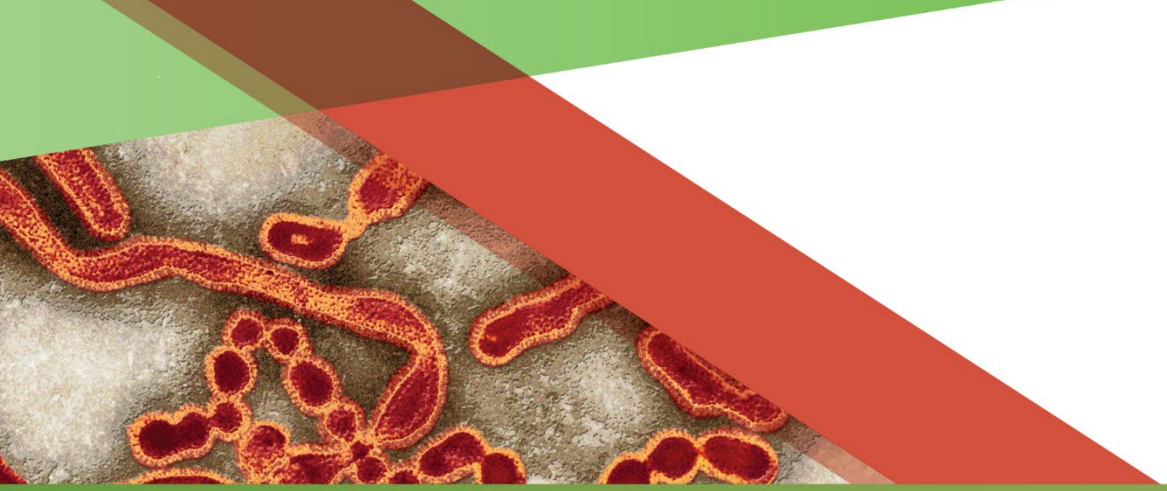

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, November 2019

Summary

This is the second influenza characterisation report for the 2019–20 influenza season. As of week 48/2019, 6 887 influenza detections across the WHO European Region had been reported; of which 84% were type A viruses, with A(H3N2) prevailing over A(H1N1)pdm09, and 16% type B viruses, with 123 of 137 (90%) ascribed to a lineage B/Victoria.

Since the October 2019 characterisation report[1], three shipments of influenza-positive specimens from EU/EEA countries were received at the London WHO Collaborating Centre (CC) - the Francis Crick Worldwide Influenza Centre (WIC). A total of 112 virus specimens, with collection dates after 31 August 2019 to be considered at the February 2020 WHO Influenza vaccine recommendation meeting, were received. HA genetic analyses reported here focus on full-length gene sequences for viruses from around the world with collection dates after 31 August 2019 and available in the Global Initiative on Sharing All Influenza Data (GISAID) as of 4 December 2019.

No A(H1N1)pdm09 test viruses from EU/EEA countries have been characterised antigenically since the last report, but the great majority of viruses from other sources have shown good reactivity with antisera raised against the 2019–20 vaccine virus, A/Brisbane/02/2018. The two viruses with collection dates after 31 August 2019, for which genetic characterisation was completed, fell in the 6B.1A5A subgroup. Globally, based on sequence data available in GISAID, subgroups 6B.1A5A (n = 96), 6B.1A5B (n = 26) and subclade 6B.1A7 (n = 19) viruses were detected recently.

Since the last report, two A(H3N2) viruses were characterised antigenically. Both were clade 3C.3a and antigenically similar to the vaccine virus, A/Kansas/14/2017. Of the 11 viruses characterised genetically, seven were subgroup 3C.2a1b+T131K, two were subgroup 3C.2a1b+T135K-A and two were clade 3C.3a. Globally, based on sequence data available in GISAID, subgroups 3C.2a1b+T131K (n = 175), 3C.2a1b+T135K-B (n = 18), 3C.2a1b+T135K-A (n = 16), clade 3C.3a (n = 10) and subclade 3C.2a2 (n =1) viruses were detected recently.

No B/Victoria-lineage viruses were characterised in this reporting period.

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, October 2019. Stockholm: ECDC; 2019. Available from (accessed 4 December 2019): https://www.ecdc.europa.eu/sites/default/files/documents/Influenza-characterisation-october-2019.pdf

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The two viruses from EU/EEA countries characterised genetically since the start of the 2019–20 season were subgroup 1A(Δ3)B, represented by B/Washington/02/2019. Globally, based on sequence data available in GISAID, subgroups 1A(Δ3)B (n = 126) and 1A(Δ2) represented by B/Colorado/06/2017 (n = 22) viruses were detected recently.

No B/Yamagata-lineage viruses have been characterised in this reporting period. Globally, based on sequence data available in GISAID, all 15 viruses detected recently have fallen in clade 3 represented by the vaccine virus B/Phuket/3073/2013 recommended for use in quadrivalent vaccines for the current northern hemisphere influenza season. While all recently circulating B/Yamagata-lineage viruses contain HA amino acid substitutions compared to B/Phuket/3073/2013, antigenic effects have been minimal.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to the European Surveillance System database since the start of the 2019–20 season (weeks 40/2019–48/2019), with a total of 6 887 detections over this period. At this early stage of the season, type A (83.5%) have predominated over type B (16.5%) viruses which is a common pattern. Of the type A viruses subtyped (n = 2 013) and the type B viruses ascribed to a lineage (n = 137), A(H3N2) (n = 1 520) have prevailed over A(H1N1)pdm09 (n = 493) viruses and 123 of 137 type B viruses have been B/Victoria-lineage. Overall, the ratio of type A to type B detections is dramatically reduced compared with the 2018–19 season (86:1 to 5:1), and dominance of both influenza A subtype and influenza B lineage is reversed compared with the 2018-19 season, with detections being highest for A(H3N2) subtype and B/Victoria lineage viruses.

