E, E224A, R259K and K308R amino acid substitutions compared to A/Victoria/2570/2019; while such viruses were well recognised by post-infection ferret antisera raised against A/Victoria/2570/2019, they were recognised less well by human post-vaccination sera.

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 of late. While 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 egg-propagated A/Darwin/9/2021 which has been recommended for egg-based vaccines to be used in the 2022 and 2023 southern hemisphere, and 2022-23 northern hemisphere seasons. Antisera raised against a range of cell culture- and egg-propagated 3C.2a1b.2a.2 viruses generally gave good recognition of the nine 3C.2a1b.2a.2 test viruses analysed here and those analysed previously.

In Europe and across the world generally, few B/Victoria-lineage viruses have been detected during weeks 40-43/2022. 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 these 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. B/Austria/1359417/2021-like (V1A.3a.2) viruses have been recommended for use in the southern hemisphere 2022 and 2023, and the northern hemisphere 2022-2023 influenza seasons. Of the V1A.3 virus cluster that emerged and spread in the Netherlands, which showed poor recognition by the panel of post-infection ferret antisera used at the WIC, a second detection in Spain has been reported. In addition, viruses detected in August in Guatemala and Zambia form separate V1A.3 clusters defined by specific HA1 amino acid substitutions.

[1]Influenza virus characterization: summary report, Europe, September 2022. 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/10665/364324, accessed 10 November 2022).

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 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 2022-2023 season (weeks 40-43/2022), compared to the same period in the 2021-2022 season. There has been a slight increase in the number of samples from patients fulfilling Influenza-Like Illness (ILI) and/or Acute Respiratory Infection (ARI) criteria being tested (5 285, 3.3%), notably from sentinel sources, but a significant rise in the number of influenza detections (3 485, ~7-fold). In the same period of 2020, during the earlier stages of the COVID-19 pandemic, just 30 336 specimens were tested (~5-fold less) and only 33 influenza detections were reported (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) residual effects of measures introduced to help curtail the spread of SARS-CoV-2, and; (iii) with large swathes of the human population now carrying a significant level of immunity to SARS-CoV-2 following either infection and/or vaccination, influenza has been able to re-establish itself after nearly two years of low-level circulation.

With these caveats, the ratio of type A to type B detections was the same for the two seasons (2021-2022 and 2022-2023), but with a reduction in dominance of A(H3N2) over A(H1N1)pdm09 viruses in 2022-2023. While the number of influenza B virus detections has increased from 76 to 537 (7-fold), the number of viruses ascribed to a lineage has increased from 0% to ~20% with all being of the B/Victoria lineage (Table 1). This is supported by sequences available in GISAID with no B/Yamagata lineage viruses, with collection dates after March 2020, having been characterised genetically. Currently, it appears that measures introduced relating to the COVID-19 pandemic are still having an effect, with greater numbers of respiratory clinical specimens being tested for influenza, but there are clear indications of a very early start to the 2022-2023 season with detections having surpassed those reported during the first four weeks of the previous season. This is also supported by the rate of influenza positivity in sentinel samples which showed a slight rise towards the end of the 2021-2022 season and continues to hover around 7%, just below the epidemic threshold which is set at 10% for the Region (Figure 1).

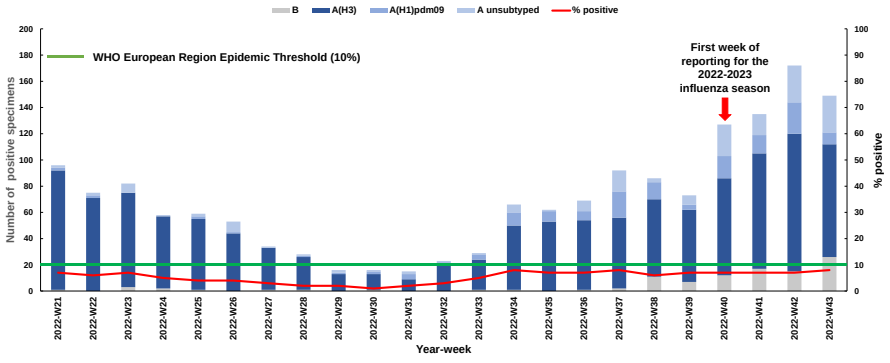
Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2022-2023 season (weeks 40-43/2022)[a]

Virus type/subtype/lineage	Cumulative number of detections for weeks 40-43/2022			Totals*		Cumulative number of detections for weeks 40-43/2021			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**513**	**3002**	**3515**	**86.7**	**6.5:1**	**46**	**445**	**491**	**86.6**	**6.5:1**
A(H1N1)pdm09	64	391	455	28.7		0	13	13	3.8	
A(H3N2)	353	777	1130	71.3	2.5:1	46	284	330	96.2	25.4:1
A not subtyped	96	1834	1930			0	148	148		
Influenza B	**70**	**467**	**537**	**13.3**		**2**	**74**	**76**	**13.4**	
Victoria lineage	29	76	105	100.0		0	0	0		
Yamagata lineage	0	0	0			0	0	0		
Lineage not ascribed	41	391	432			2	74	76		
Total detections (total tested)	**583 (8 163)**	**3 469 (>157 054)**	**4 052 (>165 217)**			**48 (3 941)**	**519 (>155 991)**	**567 (>159 932)**		

[a] Numbers taken from Flu News Europe week 43/2022, week 43/2021 and week 43/2020 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 (2022-2023) – WHO European Region[a]



[a] Figure adapted from FluNewsEurope weeks 36-39/2022 and 43/2022 reports (https://flunewseurope.org/Archives)

Genetic and antigenic characterization data generated at the WIC for viruses with collection dates after 31 August 2022 until 31 January 2023 will inform the WHO influenza vaccine composition meeting (VCM) in February 2023 when recommendations will be made for the northern hemisphere 2023-2024 influenza season. Recommendations for the 2021-2022 northern [1] and 2022 southern [2] hemisphere seasons have been made and implemented. Data presented for viruses with collection dates after 31 August 2021 until 31 January 2022 contributed to the VCM for the northern hemisphere 2022-2023 season, where it was recommended to change the A(H3N2) and B/Victoria-lineage components of influenza vaccines to match those used in 2022 southern hemisphere vaccination campaigns [3]. At the recent VCM (19-22 September), which focussed on data from viruses collected after 31 January 2022 until 31 August 2022, it was recommended to change the A(H1N1)pdm09 vaccine component for the 2023 southern hemisphere season [4].

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 WIC- and non-WIC-generated sequences available in GISAID, generated for the September report are presented (Figures 2a, 3a and 4a). Additional phylogenies (Figures 2b, 3b and 4b) are presented for HA sequences derived from viruses with collection and HA sequence submission dates from the days indicated in Table 2, with a sequence download date of 31 October 2022. 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 October 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 2022-10-31				
	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	2022-09-29	155	146	139
A(H3N2)[¥]	2022-09-01	2022-09-29	207	207	197
B/Victoria	2022-01-01	2022-09-29	58	48	48
B/Yamagata	2022-01-01	2022-09-29	0	0	0

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

[$] In addition gene sequences for 5 A(H1N2)v viruses (A/Georgia/08/2022, A/Ohio/28/2022, A/Netherlands/11748/2022, A/Michigan/42/2022 and A/Wisconsin/51/2022) and 1 A(H1N1)v virus (A/Parana/20675/2022) causing zoonoses had been submitted/released in EpiFlu™ during the period indicated

[¥] In addition gene sequences for 1 A(H3N2)v virus (A/Michigan/48/2022) causing zoonosis had been submitted/released in EpiFlu™ during the period indicated

Four shipments containing specimens (virus isolates and/or clinical specimens) with collection dates after 31 August 2022 were received at the WIC from WHO Global Influenza Surveillance and Response System (GISRS) recognised National Influenza Centres (NICs) in four WHO European Region Member States (Table 3). Due to the recent receipt of the samples (59 (98%) type A viruses and 1 (2%) type B virus) all were in the virus characterization process at the time of preparing this report.

