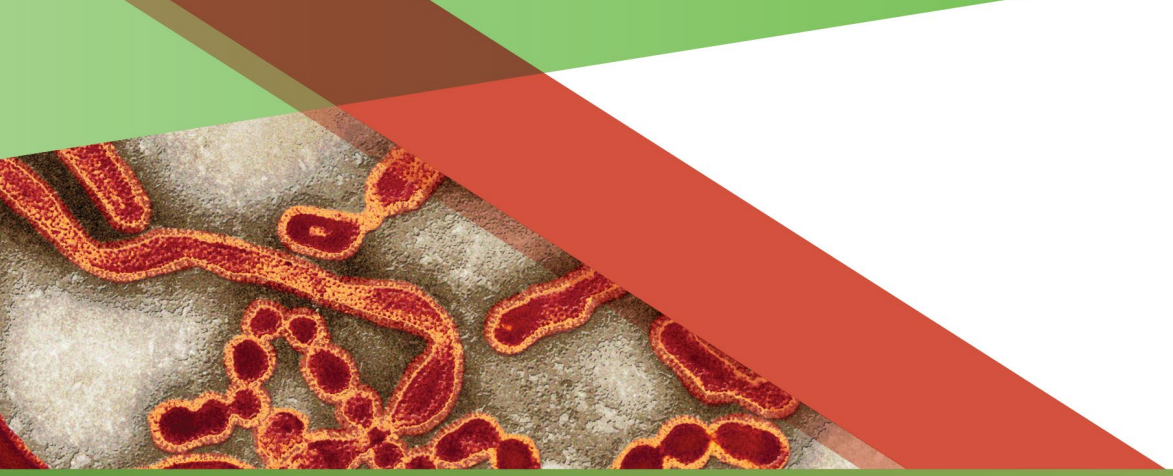

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, December 2019

Summary

This is the third report for the 2019–20 influenza season. As of week 1/2020, 42 844 influenza detections had been reported across the WHO European Region; 85% type A viruses, with A(H3N2) prevailing over A(H1N1)pdm09, and 15% type B viruses, with 531 (92%) of 576 ascribed to a B/Victoria lineage.

Since the November 2019 characterisation report[1], 12 shipments of influenza-positive specimens from EU/EEA countries have been received at the London WHO CC, the Francis Crick Worldwide Influenza Centre (WIC). A total of 397 virus specimens have been received, with collection dates after 31 August 2019, and these will be considered at the February 2020 WHO influenza vaccine recommendation meeting.

Seventeen A(H1N1)pdm09 test viruses from EU/EEA countries have been characterised antigenically since the last report, with 16 showing good reactivity with antiserum raised against the 2019–20 vaccine virus, A/Brisbane/02/2018. The 21 test viruses with collection dates from week 40/2019 genetically characterised at the WIC have fallen within subclades of clade 6B.1A: 15 6B.1A5A, 3 6B.1A5B, 1 6B.1A6 and 2 6B.1A7.

Since the last report, 17 A(H3N2) viruses have been characterised antigenically. Of the 17, 12 were clade 3C.3a viruses that were antigenically similar to the vaccine virus, A/Kansas/14/2017. The remaining five were subgroup 3C.2a1b+T135K viruses that were poorly recognised by the vaccine virus. In total, 57 viruses have been characterised genetically at the WIC: 38 clade 3C.3a, 11 3C.2a1b+T131K, three 3C.2a1b+T135K-A and five 3C.2a1b+T135K-B.

Fourteen B/Victoria-lineage viruses have been characterised in this reporting period, all of which gave antigenic profiles characteristic of subgroup 1A(Δ3)B viruses, represented by B/Washington/02/2019, the vaccine virus for the 2020 southern hemisphere season, with the subgroup having been confirmed for nine of the viruses. In total, all of 29 viruses characterised genetically at the WIC have been subgroup 1A(Δ3)B.

The single B/Yamagata-lineage virus characterised antigenically in this reporting period reacted poorly with antiserum raised against the vaccine virus B/Phuket/3073/2013 (clade 3) and only reacted well with an antiserum raised against a B/Yamagata-lineage virus carrying multiple unusual substitutions in HA1. While all recently circulating B/Yamagata-lineage viruses belong to genetic clade 3 and contain at least two HA amino acid substitutions compared to B/Phuket/3073/2013 (HA1 L172Q and M251V), antigenic effects have been minimal based on earlier reports. Genetic characterisation of B/Yamagata-lineage viruses received is pending.

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2019. Stockholm: ECDC; 2019. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/influenza-virus-characterisation-report-November-2019.pdf

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Stockholm, January 2020

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to ECDC's TESSy database since the start of the 2019–20 season (weeks 40/2019–1/2020), with a total of 42 844 detections during this period. At this early stage of the season, type A (85.4%) have predominated over type B (14.6%) viruses which is a common pattern. Of the type A viruses subtyped (n=11 324) and the type B viruses ascribed to a lineage (n=576), A(H3N2) (n=8 169) have prevailed over A(H1N1)pdm09 (n=3 156) viruses and 531 of 576 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 5.8:1), 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 2018–19 season (weeks 40/2019–1/2020)[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	**2454**	**34132**	**36586**	**85.4**	**5.8:1**	**203564**	**98.8**	**86:1**
A(H1N1)pdm09	967	2188	3155	27.9		44179	57.2	
A(H3N2)	1390	6779	8169	72.1	2.6:1	33117	42.8	0.7:1
A not subtyped	97	25165	25262			126271		
Influenza B	**1213**	**5045**	**6258**	**14.6**		**2380**	**1.2**	
Victoria lineage	255	276	531	92.2		79	47.9	
Yamagata lineage	7	38	45	7.8	0.1:1	86	52.1	1.1:1
Lineage not ascribed	951	4731	5682			2215		
Total detections (total tested)	**3667 (20172)**	**39177 (>249839)**	**42844 (>270011)**			**205947 (>849439)**		

[a] **Numbers taken from Flu News Europe week 1/2020**

*** 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, 16 shipments of specimens (virus isolates and/or clinical specimens) have been received at the Crick Worldwide Influenza Centre (WIC) with 12 of these arriving in December 2019 (weeks 49–51/2019). The packages contained 397 virus-related samples with collection dates after 31 August 2019 and were made up of 261 type A viruses, with 91 and 169 subtyped as A(H1N1)pdm09 and A(H3N2) respectively, and 136 type B viruses, with 62 and four ascribed to B/Victoria and B/Yamagata lineages respectively (Table 2), similar to the ratios reported to TESSy (Table 1). Genetic and antigenic characterisation data generated at the WIC for viruses with collection dates between 31 August 2019 and 31 January 2020 will be presented at the WHO influenza vaccine composition meeting in February 2020 when recommendations will be made for the northern hemisphere 2020–21 season. Recommendations for the current 2019–20 northern hemisphere and the subsequent 2020 southern hemisphere seasons have been published [1, 2].

