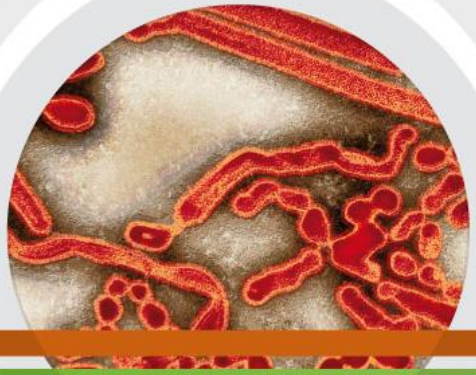

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, September 2017

Summary

In the course of the 2016–17 influenza season, over 146 000 influenza detections across the WHO Europe Region have been reported. Influenza type A viruses have prevailed over type B with A(H3N2) viruses, greatly outnumbering A(H1N1)pdm09 and B/Yamagata-lineage detections (representing 73% of the type B viruses assigned to a lineage).

Since 1 February 2017, EU/EEA countries have shared 304 influenza positive specimens with collection dates after 31 January 2017. Since the July 2017 report, 52 viruses have been characterised antigenically and 287 genetically. The HA titres of many A(H3N2) viruses were so low that they could not be characterised antigenically by haemagglutination inhibition (HI) assay.

All seven A(H1N1)pdm09 viruses characterised antigenically were similar to the 2016–17 vaccine virus, A/California/7/2009, and showed good reactivity with antiserum raised against the subclade 6B.1 2017–18 vaccine virus, A/Michigan/45/2015. Subclade 6B.1 viruses, defined by HA1 amino acid substitutions S162N and I216T, rapidly became dominant worldwide, and all (32) EU/EEA viruses with 2017 collection dates have fallen within this subclade.

Seventeen A(H3N2) viruses had sufficient HA titre for characterisation by HI assay. Over half (13/17) were recognised well by antiserum raised against egg-propagated A/Hong Kong/4801/2014 (the current vaccine component). Of 357 A(H3N2) viruses characterised genetically with collection dates in 2017, 124 (35%) were subclade 3C.2a, 228 (64%) were subclade 3C.2a1, and five (1%) were subclade 3C.3a.

Of the 13 B/Victoria-lineage viruses tested, all were antigenically similar to tissue culture-propagated surrogates of B/Brisbane/60/2008 (current vaccine component for the northern hemisphere 2017–18 season). All 55 viruses characterised with collection dates in 2017, including viruses with deletion in HA1, fell in genetic clade 1A, as do recently collected viruses worldwide.

Of the 15 B/Yamagata viruses characterised antigenically, 14 reacted well with post-infection ferret antiserum raised against egg-propagated B/Phuket/3073/2013, the recommended vaccine virus for the northern hemisphere 2015–16 influenza season, for quadrivalent vaccines since 2016 and for trivalent vaccines in the southern hemisphere 2018 season. Of the 89 viruses characterised with 2017 collection dates, all fell in genetic 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.

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Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy for the weekly reporting period (weeks 40/2016–20/2017) of the 2016–17 season. Approximately 145 000 detections had been made with type A viruses prevailing over type B at a ratio of 6.8:1. As of week 20/2016, of the type A viruses subtyped (n = 53 511) and the type B viruses ascribed to lineage (n = 2 571), A(H3N2) had prevailed over A(H1N1)pdm09 and B/Yamagata over B/Victoria by ratios of 99.0:1 and 2.5:1, respectively. While relatively few influenza detections were reported for weeks 21–39/2017, it is notable that the ratios for type A:type B and A(H3N2):A(H1N1)pdm09 dropped to 0.3:1 and 4.3:1, respectively, while the B/Yamagata:B/Victoria ratio increased to 10.4:1.