A total of 10 viruses from the WHO European Region, one A(H1N1)pdm09 and 9 A(H3N2), have been characterised antigenically since the September report (Tables 4 and 5 respectively). A single A(H3N2) has a collection date after 31 August 2022 (Table 5-2).

Table 3. Summary of seasonal influenza clinical samples and virus isolates* with collection dates after 2022-08-31 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]
2022														
September														
Germany	6					5	in process				1	in process		
Netherlands	5			5	in process									
Norway	12			12	in process									
Spain	18			8	in process	10	in process							
October														
Germany	18	1	in process			17	in process							
Netherlands	1			1	in process									
November														
TOTAL	60	1	0	26	0	32	0	0	0	0	1	0	0	0
4 Countries/areas		1.7%		43.3%		53.3%			0.0%		1.7%		0.0%	
		98.3%							1.7%					

* 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)

As of 2022-11-04

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 had emerged, with recently circulating viruses carrying the substitution **S183P** in **HA1**, although this was 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] as are egg- and cell-based A/Sydney/5/2021, recently recommended for use in the southern hemisphere 2023 season [4]. HA amino acid substitutions defining the seven subclades have been defined in the September report and earlier ones. This report focuses on subclade **6B.1A.5** viruses which have circulated recently.

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**).

The phylogeny prepared for the September report focused on HA sequences derived from viruses with collection dates after 31 May 2022 for which sequences were submitted to GISAID after July 2022. It showed that while **6B.1A.5a.1** viruses had dominated in the Region for most of the 2021-2022 season the most recent detections, in a significant number of Member States, had been **6B.1A.5a.2** viruses (Figure 2a). Subgroup **6B.1A.5a.2** viruses had been the dominant A(H1N1)pdm09 viruses in countries outside of the WHO European Region, notably those in the southern hemisphere.

The phylogeny prepared for this October report focused on HA sequences derived from viruses with collection dates after 31 December 2021 for which sequences were submitted to GISAID in the period 29 September to 31 October 2022 (Figure 2b and Table 2). As indicated in both phylogenies, recently detected viruses in subgroup **6B.1A.5a.2** all have **HA1 K54Q**, **A186T**, **Q189E**, **E224A**, **R259K** and **K308R** substitutions compared to the vaccine virus, A/Victoria/2570/2019 (Figures 2a and 2b) and virus clusters have emerged defined by amino acid substitutions: (i) **HA1 T216A** often with **D94N** , the cluster showing wide geographic distribution; (ii) **HA1 A48P**, and; (iii) **HA1 K142R**, **D260E** and **HA2 I91V**, **N124H**, frequently with **HA1 P137S**, **T277A** and **HA2 E29D**. Viruses in cluster (iii) with the additional substitutions have recently been detected in countries of the western part of the WHO European Region (Figure 2b).

The panel of post-infection ferret antisera used in HI assays, five raised against subgroup **6B.1A.5a.1** viruses and four against **6B.1A.5a.2** viruses, gives clear discrimination of test viruses in the two subgroups

(Tables 4). The single **6B.1A.5a.2** test virus analysed since the September report was recognised well, within twofold of the homologous titres, by antisera raised against all four **6B.1A.5a.2** reference viruses.

At the 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 the likelihood that many humans were unlikely to have been exposed to **6B.1A.5a.2** subgroup viruses given their low-level circulation during the COVID-19 pandemic. While the different clusters of **6B.1A.5a.2** subgroup viruses were not differentiated by post-infection ferret antisera, human serology data presented at the WHO VCM held in Dublin 19-22 September 2022 indicated poor recognition of many **6B.1A.5a.2** subgroup viruses. For this reason, egg- and cell culture-propagated A/Sydney/5/2021-like viruses, carrying the **HA1 K54Q**, **A186T**, **Q189E**, **E224A**, **R259K** and **K308R** substitutions compared to A/Victoria/2570/2019, were recommended for vaccine formulations to be used in the 2023 southern hemisphere season [4].

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

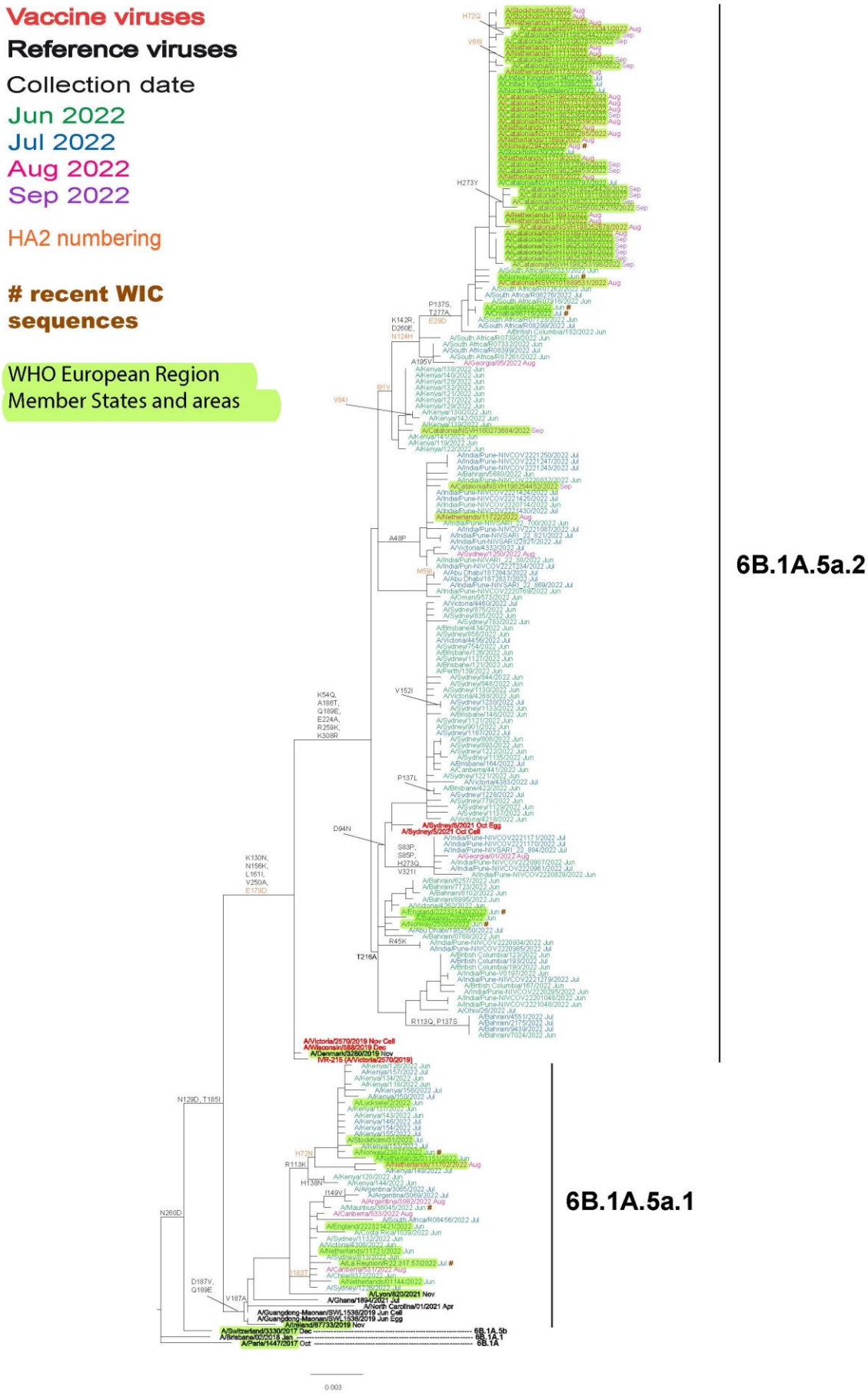


Figure 2b. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID/WIC, Oct 2022)