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 / Country	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]
SEPTEMBER														
Czech Republic	1					1	in process							
Finland	1					1	in process							
France	2					2	in process							
Norway	7			1	1	4	1	3			2	2		
Sweden	3			2	in process	1	in process							
United Kingdom	4			2	2	2	in process							
OCTOBER														
Denmark	3			2	in process	1	in process							
Finland	2			1	in process	1	in process							
France	5			3	in process						2	in process		
Germany	6			2	in process	4	in process							
Iceland	9					8	in process				1	in process		
Ireland	11			1	in process	9	in process						1	in process
Latvia	3			1	in process						2	in process		
Norway	28			5	4	19	3	15			3	2	1	0
Portugal	5			1	1	1	in process		3	in process				
Sweden	3					2	in process				1	in process		
United Kingdom	29			5	in process	21	in process				3	in process		
NOVEMBER														
Croatia	7			4	in process						3	in process		
Denmark	16			7	in process	6	in process				3	in process		
Finland	1			1	in process									
France	4			3	in process	1	in process							
Germany	5			3	in process	2	in process							
Iceland	3					2	in process		1	in process				
Ireland	49			17	in process	23	in process		7	in process	2	in process		
Latvia	10			2	in process	3	in process				5	in process		
Norway	21			6	5	9	3	4			4	4	2	1
Portugal	95	1	0	6	in process	2	in process		58	in process	28	in process		
Sweden	8			5	in process	1	in process				2	in process		
United Kingdom	44			5	in process	38	in process				1	in process		
DECEMBER														
Croatia	6			4	in process	2	in process							
Iceland	5			2	in process	2	in process		1	in process				
Latvia	1					1	in process							
13 Countries	397	1	0	91	13	169	7	22	70	0	62	8	4	1
					22.9%		42.6%					15.6%		1.0%
					65.7%							34.3%		

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

1. Propagated to sufficient titre to perform HI assay (the totalled number does not include any from batches that are in process)
2. Propagated to sufficient titre to perform HI assay in the presence of 20nM oseltamivir (the totalled number does not include any from batches that are in process)

Numbers in red indicate viruses recovered but with insufficient HA titre to permit HI assay

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

As of 2020-01-02

Influenza A(H1N1)pdm09 virus analyses

Tables 3-1 and 3-2 show the results of haemagglutination inhibition (HI) assays of A(H1N1)pdm09 viruses performed, with a panel of post-infection ferret antisera, since the November 2019 report. The 17 test viruses are sorted by date of collection and genetic group/subgroup: 11 6B.1A5A, 3 6B.1A5B, 1 6B.1A6 and 2 6B.1A7 (see below).

A total of 7/17 (41%) A(H1N1)pdm09 test viruses were antigenically indistinguishable from the A/Michigan/45/2015 northern hemisphere 2018–19 influenza season vaccine virus [3], being recognised at titres within two-fold of the titre of the post-infection ferret antiserum with the homologous virus, the number increasing to 15/17 (88%) for titres within four-fold. Somewhat better recognition was observed with the ferret antiserum raised against the A/Brisbane/02/2018 northern hemisphere 2019–20 influenza season vaccine virus [1], with 12/17 (71%) and 16/17 (94%) being recognised at titres within two-fold and four-fold, respectively. Similar good recognition was observed with antiserum raised against egg-propagated A/Switzerland/3330/2017 (genetic subgroup 6B.1A5B) but antisera raised against egg-propagated A/Slovenia/2903/2015 (clade 6B.1) and A/Switzerland/2656/2017 (clade 6B.1A) recognised only 8/17 (47%) and 7/17 (41%) test viruses respectively, at titres within four-fold of homologous titres.

Good recognition was observed with antisera raised against four cell culture-propagated viruses (A/Bayern/69/2009, A/Paris/1447/2017, A/Norway/3422/2018 and A/Ireland/84630/2018) with 94–100% of test viruses being recognised at titres within four-fold of the respective homologous titres. The antiserum raised against cell culture-propagated A/Lviv/N6/2009 is an unusual virus/antiserum combination, with A/Lviv/N6/2009 encoding **HA1** amino acid polymorphism of **G155G/E**, with E predominating, and **D222G** substitution: this antiserum recognised only 12 test viruses at a titre within four-fold of the homologous titre.

Full-length HA gene sequences from seasonal influenza viruses with collection dates after 31 August 2019, deposited in GISAID during the period 5 December 2109 to 2 January 2020, were downloaded from GISAID and combined with those generated at the WIC. From the large phylogenies generated, for both influenza A subtypes and both influenza B lineages, representative sets of sequences were used to produce the phylogenies presented here (Figures 1 to 4).

Figure 1 shows an HA gene-based phylogeny for a representative set of these recently circulating A(H1N1)pdm09 viruses. All recently circulating viruses fell 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. 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 majority of recently circulating viruses have fallen into subgroup **6B.1A5A** which contains a number of virus clusters, two of which have been detected in significant numbers, one defined by **HA1 D187A** and **Q189E** substitutions and the other by **HA2 V193A** substitution. Significant numbers of viruses in subgroup **6B.1A5B** (with additional **HA1** substitutions of **K130N**, **K160M** and **T216K**) and subclade **6B.1A7** (with additional **HA1** substitutions of **E68D**, **T120A**, **S121N** and **L161I**) have also been detected (Figure 1). The great majority of viruses in the various subgroups have remained antigenically similar to A/Brisbane/02/2018, as assessed with post-infection ferret antisera, and shown in earlier characterisation reports.