Since 1 February 2017, 27 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC), from 22 National Influenza Centres in the EU/EEA. These packages contained 304 specimens, a mix of clinical samples and virus isolates originating from 22 countries in EU/EAA, with specimen collection dates after 31 January 2017 (Table 2). The majority (57%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 6.2:1. Of the 131 type B specimens received (43% of the specimens), 58 were B/Victoria-lineage and 72 were B/Yamagata-lineage. The antigenic and genetic properties of influenza viruses, characterised since the July 2017 report[1], are presented and discussed in this surveillance report.

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2016–17 season (week 40/2016)

Virus type/subtype/lineage	Cumulative number of detections						Totals*			
	Sentinel sources		Non-sentinel sources		Totals		%		Ratios	
	Weeks 40/2016-20/2017	Weeks 21-39/2017	Weeks 40/2016-20/2017	Weeks 21-39/2017	Weeks 40/2016-20/2017	Weeks 21-39/2017	Weeks 40/2016-20/2017	Weeks 21-39/2017	Weeks 40/2016-20/2017	Weeks 21-39/2017
Influenza A	**16 240**	**15**	**110 018**	**341**	**126 258**	**356**	**87.2**	**25.3**	**6.8:1**	**0.3:1**
A(H1N1)pdm09	187	7	370	27	557	34	1.0	18.8		
A(H3N2)	13 574	5	39 380	142	52 954	147	99.0	81.2	99.0:1	4.3:1
A not subtyped	2 479	3	70 268	172	72 747	175				
Influenza B	**1 961**	**25**	**16 557**	**1 027**	**18 518**	**1 052**	**12.8**	**74.7**		
Victoria lineage	386	5	346	12	732	17	28.5	8.8		
Yamagata lineage	481	2	1 358	175	1 839	177	71.5	91.2	2.5:1	10.4:1
Lineage not ascribed	1 094	18	14 853	840	15 947	858				
Total detections (total tested)	**18 201 (50 975)**	**40 (2 060)**	**126 575 (589 447)**	**1 368 (43 995)**	**144 776 (640 422)**	**1 408 (46 055)**				

* 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, July 2017. Stockholm: ECDC; 2017. Available from: https://ecdc.europa.eu/sites/portal/files/documents/ERLI-Net-report-Jul-2017.pdf

Table 2. Summary of clinical samples and virus isolates, with collection dates after 31 January 2017, received from EU/EEA Member States

MONTH* / Country	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
		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 FEBRUARY														
Austria	16			3	3	7	0	7					6	6
Belgium	9					7	0	7			1	1	1	1
Bulgaria	12			2	2	7	1	6			3	2		
France	7					4	2	2			2	2	1	1
Germany	14			4	4	4	2	2			2	2	4	4
Greece	7			1	0	5	0	0			1	0		
Iceland	13					10	7	3					3	3
Ireland	1										1	1		
Italy	9			2	1	7	2	3						
Latvia	9					5	3	2			1	1	3	3
Lithuania	5					4	3	1			1	1		
Norway	31			2	1	14	2	12			8	5	7	5
Poland	10					10	0	5						
Portugal	2					2	1	1						
Slovakia	9			2	2	3	1	2			3	3	1	1
Slovenia	7					5	1	4					2	2
Spain	1					1	1	0						
Sweden	4					3	3	0			1	1		
United Kingdom	3					3	0	3						
2017 MARCH														
Austria	3					1	0	1			1	1	1	1
Bulgaria	1					1	0	1						
France	5			1	1	3	2	1					1	1
Germany	13					8	7	1			3	3	2	2
Iceland	6					4	2	2					2	2
Ireland	1												1	1
Italy	3												3	2
Latvia	2					1	0	1					1	1
Lithuania	6					1	1	0			1	1	4	4
Norway	17			1	1	11	4	5			1	0	4	3
Poland	6					6	0	2						
Romania	7										7	5		
Slovakia	1												1	1
Slovenia	7					2	2	0			1	1	4	4
United Kingdom	1										1	1		
2017 APRIL														
Austria	2												2	2
Germany	4					2	1	1			1	1	1	1
Ireland	2												2	2
Latvia	2					1	1	0					1	1
Norway	24			3	3	4	1	3			9	8	8	8
Poland	1								1	0				
Romania	8										7	5	1	1
Slovakia	1										1	1		
Slovenia	1												1	1
United Kingdom	3			1	1						1	1	1	1
2017 MAY														
France	2			2	2									
Norway	5					3	1	1					2	2
United Kingdom	1												1	1
	304	0	0	24	21	149	51	79	1	0	58	47	72	68
		0.0%		7.9%		49.0%			0.3%		19.1%		23.7%	
20 Countries		56.9%							43.1%					