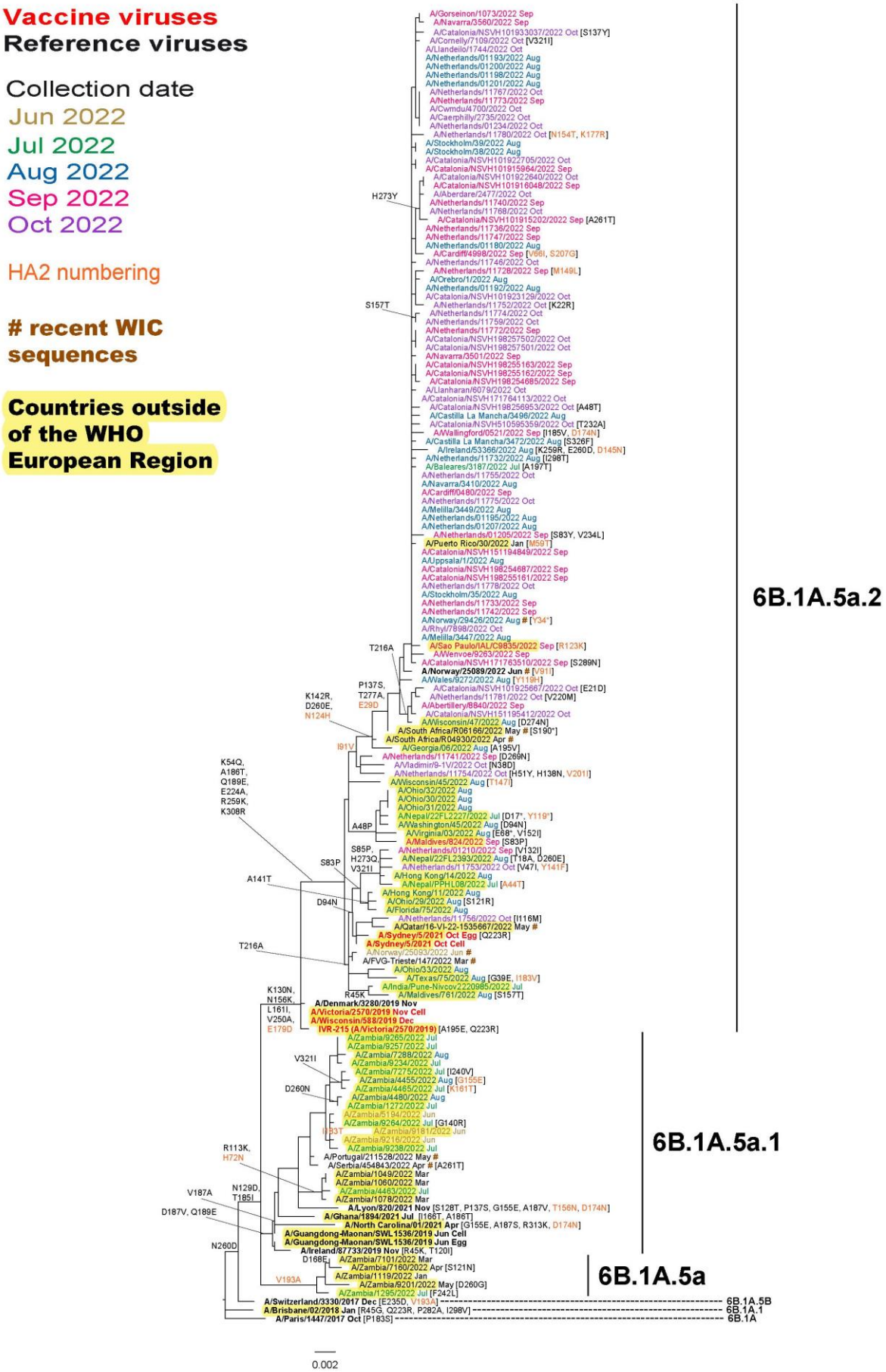


Table 4. Antigenic analysis of influenza A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection fereret antisera										NEW	
				A/Ire	A/G-M	A/G-M	A/Ghana	A/Lyon	A/Denmark	A/Nor	A/Sydney	IVR-215	A/Sydney	A/Sydney	
				87733/19	SWL1536/19	SWL1536/19	1894/21	820/21	3280/19	25089/22	5/21	A/Vic/2570/19	5/21	5/21	
				Egg	MDCK	Egg	Egg	Egg	MDCK	MDCK	MDCK	Egg	Egg	Egg	
	Passage history			St Jude's							CDC Ferret				
	Ferret number			F18/20	F09/20	F12/20	F02/22	F06/22	F28/20	F38/22	A96111	F37/21	F04/22	F40/22	
	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	6B.1A.5a.2	6B.1A.5a.2	6B.1A.5a.2
REFERENCE VIRUSES															
A/Ireland/87733/2019	6B.1A5a.1	2019-11-03	E4	640	5120	1280	1280	320	40	40	<40	80	40	40	
A/Guangdong-Maonan/SWL1536/2019	6B.1A5a.1	2019-06-17	C2/MDCK1	640	1280	2560	1280	320	40	40	<40	80	40	<40	
A/Guangdong-Maonan/SWL1536/2019	6B.1A5a.1	2019-06-17	E3/E2	320	640	1280	320	160	<40	<40	<40	40	<40	40	
A/Ghana/1894/2021	6B.1A5a.1	2021-07-21	E2/E1	640	2560	2560	1280	320	80	<40	40	160	80	40	
A/Lyon/820/2021	6B.1A5a.1	2021-11-16	E1/E2	160	320	320	160	320	40	40	<40	80	40	40	
A/Denmark/3280/2019	6B.1A5a.2	2019-11-10	MDCK4/MDCK5	40	80	80	40	40	1280	1280	320	2560	1280	640	
A/Norway/25089/2022	6B.1A5a.2	2022-06-15	MDCK2	<40	<40	40	<40	<40	640	1280	320	1280	1280	640	
A/Sydney/5/2021	6B.1A5a.2	2021-10-16	MDCK3/MDCK1	<40	<40	<40	<40	<40	640	640	320	1280	640	640	
IVR-215 (A/Victoria/2570/2019)	6B.1A5a.2	2018-11-22	E4/D7/E2	40	160	80	40	80	640	640	320	1280	640	640	
A/Sydney/5/2021	6B.1A5a.2		E3/E2	<40	40	40	<40	<40	640	640	160	640	640	640	
TEST VIRUSES															
A/Catalonia/NSVH101883797/2022	6B.1A5a.2	2022-07-31	SIAT1/MDCK1	<40	<40	40	<40	<40	640	1280	320	640	640	640	
						Vaccine NH 2020-21						Vaccine SH 2021 NH 2021-22 SH 2022 NH 2022-23	Vaccine SH 2023		

< relates to the lowest dilution of antiserum used
ND = Not Done

Influenza A(H3N2) virus analyses

A(H3N2) viruses with HA sequences 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. While both 3C.2a1b and 3C.3a viruses continued to evolve (see the September report and earlier ones), since 2019-2020 group **3C.2a1b** viruses have dominated.