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
	Passage history			A/Mich 45/15	A/Bayern 69/09	A/Lviv N6/09	A/Slov 2903/2015	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18	A/Ire 84630/18	A/Bris 02/18
	Ferret number			F31/16^{-1}	F09/15^{-1}	F13/18^{-1}	NIB F48/16^{-1}	F03/18^{-2}	F20/18^{-1}	F23/18^{-1}	F04/19^{-1}	F08/19^{-1}	F09/19^{-1}
	Genetic group			6B.1			6B.1	6B.1A	6B.1A	6B.1A5B	6B.1A5A	6B.1A6	6B.1A1
REFERENCE VIRUSES													
A/Michigan/45/2015	6B.1	2015-09-07	E3/E4	2560	640	640	2560	2560	2560	1280	2560	2560	1280
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	80	320	320	40	160	160	80	320	40	80
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK3	320	640	640	160	640	320	160	640	160	320
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	2560	640	1280	5120	5120	5120	1280	5120	1280	2560
A/Paris/1447/2017	6B.1A	2017-10-20	MDCK1/MDCK3	640	320	160	1280	2560	2560	640	2560	1280	1280
A/Switzerland/2656/2017	6B.1A	2017-12-21	E5/E3	2560	640	640	2560	2560	5120	2560	5120	2560	2560
A/Switzerland/3330/2017	clone 35 6B.1A5B	2017-12-20	E6/E2	640	320	160	1280	1280	1280	1280	640	640	640
A/Norway/3433/2018	6B.1A5A	2018-10-30	MDCK3	320	80	40	320	640	640	320	640	320	320
A/Ireland/84630/2018	6B.1A6	2018-11-28	MDCK1/MDCK3	640	160	160	1280	1280	1280	640	640	1280	640
A/Brisbane/02/2018	6B.1A1	2018-01-04	E3/E1	1280	320	320	1280	2560	2560	1280	1280	1280	1280
TEST VIRUSES													
A/England/292/2019	6B.1A5A	2019-09-06	SIAT1/MDCK1	320	160	80	320	640	320	320	1280	320	320
A/England/296/2019	6B.1A5A	2019-09-13	SIAT1/MDCK1	640	320	160	640	1280	640	640	1280	640	640
A/England/298/2019	6B.1A5A	2019-10-10	SIAT1/MDCK1	640	160	80	640	1280	640	320	1280	640	320
A/Norway/2316/2019	6B.1A5A	2019-10-16	MDCK1	640	160	160	640	1280	640	640	1280	640	320
A/Norway/2347/2019	6B.1A5A	2019-10-23	MDCK1	320	80	40	160	320	160	160	640	160	160
A/Norway/2368/2019	6B.1A5A	2019-11-03	SIAT1/MDCK1	640	160	160	640	640	640	640	1280	640	640
A/Norway/2317/2019	6B.1A5B	2019-10-21	MDCK1	640	80	40	640	640	320	320	640	640	320
A/Norway/2412/2019	6B.1A5B	2019-11-06	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Norway/2406/2019	6B.1A5B	2019-11-08	MDCK1	640	160	80	640	640	640	640	1280	640	640
A/England/297/2019	6B.1A6	2019-10-08	SIAT1/MDCK1	640	320	160	640	1280	640	640	1280	640	640
A/Norway/2471/2019	6B.1A7	2019-11-14	MDCK1	640	320	160	1280	2560	1280	1280	2560	1280	1280
A/Norway/2475/2019	6B.1A7	2019-11-16	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)	Vaccine
1 < = <40; 2 < = <80; ND =Not Done	NH 2018-19
Sequences in phylogenetic trees	SH 2019

Vaccine
NH 2019-20
SH 2020

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				A/Mich 45/15 Egg F31/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F13/18[*1]	A/Slov 2903/2015 Egg NIB F-48/16[*1]	A/Paris 1447/17 MDCK F03/18[*2]	A/Swit 2656/17 Egg F20/18[*1]	A/Swit 3330/17 Egg F23/18[*1]	A/Norway 3433/18 MDCK F04/19[*1]	A/Ire 84630/18 MDCK F08/19[*1]	A/Bris 02/18 Egg F09/19[*1]
Passage history													
Ferret number													
Genetic group				6B.1			6B.1	6B.1A	6B.1A	6B.1A5B	6B.1A5A	6B.1A6	6B.1A1
REFERENCE VIRUSES													
A/Michigan/45/2015		6B.1	2015-09-07	E3/E4	1280	320	320	1280	2560	2560	1280	2560	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	160	320	320	40	320	160	160	640	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	640	80	320	320	160	640	80	160
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	2560	640	640	2560	2560	2560	1280	2560	2560	2560
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	1280	320	80	1280	1280	1280	640	1280	1280	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	5120	640	1280	5120	5120	5120	5120	5120	5120	2560
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	1280	320	160	640	1280	1280	1280	1280	1280	640
A/Norway/3433/2018		6B.1A5A	2018-10-30	MDCK3	640	160	40	640	640	640	640	1280	640	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	320	160	1280	1280	1280	1280	1280	1280	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	320	320	1280	1280	1280	640	1280	1280	640
TEST VIRUSES													
A/Azores/9/2019		6B.1A5A	2019-10-31	MDCK2	1280	320	320	640	1280	1280	320	1280	640	640
A/Azores/10/2019		6B.1A5A	2019-11-07	MDCK1	1280	320	160	640	1280	1280	640	2560	640	640
A/Azores/11/2019		6B.1A5A	2019-11-11	MDCK2	1280	320	320	1280	1280	1280	640	2560	1280	640
A/Azores/12/2019		6B.1A5A	2019-11-19	MDCK2	1280	320	320	1280	1280	1280	640	1280	1280	1280
A/Azores/13/2019		6B.1A5A	2019-11-21	MDCK1	640	320	160	640	1280	640	320	1280	640	640