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2019-20 season (weeks 40/2019–48/2019)[a]

	Cumulative number of detections			Totals*		Totals for 2018-19 season*		
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Number	%	Ratios
Influenza A	**359**	**5389**	**5748**	**83.5**	**5:1**	**203564**	**98.8**	**86:1**
A(H1N1)pdm09	125	368	493	24.5		44179	57.2	
A(H3N2)	215	1305	1520	75.5	3.1:1	33117	42.8	0.7:1
A not subtyped	19	3716	3735			126271		
Influenza B	**189**	**950**	**1139**	**16.5**		**2380**	**1.2**	
Victoria lineage	54	69	123	89.8		79	47.9	
Yamagata lineage	2	12	14	10.2	0.11:1	86	52.1	1.1:1
Lineage not ascribed	133	869	1002			2215		
Total detections (total tested)	**548 (7833)**	**6339 (>124781)**	**6887 (>132614)**			**205947 (>849439)**		

[a] **Numbers taken from Flu News Europe week 48/2019**

*** 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 Yamagata:Victoria lineages.**

Since week 40/2019, four shipments of specimens (virus isolates and/or clinical specimens) were received at the Crick Worldwide Influenza Centre (WIC). The packages contained 112 virus-related samples received with collection dates after 31 August 2019, and were made up of 20 A(H1N1)pdm09, 80 A(H3N2), nine B/Victoria lineage and three B/Yamagata lineage viruses (Table 2), similar to the ratios reported to the European Surveillance System (Table 1). Genetic and antigenic characterisation data generated at the WIC for viruses with collection dates after 31 August 2019 until 31 January 2020 will be presented at the WHO influenza vaccine composition meeting in February 2020, when recommendations for the northern hemisphere 2020–21 season will be made. Recommendations have already been published [1,2] for the current 2019–20 northern hemisphere and the subsequent 2020 southern hemisphere seasons.

Table 2. Summary of clinical samples and virus isolates, with collection dates from 1 September 2019, contained in packages received from EU/EEA Member States since week 40/2019

MONTH	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country	Seasonal viruses	Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[1]
SEPTEMBER														
Norway	7			1	1	4	1	3			2	2		
United Kingdom	2			2	in process									
OCTOBER														
Norway	28			5	in process	19	in process				3	3	1	in process
United Kingdom	20			2	in process	18	in process							
NOVEMBER														
Norway	21			6	in process	9	in process				4	in process	2	in process
United Kingdom	34			4	0	30	in process							
2 Countries	112	0	0	20	1	80	1	3	0	0	9	5	3	0
					17.9%		71.4%					8.0%		2.7%
					89.3%							10.7%		

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

Includes clinical samples from Northern Ireland, in lysis-mix, for which genetic characterisation only can be performed

As of 2019-12-04

Influenza A(H1N1)pdm09 virus analyses

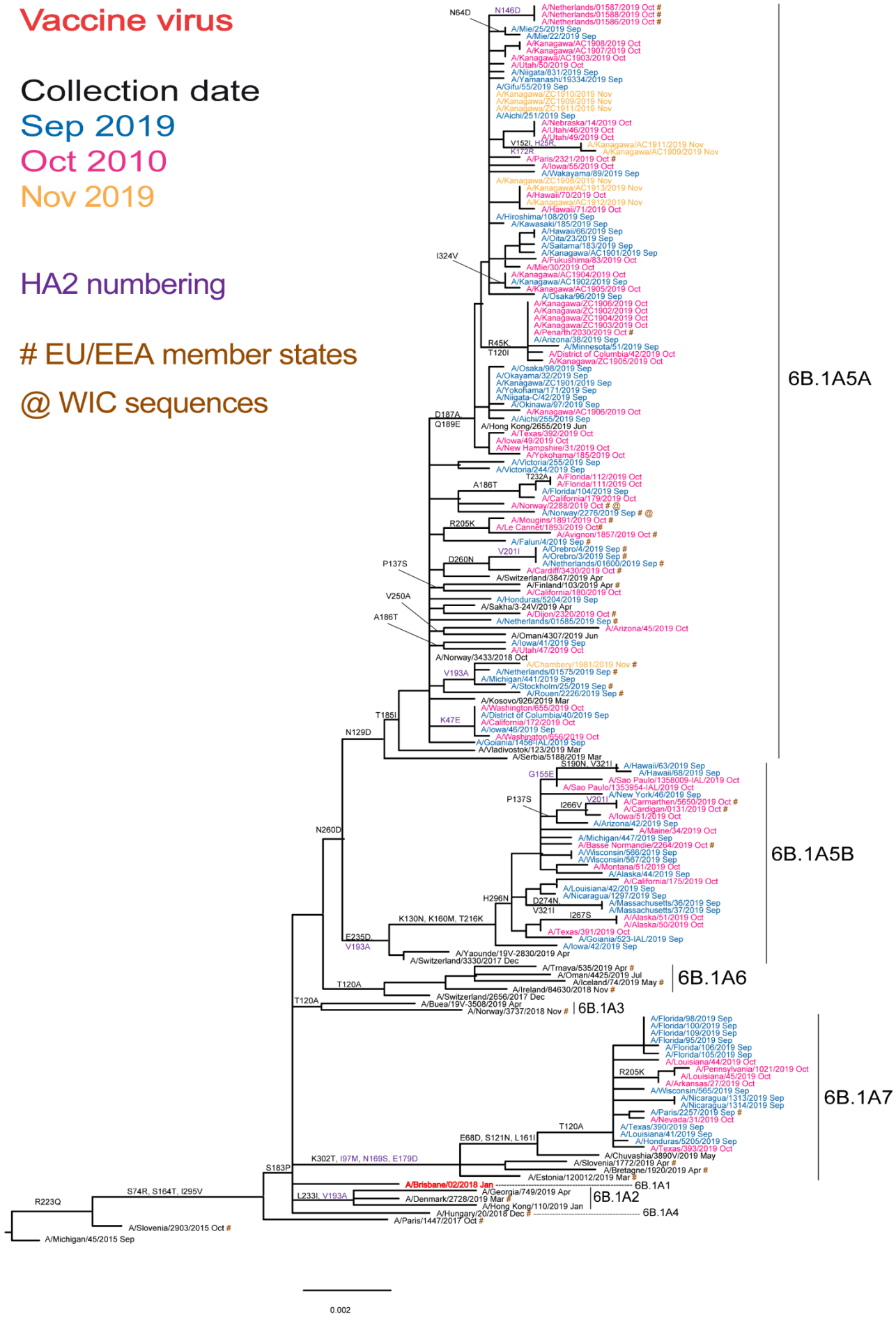
Since the October 2019 characterisation report, no A(H1N1)pdm09 viruses from EU/EEA countries have been assessed antigenically by haemagglutination inhibition (HI) assays with a panel of post-infection ferret antisera. However, as indicated in previous reports for viruses from EU/EEA countries, recently circulating viruses from Mauritius and Qatar received at the WIC were recognised well by antisera raised against A/Michigan/45/2015, the northern hemisphere 2018–19 influenza season vaccine virus [3], and A/Brisbane/02/2018, the northern hemisphere 2019-20 influenza season vaccine virus [1].