*** 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 July 2017 report are shown in Table 3. All seven A(H1N1)pdm09 viruses from EU/EEA countries antigenically characterised were similar to the vaccine virus for the forthcoming northern hemisphere 2017–18 influenza season, A/Michigan/45/2015 [1], with all viruses being recognised at titres within twofold of the homologous titre of the antiserum. The antiserum raised against A/California/7/2009, the vaccine virus recommended for use for the northern hemisphere 2016–17 influenza season, also recognised all of the test viruses at titres within twofold of the homologous titre of the antiserum. All seven test viruses were recognised by the antiserum panel at titres within fourfold of the titres of the antisera with their respective homologous viruses. Furthermore, 90% of the individual titres of the test viruses were within twofold of the titres of the antisera with their homologous viruses.

As observed for all EU/EEA A(H1N1)pdm09 viruses characterised throughout the 2016–17 season, those in Table 3 fell within subclade 6B.1. A representative phylogenetic tree is shown in Figure 1. Significant numbers of HA genes of viruses from EU/EAA countries cluster in two genetic subgroups defined by HA1 amino acid substitutions of D274N with I324V and S74R with I295V.

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/E2	1280	2560	5120	640	2560	1280	5120	2560	2560	5120	2560	
A/California/7/2009	clone 38-32		2009-04-09	E3/E4	1280	1280	320	640	1280	640	2560	1280	1280	2560	1280	G155E
A/Bayern/69/2009			2009-07-01	MDCK5	<	40	320	320	40	40	40	40	80	80	40	
A/Lviv/N6/2009			2009-10-27	MDCK4/SIAT1/MDCK3	40	80	320	640	80	80	80	80	80	160	80	G155E>G, D222G
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK6	640	640	320	320	1280	320	2560	1280	640	1280	640	
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	640	640	640	320	640	320	2560	1280	640	2560	640	
A/St. Petersburg/100/2011		7	2011-03-14	E1/E4	640	640	640	320	640	320	2560	640	640	2560	640	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	320	160	80	320	160	1280	640	640	640	320	
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	640	320	640	640	640	1280	640	1280	640	640	
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E1	1280	1280	640	640	1280	640	2560	1280	1280	2560	2560	
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	640	320	640	320	1280	640	640	1280	1280	
TEST VIRUSES																
A/Austria/971790/2017		6B.1	2017-02-20	C2/MDCK1	1280	640	640	320	640	640	1280	1280	1280	2560	1280	
A/Austria/971917/2017		6B.1	2017-02-13	C2/MDCK1	640	640	320	160	640	320	1280	1280	1280	1280	1280	
A/Austria/971919/2017		6B.1	2017-02-13	C1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	
A/Bretagne/1184/2017		6B.1	2017-03-22	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	1280	
A/England/41/2017		6B.1	2017-04-12	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	
A/Paris/1226/2017		6B.1	2017-05-03	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	
A/Paris/1227/2017		6B.1	2017-05-03	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	