Vaccine
NH 2018-19
SH 2019

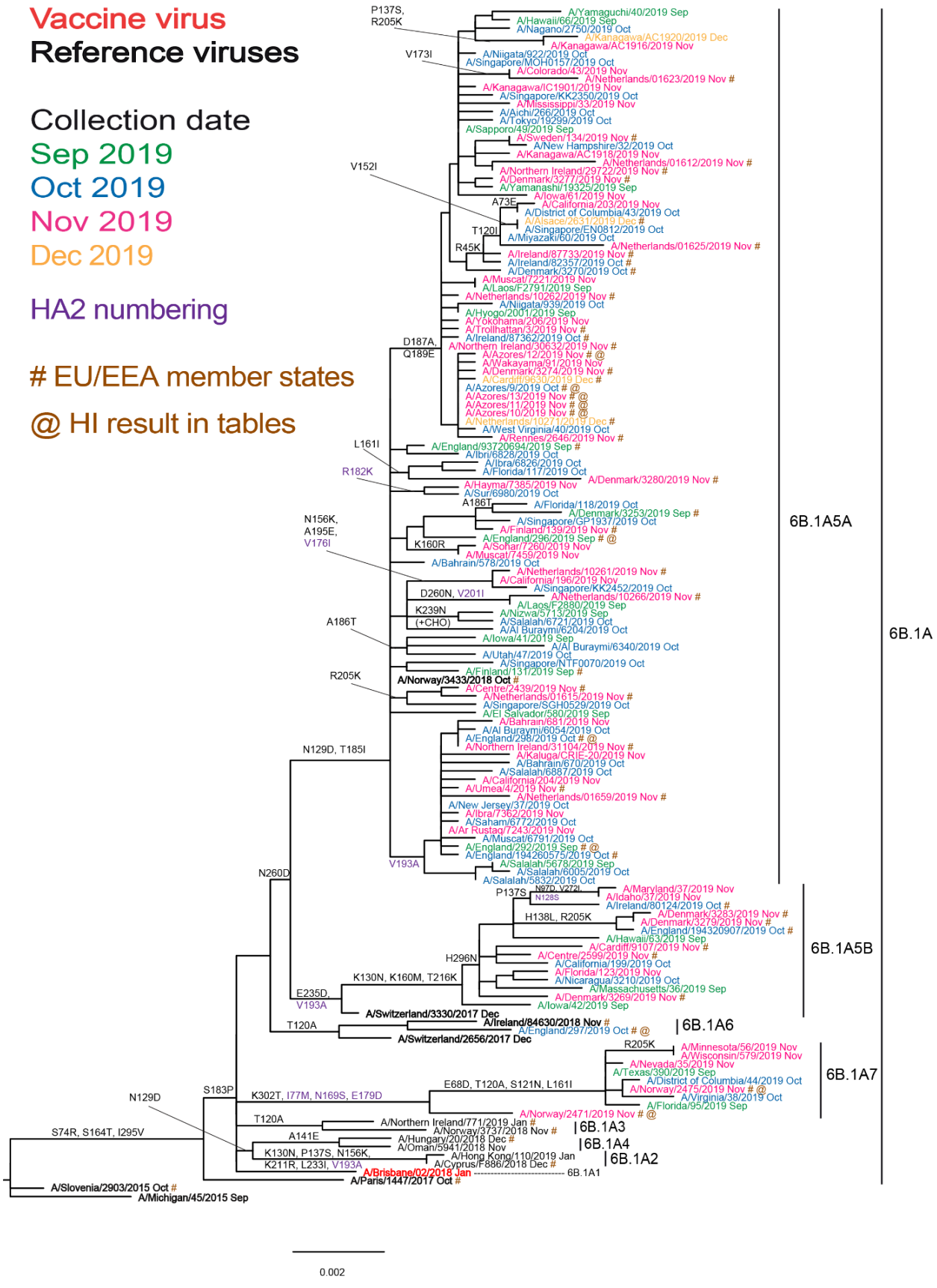
Vaccine
NH 2019-20
SH 2020

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

1 < = <40; 2 < = <80; ND =Not Done

Sequences in phylogenetic trees

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 first in the November 2014 report[3], this is a particular problem for most viruses that fall in genetic clade 3C.2a.

Since the November 2019 characterisation report of the viruses recovered, based on positive neuraminidase activity, 17 retained sufficient HA activity to allow antigenic analysis by HI (Tables 4-1 to 4-2). All test viruses were poorly recognised by antisera raised against subclade 3C.2a2 viruses, cell culture-propagated A/Bretagne/1413/2017 and egg-propagated A/Switzerland/8060/2017 (the vaccine virus for the 2019 southern hemisphere season [4], and the egg-propagated subgroup 3C.2a1b+T131K vaccine virus for the southern hemisphere 2020 season [2], A/South Australia/34/2019. Similarly, antisera raised against two cell culture-propagated subgroup 3C.2a1b viruses, A/La Rioja/2202/2018 (3C.2a1b+T135K) and A/Norway/3275/2018 (3C.2a1b+T131K), for which no homologous titres are given due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, each recognised only one test virus at titres of 160. Test viruses reacted better with antiserum raised against the northern hemisphere 2018–19 vaccine virus [3], egg-propagated A/Singapore/INFOMH-16-0019/2016 (3C.2a1), with 11 (65%) and 14 (82%) test viruses being recognised at titres within two-fold and four-fold of the homologous titre, respectively.

Antisera raised against two cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, each recognised 12/17 (71%) and 13/17 (76%) test viruses at titres within two-fold and four-fold of homologous titres, respectively. However, the antiserum raised against egg-propagated A/Kansas/14/2017, the vaccine virus for the northern hemisphere 2019–2020 season [1], recognised only six (35%) test viruses at titres within four-fold of the homologous titre. Antiserum raised against cell culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised all test viruses at titres within four-fold of the homologous titre.

Overall, the HI data show poor recognition of test viruses by post-infection ferret antisera raised against three of four egg-propagated vaccine/reference viruses. The HA genes of the 17 test viruses fell in two clusters, 12 in clade 3C.3a and five in subgroup 3C.2a1b+T135K (Tables 4-1 and 4-2), so the HI data indicates: (i) poor cross-reactivity of antisera raised against subclade 3C.2a2 viruses, (ii) significant clade specificity of the antisera raised against cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, and (iii) of the six antisera raised against cell culture-propagated viruses, the one raised against A/Hong Kong/5738/2014 (clade 3C.2a) gives the broadest cross-clade/subclade reactivity.

Viruses in clade 3C.2a have been predominant since the 2014–15 influenza season and subgroup 3C.2a1b viruses prevailed during 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.

[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 10 January 2020): 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 10 January 2020): https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf

- 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 an HA gene-based phylogeny for a representative set of recently circulating A(H3N2) viruses. Globally, based on sequences deposited in GISAID, viruses in the **3C.2a1b** subgroup have circulated recently in the greatest numbers with the majority falling in the **3C.2a1b+T131K** cluster. Diversification of subgroup **3C.2a1b** viruses with **HA1 T135K** substitution is occurring, notably with significant geographic spread of viruses in the antigenically distinct **3C.2a1b+T135K-B** cluster. The geographic distribution of clade 3C.3a viruses appears more restricted, with the majority being reported from the European Region, notably by the United Kingdom.

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.

