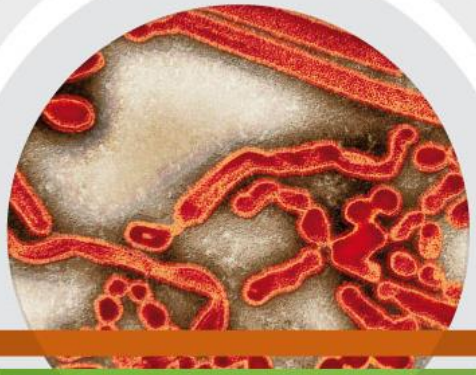


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, December 2017

Summary

This is the second report of the 2017–18 influenza season. As of week 1/2018, nearly 37 000 influenza detections across the WHO European Region have been reported. Types A and B viruses have been detected in equal proportions (~1:1), with A(H3N2) being slightly more prevalent than A(H1N1)pdm09 viruses (1.7:1) and B/Yamagata being significantly more prevalent than B/Victoria viruses (28.7:1).

Ten EU/EEA countries have shared influenza-positive specimens with the London WHO CC since week 40/2017. Of the 280 specimens received, 268 have collection dates after 31 August 2017.

The 20 A(H1N1)pdm09 test viruses characterised antigenically showed good reactivity with antiserum raised against the 2017–18 vaccine virus, A/Michigan/45/2015. The 12 test viruses with collection dates from week 40/2017 genetically characterised at the Crick Worldwide Influenza Centre (WIC), as others from the European Region with collection dates after 31 August 2017 deposited in GISAID, have all fallen in subclade 6B.1, defined by HA1 amino acid substitutions S162N and I216T, the great majority with additional substitutions of S74R, S164T and I295V.

Of 50 viruses successfully recovered to date, only eight (16%) had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir. Six of the eight viruses were recognised well by an antiserum raised against a cell culture-propagated virus genetically similar to the currently used vaccine virus (egg-propagated A/Hong Kong/4801/2014). The antiserum raised against this vaccine virus recognised only the minority (25%) of viruses well. While genetic analysis of these viruses is pending, others from the European Region with collection dates after 31 August 2017 as deposited in GISAID, fall within the 3C.2a genetic clade, with a minority falling in the 3C.2a1 genetic subclade. Of the 14 viruses with collection dates from week 40/2017 characterised at the WIC, 10 were clade 3C.2a and four subclade 3C.2a1.

Of the five B/Victoria-lineage viruses tested, three reacted well with post-infection ferret antisera raised against tissue culture-propagated surrogates of B/Brisbane/60/2008. The remaining two, one each from France and Spain, reacted well with an antiserum raised against tissue culture-propagated B/Norway/2409/2017 that carries an HA1 double amino acid deletion (Δ162-163). Of the four viruses characterised genetically at the WIC, three fell within clade 1A (including the only one with a collection date after week 40/2017) while the fourth fell within the subgroup (1A(Δ2)) carrying the HA1 double amino acid deletion.

All 16 B/Yamagata viruses characterised antigenically reacted well (within fourfold of the homologous titre) with post-infection ferret antiserum raised against egg-propagated B/Phuket/3073/2013, the recommended vaccine virus for use in quadrivalent vaccines for the northern hemisphere 2017–18 and for trivalent vaccines in the southern hemisphere 2018 seasons. The nine viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others recently circulating in the European Region and reported to GISAID, fall within clade 3.

This report was prepared by Rod Daniels, Vicki Gregory, Burcu Ermetal, Aine Rattigan and John McCauley for the European Centre for Disease Prevention and Control (ECDC) under an ECDC framework contract.

Suggested citation: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, December 2017. Stockholm: ECDC; 2018.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy since the start of the 2017–18 season (weeks 40/2017–1/2018), compared to numbers reported for the 2016–17 season. Nearly 37 000 detections have been reported, an increase of approximately 34 000 compared to the situation as of week 48/2017, with equal proportions of types A and B viruses. Of the type A viruses subtyped (n = 7 493) and the type B viruses ascribed to lineage (n = 1 398), A(H3N2) still prevailed over A(H1N1)pdm09, at a ratio of 1.7:1, and B/Yamagata prevailed over B/Victoria, at a ratio of 28.7:1; these ratios represent a decrease and an increase in relative prevalence, respectively, compared to the situation as of week 48/2017 (as summarised in the November 2017 report[1]). Compared to the 2016–17 season, significant numbers of influenza type B viruses have been detected early in the 2017–18 season, and the dominance of B/Yamagata over B/Victoria has increased from 2.7:1, seen in the 2016–2017 winter, to 28.7:1 currently reported; with these early type B virus detections the ratio of type A to type B detections has decreased significantly compared to the 2016–17 season (~1:1 from 6.5:1), and of the A subtyped viruses, a significant increase in the proportion of A(H1N1)pdm09 has been seen (36.4% in 2017–2018 compared to 1.1% in 2016–2017).

Since week 40/2017, 12 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC) from ten national influenza centres in the EU/EEA. These packages contained 280 specimens, a mix of clinical samples and virus isolates, with specimen collection dates after May 2017 (Table 2). The majority (59%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 1.4:1. Of the 116 type B specimens received (41% of the specimens), 23 were B/Victoria-lineage and 65 were B/Yamagata-lineage. The antigenic and genetic properties of influenza viruses, characterised since the November 2017 report, are presented and discussed in this surveillance report. Since six of the shipments were received after week 50/2017, the great majority of specimens have not yet been characterised (in process: Table 2).

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2017–18 season (weeks 40/2017–1/2018)

	Cumulative number of detections			Totals*		Totals for 2016-17 season*		
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Number	%	Ratios
Influenza A	**1 239**	**17 022**	**18 261**	**49.6**	**1.0:1**	**126 614**	**86.6**	**6.5:1**
A(H1N1)pdm09	672	2 056	2 728	36.4		591	1.1	
A(H3N2)	455	4 310	4 765	63.6	1.7:1	53 101	98.9	89.8:1
A not subtyped	166	10 656	10 822			**72 922**		
Influenza B	**2 413**	**16 065**	**18 478**	**50.4**		**19 570**	**13.4**	
Victoria lineage	33	14	47	3.4		749	27.1	
Yamagata lineage	696	655	1 351	96.6	28.7:1	2 016	72.9	2.7:1
Lineage not ascribed	1 684	15 396	17 080			16 805		
Total detections (total tested)	**3 706 (16 841)**	**33 087 (227 879)**	**36 793 (244 720)**			**146 184 (686 477)**		

* 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.