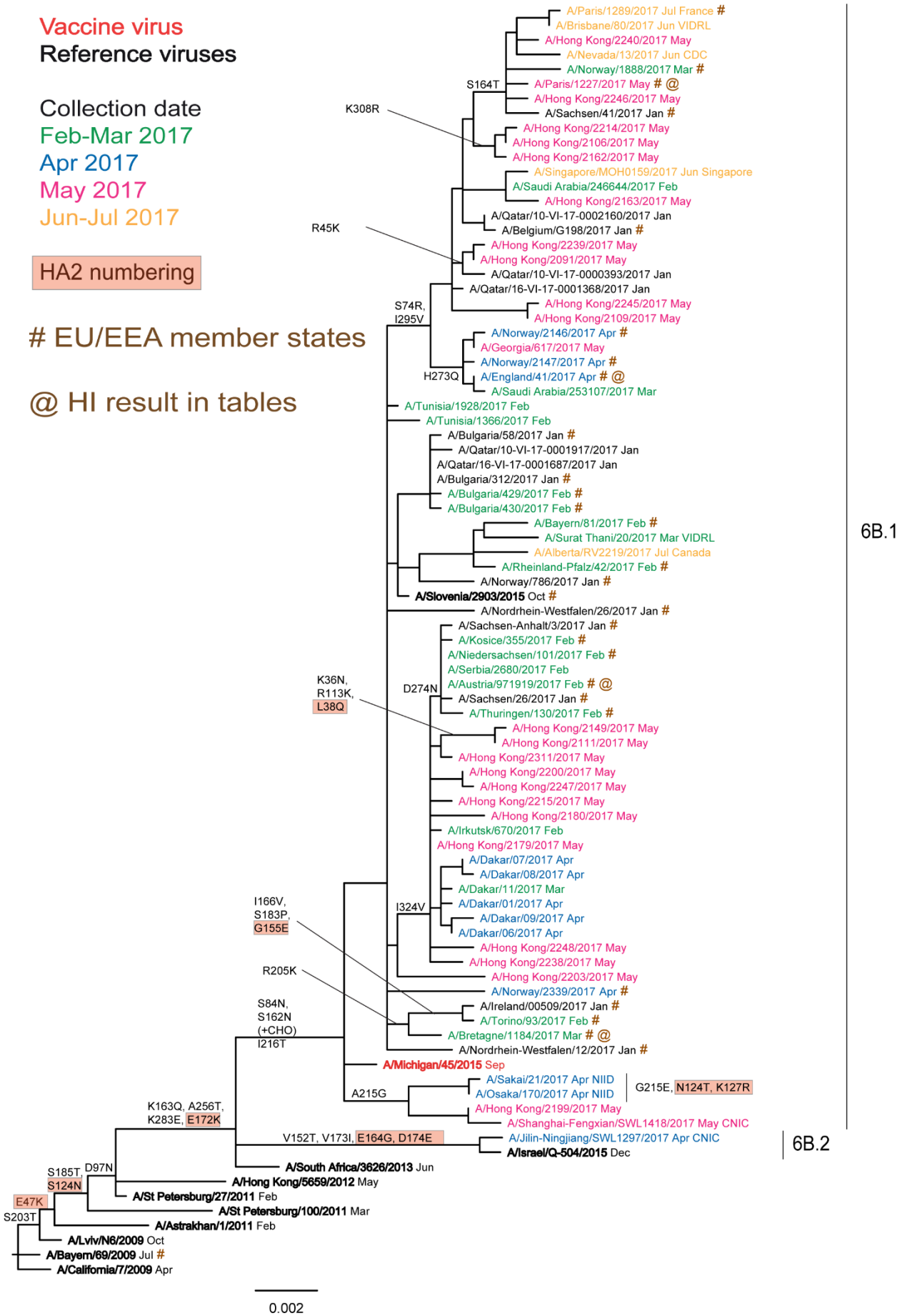
Vaccine

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

1 < = <40; 2 < = <80

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 subclade 3C.2a.