Group **3C.2a1b** viruses contain HA amino acid substitutions found in subclade **3C.2a1** (those in clade **3C.2a** plus **N171K** in **HA1** and **I77V** and **G155E** in **HA2**, with most carrying **N121K** in **HA1**, e.g. **A/Singapore/INFIMH-16-0019/2016,** a former vaccine virus), plus **E62G, R142G** and **H311Q** in **HA1**, often with additional amino acid substitutions – notably either **HA1 T135K** commonly with **T128A** (both of which result in loss of potential glycosylation sites) yielding the **3C.2a1b.1** subgroup (e.g., **A/La Rioja/2202/2018**) or **HA1 T131K** and **HA2 V200I** producing 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)**.

The first phylogeny was based on a representative set of HA sequences derived from viruses with collection dates after 31 July 2022 made available in GISAID and generated at the WIC from 01 August 2022 up to 28 September 2022, being largely dominated by viruses detected in Catalonia, Spain (Figure 3a). Small numbers of 'Cambodia-like' **3C.2a1b.2a.1** viruses, from China were reported on. The vast majority of recently collected viruses 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 major subgroups defined by specific **HA1** amino acid substitutions: (i) **E50K** with a range of additional substitutions, e.g., **F79V**, **I140K**, **S262N** and **R33Q**; (ii) **D53N** and **P289S**; (iii) **D53N**, **N96S** (gain a glycosylation site) and **I192F**, some with additional substitutions; (iv) **D53G** often with **D104G** and **K276R**, and **I140K** and **R299K**. Subgroups (ii), (iii) and (iv) also share **HA1 H156S** amino acid substitution. Sequences derived from samples collected in the WHO European Region were dispersed throughout the 'Bangladesh-like' (**3C.2a1b.2a.2**) portion of the phylogeny with viruses falling into multiple virus clusters defined by specific amino acid substitutions (Figure 3a).

The second phylogeny is based on HA sequences derived from viruses with collection dates after 31 August 2022 made available in GISAID and generated at the WIC from 29 September to 31 October 2022 and shows a very similar profile to the first phylogeny but for a lack of recently submitted sequences from **3C.2a1b.2a.1** viruses (Table 2 and Figure 3b). Again, sequences from **3C.2a1b.2a.2** viruses in Catalonia and wider regions of Spain dominated sequence submissions from the WHO European Region but with significant contributions from the Netherlands and Wales, together with small numbers from other countries (e.g., Ireland, the Russian Federation and Sweden). Sequences from these viruses fell in subgroups (i), (iii) and (iv). Relatively few sequences from viruses detected in countries outside of the WHO European Region had been submitted to GISAID, but these also fell in subgroups (i), (iii) and (iv).

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 in red on the phylogenies, as are egg- and cell-culture based 'Bangladesh-like' vaccines to be used in the 2022 and 2023 southern hemisphere and 2022-2023 northern hemisphere seasons, A/Darwin/9/2021 and A/Darwin/6/2021 (**3C.2a1b.2a.2**) respectively [2, 4, 3] (Figures 3a and 3b).

As described in many previous reports[2], influenza A(H3N2) viruses had been difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells (RBCs) from guinea pigs, turkeys, and humans, often with the loss of ability to agglutinate any of these RBCs. As was highlighted first in the November 2014 report[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

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

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

guinea pig RBCs well, allowing HI assays to be performed with single A(H3N2) viruses from Croatia and the Netherlands failing to yield a sufficient HA titre with guinea pig RBCs to allow HI analysis.

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.

Results for nine A(H3N2) 'Bangladesh-like' (**3C.2a1b.2a.2)** test viruses fully characterised antigenically since the September report, only one of which has a collection date after 31 August 2022 (A/Catalonia/NSVH161512067/2022), are shown in Tables 5-1 to 5-2. All test viruses were recognised well, within fourfold of the respective homologous titres (most within twofold), by post-infection ferret antisera raised against the four **3C.2a1b.2a.2** viruses, which included the egg-propagated A/Darwin/9/2021 vaccine virus.

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.

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

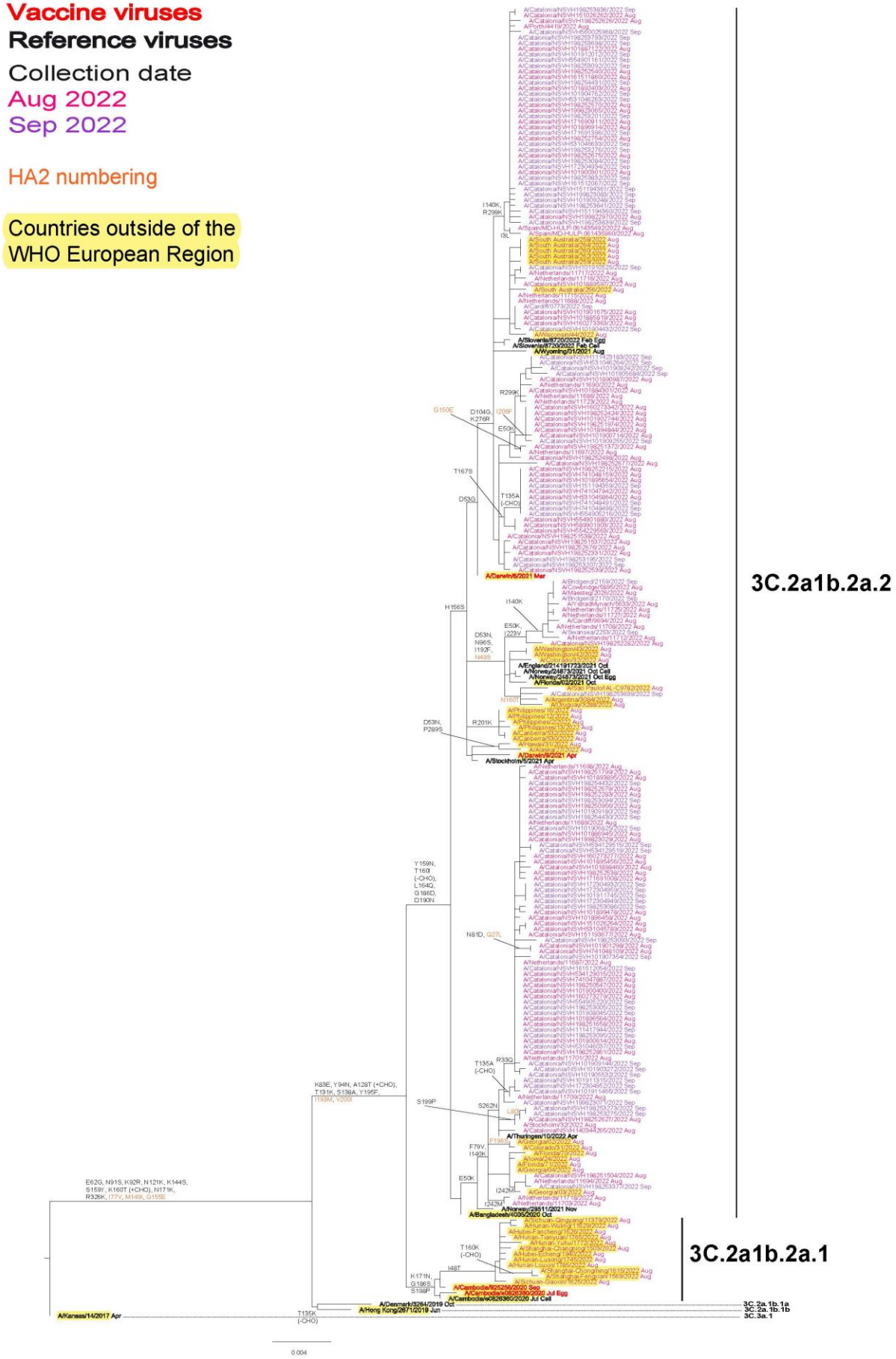


Figure 3b. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID/WIC, Oct 2022)