Figure 1 shows a phylogenetic tree for the HA genes of A(H1N1)pdm09 viruses. Full-length gene sequences of viruses with collection dates after 31 August 2019 were downloaded from GISAID on 4 December 2019 (n = 141) and combined with the 2019–20 reference set provided in relation to the European Surveillance System reporting. All recently circulating viruses fell into subclade 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 subclade 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. Figure 1 is annotated with **HA1 S183P** substitution groups assigned for the February 2019 WHO Vaccine Consultation Meeting (6B.1A/183P-1 to -7, abbreviated to 6B.1A1 to 6B.1A7), and the recommended vaccine virus A/Brisbane/02/2018, is shown in red [1]. The seven subclades are defined by the following HA amino acid substitutions:

1. Subclade **6B.1A1** viruses, represented by the current vaccine virus **A/Brisbane/02/2018**, carry an HA gene mutation encoding **HA1 S183P** amino acid substitution;
2. Subclade **6B.1A2** viruses, represented by **A/Denmark/2728/2019**, carry HA gene mutations encoding **HA1 S183P** and **L233I** with **HA2 V193A** amino acid substitutions - a subgroup 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.1A3** viruses, represented by **A/Norway/3737/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions;
4. Subclade **6B.1A4** represented by **A/Hungary/20/2018** carries HA gene mutations encoding **HA1 N129D, A144E** and **S183P** amino acid substitutions;
5. Subclade **6B.1A5** viruses carry HA gene mutations encoding **HA1 S183P** and **N260D** amino acid substitutions and splits into two subgroups designated **6B.1A5A** represented by **A/Norway/3433/2018** with additional **HA1** amino acid substitutions of **N129D** and **T185A**, and **6B.1A5B** represented by **A/Switzerland/3330/2017** with additional amino acid substitutions of **HA1 E235D** and **HA2 V193A**;
6. Subclade **6B.1A6** viruses, represented by **A/Ireland/84630/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions, like subclade **6B.1A3** viruses, but fall within a separate phylogenetic branch which is closer to subclade **6B.1A5** viruses;
7. Subclade **6B.1A7** 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 subgroup of this subclade has emerged with **P183S** (reversion)**, T185I, I240V** and **I286L** substitutions in **HA1** (e.g. **A/Estonia/120012/2019**).

The great majority of viruses (n = 122) with collection dates after 31 August 2019 fell within the 6B.1A5 subclade, mostly in the 6B.1A5A subgroup (n = 96) with 62 of these viruses carrying additional HA1 substitutions of D187A and Q189E. The 26 viruses in the 6B.1A5B subgroup all contain additional HA1 amino acid substitutions of T126K, K130N, and K160M. The remaining 19 viruses with collection dates after 31 August 2019 all fell in subclade 6B.1A7 with the additional HA1 amino acid substitutions observed in A/Moscow/193/2019, together with T120A substitution.

Figure 1. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes



Influenza A(H3N2) virus analyses

As described in many previous reports[2], influenza A(H3N2) viruses have continued to be 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 for the first timein the November 2014 report[3], this is a particular problem for most viruses that fall in genetic clade 3C.2a.

Since the October 2019 characterisation report, two viruses from Norway, both clade 3C.3a, have been characterised antigenically. Both viruses were recognised at titres within twofold of the respective homologous titres with antisera raised against cell culture-propagated clade 3C.3a viruses, A/England/528/2018 and A/Kansas/14/2017, and within fourfold for the antisera raised against the current vaccine virus, egg-propagated A/Kansas/14/2017. Antisera raised against clade 3C.2a2 and subgroup 3C.2a1b viruses recognised the test viruses poorly. Antisera raised against a cell culture-propagated clade 3C.2a virus (A/Hong Kong/5738/2014) and an egg-propagated subclade 3C.2a1 virus (A/Singapore/INFIMH-16-0019/2016, a former vaccine virus) recognised the test viruses at titres with fourfold of the respective homologous titres.