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2017. Stockholm: ECDC; 2017. Available from: https://ecdc.europa.eu/sites/portal/files/documents/ERLI-Net-report-Nov-2017.pdf

Table 2. Summary of clinical samples and virus isolates, contained in packages received from EU/EEA Member States since week 40/2017

MONTH*	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country		Number received	Number propagated	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated	Number received	Number propagated[1]	Number received	Number propagated[1]
2017														
JUNE														
Norway	3										2	2	1	1
Sweden	1			1	1									
JULY														
Norway	1												1	1
Sweden	1					1	0	1						
AUGUST														
Finland	1					1	in process							
France	1			1	in process									
Norway	4			3	2						1	0		
SEPTEMBER														
Finland	2					2	in process							
France	4			2	in process						1	1	1	1
Germany	1												1	in process
Norway	2			1	1								1	1
Spain	1			1	1									
Sweden	1					1	0	1						
United Kingdom	2					1	0	1			1	1		
OCTOBER														
Finland	1					1	in process							
France	7			4	in process	2	2	0					1	1
Norway	21			3	2	15	in process						3	in process
Slovenia	1					1	in process							
Spain	7			1	1	5	in process						1	in process
Sweden	3					3	2	1						
United Kingdom	7			2	2	3	in process				1	1	1	1
NOVEMBER														
Austria	1	1	0											
Finland	7					3	in process				1	in process	3	in process
France	15			7	in process	4	in process				1	1	3	3
Germany	6			2	in process	2	in process						2	in process
Latvia	6			1	1	3	3						2	in process
Norway	21			3	in process	10	in process				1	in process	7	in process
Slovenia	2												2	in process
Spain	24			1	in process	5	in process		6	in process	5	in process	7	in process
Sweden	7					5	in process						2	in process
United Kingdom	4					3	in process						1	in process
DECEMBER														
Austria	37			17	in process	8	in process		12	in process				
Finland	1					1	in process							
Germany	17			5	in process	5	in process						7	in process
Latvia	2			2	2									
Norway	10			2	in process	3	in process						5	in process
Slovenia	12			4	in process	3	in process				3	in process	2	in process
Spain	31			3	in process	4	in process		7	in process	6	in process	11	in process
2018														
JANUARY														
Slovenia	5	2	in process						3	in process				
	280	3	0	66	13	95	7	4	28	0	23	6	65	9
		1.1%		23.6%		33.9%			10.0%		8.2%		23.2%	
10 Countries		58.6%							41.4%					

*** Month indicates the months in which the clinical specimens were collected**
1. Propagated to sufficient titre to perform HI assay
2. Propagated to sufficient titre to perform HI assay in presence of 20nM oseltamivir; numbers in red indicate viruses recovered but with insufficient HA titre to permit HI assay

Influenza A(H1N1)pdm09 virus analyses

Results of haemagglutination inhibition (HI) analyses of viruses performed since the November 2017 report are shown in Table 3. All 20 A(H1N1)pdm09 test viruses antigenically characterised were similar to the vaccine virus for the present northern hemisphere 2017–18 influenza season, A/Michigan/45/2015 [1], with all viruses being recognised at titres within twofold of the titre of the antiserum for the homologous virus. The antiserum raised against A/California/7/2009, the vaccine virus recommended for use for the northern hemisphere 2016–17 influenza season, recognised all but two of the test viruses at titres within twofold, and all within fourfold, of the homologous titre of the antiserum. Similarly, all but three of the test viruses were recognised by the antiserum panel at titres within twofold of the titres of the antisera with their respective homologous viruses; the three fourfold reductions were observed with antiserum raised against A/Lviv/N6/2009.

Genetic analyses of many test viruses are in process but the HA sequences of A(H1N1)pdm09 viruses from European countries (as defined in GISAID) with collection dates after 31 August 2017 all fall within subclade 6B.1 (Figure 1), as shown for 10 of the antigenically characterised viruses (Table 3), as was observed for all EU/EEA A(H1N1)pdm09 viruses characterised throughout the 2016–17 season. The majority of HA genes of recently circulating viruses from EU/EAA countries cluster in a genetic subgroup defined by HA1 amino acid substitutions of S74R, S164T and I295V (Figure 1).

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

Viruses	Other information[$]	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera: A/Mich 45/15 Egg NIB F42/16[*1] 6B.1	A/Cal 7/09 Egg F06/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F14/13[*1]	A/Astrak 1/11 MDCK F22/13[*1] 5	A/St. P 27/11 Egg F26/14[*1] 6	A/St. P 100/11 Egg F24/11[*1] 7	A/HK 5659/12 MDCK F30/12[*1] 6A	A/Sth Afr 3626/13 Egg F03/14[*1] 6B	A/Slov 2903/2015 Egg F02/16[*2] 6B.1	A/Israel Q-504/15 MDCK F08/16[*2] 6B.2
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	1280	640	320	320	640	640	2560	640	640	1280	1280
A/California/7/2009	clone38-32		2009-04-09	E3/E3	1280	1280	640	640	1280	1280	2560	1280	1280	2560	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	40	320	320	40	40	80	40	40	80	<
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	80	640	640	80	160	160	160	160	320	80
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	320	640	320	320	640	640	2560	640	640	1280	640
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	2560	640	1280	2560	1280
A/St. Petersburg/100/2011		7	2011-03-14	E1/E4	640	320	320	320	640	320	1280	640	320	1280	640
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	160	160	160	80	320	160	640	320	320	640	160
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	320	640	640	640	640	1280	640	1280	1280	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	640	320	320	1280	640	2560	1280	1280	2560	1280
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	320	640	320	2560	640	640	1280	1280
TEST VIRUSES															
A/Stockholm/34/2017			2017-06-01	MDCK1/MDCK1	640	320	320	320	640	320	1280	640	640	1280	640
A/Andalucia/2283/2017			2017-09-13	SIAT1/MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280
A/Norway/3168/2017		6B.1	2017-09-18	MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	5120	1280
A/England/69/2017		6B.1	2017-10-01	MDCK2/MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	5120	2560
A/England/75/2017		6B.1	2017-10-06	SIAT1/MDCK1	640	640	640	160	640	320	2560	640	640	2560	640
A/Paris/1458/2017		6B.1	2017-10-17	MDCK1/MDCK1	1280	640	640	320	640	640	2560	1280	1280	2560	1280
A/Paris/1459/2017		6B.1	2017-10-20	MDCK1/MDCK1	640	640	320	320	640	320	1280	640	640	1280	640
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK1	1280	1280	640	640	1280	640	2560	1280	1280	5120	2560
A/Haute Normandie/1469/2017		6B.1	2017-10-26	MDCK1/MDCK1	2560	2560	640	640	2560	1280	5120	1280	1280	5120	2560
A/Andalucia/2280/2017			2017-10-26	SIAT1/MDCK1	1280	1280	640	640	1280	640	2560	1280	1280	2560	2560
A/Lyon/2044/2017			2017-11-06	MDCK2/MDCK1	640	640	320	320	640	320	1280	640	640	2560	1280
A/Nord Pas de Calais/1505/2017		6B.1	2017-11-08	MDCK2/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640
A/Paris/1516/2017		6B.1	2017-11-11	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640
A/Paris/1509/2017		6B.1	2017-11-13	MDCK2/MDCK1	640	320	320	320	640	320	1280	640	640	2560	1280
A/Clermont-Ferrand/2061/2017			2017-11-13	MDCK2/MDCK1	640	640	640	320	1280	320	2560	640	1280	2560	1280
A/Norway/3498/2017			2017-11-16	MDCK1/MDCK1	1280	640	640	320	1280	640	2560	640	640	2560	1280
A/Bourgoin-Jallieu/2175/2017			2017-11-17	MDCK2/MDCK1	640	1280	1280	640	1280	640	2560	1280	1280	2560	1280
A/Latvia/11-082656/2017			2017-11-30	MDCK1/MDCK1	640	640	640	320	640	320	1280	640	640	1280	1280
A/Latvia/12-027589/2017			2017-12-11	MDCK1/MDCK1	1280	640	640	320	1280	640	2560	640	640	2560	1280
A/Latvia/12-027887/2017			2017-12-11	MDCK1/MDCK1	640	640	640	320	640	320	1280	640	640	2560	1280