Results of HI tests performed with guinea pig RBCs in the presence of 20nM oseltamivir, added to circumvent NA-mediated binding of A(H3N2) viruses to the RBCs, are shown in Tables 4-1 and 4-2. Since the July 2017 report, 17 EU/EAA viruses retained sufficient HA titre to be analysed by HI assay. A further 10 viruses were successfully propagated as shown by positive neuraminidase activity but they could not be analysed by HI due to insufficient HA activity in the presence of 20nM oseltamivir.

An antiserum raised against egg-propagated A/Hong Kong/4801/2014, the virus recommended for use in vaccines for the northern hemisphere 2016–17, 2017–18 and southern hemisphere 2017 influenza seasons, recognised 13/17 (76%) test viruses at titres within fourfold compared to the titre of the antiserum with the homologous virus. Antiserum raised against the cell culture-propagated cultivar of A/Hong Kong/4801/2014 was slightly more effective with 14/17 (82%) giving titres within fourfold of that for the homologous virus. Antisera have been raised against three cell culture-propagated reference viruses in the 3C.2a1 subclade, A/Oman/2585/2016, A/Norway/4436/2016 and A/Greece/4/2017, but these reference viruses are unable to agglutinate RBCs.

Nevertheless, significant numbers of test viruses, 13/17 (76%), 9/10 (90%) and 7/7 (100%) were recognised by these antisera respectively, at a range of titres within fourfold of the highest titre for each antiserum. An antiserum raised against egg-propagated A/Switzerland/9715293/2013 (3C.3a), the northern hemisphere 2015–16 vaccine component, reacted well with all but two (12%) test viruses at titres within fourfold of the homologous titre. Antisera raised against egg-propagated A/Norway/4849/2016 (3C.2a) and A/Greece/4/2017 (3C.2a1) were assessed against ten cell culture-propagated test viruses, none of which were recognised at titres within fourfold of the antisera with their respective homologous viruses.

Phylogenetic analysis of the HA genes of representative A(H3N2) viruses with recent collection dates is shown in Figure 2. Viruses in subclades 3C.2a and 3C.3a have been in circulation since the 2013–14 northern hemisphere influenza season, with subclade 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 subclades, and one of these clusters has been designated 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 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 subclades 3C.2a and 3C.2a1. The location of A/Singapore/INFIMH-16-0019/2016 (3C.2a1), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2018 season [2], is indicated in Figure 2.

[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

Table 4-1. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre						NEW	NEW
					Post-infection ferret antisera							
					A/Stock 6/14 SIAT F14/14*1 3C.3a	A/Switz 9715293/13 SIAT F18/15*1 3C.3a	A/HK 4801/14 MDCK F43/15*1 3C.2a	A/HK 4801/14 Egg F12/15*1 3C.2a	A/Oman 2585/16 SIAT NIB F50/16*1 3C.2a1	A/Nor 4436/16 SIAT F03/17*1 3C.2a1	A/Nor 4849/16 Egg F23/17*1 3C.2a	A/Greece 4/17 Egg F28/17*1 3C.2a1
REFERENCE VIRUSES												
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT2	640	160	320	160	320	320	80	160
A/Switzerland/9715293/2013		3C.3a	2013-12-06	SIAT1/SIAT3	640	80	160	40	160	160	<	80
A/Hong Kong/4801/2014		3C.2a	2014-02-26	MDCK4/MDCK1	320	160	640	160	320	320	80	160
A/Hong Kong/4801/2014	isolate 1	3C.2a	2014-02-26	E6/E2	80	80	640	320	640	320	640	1280
A/Norway/4849/2016		3C.2a	2016-12-02	E7	80	80	640	160	320	320	640	1280
A/Greece/4/2017		3C.2a1	2017-01-02	E9	160	80	640	160	640	320	320	2560
TEST VIRUSES												
A/Stockholm/60/2016		3C.2a1	2016-12-28	MDCK1/SIAT2	160	40	160	80	160	160	<	80
A/Thuringen/165/2017		3C.2a	2017-01-13	C1/SIAT2	320	80	320	80	160	320	<	40
A/Stockholm/11/2017		3C.2a1	2017-01-14	MDCK0/SIAT2	160	40	160	80	160	160	<	80
A/England/19/2017		3C.2a1	2017-01-31	SIAT1/SIAT1	160	80	320	80	80	160	40	320
A/Paris/1023/2017		3C.2a1	2017-02-16	MDCK1/SIAT1	80	40	80	40	80	160	<	80
A/Linkoping/1/2017		3C.2a1	2017-02-17	MDCK2/SIAT2	320	80	320	80	320	320	40	160
A/Basse Normandie/1055/2017		3C.2a1	2017-02-20	MDCK1/SIAT1	80	40	160	40	160	160	<	40
A/Paris/1145/2017		3C.2a1	2017-03-06	MDCK1/SIAT1	160	<	80	40	80	160	<	40
A/Dijon/1176/2017		3C.2a1	2017-03-14	MDCK1/SIAT1	80	<	80	40	80	40	<	40
A/Niedersachsen/186/2017		3C.2a1	2017-03-21	C2/SIAT2	320	80	160	80	320	320	<	160
								Vaccine				