Viruses in clade 3C.2a have been dominant since the 2014–15 influenza season and subgroup 3C.2a1b viruses predominated over the course of the 2018–19 season, but the HA gene sequences of viruses in both clades 3C.2a and 3C.3a continue to diverge. Notably, clade 3C.3a viruses have evolved to carry **HA1** amino acid substitutions of **L3I, S91N**, **N144K** (loss of a N-linked glycosylation motif at residues 144-146), **F193S** and **K326R**, and **D160N** in **HA2**, compared with A/Stockholm/6/2014, and levels of detection since January 2019 had increased in a number of WHO European Region countries and North America. Greater variation has been observed among clade 3C.2a viruses, resulting in the designation of new subclades/subgroups. Amino acid substitutions that define these subclades/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);
- Subgroup **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**;
- Subgroup **3C.2a1b**: Those in subclade **3C.2a1** plus **E62G, R142G** and **H311Q** in **HA1**, often with additional amino acid substitutions – notably **HA1 T131K** and **HA2 V200I**, the **3C.2a1b+T131K** cluster (e.g. **A/South Australia/34/2019**) or **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+T135K-A** cluster (e.g. **A/La Rioja/2202/2018**) or a recently emerged, antigenically distinct group with **HA1 T135K, T128A, S137F, A138S** and **F193S**, the **3C.2a1b+T135K-B** cluster (e.g. **A/Hong Kong/2675/2019**);
- Subclade **3C.2a2**: Those in clade **3C.2a** plus **T131K**, **R142K** and **R261Q** in **HA1**, e.g. **A/Switzerland/8060/2017** (a former vaccine virus);
- Subclade **3C.2a3**: Those in clade **3C.2a** plus **N121K** and **S144K** in **HA1**, e.g. **A/Cote d'Ivoire/544/2016**, sometimes with additional substitutions;
- Subclade **3C.2a4**: Those in clade **3C.2a** plus **N31S, D53N, S144R, N171K, I192T and Q197H** in **HA1**, e.g. **A/Valladolid/182/2017**, sometimes with additional substitutions;
- Clade **3C.3a**: represented by **A/Switzerland/9715293/2013** (see above), but recently a resurgence of clade **3C.3a** 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 2019-20 influenza season.

Figure 2 shows a HA gene phylogeny using the 2019–20 reference set provided in relation to the European Surveillance System reporting, and full length gene sequences available in GISAID for viruses with collection dates after 31 August 2019 (n = 220) and as of 4 December 2019. Globally, the great majority of viruses (n = 175) with collection dates after 31 August 2019 have HA genes that fall within the 3C.2a1b+T131K cluster with the majority (n = 125) carrying substitutions (**HA1 S219F** and **HA2 V18M**) seen in the vaccine virus, A/South Australia/34/2019. The next most numerous group is that with HA1 T135K substitution (n = 34 in total) with 16 viruses in the 3C.2a1b+T135K-A cluster and 18 in the 3C.2a1b+T135K-B cluster. Sequences from viruses in clade 3C.3a (n = 10) and clade 3C.2a2 (n = 1) make up the remainder of the 220, derived from recently collected viruses, that were downloaded from GISAID.

The locations of A/Kansas/14/2017 (3C.3a), the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2019–20 influenza season [1], and A/South Australia/34/2019 (3C.2a1b+T131K), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2020 influenza season [2], are indicated in Figure 2 in red.

[2] For example, the September 2013 report: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2013. Stockholm: ECDC; 2014. Available from (accessed 4 December 2019): 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 (accessed 4 December 2019): https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf