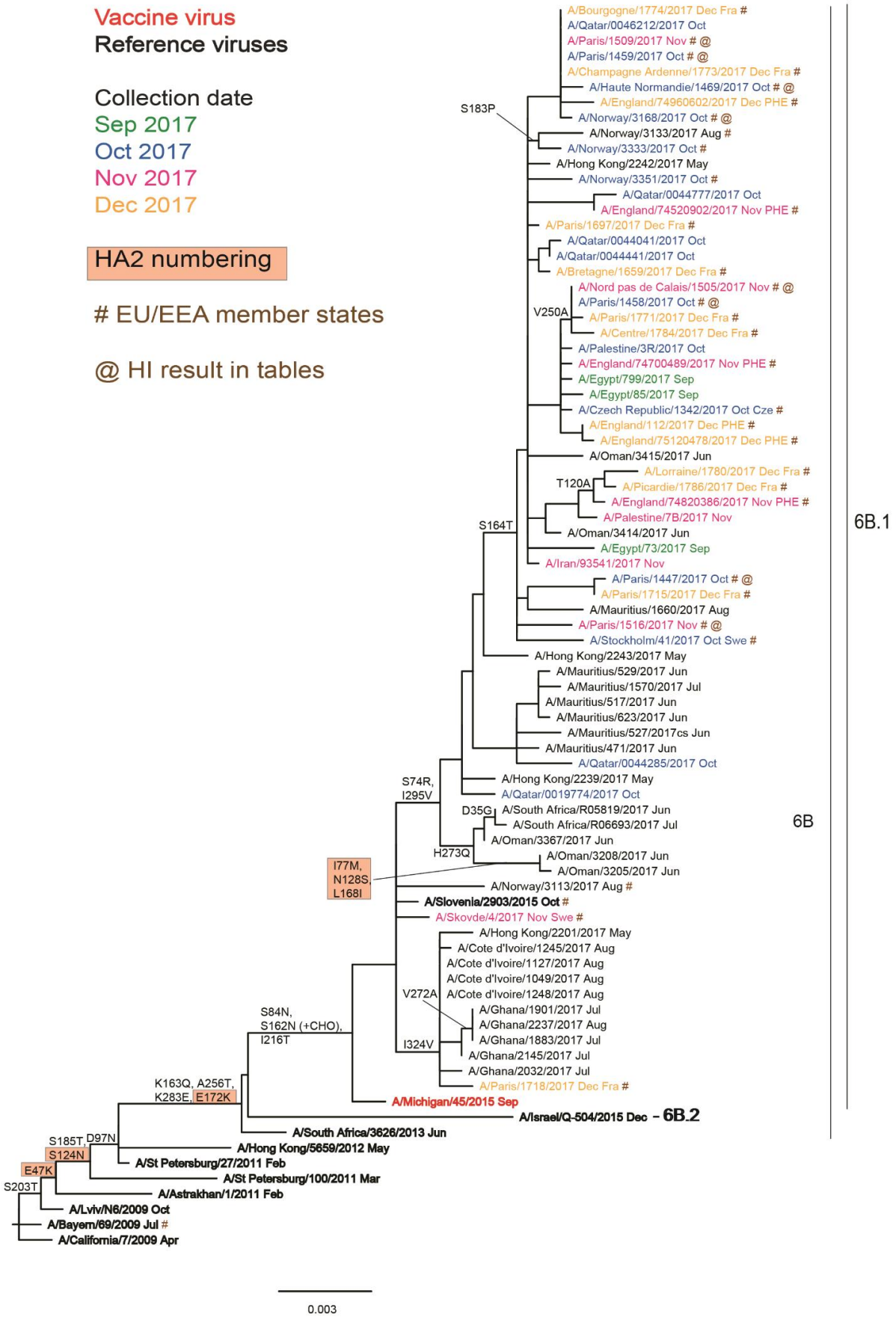
* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80

Vaccine

[$] Virus clone indicated and significant HA1 amino acid substitutions

Sequences in phylogenetic tree

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.

Most of the 89 A(H3N2) virus specimens with collection dates after week 40/2017 are in process for antigenic and genetic characterisation. However, of those successfully isolated to date (n = 50), as shown by positive neuraminidase activity, only eight (16%) had sufficient HA activity in the presence of 20nM oseltamivir to allow antigenic analysis by HI assay (Table 4).