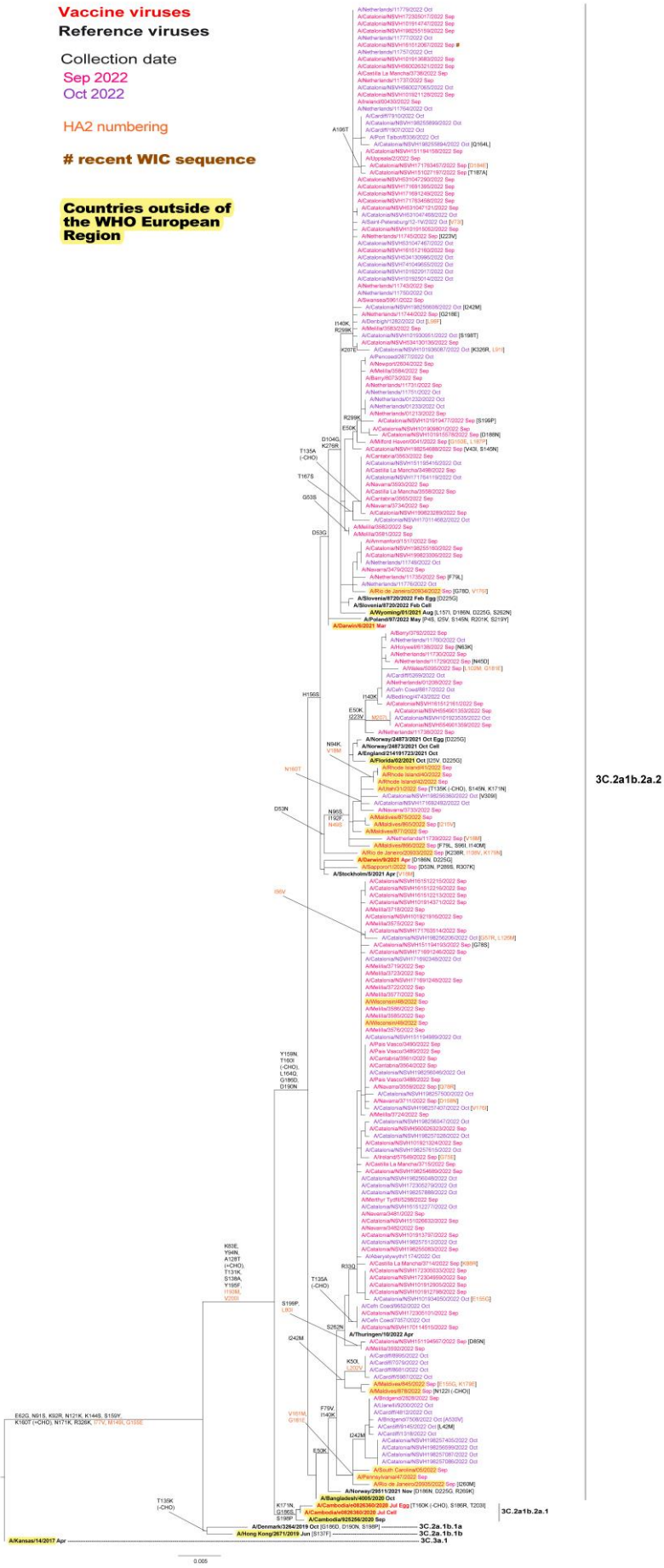


Table 5-1. Antigenic analysis of influenza A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
				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	214191723/21	9/21	14/17
				SIAT	Cell	SIAT	Egg	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			F19/20	St Judes F21/20	F03/21	F10/21	F07/21	F35/21	F07/22	F39/21	F17/19
	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/SIAT5	320	320	640	160	160	160	40	160	80
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT5	160	160	640	80	80	80	<40	160	40
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	80	160	640	160	160	160	<40	160	80
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	80	<40	80	640	160	160	160	320	40
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	40	160	160	320	320	320	320	160
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	80	<40	80	80	160	320	320	320	<40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT3	40	<40	40	80	160	320	640	320	<40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E4	80	40	80	320	320	640	640	640	40
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<40	80	40	40	80	40	160	320
TEST VIRUSES												
A/Pays de Loire/21194/2022	3C.2a1b.2a.2	2022-03-14	C1/SIAT1	80	<40	40	80	160	320	320	320	40
A/Coquelles/21188/2022	3C.2a1b.2a.2	2022-03-15	C1/SIAT1	40	<40	40	40	160	320	160	320	<40
A/Lorraine/20876/2022	3C.2a1b.2a.2	2022-03-16	C1/SIAT1	40	<40	40	40	160	320	160	320	<40
A/Nord Pas de Calais/27131/2022	3C.2a1b.2a.2	2022-04-05	C1/SIAT1	40	<40	40	40	160	320	320	320	<40
A/Bretagne/32468/2022	3C.2a1b.2a.2	2022-04-26	C1/SIAT1	40	<40	40	40	80	160	160	160	<40
A/Champagne Ardenne/32870/2022	3C.2a1b.2a.2	2022-04-29	C1/SIAT1	80	<40	40	80	80	160	320	320	<40
							Vaccine NH 2021-22				Vaccine SH 2022 NH 2022-23 SH 2023	

< relates to the lowest dilution of antiserum used
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									NEW		
				A/Denmark 3264/19 SIAT F19/20 3C.2a1b.1a	A/HK 2671/19 Cell St Judes F21/20 3C.2a1b.1b	A/Camb 925256/20 SIAT F03/21 3C.2a1b.2a.1	A/Camb e0826360/20 Egg F10/21 3C.2a1b.2a.1	A/Bang 4005/20 SIAT F07/21 3C.2a1b.2a.2	A/Stock 5/21 SIAT F35/21 3C.2a1b.2a.2	A/Eng 214191723/21 SIAT F07/22 3C.2a1b.2a.2	A/Thuringen 10/22 SIAT F36/22 3C.2a1b.2a.2	A/Poland 97/22 SIAT F39/22 3C.2a1b.2a.2	A/Darwin 9/21 Egg F39/21 3C.2a1b.2a.2	A/Kansas 14/17 SIAT F17/19 3C.3a.1
REFERENCE VIRUSES															
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT5	320	320	640	160	160	160	40	ND	ND	160	160	80
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT5	320	320	640	80	160	80	40	40	ND	160	160	80
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	80	160	640	160	160	160	<40	ND	ND	ND	160	80
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	160	<40	160	1280	160	160	320	80	80	80	320	80
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	160	<40	160	160	640	320	320	320	320	320	160	80
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	SIAT0/SIAT3	40	<40	40	40	160	320	320	160	160	640	320	<40
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT3	40	<40	40	40	80	320	640	160	160	320	320	<40
A/Thuringen/10/2022	3C.2a1b.2a.2	2022-04-01	P1/SIAT2	160	<40	80	160	320	640	320	320	ND	ND	160	80
A/Poland/97/2022	3C.2a1b.2a.2	2022-05-09	SIAT2	80	<40	80	160	160	640	640	ND	ND	1280	640	40
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E4	80	40	40	320	160	320	320	160	640	640	640	<40
A/Kansas/14/2017	3C.3a.1	2017-12-14	SIAT3/SIAT2	40	<40	80	40	40	320	40	40	80	80	80	320
TEST VIRUSES															
A/Croatia/7736?/2022	3C.2a1b.2a.2	2022-05-07	SIAT1	40	<40	40	40	160	160	320	ND	ND	ND	320	<40
A/Catalonia/NSVH10189240?/2022	3C.2a1b.2a.2	2022-08-13	SIAT1/SIAT1	80	<40	40	80	160	320	320	80	ND	ND	320	<40
A/Catalonia/NSVH16151206?/2022	3C.2a1b.2a.2	2022-09-14	SIAT1/SIAT1	160	<40	80	160	160	640	640	160	ND	ND	640	40
							Vaccine NH 2021-22						Vaccine SH 2022 NH 2022-23 SH 2023		