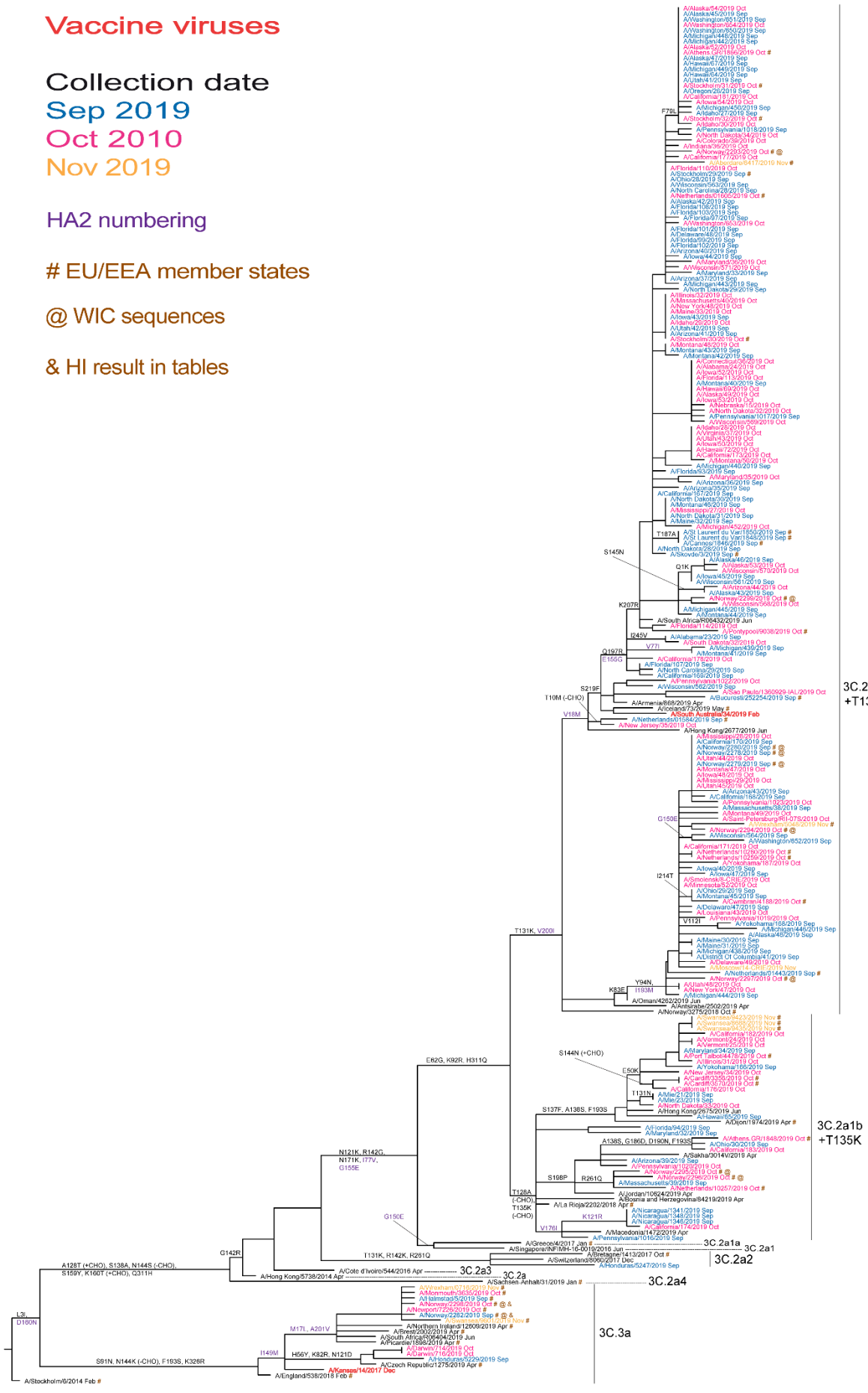
Table 3. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
	Passage history			A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/La Rioja 2202/18	A/Switz 8060/17	A/Eng 538/18	A/Norway 3275/18	NYMC X-327 A/Kansas/14	A/Kansas 14/17	IVR-197 A/Sth Aus/34/19
				MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	SIAT	Egg	SIAT	Egg
	Ferret number			St Judes F60/17[-1]	F01/18[-1]	F13/19[-1]	F26/18[-1]	F27/18[-1]	F31/18[-1]	F03/19[-1]	F16/19[-1]	F17/19[-1]	F39/19[-1]
	Genetic group			3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a	3C.2a1b+T131K
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	160	160	160	160	160	320	160	160	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	160	80	320	160	160	160	80	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	80	40	160	160	80	40	40	40	<	40
A/Switzerland/8060/2017	clone 57 3C.2a2	2017-12-12	E7/E1	160	1280	160	80	640	80	80	40	<	80
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT4	<	40	40	<	<	640	<	160	320	<
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	<	<	<	<	<	160	<	640	160	<
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	40	80	<	40	640	40	160	320	<
IVR-197 (A/South Australia/34/2019)	3C.2a1b+T131K	2019-02-06	E5/D8/E1	160	320	160	40	320	80	640	40	40	640
TEST VIRUSES													
A/Norway/2282/2019	3C.3a	2019-09-25	SIAT1	40	40	40	<	40	320	<	160	160	<
A/Norway/2298/2019	3C.3a	2019-10-10	SIAT1	40	40	40	<	40	320	<	160	320	<
						Vaccine NH 2018-19		Vaccine SH 2019			Vaccine NH 2019-20		Vaccine SH 2020

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)[-1] < = <40

Sequences in phylogenetic trees

Figure 2. Phylogenetic comparison of influenza A(H3N2) HA genes



Influenza B virus analyses

A total of 12 influenza type B viruses with collection dates after 31 August 2019 have been received at the WIC: nine B/Victoria-lineage and three B/Yamagata-lineage (Table 2).

Influenza B/Victoria-lineage

No B/Victoria-lineage viruses from EU/EEA countries have been assessed by HI assay since the October 2019 report, but the two characterised in that report are now known to be subclade 1A(△3)B viruses (see below).

All recently circulating B/Victoria-lineage viruses have fallen in genetic **clade 1A**, represented by **B/Brisbane/60/2008** a former vaccine virus, but with additional **HA1** amino acid substitutions of **I117V, N129D** and **V146I** (e.g. **B/Ireland/3154/2016**). Those viruses retaining full-length HAs have remained antigenically similar to A/Brisbane/60/2008. However, three genetic groups (described below with amino acid substitutions/deletions relative to B/Brisbane/60/2008 indicated) containing deletions of HA gene codons have emerged, and the viruses in these groups are antigenically distinct from A/Brisbane/60/2008 and each other (as noted in the September 2018 characterisation report[4] and earlier ones), such that four antigenically distinguishable groups have been circulating:

- A group with double deletion of **HA1** residues **162** and **163** (**subclade △162-163** or **1A(△2)**) with amino acid substitutions of **D129G** and **I180V**, and **HA2 R151K** that has spread worldwide and is represented by the current vaccine virus, **B/Colorado/06/2017**;
- A group with triple deletion of **HA1** residues **162** to **164** (**subclade △162-164A** or **1A(△3)A**), first detected in Asia, with amino acid substitutions of **I180T** and **K209N** that has shown limited spread worldwide and is represented by **B/Hong Kong/269/2017**;
- A group with triple deletion of **HA1** residues **162** to **164** (**subclade △162-164B** or **1A(△3)B**), first detected in Africa, with amino acid substitution **K136E** often with **G133R** that has shown geographic spread in recent months and is represented by the recently recommended vaccine virus **B/Washington/02/2019**.