Of the eight viruses able to be analysed by HI assay, only two were recognised by the antiserum raised against the currently used vaccine virus, egg-propagated A/Hong Kong/4801/2014, at titres within fourfold of the titre of the antiserum for the homologous virus. However, the converse was observed with an antiserum raised against cell culture-propagated A/Hong Kong/5738/2014, a virus closely related genetically to A/Hong Kong/4801/2014, which recognised six viruses at titres within twofold of the homologous titre of the antiserum; the other two viruses, A/Latvia/11-046717/2017 and A/Latvia/11-060108/2017 were recognised less well. Similarly, antisera raised against cell culture-propagated cultivars of the former vaccine virus A/Switzerland/9715293/2013 and A/Stockholm/6/2014, both 3C.3a viruses, also recognised A/Latvia/11-046717/2017 and A/Latvia/11-060108/2017 at titres lower than they recognised the other six test viruses: these six were all recognised at titres within twofold and fourfold, respectively, of the titres of the antisera for the homologous viruses.

Six antisera for which no homologous titres are given, due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, were used. A/Norway/4293/2017, A/Norway/4465/2017 and A/Hong Kong/4018/2017 all had HA genes that fell into a genetic subgroup within the 3C.2a clade encoding the amino acid substitutions T131K, R142K and R261Q in HA1. These antisera recognised three of the test viruses at high titres of 640 or 1280 but each recognised A/Stockholm/44/2017, A/Latvia/11-046717/2017 and A/Latvia/11-060108/2017 poorly, and A/Uppsala/2/2017 and A/Stockholm/44/2017 were recognised at intermediate titres. A/Oman/2585/2016, A/Norway/4436/2016 and A/Greece/4/2017 all had HA genes that fell into the 3C.2a1 subclade. These three antisera, respectively, recognised all the test viruses but for A/Latvia/11-046717/2017, recognised all viruses but for A/Latvia/11-046717/2017 and A/Latvia/11-060108/2017 and recognised all the test viruses at titres similar to the titres of the antisera for the majority of the panel of reference viruses.

Antisera raised against the egg-propagated cultivars of A/Norway/4465/2017 and A/Singapore/INFIMH-16-0019/2016, 3C.2a1 subclade viruses, were used. The antiserum raised against the egg-propagated cultivar of A/Singapore/INFIMH-16-0019/2016 recognised all eight test viruses at titres within fourfold of the titre of the antiserum for the homologous virus, seven at titres twofold lower than, equal to or twofold higher than the homologous titre of the antiserum. The antiserum raised against A/Norway/4465/2017 recognised none of the test viruses at a titre within fourfold of the titre of the antiserum for the homologous virus.

Phylogenetic analysis of the HA genes of representative A(H3N2) viruses from Europe with recent collection dates, after 31 August 2017 as available in GISAID, is shown in Figure 2. Viruses in clades 3C.2a and 3C.3a have been in circulation since the 2013–14 northern hemisphere influenza season, with clade 3C.2a viruses predominating since the 2014–15 influenza season and continuing to predominate in recent months (Figure 2). Clusters of viruses have emerged in both clades and one of these clusters has been designated subclade 3C.2a1. Amino acid substitutions that define these subdivisions and subclades are:

- 3C.2a: **N145S** in **HA1**, and **D160N** in **HA2**, which defined clade 3C.2, plus **L3I**, **N144S** (resulting in the loss of a potential glycosylation site), **F159Y**, **K160T** (in the majority of viruses, resulting in the gain of a potential glycosylation site), **N225D** and **Q311H** in **HA1**, e.g. A/Hong Kong/4801/2014
- 3C.2a1: those in 3C.2a, plus **N171K** in **HA1** and **I77V** and **G155E** in **HA2**, e.g. A/Bolzano/7/2016 and A/Iasi/206625/2017, often with **N121K** in **HA1**, e.g. A/Scotland/63440583/2016, A/Singapore/INFIMH-16-0019/2016 and A/Bulgaria/471/2017
- 3C.3a: **T128A** (resulting in the loss of a potential glycosylation site), **R142G** and **N145S** in **HA1** which defined clade 3C.3 plus **A138S**, **F159S** and **N225D** in **HA1**, many with **K326R**, e.g. A/Switzerland/9715293/2013.

Currently circulating viruses fall into genetic groups within both clade 3C.2a and subclade 3C.2a1, with the majority of recently circulating viruses in EU/EEA countries falling in clade 3C.2a predominantly in a cluster of viruses defined by **T131K**, **R142K** and **R261Q** substitutions in **HA1**. The location of A/Singapore/INFIMH-16-

[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: 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: http://www.ecdc.europa.eu/en/publications/Publications/ERLI-Net report November 2014.pdf

0019/2016 (3C.2a1), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2018 season [2], is indicated in Figure 2.