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
				A/HK	A/Bretagne	A/Singapore	A/La Rioja	A/Switz	A/Eng	A/Norway	NYMC X-327	A/Kansas	IVR-197
				5738/14	1413/17	0019/16	220218	8060/17	538/18	3275/18	A/Kansas/14	14/17	A/Sth Aus/34/19
	Passage history			MDCK St Judes	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	SIAT	Egg	SIAT	Egg
	Ferret number			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+T135K-A	3C.2a2	3C.3a	3C.2a1b+T131K	3C.3a	3C.3a	3C.2a1b+T131K
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK3/SIAT2	160	160	160	160	160	320	160	160	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	160	160	640	320	320	160	160	320
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	80	40	160	320	80	80	40	40	<	80
A/Switzerland/8060/2017	clone 57 3C.2a2	2017-12-12	E7/E1	160	1280	160	80	640	80	80	80	<	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT4	<	40	40	40	<	640	<	160	640	<
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	<	<	<	<	<	320	<	1280	320	<
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	80	40	80	<	40	640	40	320	640	<
IVR-197 (A/South Australia/34/2019)	3C.2a1b+T131K	2019-02-06	E5/D8/E1	1280	1280	320	160	320	160	2560	40	80	2560
TEST VIRUSES													
A/England/307/2019	3C.3a	2019-10-05	SIAT1/SIAT1	40	40	80	40	<	640	<	160	320	<
A/England/320/2019	3C.3a	2019-10-07	MDCK1/SIAT1	80	80	160	40	40	640	<	320	320	<
A/England/323/2019	3C.3a	2019-10-14	SIAT1/SIAT1	40	80	80	40	40	640	<	320	320	<
A/England/309/2019	3C.3a	2019-10-15	SIAT1/SIAT1	40	80	80	40	40	640	<	160	320	<
A/England/325/2019	3C.3a	2019-10-16	SIAT1/SIAT1	80	80	80	40	40	640	<	320	640	<
A/England/344/2019	3C.3a	2019-10-21	SIAT1/SIAT1	40	80	80	40	40	640	<	160	640	<
A/England/330/2019	3C.3a	2019-10-24	SIAT1/SIAT1	40	80	80	40	40	640	<	160	320	<
A/England/331/2019	3C.3a	2019-10-25	MDCK1/SIAT1	80	80	160	40	40	640	40	320	640	<
A/England/335/2019	3C.3a	2019-10-28	SIAT1/SIAT1	40	40	40	<	40	640	<	160	320	<
A/England/347/2019	3C.3a	2019-10-30	SIAT1/SIAT1	80	80	80	40	<	640	40	320	640	40
A/England/350/2019	3C.3a	2019-11-11	SIAT1/SIAT1	80	40	40	<	<	640	<	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

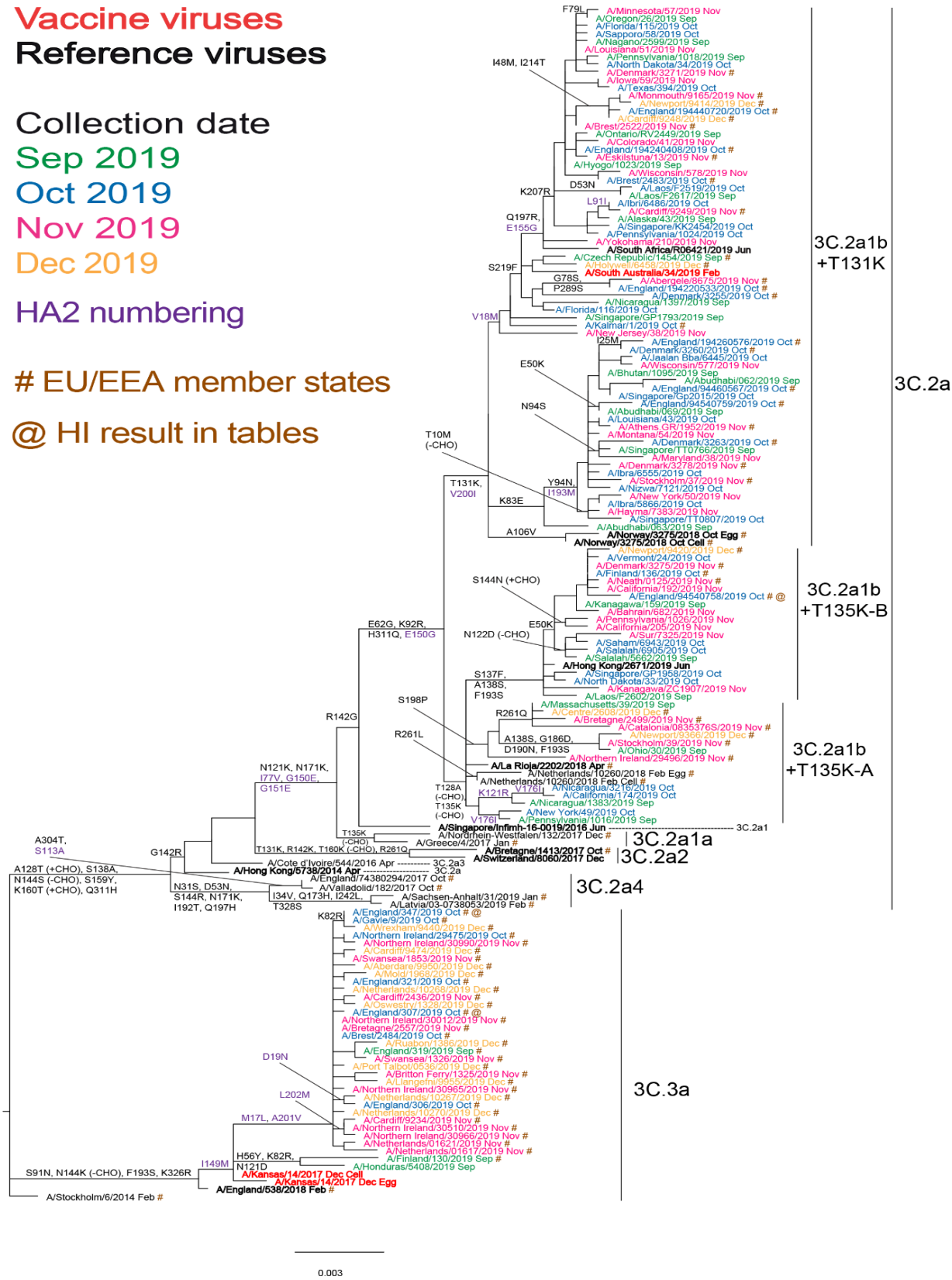
Table 4-2. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				A/HK	A/Bretagne	A/Singapore	A/La Rioja	A/Switz	A/Eng	A/Norway	NYMC X-327	A/Kansas	IVR-197
			Passage history	5738/14	1413/17	0019/16	2202/18	8060/17	538/18	3275/18	A/Kansas/14	14/17	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+T135K-A	3C.2a2	3C.3a	3C.2a1b+T131K	3C.3a	3C.3a	3C.2a1b+T131K
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK3/SIAT2	160	160	320	160	160	320	160	160	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	320	160	640	320	320	160	160	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	160	80	320	160	160	80	40	40	<	40
A/Switzerland/8060/2017 clone 57	3C.2a2	2017-12-12	E7/E1	160	1280	320	160	1280	160	80	40	40	80
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	80	40	80	40	40	640	<	320	640	<
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	E×/E1	40	40	80	40	<	320	<	1280	320	40
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	80	40	80	40	40	640	40	320	320	<
IVR-197 (A/South Australia/34/2019)	3C.2a1b+T131K	2019-02-06	E5/D8/E1	320	640	640	80	320	80	1280	40	40	1280
A/South Australia/34/2019	3C.2a1b+T131K	2019-02-06	E6/E1	160	640	640	80	320	80	1280	40	40	1280
TEST VIRUSES													
A/Norway/2323/2019	3C.2a1b+T135K-B	2019-10-06	SIAT1/SIAT1	160	40	160	160	80	160	160	80	80	160
A/England/945/407/58/2019	3C.2a1b+T135K-B	2019-10-25	SIAT1/SIAT1	40	<	40	40	<	40	80	<	<	<
A/Norway/2356/2019	3C.2a1b+T135K-B	2019-10-28	SIAT1/SIAT1	40	<	40	40	<	40	80	<	<	<
A/Norway/2425/2019	3C.2a1b+T135K-B	2019-11-05	SIAT1	40	<	40	40	<	40	80	<	<	<
A/Norway/2408/2019	3C.2a1b+T135K-B	2019-11-12	SIAT1	40	<	80	80	<	40	80	<	40	<
A/Norway/2379/2019	3C.3a	2019-11-06	SIAT1/SIAT1	80	80	160	40	80	640	40	320	640	40
						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 136 influenza type B viruses with collection dates after 31 August 2019 have been received at the WIC (Table 2). Of these, 66 were sent with pre-assignment to a lineage: 62 B/Victoria and four B/Yamagata.