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

Sequences in phylogenetic trees

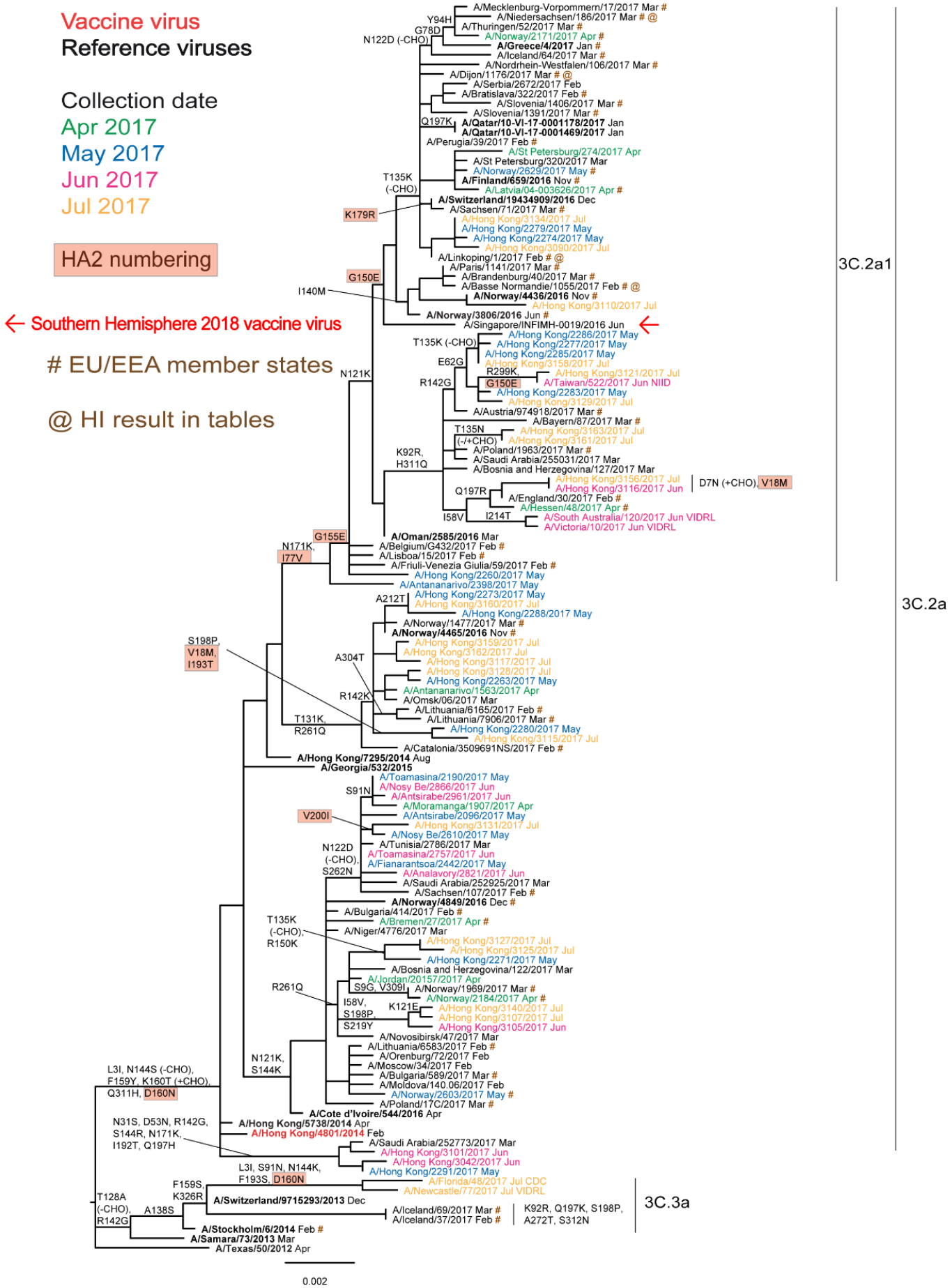
Table 4-2. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre					
				Post-infection ferret antisera					
				A/Stock 6/14 SIAT F14/14*1	A/Switz 9715293/13 SIAT F18/15*1	A/HK 4801/14 MDCK F43/15*1	A/HK 4801/14 Egg F12/15*1	A/Oman 2585/16 SIAT NIB F50/16*1	A/Greece 4/17 SIAT F27/17*1
Passage history / Ferret number				3C.3a	3C.3a	3C.2a	3C.2a	3C.2a1	3C.2a1
Genetic group									
REFERENCE VIRUSES									
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	1280	320	320	160	320	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	640	160	160	80	160	160
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1	640	160	640	160	320	640
A/Hong Kong/4801/2014	isolate 1 3C.2a	2014-02-26	E6/E2	160	160	640	320	640	320
TEST VIRUSES									
A/St Etienne/951/2017	3C.2a1	2017-01-05	MDCK2/SIAT1	640	160	640	160	320	320
A/Lisboa/2/2017	3C.2a1	2017-01-05	SIAT1/SIAT1	320	80	160	80	320	320
A/Lisboa/4/2017	3C.2a	2017-01-05	SIAT1/SIAT1	320	80	160	80	320	160
A/Lisboa/12/2017	3C.2a	2017-01-05	SIAT1/SIAT1	320	80	160	80	320	320
A/Lisboa/5/2017	3C.2a1	2017-01-12	SIAT1/SIAT1	160	40	160	80	160	320
A/Lisboa/17/2017	3C.2a1	2017-01-22	SIAT2/SIAT2	320	160	320	160	320	320
A/Lisboa/16/2017	3C.2a	2017-02-10	SIAT1/SIAT1	160	40	160	80	160	320
							Vaccine		

* 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

EU/EEA countries have provided 131 influenza type B-positive specimens with collection dates after 31 January 2017; 130 were ascribed to a lineage: 58 B/Victoria-lineage and 72 B/Yamagata-lineage (Table 2).

Influenza B – Victoria lineage

Since the July 2017 report, 13 viruses of the B/Victoria lineage have been characterised antigenically. All viruses sequenced to date belong to genetic clade 1A; HI results are shown in Tables 5-1 to 5-3.