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

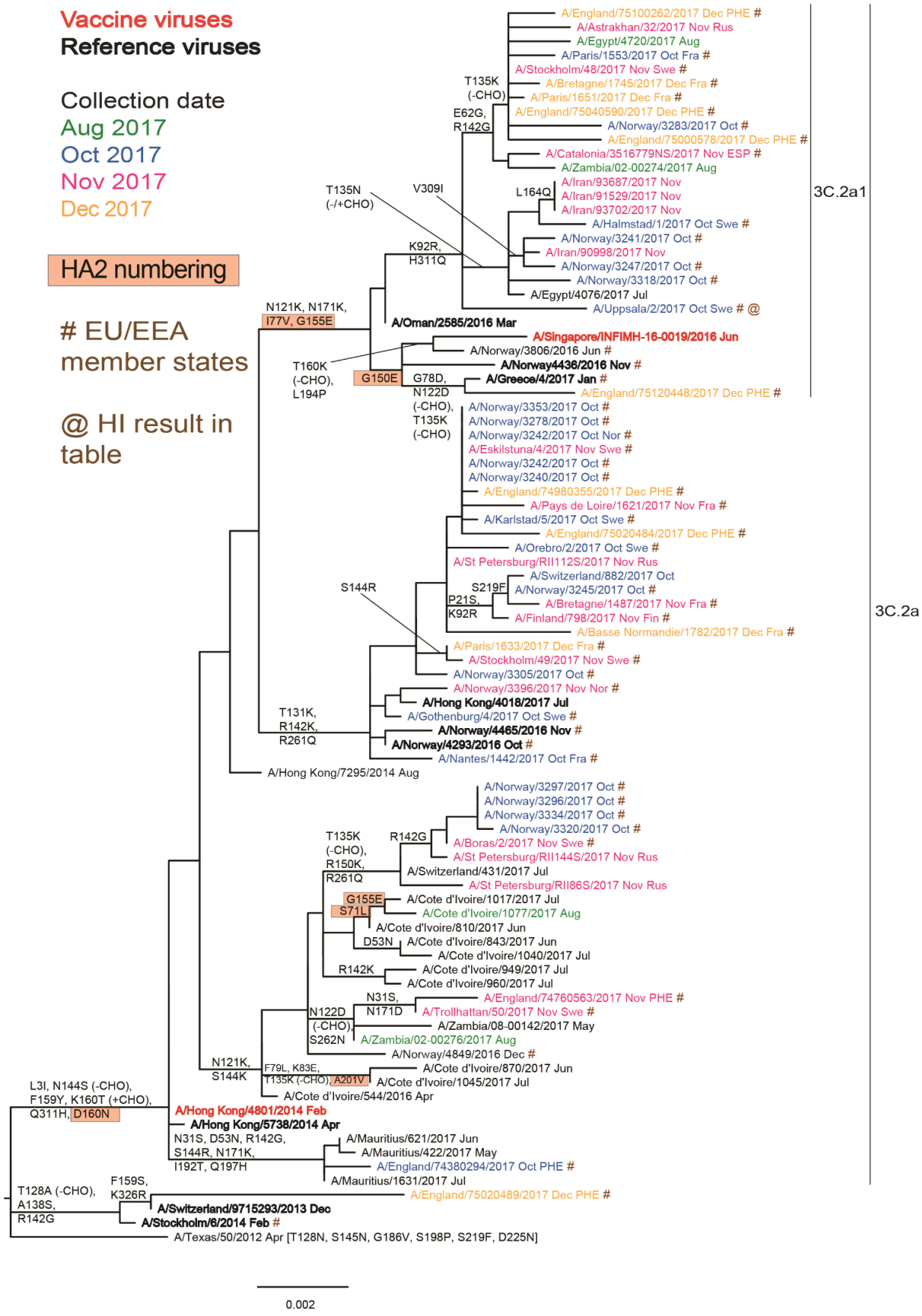
Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera											
					A/Stock 6/14 SIAT	A/Switz 9715293/13 SIAT	A/HK 5738/14 MDCK	A/HK 4801/14 Egg	A/Nor 4293/17 SIAT	A/Nor 4465/17 SIAT	A/Nor 4465/17 Egg	A/HK 4018/17 SIAT	A/Oman 2585/16 SIAT	A/Nor 4436/16 SIAT	A/Greece 4/17 SIAT	A/Singapore 0019/16 Egg 10^{-4}
		Ferret number			F14/14[*1]	F18/15[*1]	F30/14[*1]	F42/15[*1]	F04/17[*1]	F11/17[*1]	F12/17[*1]	F48/17[*1]	NIB F50/16[*1]	F03/17[*1]	F27/17[*1]	F41/17[*1]
		Genetic group			3C.3a	3C.3a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a1	3C.2a1	3C.2a1	3C.2a1
REFERENCE VIRUSES																
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT2	640	160	160	160	320	80	40	320	320	320	160	320
A/Switzerland/9715293/2013		3C.3a	2013-12-06	SIAT1/SIAT3	320	160	160	40	80	40	<	160	160	320	80	80
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	320	80	320	80	320	160	80	320	320	320	160	320
A/Hong Kong/4801/2014	isolate 1	3C.2a	2014-02-26	E6/E2	40	40	320	640	640	320	1280	320	320	160	320	2560
A/Norway/4465/2016		3C.2a	2016-11-07	E6	<	<	160	640	2560	2560	2560	2560	320	160	640	640
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-06-14	E5/E2	<	<	40	160	40	40	320	80	160	80	160	640
TEST VIRUSES																
A/Uppsala/2/2017		3C.2a1	2017-10-03	MDCK1/SIAT1	160	80	160	40	160	160	<	160	160	320	160	320
A/Bretagne/1413/2017		3C.2a	2017-10-09	MDCK1/SIAT3	320	80	160	80	640	1280	160	1280	320	320	160	320
A/Nantes/1441/2017		3C.2a	2017-10-10	MDCK2/SIAT2	320	80	160	80	640	640	160	640	320	320	160	320
A/Stockholm/43/2017		3C.2a1	2017-10-17	MDCK2/SIAT1	160	80	160	80	80	160	40	160	160	160	160	320
A/Latvia/11-002559/2017			2017-11-01	MDCK2/SIAT1	160	80	160	80	640	640	160	640	160	160	160	160
A/Stockholm/44/2017		3C.2a1	2017-11-03	MDCK1/SIAT1	160	80	160	40	80	40	<	80	160	160	160	320
A/Latvia/11-046717/2017			2017-11-17	MDCK2/SIAT1	40	40	40	160	40	40	320	80	80	80	160	640
A/Latvia/11-060108/2017			2017-11-22	MDCK2/SIAT1	40	40	80	320	80	80	320	80	160	80	160	1280
								Vaccine NH 2017-18								Vaccine SH 2018

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

ND = not done

Sequences in phylogenetic tree

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



Influenza B virus analyses

A total of 116 influenza type B-positive specimens with collection dates after May 2017 have been received, with 88 being ascribed to a lineage: 23 B/Victoria-lineage and 65 B/Yamagata (Table 2).

Influenza B – Victoria lineage

HI results for the five tissue culture-propagated test viruses analysed since the November 2017 report are shown in Table 5. Only one test virus reacted with post-infection ferret antiserum raised against B/Brisbane/60/2008 egg-propagated vaccine virus at a titre within twofold of the serum's homologous titre; this virus, B/England/71/2017, showed polymorphism (NK[A/T]) at the 197-199 N-linked glycosylation site which is commonly lost on egg-isolation. Similar reactivity profiles were seen with post-infection ferret antisera raised against all other egg-propagated reference viruses (B/Malaysia/2506/2004, B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012). Conversely, three of the test viruses reacted within twofold of the respective homologous titres with antisera raised against clade 1A tissue culture-propagated surrogates for B/Brisbane/60/2008; these sera were raised against B/Formosa/V2367/2012, B/Ireland/3154/2016 and B/Nordrhein-Westfalen/1/2016. The same three test viruses showed reactivity with an antiserum raised against a cell culture-propagated clade 1B virus, B/Hong Kong/514/2009, one within twofold and two within fourfold of the homologous titre. Two of the test viruses, B/Clermont-Ferrand/1894/2017 and B/Galicia/2465/2017 from France and Spain respectively, showed good reactivity only with antiserum raised against cell culture-propagated B/Norway/2409/2017, a virus carrying a double amino acid deletion in HA1, Δ162-163 (1A(Δ2)) (Table 5). The B/Galicia/2465/2017 virus has been shown to fall in the 1A(Δ2) genetic group.