Influenza B/Victoria-lineage

Fourteen B/Victoria-lineage viruses from EU/EEA countries have been assessed by HI assay since the November 2019 report (Table 5). The reactivity profiles of all test viruses were similar. Poor reactivity with ferret antisera raised against seven viruses in **clade 1A** (n=4) and **subclade 1A(△2)** (n=3) was observed, with only the antiserum raised against cell culture-propagated B/Colorado/06/2017 **1A(△2)** recognising eight (57%) of the test viruses at a titre within four-fold of the homologous titre. Reactivity with antisera raised against three **subclade 1A(△3)B** was much better, with only two test viruses reacting at titres ≥four-fold reduced compared to the respective homologous titres. The nine viruses for which genetic characterisation was completed are all in **subclade 1A(△3)B**. The two viruses showing low reactivity with antisera raised against B/Washington/02/2019, B/Norway/2386/2019 and B/Norway/2429/2019, have unusual **HA1** substitutions of **N126K** and **G256R**, respectively (Table 5).

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 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 showed 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 showed 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 sequences available in GISAID for a set of recently circulating viruses. Over the last three months, viruses in **subclade 1A(△3)B** have been predominant, with the great majority having **HA1 K136E** and **G133R** substitutions, and a number of virus clusters have emerged defined by specific amino acid substitutions - e.g. **HA1 E128K** or **N150K** with **G184E**, **N197D** (loss of a glycosylation site) and **R279K**. Relatively few **subclade 1A(△2)** viruses have been detected.

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. The recent predominance of **1A(Δ3)B** viruses led to the 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

A single B/Yamagata-lineage virus from Norway has been assessed by HI assay since the November 2019 report (Table 6). It reacted poorly with the panel of post-infection ferret antisera, with only that raised against B/Norway/2134/2019 giving reactivity four-fold reduced compared to the homologous titre. While genetic characterisation of B/Norway/2465/2019 is pending, B/Norway/2134/2019 is an unusual virus carrying multiple substitutions in **HA1** that include **G141R**, **K149E**, **I150N**, **G183E** and **N196I** (loss of a glycosylation site).

The HA phylogeny (Figure 4) was constructed using the most recently submitted sequences to GISAID, for viruses with collection dates after 31 August 2019, together with sequences from a selection of viruses with earlier collection dates. 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 sub-clustering of sequences from recently collected viruses, defined by specific amino acid substitutions (e.g. **HA1 D229N** or **D232N** [introducing a potential N-linked

[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2018. Stockholm: ECDC; 2018. Available from (accessed 12 January 2020): https://ecdc.europa.eu/sites/portal/files/documents/ECDC-Flu-Characterisation-Report-Sep-2018.pdf

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.

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
	Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Sth Aus 81/12 Egg	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Norway 2409/17 MDCK	B/Colorado 06/17 MDCK	B/Colorado 06/17 Egg	B/Clv 1662/18 MDCK	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[1,3]	F44/17[*2]	F25/16[*4]	F15/16[*2]	F16/16[*2]	F40/17[*2]	F09/18[*4]	F11/18[*2]	F37/18[*4]	F37/19[*4]	F38/19[*4]
	Genetic group			1A	1A	1A	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES														
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	640	640	80	40	<	20	80	<	<	320
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	640	640	40	20	<	20	80	<	<	160
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	160	40	160	80	<	<	<	<	<	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	2560	160	40	160	80	<	<	<	<	<	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	20	10	<	<	40	40	80	<	<	<
B/Colorado/06/2017	1A(Δ2)	2017-02-05	MDCK1/MDCK2	80	20	20	<	<	40	40	80	<	<	20
B/Colorado/06/2017	1A(Δ2)	2017-02-05	E5/E2	1280	320	80	<	<	40	80	320	<	<	160
B/Cote D'Ivoire/1662/2018	1A(Δ3)B	2018-07-25	P0/MDCK3	320	40	40	<	<	<	<	20	20	80	80
B/Washington/02/2019	1A(Δ3)B	2019-01-19	C2/MDCK2	640	160	80	<	<	<	40	160	80	80	320
B/Washington/02/2019	1A(Δ3)B	2019-01-19	E3/E2	640	160	40	<	<	<	20	160	40	<	320
TEST VIRUSES														
B/Norway/2386/2019	1A(Δ3)B	2019-10-29	MDCK1/MDCK1	80	20	10	<	<	<	<	<	20	20	40
B/Norway/2375/2019	1A(Δ3)B	2019-10-31	MDCK1/MDCK1	160	40	10	<	<	<	10	<	20	80	320
B/Norway/2426/2019	1A(Δ3)B	2019-11-07	MDCK1	320	40	40	<	<	<	10	10	40	80	320
B/Norway/2429/2019	1A(Δ3)B	2019-11-08	MDCK1	160	40	10	<	<	<	<	<	40	20	80
B/Norway/2446/2019		2019-11-12	MDCK2	320	40	10	<	<	<	<	<	10	80	320
B/Norway/2464/2019	1A(Δ3)B	2019-11-14	MDCK1	80	40	10	<	<	<	<	<	20	40	320
B/Madeira/67/2019		2019-11-22	MDCK1	80	40	10	<	<	<	<	<	20	40	160
B/Madeira/68/2019		2019-11-23	MDCK2	640	40	40	<	<	<	20	80	40	80	320
B/Lisboa/36/2019		2019-11-23	MDCK2	640	160	80	<	<	<	<	40	40	80	160
B/Guarda/171/2019	1A(Δ3)B	2019-11-24	MDCK1	320	40	20	<	<	<	10	<	40	40	320
B/Guarda/170/2019	1A(Δ3)B	2019-11-24	MDCK2	640	80	40	<	<	<	40	40	40	80	320
B/Madeira/69/2019		2019-11-24	MDCK1	320	40	20	<	<	<	10	<	40	40	160
B/Madeira/70/2019	1A(Δ3)B	2019-11-26	MDCK1	320	40	20	<	<	<	10	<	40	80	320
B/Braga/135/2019	1A(Δ3)B	2019-11-27	MDCK1	160	40	10	<	<	<	10	<	40	80	320