The HA phylogeny (Figure 3) was constructed using the 2019–20 reference set provided in relation to the European Surveillance System reporting, and full length gene sequences available in GISAID for viruses with collection dates after 31 August 2019 (n = 148) and as of 4 December 2019. Over the last three months, viruses in subclade 1A(△3)B (n = 126) have dominated with the great majority (n = 120) having HA1 K136E and G133R substitutions. The remaining 22 viruses have HA genes falling in subclade 1A(△2).

Following the spread of 1A(Δ2) viruses a representative, B/Colorado/06/2017, was recommended for use in trivalent influenza vaccines for the 2018–19 and 2019–20 northern hemisphere [3, 1] and 2019 southern hemisphere [4] seasons. Recent predominance of 1A(Δ3)B viruses led to recommendation of a representative (B/Washington/02/2019) for use in trivalent influenza vaccines for the 2020 southern hemisphere season [2].

Influenza B/Yamagata-lineage

No B/Yamagata-lineage viruses from EU/EEA countries, or others that share influenza-positive samples with the WIC, have been assessed by HI assay since the October 2019 report.

The HA phylogeny (Figure 4) was constructed using the 2019–20 reference set provided in relation to the European Surveillance System reporting and full length gene sequences available in GISAID for viruses with collection dates after 31 August 2019 (n = 15) as of 4 December 2019. All recently collected viruses have HA genes that continue to fall in genetic clade 3, 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. Some subclustering of sequences from recently collected viruses, defined by specific amino acid substitutions (e.g. **HA1 D229N** or **D232N** [introducing a potential N-linked glycosylation site] with **R48K**), is occurring. It has been noted in previous characterisation reports for 2018 that 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, which has been recommended for inclusion in quadrivalent vaccines for the 2018–2019 and 2019–20 [3, 1] northern hemisphere, and the 2019 and 2020 [4, 2] southern hemisphere seasons.

[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2018. Stockholm: ECDC; 2018. Available from (accessed 5 December 2019): https://ecdc.europa.eu/sites/portal/files/documents/ECDC-Flu-Characterisation-Report-Sep-2018.pdf