Full-length HA gene sequences derived from 66 B/Victoria lineage viruses with collection dates after 31 August 2017 have been deposited in GISAID. These recently circulating viruses, like those earlier viruses from Europe and elsewhere, continue to have HA genes that fall in the B/Brisbane/60/2008 clade (clade 1A; Figure 3). The great majority of viruses, with collection dates since October 2015, fall in a major subcluster defined by **HA1** amino acid substitutions **I117V**, **N129D** and **V146I** within clade 1A. Two new groups have emerged with deletions in the HA gene. For one group, the HA gene encodes an HA with deletion of residues 162 and 163 of HA1 (exemplified by B/Norway/2409/2017; Δ162-163), with recently circulating examples being detected in Canada, Trinidad, the USA and now France and Spain while the other group encodes an HA with deletion of residues 162, 163 and 164 of HA1 (exemplified by B/Hong Kong/269/2017; Δ162-164). The Δ162-163 viruses have additional substitutions **D129G, I180V** in **HA1** and **R151K** in **HA2** and the Δ162-164 viruses from Hong Kong have additional substitutions **I180T** and **K209N** in **HA1**.

Influenza B – Yamagata lineage

HI results for 16 B/Yamagata-lineage test viruses analysed since the November 2017 report are shown in Table 6. The six viruses analysed genetically to date belong to genetic clade 3, the B/Wisconsin/1/2010-B/Phuket/3073/2013 clade.

The antiserum raised against egg-propagated B/Phuket/3073/2013, recommended recently for inclusion in trivalent vaccines for the southern hemisphere 2018 season [2], recognised all 16 test viruses at titres within fourfold of the titre of the antiserum with the homologous virus and two within twofold. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised all test viruses at titres within fourfold of the homologous titre of the antiserum and 13 within twofold. An antiserum raised against a former vaccine virus, egg-propagated B/Wisconsin/1/2010 with a homologous titre of 160, recognised 14 of the test viruses at titres within fourfold of the homologous titre of the antiserum, while two viruses (B/Paris/1502/2017 and B/Lorraine/1510/2017) were not recognised. Antisera raised against egg-propagated B/Stockholm/12/2011 and B/Hong Kong/3417/2014 both gave homologous titres of 80 and recognised all test viruses at titres within fourfold of the homologous titre with 16 and one, respectively, being recognised within twofold.

Antisera raised against both egg- and cell culture-propagated clade 2 viruses, generally recognised none of the test viruses well (most were recognised at titres at least eightfold reduced compared to the respective homologous titres of the antisera); however, the antisera raised against cell culture-propagated B/Estonia/55669/2011 and egg-propagated B/Massachusetts/02/2012 recognised seven and two test viruses, respectively, at titres within fourfold of the titres of the antisera with the homologous viruses.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses, including recently circulating ones. Worldwide, the vast majority of HA genes from viruses collected in 2017 have fallen in clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade. The vast majority of viruses, including those with collection dates after 31 August from Europe as deposited in GISAID, fall in a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions.

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 Sh 539, 540, 543, 544, 570, 571, 574[1,3]	B/Mal 2506/04 Egg F-41/14[*2]	B/Bris 60/08 Egg NIB F52/16[*2]	B/Malta 636714/11 Egg F29/13[*2]	B/Jhb 3964/12 Egg F04/16[*2]	B/For V2367/12 MDCK F09/16[*2]	B/Sth Aus 81/12 Egg F42/16[*2]	B/HK 514/09 MDCK F09/13[*2]	B/Ireland 3154/16 MDCK F15/16[*2]	B/Nord-West 1/16 MDCK F16/16[*2]	B/Nor 2409/17 MDCK F40/17[*2]
	Ferret number														
	Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A	1A
REFERENCE VIRUSES															
B/Malaysia/2506/2004		2004-12-06	E3/E6	2560	640	320	80	40	160	80	20	<	<	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	160	640	320	320	320	640	80	80	80	<
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	160	640	320	160	320	320	40	40	40	<
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	640	1280	1280	1280	1280	1280	320	320	320	20
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	80	640	320	160	320	320	80	80	80	<
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	160	640	320	320	320	640	80	80	80	<
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	10	80	80	80	320	40	160	160	160	<
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	40	40	80	160	40	40	160	160	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	1280	<	40	40	40	160	10	40	80	80	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK2	160	<	<	<	<	<	10	<	20	20	160
TEST VIRUSES															
B/Clermont-Ferrand/1894/2017		2017-09-12	MDCK2/MDCK1	160	<	<	<	<	<	10	<	10	10	80
B/England/66/2017	1A	2017-09-12	SIAT1/MDCK1	2560	10	80	40	80	160	20	80	80	80	<
B/England/71/2017	NK(A/T)	2017-10-11	SIAT1/MDCK1	5120	80	640	160	160	160	320	40	80	40	<
B/Centre/1582/2017	1A	2017-11-27	MDCK1	2560	10	40	40	80	160	80	40	80	80	<
B/Galicia/2465/2017	1A(Δ2)	2017-12-02	SIAT1/MDCK1	160	<	<	<	<	<	10	<	10	10	80