Vaccine	Vaccine SH 2020
NH 2018-19	
SH 2019	
NH 2019-20	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; ND = Not Done

Sequences in phylogenetic trees

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

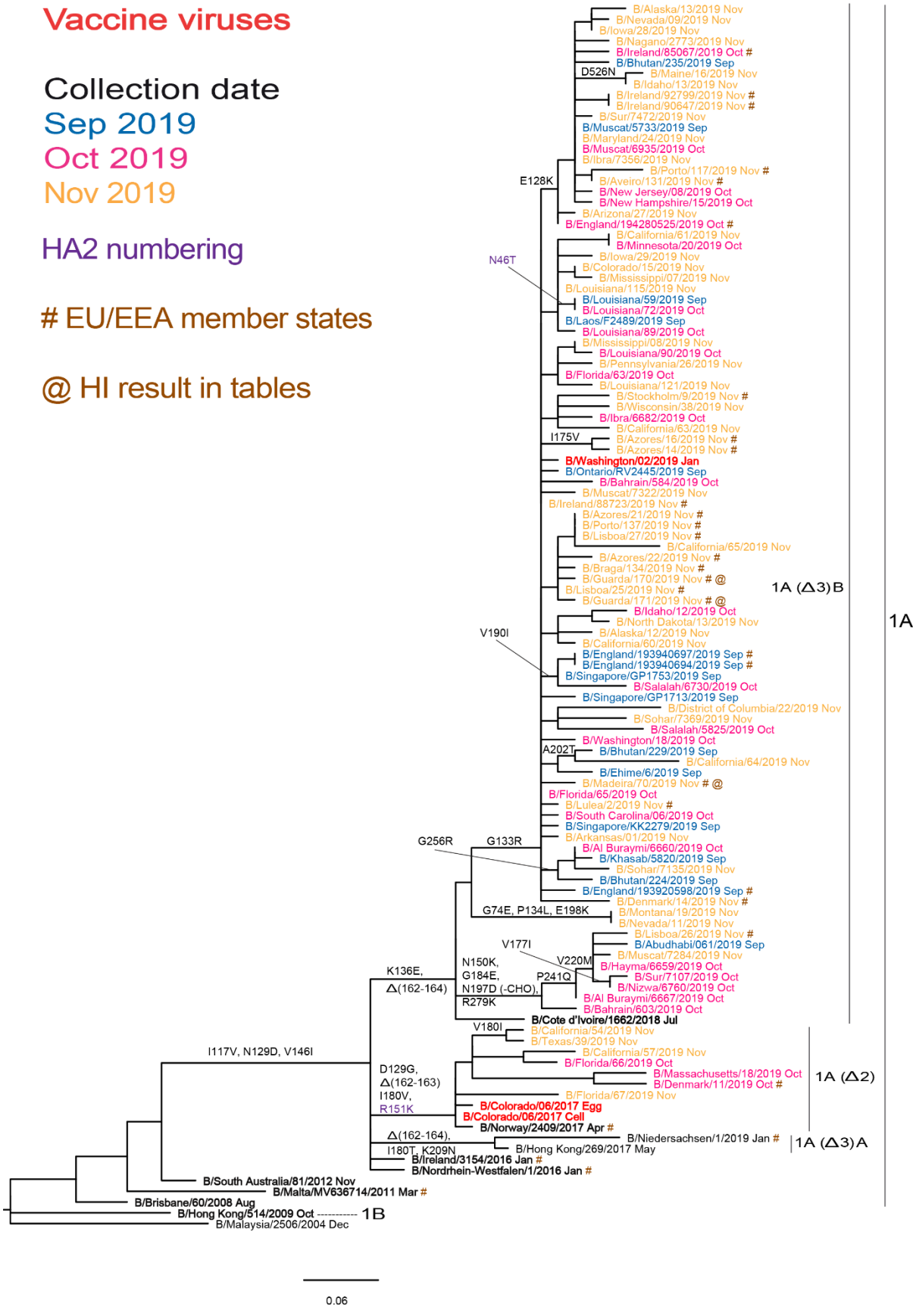


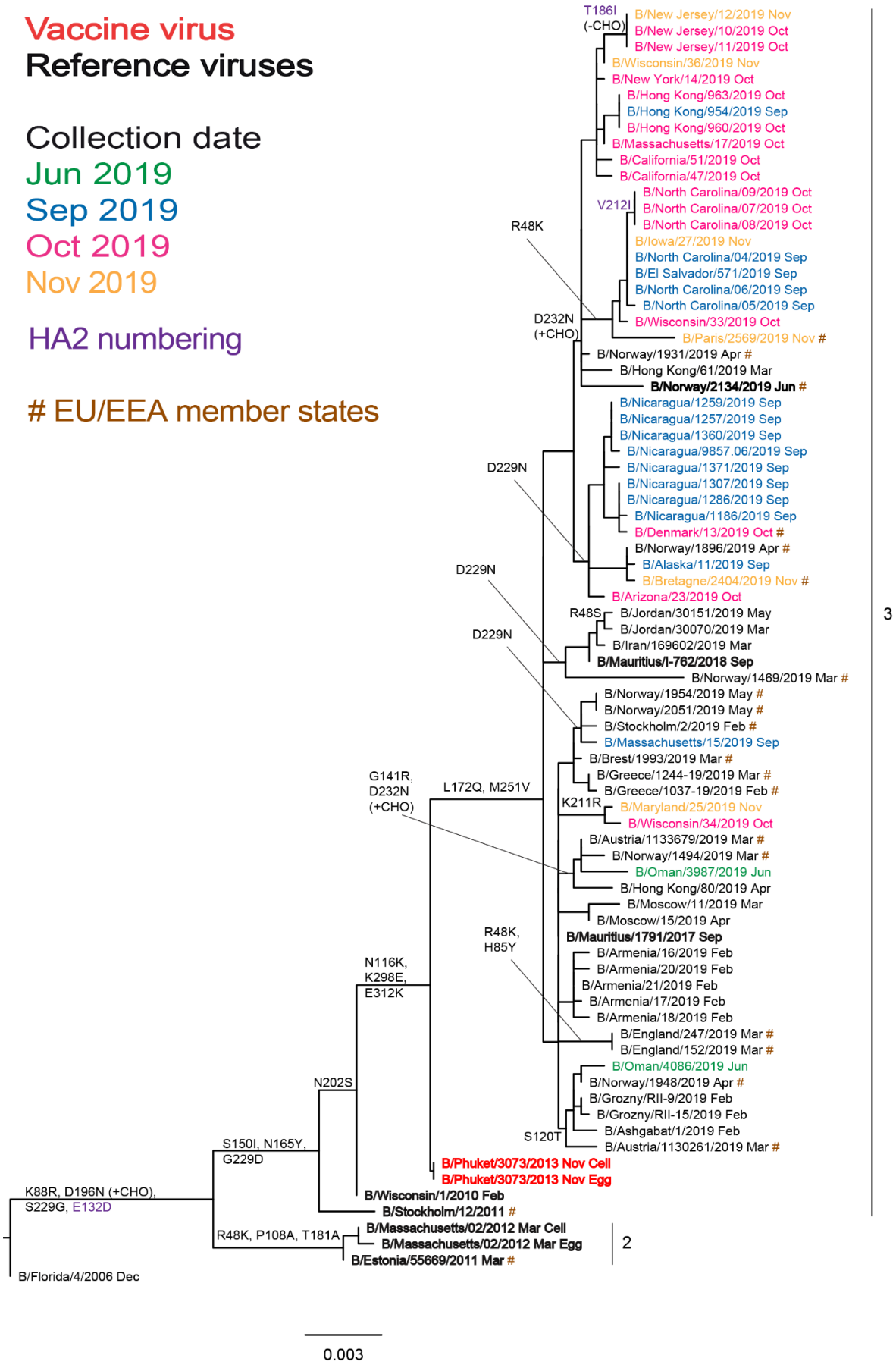
Table 6. **Antigenic analysis of influenza B/Yamagata-lineage viruses by HI**