Figure 3. Phylogenetic comparison of influenza B/Victoria-lineage HA genes

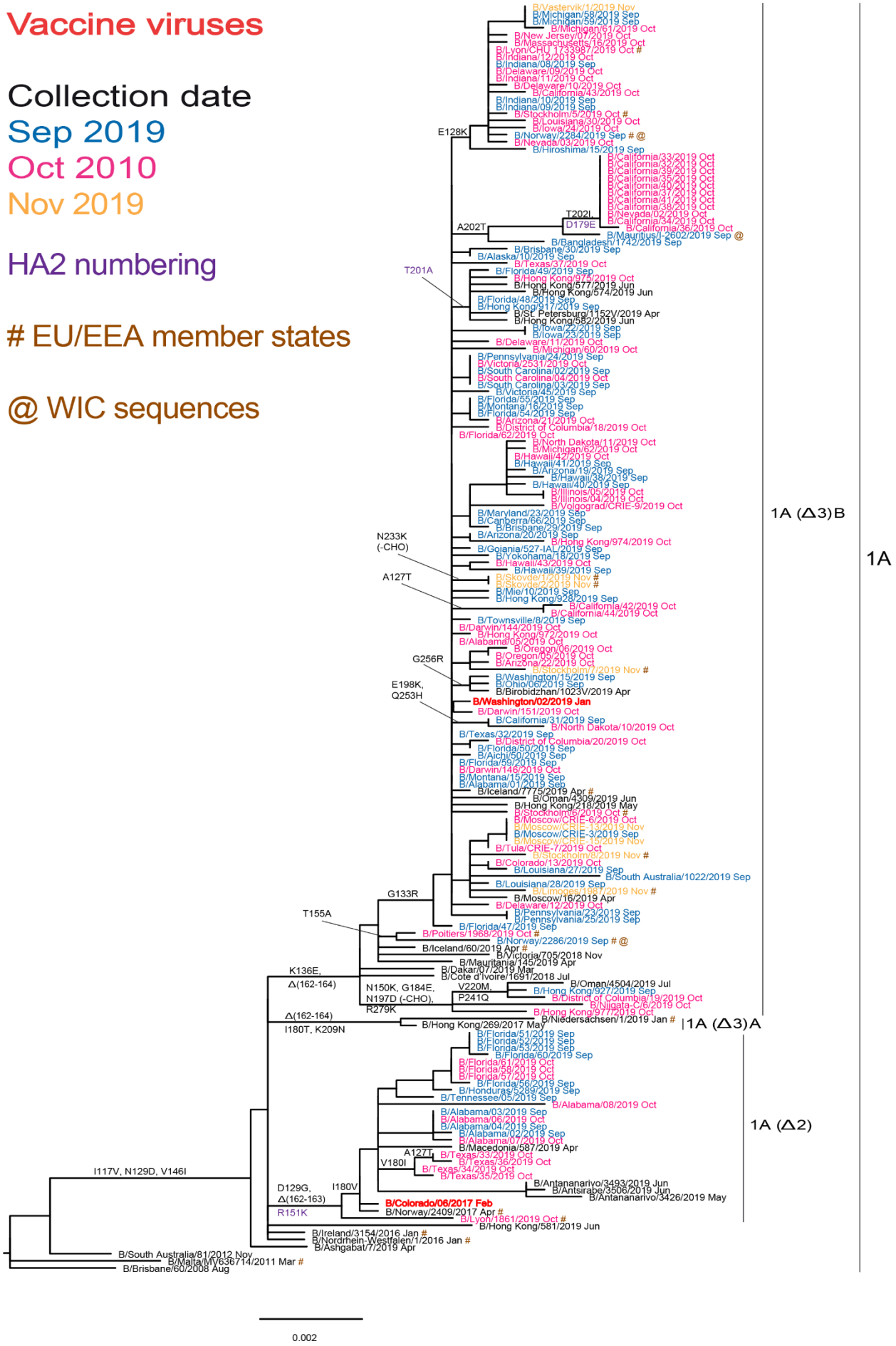
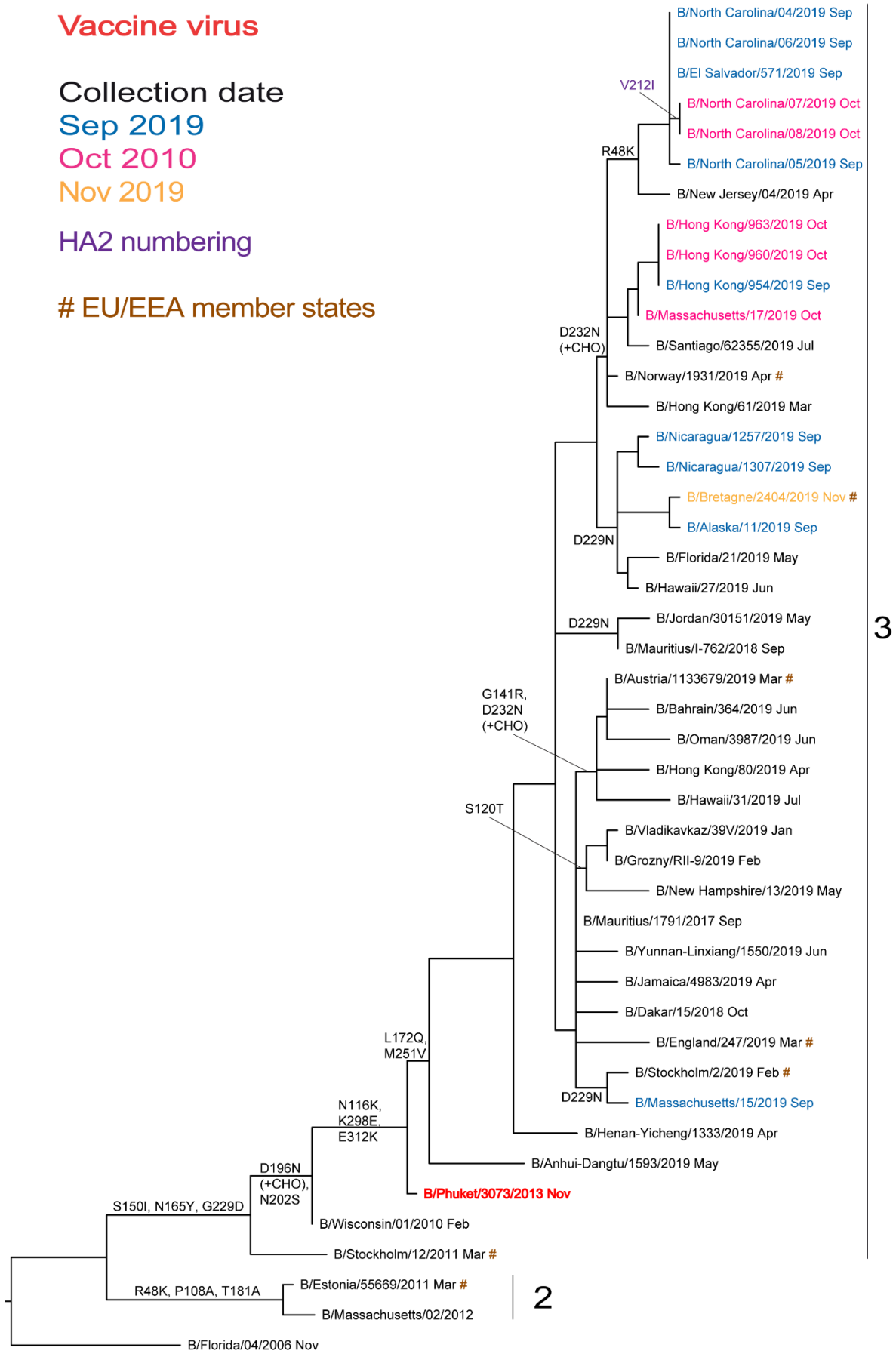


Figure 4. Phylogenetic comparison of influenza B/Yamagata-lineage HA genes



Summaries of data submitted to the European Surveillance System

Genetic characterisation

For the 2019–20 season, as of week 48/2019, 131 viruses had been characterised genetically and ascribed to a genetic clade:

- 33 A(H1N1)pdm09 were subclade 6B.1A5, with 22 falling in subgroup 6B.1A5A represented by A/Norway/3433/2018 and 11 in subgroup 6B.1A5B represented by A/Switzerland/3330/2018;
- 74 were A(H3N2) viruses, with 36 being subgroup 3C.2a1b+T131K represented by A/South Australia/34/2019, 26 being clade 3C.3a represented by A/Kansas/14/2017, nine being subgroup 3C.2a1b+T135K-D represented by A/Hong Kong/2675/2019 and 3 being subgroup 3C.2a1b+T135K-A represented by A/La Rioja/2202/2018;
- two were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013;
- 22 were B/Victoria-lineage viruses, with 17 being subclade 1A(Δ3)B represented by B/Washington/02/2019, three being subclade 1A(Δ3)A represented by B/Hong Kong/269/2017 and two being subclade 1A(Δ2) represented by the vaccine virus B/Colorado/06/2017.

Antiviral susceptibility

All of the 46 viruses (22 A(H3N2), 20 A(H1N1)pdm09 and 4 type B) collected in the course of the 2019–20 season tested for susceptibility to neuraminidase inhibitors, oseltamivir and zanamivir, up to week 48/2019, showed normal inhibition (NI).