< relates to the lowest dilution of antiserum used
ND = Not Done

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 B/Brisbane/60/2008-like antigenically. 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 and displaced viruses with full-length HAs. 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 first recommended for use in the 2020 southern hemisphere season and thereafter up to the 2021-2022 northern hemisphere season.

The phylogeny generated for the September report, was based on sequences from viruses with collection dates after 28 February 2022 that were submitted to GISAID after July 2022 (Figure 4a). All viruses were **V1A.3** subclade represented by **B/Washington/02/2019**, with single viruses from China and Germany having identical HA amino acid sequences. Overall, the great majority of viruses fell in the **V1A.3a** group characterised by **HA1 N150K**, **G184E**, **N197D** (resulting in loss of a glycosylation site) and **R279K**, with this group splitting into two subgroups designated **V1A.3a.1** (characterised by **HA1 V220M** and **P241Q** substitutions, detected in China in the early months of 2022) and **V1A.3a.2** (characterised by **HA1 A127T**, **P144L** and **K203R**, often with additional substitutions, which has spread worldwide and is represented by the **B/Austria/1359417/2021** vaccine virus). Virus clusters defined by specific **HA1** amino acid substitutions in some countries, e.g., **H122Q** in China, **K56N** in Timor-Leste and **Q200P** in Brazil had emerged in the **V1A.3a.2** subgroup. Sequences submitted by the Netherlands split between the **V1A.3a.2** subgroup and subclade **V1A.3** with the latter viruses having **HA1 K75E**, **E128K**, **T155A** and **G230N** substitutions, first detected in viruses in Kenya, but with an additional **HA1 G184R** substitution (Figure 4a). These **V1A.3** viruses have spread throughout the Netherlands and **B/Catalonia/NSVH534129036/2022** represents the first reported detection of such viruses outside of the Netherlands.

The phylogeny generated for this October report contains HA sequences from viruses with collection dates after 31 December 2021 that were submitted to GISAID in the period 29 September to 31 October 2022 (Figure 4b). While the phylogeny has the same structure as that generated for the September report there is greater diversity within the **B/Washington/02/2019 V1A.3** subclade with viruses carrying **HA1** substitutions of (i) **N223K** (resulting in loss of a glycosylation site) and either **K52N** (detected in Zambia) or **T73I** (detected in Guatemala) or (ii) **K75E**, **E128K**, **T155A** and **A202V** (detected in Zambia). HA sequence from another case of 'Netherlands-like' virus infection also became available. Sequences derived from **V1A.3a.2** viruses were still in the majority, notably so for those with collection dates in September and October reported by the Netherlands, Spain and Wales.

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 characterised 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 160 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 2023, and northern hemisphere 2022-2023 influenza seasons [2, 4, 3].

[4] 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

No B/Victoria-lineage viruses have been characterised antigenically at the WIC since the September report where it was shown that **V1A.3a.2** viruses were generally well recognised by post-infection ferret antisera raised against **V1A.3a.2** viruses including the vaccine virus, **B/Austria/1359417/2021**. Conversely, **V1A.3** viruses from the Netherlands were poorly recognised by antisera raised against **V1A.3a.1/2** viruses, while egg-propagated cultivars were recognised well by sheep hyperimmune serum raised against egg-propagated **B/Brisbane/60/2008**, less efficiently by post-infection ferret antiserum raised against cell culture-propagated B/Netherlands/11267/2022 and somewhat better by ferret antisera raised against **B/Colorado/06/2017** (**V1A.1**) and **B/Washington/02/2019** (**V1A.3**). The latter is related to loss of a **HA1** glycosylation sequon at positions **194-196** (**V1A.3** numbering) or **197-199** (**V1A** numbering) on adaptation to replication in hens' eggs.

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 31 October 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 was recommended for inclusion in quadrivalent vaccines for the 2021-2022 and 2022-2023 northern and, 2022 and 2023 southern hemisphere seasons [1, 3, 2, 4]. 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.

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 not LAIV-related.