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
	Passage history			B/Phuket	B/Estonia	B/Mass	B/Mass	B/Wis	B/Stock	B/Phuket	B/Phuket	B/Maur	B/Maur	B/Maur	B/Nor
	Ferret number			3073/13	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13	1791/17	I-762	I-762	2134/19
				Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK	Egg
				SH614[1,3]	F39/17[*2]	F10/16[*2]	F06/17[4]	F36/15[*2]	F05/17[*2]	F27/15[*2]	F25/17[*2]	F04/18[*2]	F05/19[*2]	F05/19[*2]	F48/19[*2]
	Genetic Group			3	2	2	2	3	3	3	3	3	3	3	3
REFERENCE VIRUSES															
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	40	20	80	40	40	40	80	20	40	<	<
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK4	1280	160	320	320	160	160	160	320	160	320	10	10
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	320	10	<	160	40	80	10	80	<	10	40	40
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	1280	<	<	160	80	320	40	320	40	40	40	40
B/Stockholm/12/2011	3	2011-03-28	E4/E2	320	<	<	40	40	80	20	80	10	20	20	20
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	2560	80	320	160	320	160	320	160	160	640	40	40
B/Phuket/3073/2013	3	2013-11-21	E4/E3	640	<	<	80	80	80	20	160	20	40	20	20
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK4	1280	<	40	40	40	80	80	80	80	80	<	<
B/Mauritius/I-762/2018	3	2018-09-02	MDCK1/MDCK3	1280	<	40	40	40	80	80	80	80	160	<	<
B/Norway/2134/2019	3	2019-06-06	E2(am1/a1)	160	<	<	<	<	<	<	<	<	<	2560	
TEST VIRUSES															
B/Norway/2465/2019		2019-11-14	MDCK1	160	<	<	<	<	<	<	<	<	<	640	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
1 < = <40; 2 < = <10; 3 hyperimmune sheep serum
B/Yamagata-lineage virus recommended for use in quadravalent vaccines SH 2019, NH 2019-20 and SH 2020

Vaccine#

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



Summaries of data submitted to TESSy

Genetic characterisation

For the 2019–20 season, as of week 1/2020, 456 viruses had been characterised genetically and ascribed to a genetic clade:

- A total of 97 A(H1N1)pdm09 were subclade 6B.1A5, with 82 falling in subgroup 6B.1A5A represented by A/Norway/3433/2018 and 15 in subgroup 6B.1A5B represented by A/Switzerland/3330/2018. A further six fell in subclade 6B.1A7 represented by A/Slovenia/1489/2019.
- A total of 261 were A(H3N2) viruses, with 93 being subgroup 3C.2a1b+T131K represented by A/South Australia/34/2019, 116 being clade 3C.3a represented by A/Kansas/14/2017, 42 being subgroup 3C.2a1b+T135K-B represented by A/Hong Kong/2675/2019 and 10 being subgroup 3C.2a1b+T135K-A represented by A/La Rioja/2202/2018.
- A total of 10 were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013.
- A total of 82 were B/Victoria-lineage viruses, with 79 being subclade 1A(Δ3)B represented by B/Washington/02/2019 and three being subclade 1A(Δ2) represented by the vaccine virus B/Colorado/06/2017.

Antiviral susceptibility

All of the 185 viruses (67 A(H3N2), 101 A(H1N1)pdm09 and 17 type B) collected during the course of the 2019–20 season tested for susceptibility to neuraminidase inhibitors, oseltamivir and zanamivir, up to week 1/2020, showed normal inhibition (NI).

At the WIC this season, 60 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 15 A(H1N1)pdm09, 28 A(H3N2), 16 B/Victoria-lineage and one B/Yamagata-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 had notified WHO of three cases of human infection with influenza A(H7N9). A description of the characteristics of H7N9 viruses can be found on WHO's 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. This wave 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 25 November 2019 reports that no new cases of human infection had been detected since the 27 September report and indicates that there have been no A(H7N9) detections in samples collected in July and August 2019, according to publicly available reports from animal health authorities in China [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 20 December 2019 and can be found on ECDC's website [12].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 25 November 2019. While no new human cases were reported, detections of various A(H5Nx) subtypes have continued in birds in Africa, Europe and Asia [10]. No new human cases of A(H5N1) infection have been detected since the case in Nepal in March. There have been reports of A(H5N1) infection in domestic birds in Nepal since February 2019, however 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 20 December 2019 and this can be found on ECDC's website [12].

Influenza A(H9N2) virus

The most recent monthly risk assessment of influenza at the human–animal interface, published by WHO on 25 November 2019, reported three new cases of human infection by A(H9N2) viruses (two in China and one in India) since the last update on 27 September 2019 [10]. Direct poultry contact was confirmed in the two cases from China.

WHO CC reports

A description of results generated by the London WHO CC at the WIC, and used at the most recent WHO vaccine composition meeting (held in Geneva, Switzerland, 23–27 September 2019) and previous meetings, can be found at: https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports (accessed 10 January 2020).

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 who submitted sequences directly to WHO CC London.

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