At the WIC this season, 14 viruses from EU/EEA countries were assessed phenotypically against oseltamivir and zanamivir: 2 A(H1N1)pdm09, 10 A(H3N2) and 2 B/Victoria-lineage. All viruses showed NI by the two neuraminidase inhibitors.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [5] reported that the China Health and Family Planning Commission notified them of three cases of human infection with influenza A(H7N9). A description of the characteristics of H7N9 viruses can be found on the WHO website [6]. 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, though few human cases were reported during the 2017–18 season [7]. WHO posted an analysis of information on A(H7N9) viruses on 10 February 2017 [8] and ECDC published a rapid risk assessment on the implications of A(H7N9) for public health on 3 July 2017 [9]. A summary and assessment of influenza viruses at the human-animal interface on 27 September 2019 reports that no new cases of human infection had been detected since the 24 June report, and indicates that there have been no publically available reports from animal health authorities in China of influenza A(H7N9) virus detections in animals in recent months [10]. The most recent human case was detected in mid-March 2019 [11]. 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 published on 27 September 2019, and is available on the ECDC website [12].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 27 September 2019, indicating that various A(H5Nx) subtypes continue to be detected in birds in Africa, Europe and Asia, with a new case of human infection with an A(H5N6) virus being reported by China on 18 August 2019 [10]. No new human cases of A(H5N1) infection have been detected since those in Nepal in March, where there were reports of A(H5N1) infection in domestic birds, this was the first human case of A(H5N1) infection reported to WHO since 2017 [13]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [14]. As described above, the EU Reference Laboratory for Avian Influenza, in collaboration with ECDC and the European Food Standards Agency, published the latest overview of avian influenza on 27 September 2019 which is available on the ECDC website [12].

WHO Collaborating Centre reports

A description of results generated by the London WHO CC at the WIC and used in previous and the most recent WHO vaccine composition meeting (held in Geneva, Switzerland 23-27 September 2019) can be found at:https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports (accessed 4 December 2019).

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 of sample collection. Isolates from WHO NICs in EU/EEA countries are marked (#). Sequences for most viruses from non-EU/EEA countries were recovered from the GISAID EpiFlu database. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from the GISAID EpiFlu database, which were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website), along with all laboratories that submitted sequences directly to WHO CC London.

References

1. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2019–2020 northern hemisphere influenza season. Wkly Epidemiol Rec. 2019 Mar 22;94(12):141-150. https://apps.who.int/iris/bitstream/handle/10665/311441/WER9412-141-150.pdf
2. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2020 southern hemisphere influenza season. Wkly Epidemiol Rec. 2019 Oct 18;94(42):473-496. https://apps.who.int/iris/bitstream/handle/10665/329390/WER9442-eng-fre.pdf
3. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2018–2019 northern hemisphere influenza season. Wkly Epidemiol Rec. 2018 Mar 23;93(12):133-152. http://apps.who.int/iris/bitstream/handle/10665/260550/WER9312.pdf
4. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2019 southern hemisphere influenza season. Wkly Epidemiol Rec. 2018 Oct 19;93(42):553-576. http://apps.who.int/iris/bitstream/handle/10665/275475/WER9342.pdf
5. World Health Organization. Emergencies preparedness, response – Human infection with influenza A(H7N9) virus in China. 1 April 2013 [internet]. Geneva: WHO; 2013 [accessed 5 December 2019]. Available from: http://www.who.int/csr/don/2013_04_01/en/index.html
6. World Health Organization. Influenza – Avian influenza A(H7N9) virus [internet]. Geneva: WHO; 2017 [accessed 5 December 2019]. Available from: http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/
7. World Health Organization. Emergencies preparedness, response –Human infection with avian influenza A(H7N9) virus – China [internet]. Geneva: WHO; 2017 [accessed 5 December 2019]. Available from: http://www.who.int/csr/don/26-october-2017-ah7n9-china/en/
8. World Health Organization. Analysis of recent scientific information on avian influenza A(H7N9) virus. 10 February 2017 [internet]. Geneva: WHO, 2017 [accessed 5 December 2019]. Available from: http://www.who.int/influenza/human_animal_interface/avian_influenza/riskassessment_AH7N9_201702/en
9. European Centre for Disease Prevention and Control. Influenza A(H7N9) virus in China - implications for public health - 7th update, 3 July 2017. Stockholm: ECDC; 2017 [accessed 5 December 2019]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/2017-07-03-RRA-Disease-China_H7N9_0.pdf
10. World Health Organization. Influenza at the human-animal interface. Summary and assessment, 25 June to 27 September 2019 [internet]. Geneva: WHO, 2019 [accessed 5 December 2019]. Available from: https://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_27_09_2019.pdf
11. World Health Organization. Influenza at the human–animal interface. Summary and assessment, 13 February to 9 April 2019 [internet]. Geneva: WHO; 2019 [accessed 5 December 2019]. Available from: https://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_09_04_2019.pdf
12. European Centre for Disease Prevention and Control, European Food Safety Authority, European Union Reference Laboratory for Avian influenza. Avian influenza overview, February – August 2019. Parma and Stockholm: EFSA, ECDC; 2019 [accessed 5 December 2019]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/avian-influenza-overview-february-august-2019.pdf
13. World Health Organization. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003–2019. Geneva: WHO; 2019 [accessed 5 December 2019]. Available from: https://www.who.int/influenza/human_animal_interface/2019_09_27_tableH5N1.pdf
14. European Centre for Disease Prevention and Control. Outbreak of highly pathogenic avian influenza A(H5N8) in Europe – 18 November 2016. Stockholm: ECDC; 2016 [accessed 5 December 2019]. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/risk-assessment-avian-influenza-H5N8-europe.pdf