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

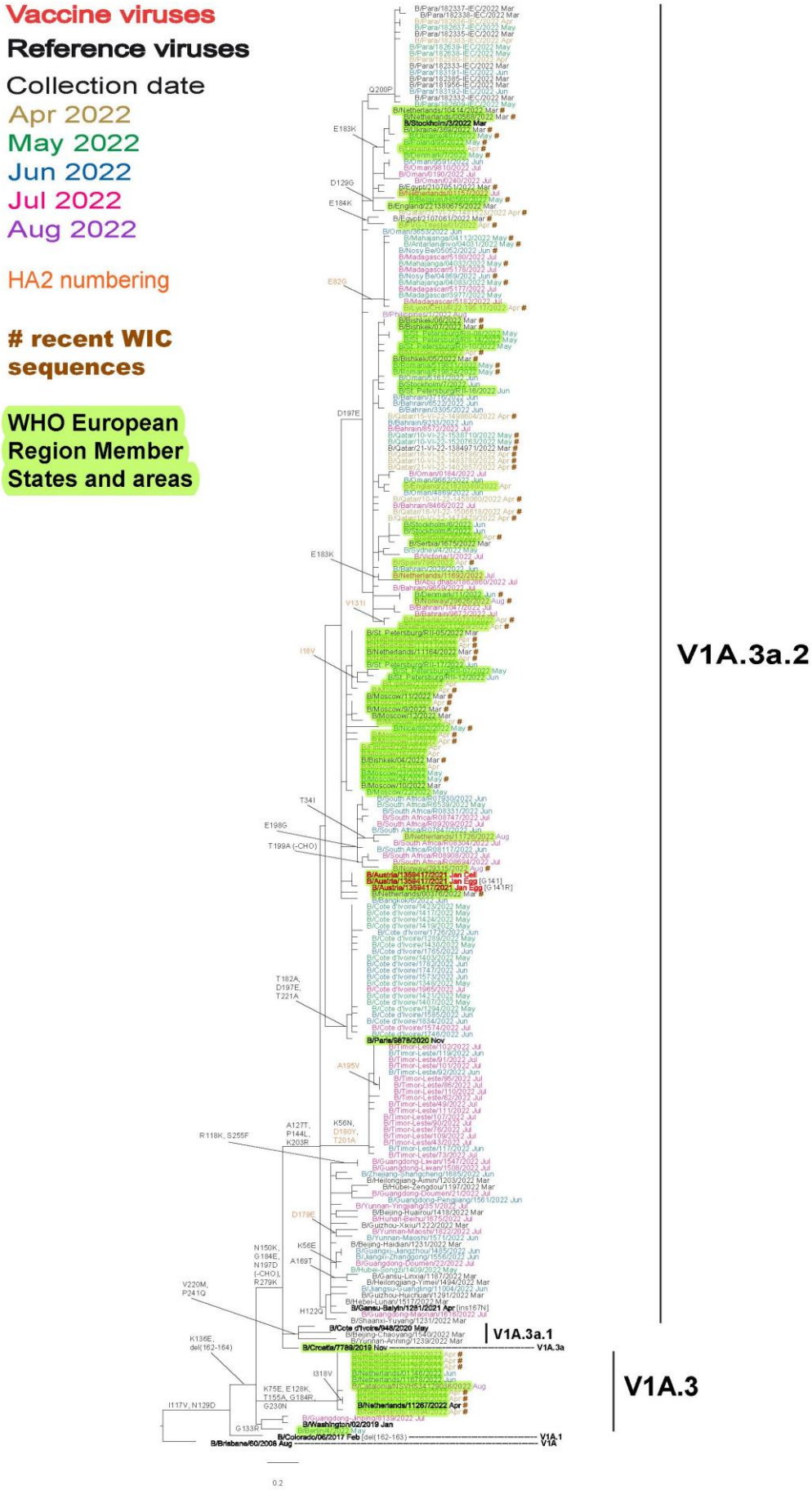


Figure 4b. Phylogenetic comparison of B/Victoria-lineage HA genes (GISAID/WIC, Oct 2022)

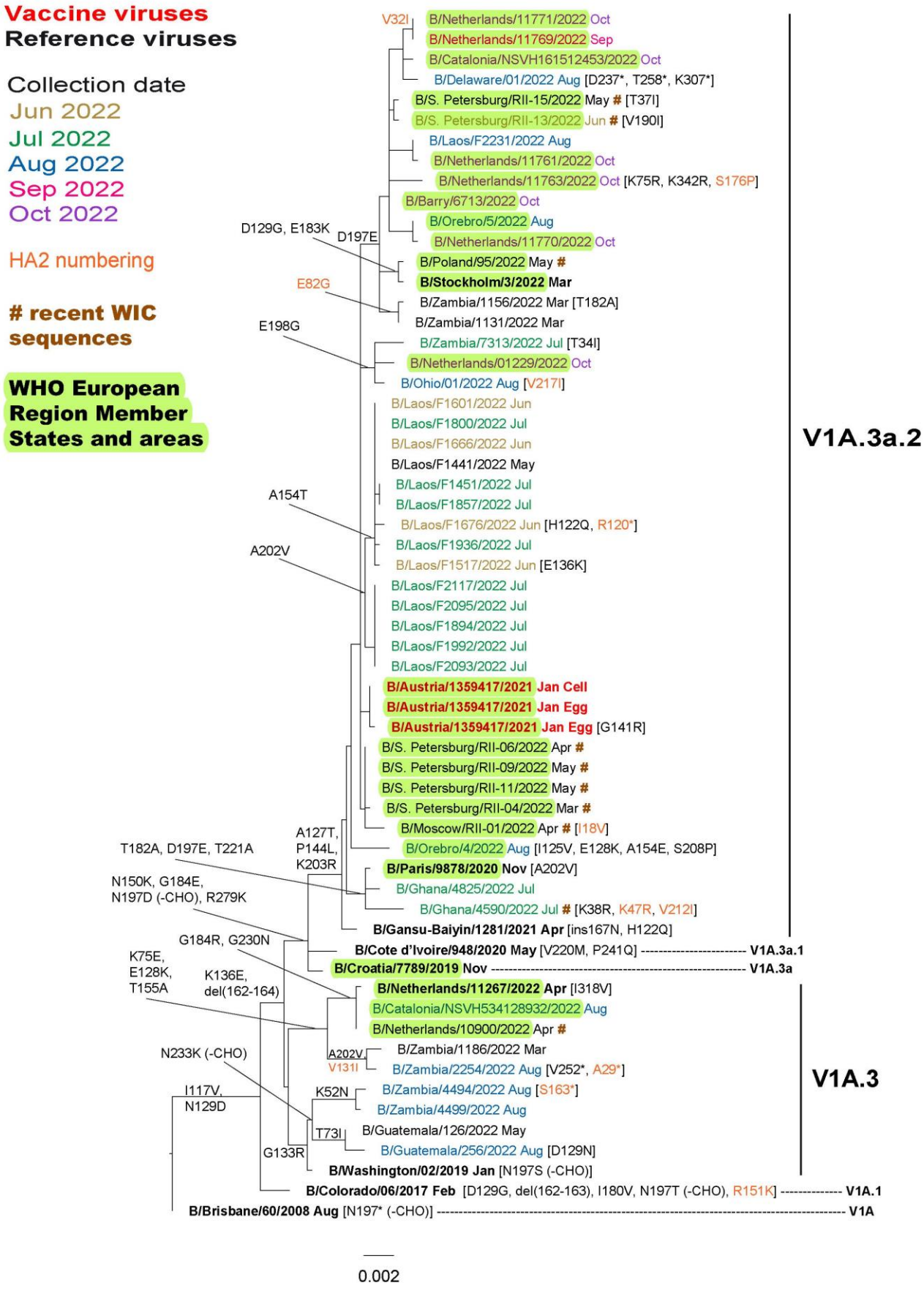
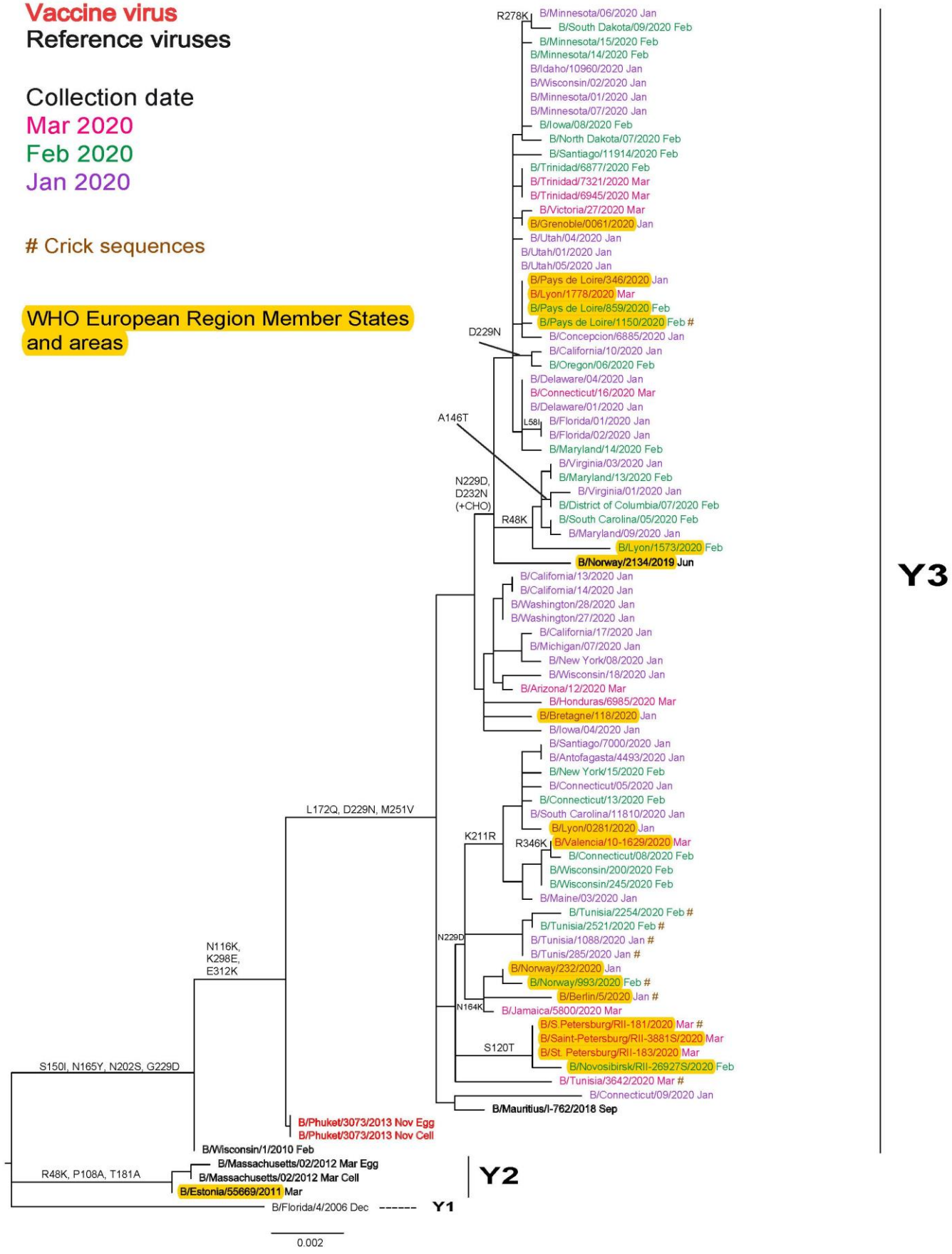