Vaccine

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum

[$] Polymorphism resulting in partial loss of the HA1 197-199 glycosylation site

Sequences in phylogenetic tree

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

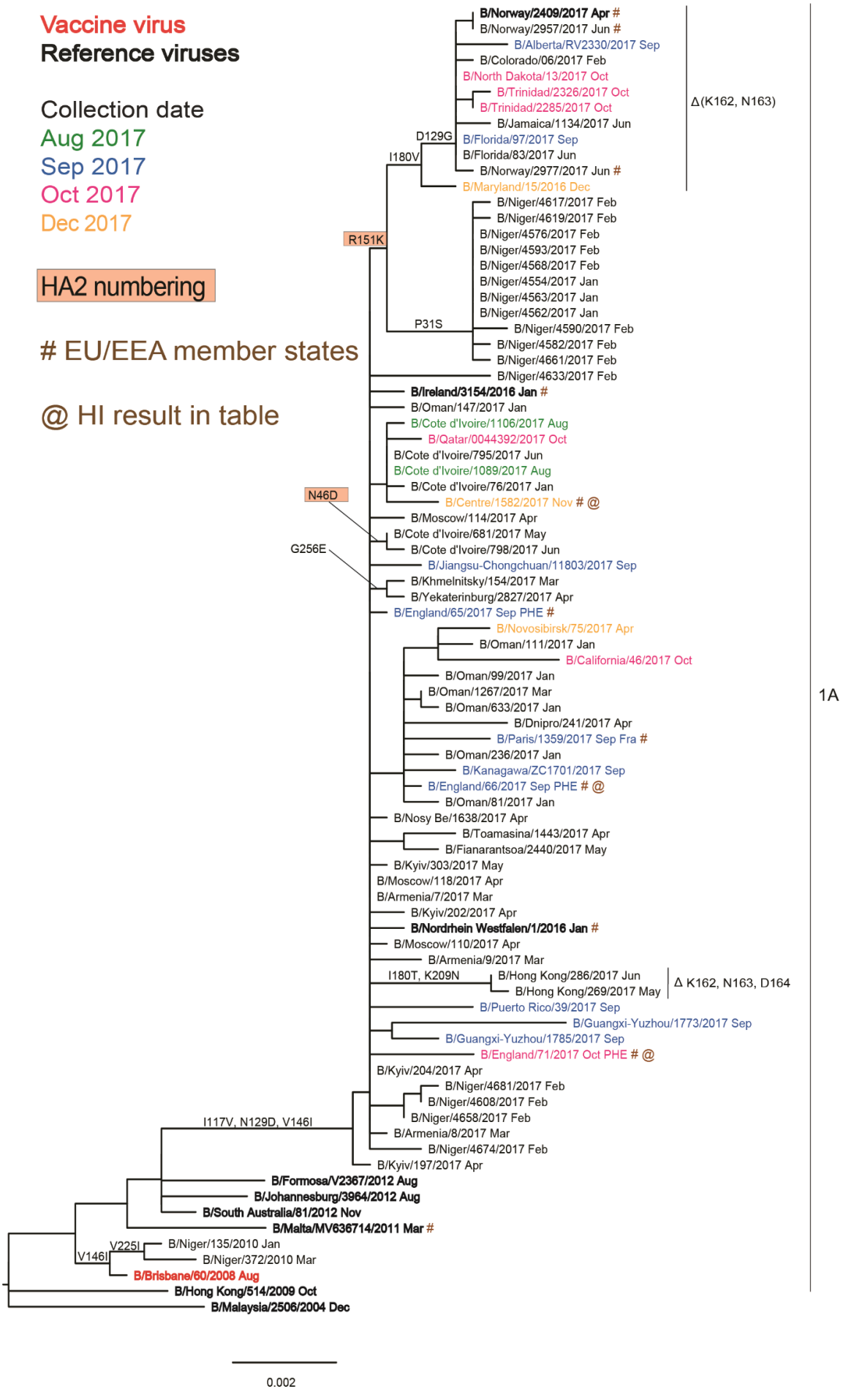


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

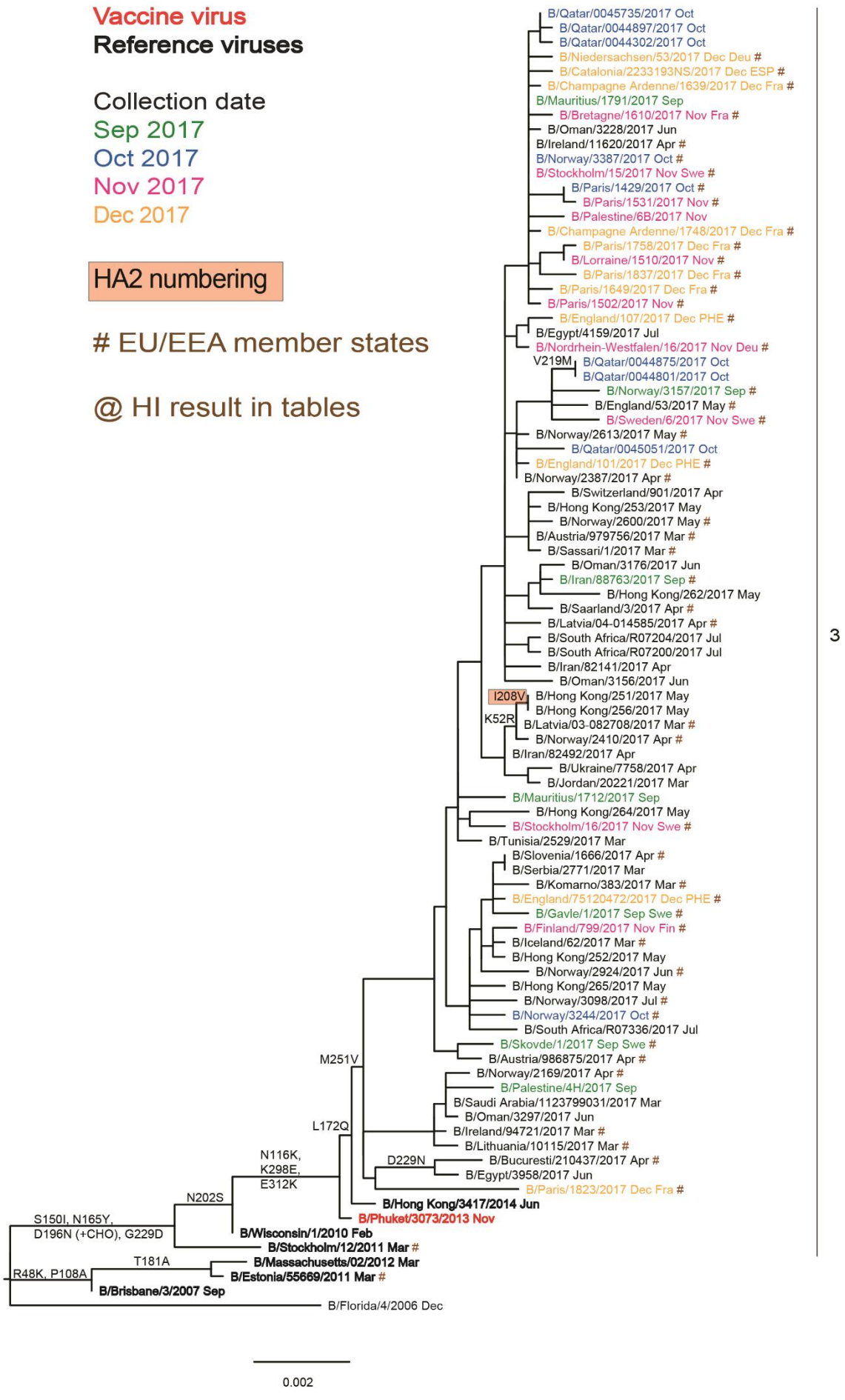
Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg	B/HK 3417/14 Egg
		Ferret number			SH614*1,3	F38/14*2	F27/13*2	F05/15*2	F16/14*2	F36/15*2	F06/15*2	F27/15*2	NIB F51/16*2	St Judes F716/14*2
		Genetic Group			3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	640	320	320	1280	320	320	40	1280	80
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	1280	1280	640	320	160	80	20	40	80	20
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	2560	320	640	640	1280	320	160	80	640	80
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	640	160	80	640	80	80	20	320	40
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	160	40	20	320	160	80	40	640	40
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	80	40	10	160	80	80	20	160	20
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	5120	80	160	160	160	160	80	160	320	40
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	80	40	20	160	160	80	20	640	20
B/Hong Kong/3417/2014		3	2014-06-04	E4/E3	1280	40	40	10	80	80	40	20	160	80
TEST VIRUSES														
B/Lyon-Croix-Rousse/1919/2017			2017-09-24	MDCK2/MDCK1	2560	80	80	40	80	160	40	80	160	20
B/England/70/2017			2017-10-04	MDCK1/MDCK1	2560	80	80	80	80	160	40	80	160	20
B/Paris/1429/2017		3	2017-10-14	MDCK1/MDCK1	2560	40	160	40	80	80	40	80	160	20
B/Paris/1502/2017		3	2017-11-03	MDCK1/MDCK1	2560	40	160	40	80	<	40	80	160	20
B/Norway/3416/2017			2017-11-07	MDCK1/MDCK1	2560	80	160	80	160	160	40	80	320	20
B/Lorraine/1510/2017		3	2017-11-09	MDCK2/MDCK1	2560	40	160	80	160	<	40	80	160	20
B/Stockholm/16/2017		3	2017-11-09	MDCK1/MDCK1	2560	80	160	80	80	160	40	160	320	40
B/England/74/2017			2017-11-14	SIAT1/MDCK1	2560	40	80	40	80	160	40	80	160	20
B/Finland/799/2017		3	2017-11-15	MDCK1/MDCK1	2560	80	80	80	80	160	40	80	160	20
B/Navarra/2484/2017			2017-11-16	SIAT1/MDCK1	2560	40	160	80	80	160	40	80	160	20
B/Finland/807/2017			2017-11-18	MDCK1/MDCK1	2560	80	80	40	80	160	40	80	160	20
B/Paris/1531/2017		3	2017-11-20	MDCK1	2560	40	80	40	80	80	40	40	160	20
B/Falun/1/2017			2017-11-20	MDCK0/MDCK1	2560	40	80	40	80	80	40	80	160	20
B/Norway/3550/2017			2017-11-22	MDCK1/MDCK1	2560	40	80	40	80	160	40	40	160	20
B/Navarra/2483/2017			2017-12-05	SIAT1/MDCK1	2560	40	80	40	80	80	40	40	160	20
B/Navarra/2482/2017			2017-12-06	SIAT1/MDCK1	2560	40	160	80	80	160	40	80	320	20
													Vaccine#	

* 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 NH 2017-18

Sequences in phylogenetic tree

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



Summary of genetic data submitted to TESSy

For the 2017–18 season, weeks 40/2017—1/2018, 298 viruses have been characterised genetically:

- 32 were defined as A(H1N1)pdm09 subclade 6B.1 as represented by A/Michigan/45/2015, with one not attributed to a clade
- 88 were A(H3N2) clade 3C.2a represented by A/Hong Kong/4801/2014 and 49 were subclade 3C.2a1 represented by A/Singapore/INFIMH-16-0019/2016, with one not attributed to a clade
- 14 were B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008, with six falling in the 1A Δ162-163 subclade
- 110 were B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013, with three that were not attributed to a clade.

Antiviral susceptibility

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 28 viruses with collection dates from week 40/2017 at the WIC: 8 A(H1N1)pdm09, 13 A(H3N2), 1 B/Victoria-lineage and 6 B/Yamagata-lineage viruses. All showed normal inhibition (NI) by both neuraminidase inhibitors.

For weeks 40/2017–1/2018 of the 2017–18 influenza season, countries reported on the antiviral susceptibility of 28 A(H1N1)pdm09 viruses, 60 A(H3N2) viruses and 35 influenza type B viruses from sentinel and non-sentinel sources to TESSy. All but one showed no molecular or phenotypic evidence of reduced inhibition (RI) by neuraminidase inhibitors (oseltamivir and zanamivir); a single A(H3N2) isolate showed RI by both oseltamivir and zanamivir.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [3] reported that the China Health and Family Planning Commission notified the WHO 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 [4]. Increased numbers of cases have been reported over the course of the following seasons and cases have been reported in 2017, during the fifth and largest wave to date, which has included the emergence of Highly Pathogenic Avian Influenza (HPAI) strains that have caused some zoonoses [5]. A revised Rapid Risk Assessment [6] for these A(H7N9) viruses was carried out by ECDC and posted on 11 February 2015 and most recently updated on 3 July 2017 [7]. WHO posted an analysis of recent information on A(H7N9) viruses on 10 February 2017 [8] and a summary and assessment of influenza viruses at the human-animal interface on 7 December 2017 [9], with the latest cases being reported on 26 October 2017 [5].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 7 December 2017 [9]. ECDC published a rapid risk assessment update on the situation in Egypt on 13 March 2015 [10] and an epidemiological update on 10 April 2015 [11]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [12]. ECDC, in collaboration with the European Food Safety Authority and the EU Reference Laboratory for Avian Influenza also published a joint overview of avian influenza in October 2017 [13].

WHO CC reports

A description of results generated by the WHO Collaborating Centre for Reference and Research on Influenza at the Crick Worldwide Influenza Centre (Francis Crick Institute) and used at the WHO vaccine composition meetings held at WHO Geneva 27 February–1 March 2017 and held at The Peter Doherty Institute, University of Melbourne, 25–27 September 2017 can be found at:

https://www.crick.ac.uk/media/358671/crick_nh_vcm_report_feb_2017_v2.pdf

and

https://www.crick.ac.uk/media/393884/crick_sh2017_vcm_report_to_post.pdf

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 some viruses from non-EU/EEA countries were recovered from GISAID. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from GISAID's 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 the London WHO Collaborating Centre.

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