Figure 5. Phylogenetic comparison of B/Yamagata-lineage HA genes (GISAID, September 2021)



Summaries of data submitted to TESSy

Genetic characterization

26 viruses detected over the course of the 2022-2023 season (weeks 40-43/2022) were genetically characterised:

- Of 14 A(H1N1)pdm09 viruses, all belonged to clade 6B.1A.5a.2 with 10 represented by A/Norway/25089/2022, 3 by A/Sydney/5/2021 and 1 by A/Victoria/2570/2019.
- Of 9 A(H3N2) viruses, 8 belonged to the 'Bangladesh-like' clade (3C.2a1b.2a.2) represented by A/Slovenia/8720/2022, and 1 was not attributed to a clade.
- 3 B/Victoria-lineage viruses were characterised but no subgroup was assigned.

Antiviral susceptibility

Up to week 43/2022, 43 viruses were assessed for susceptibility to neuraminidase inhibitors (NAIs): 9 A(H3), 14 A(H1)pdm09 and 3 B virus were assessed genotypically, and 16 A(H3) and 1 B virus were assessed phenotypically. Susceptibility to the PA inhibitor baloxavir marboxil (BXM) was assessed genotypically for 25 viruses: 9 A(H3), 13 A(H1)pdm09 and 3 B viruses. Phenotypically no viruses exceeded IC_{50}-fold-change thresholds for reduced susceptibility to NAIs and, genotypically, no markers associated with reduced susceptibility to NAIs or BXM were identified.

At the WIC, no antiviral data relating to WHO European Region influenza viruses collected during the 2022-2023 season has been generated.

Animal influenza and zoonotic events

Influenza A(H7N9) virus

On 1 April 2013, the WHO Global Alert and Response System [5] 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 caused some zoonoses, although few human cases were reported during the 2017-18 season [6]. 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 08 November 2022). The assessment published on 05 October 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 [7]. 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 [8]. 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 28 September 2022 and can be found on ECDC's website [9].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 5 October 2022. Since the previous risk assessment on 30 August 2022, one human case of infection with an A(H5N6) avian influenza virus was reported by China [7]. The case was in a 3-year-old male who had disease onset on 1 September 2022, being hospitalised with severe pneumonia on 11 September, and remaining in a severe condition at the time of reporting. He had been exposed to backyard poultry before illness onset, but environmental samples tested for influenza were negative and no family members had developed symptoms at the time of reporting.

The first case of human infection with an A(H5N1) virus in the western area of the WHO European Region was detected in England in January 2020 and a report into the investigation of this case has been published [10]. The person was asymptomatic but had close contact with ducks infected with HPAI A(H5N1). Currently, two cases of potential human infection with HPAI A(H5N1) involving poultry workers in Spain known to of had contact with infected poultry are under investigation through collaborations between the relevant

authorities/laboratories in Spain, WHO and WIC with the animal health context provided through national authorities, WOAH and FAO. Respiratory samples from both workers were positive for A(H5N1) by real-time RTPCR assay, but at high Ct values such that environmental contamination of the respiratory tract, rather than true infection, cannot be ruled out at this stage.

The latest collaborative report from ECDC and the European Food Safety Authority (EFSA), reported 788 highly pathogenic avian influenza (HPAI) A(H5) detections between 11 June and 09 September 2022, 56 in poultry, 710 in wild birds and 22 in captive birds [9]. Detections occurred in 16 European countries and high mortality was observed in colony-breeding seabird species along the northwest coast of Europe involving HPAI A(H5N1). Overall, the HPAI epidemic season in 2021-2022 is the largest so far observed in Europe with 2 467 outbreaks in poultry and 47.7 million birds culled, 187 outbreaks in captive birds, and 3 573 detections in wild birds. Genetic analyses indicated that the circulating viruses belonged to clade 2.3.4.4b. Such viruses have been circulating in Europe since October 2020 and now exist as seven genotypes, three of which were identified over the summer period. 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 26 October 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 28 September 2022 a total of 696 HPAI outbreaks (72 H5Nx, 620 H5N1, one H5N2, one H5N4, one H5N5 and one HPAI not confirmed as H5) and no low pathogenic avian influenza (LPAI) outbreaks had been reported [11].

HPAI A(H5) viruses have also been detected in wild mammal species in Europe and North America, with some viruses showing genetic markers of adaptation to replication in mammals.

Influenza A(H9N2) virus

Since the previous WHO risk assessment on 30 August 2022, no zoonotic cases of A(H9N2) infection had been reported to WHO [7]. Public Health England published an updated risk assessment for avian influenza A(H9N2) in August 2021 [12]. 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 30 August 2022 five cases of human infection with swine viruses were reported [7]. China reported a case of A(H1N1)v infection in a 6-year-old female who had mild respiratory symptoms not requiring hospitalization and had no known source of exposure with environmental samples and family members testing negative for influenza.

The United States, Centers for Disease Control and Prevention (CDC) reported four human cases of A(H1N2)v infection three of which were in children less than 18 years of age. The case detected in Wisconsin was still under investigation, while the other three had attended agricultural fairs, one in Georgia and two in Michigan (family members attending the same fair). No evidence of human-to-human transmission was found.

In addition, a new (second) case of human A(H10N3) infection, following a case in April 2021, was reported by China. A 33-year-old male butcher with fever, cough and chest pain was hospitalized and treated for severe pneumonia and respiratory failure, resulting in recovery. He had exposure to backyard poultry but neither samples from his workplace nor residence were influenza-positive and sampling of close contacts/family members revealed no further cases.

WHO Collaborating Centre reports

A description of results generated by the London WHO Collaborating Centre at the WIC and used at the September 2022 WHO VCM (19-22 September 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 08 November 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.

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