All 13 test viruses showed similar HI reactivity patterns to those observed throughout the 2014–15 and 2015–16 influenza seasons. Only one test virus gave a titre within fourfold of the titre with the homologous virus for an antiserum raised against the egg-propagated vaccine virus, B/Brisbane/60/2008, recommended for use in both trivalent and quadrivalent vaccines. The test viruses were also not recognised well by post-infection ferret antisera raised against egg-propagated B/Malta/636714/2011 and B/Johannesburg/3964/2012 although the antiserum raised against egg-propagated B/South Australia/81/2012 recognised 11/13 test viruses at titres within fourfold of the homologous titres of the antiserum. By contrast, all 13 test viruses showed reactivity within fourfold – the majority within twofold – of the titres for the corresponding homologous viruses with antisera raised against viruses that are considered to be surrogate tissue culture-propagated antigens representing the egg-propagated B/Brisbane/60/2008 prototype virus. These antisera were raised against tissue culture-propagated viruses B/Hong Kong/514/2009 (clade 1B), B/Formosa/V2367/2012, B/Ireland/3154/2016 and B/Nordrhein-Westfalen/1/2016 (all clade 1A).

Antisera raised against representative cell culture-propagated viruses of the clade 1A group with a double amino acid deletion (Δ) in HA1 positions 162-163 (Δ162-163), A/Maryland/15/2016 and A/Norway/2409/2017, showed poor recognition of all viruses (reference and test) that retained these two amino acids. The antiserum raised against egg-propagated A/Maryland/15/2016, which had lost the HA1 197-199 glycosylation site, showed somewhat better recognition of some reference viruses – those that had also lost the glycosylation site. All four antisera showed good reactivity with Δ162-163 viruses.

Phylogenetic analysis of the HA gene of representative B/Victoria lineage viruses is shown in Figure 3. Viruses from Europe, and elsewhere, continue to have HA genes that fall in the B/Brisbane/60/2008 clade (clade 1A). The great majority of viruses, with collection dates since October 2015, fall in a major subcluster defined by 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) 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 have additional substitutions **I180T** and **K209N** in **HA1**.

Influenza B – Yamagata lineage

HI results for 15 B/Yamagata-lineage test viruses analysed since the July 2017 report are shown in Table 6. All viruses belonged to genetic clade 3.

Five antisera were raised against clade 3 viruses. That raised against egg-propagated B/Phuket/3073/2013, recommended for inclusion in quadrivalent influenza vaccines since the southern hemisphere 2016 season and recently for inclusion in trivalent vaccines for the southern hemisphere 2018 season [2], recognised 14/15 (93%) test viruses at titres within fourfold of the titre of the antiserum with the homologous virus. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised 87% of test viruses at titres within fourfold of the homologous titre of the antiserum. An antiserum raised against a former vaccine virus, egg-propagated B/Wisconsin/1/2010 with a homologous titre of 80, recognised all of the test viruses at titres within twofold of the homologous titre as did the antiserum raised against egg-propagated B/Hong Kong/3417/2014. That raised against egg-propagated B/Stockholm/12/2011 recognised all but one test virus at titres within fourfold of the homologous titre of the antiserum.

Antisera raised against both egg- and cell-propagated clade 2 viruses, recognised the test viruses less well, with three to eight of the 15 viruses (20–53%) being recognised at titres within fourfold of the homologous titres of the antisera.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. Worldwide, the vast majority of HA genes from recently collected viruses have fallen in clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade, with the great majority falling in a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions. One virus, B/Nordrhein-Westfalen/1/2017, annotated in the phylogenetic tree, is a reassortant virus carrying an NA gene most closely related to NA genes of viruses of the B/Victoria-lineage.

Table 5-1. 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	B/Mal 2506/04 Egg	B/Bris 60/08 Egg	B/Malta 636714/11 Egg	B/Jhb 3964/12 Egg	B/For V2367/12 MDCK	B/Sth Aus 81/12 Egg	B/HK 514/09 MDCK	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK
	Ferret number			539, 540, 543, 544, 570, 571, 574[#1,3]	F41/14[*2]	NIB F52/16[*2]	F29/13[*2]	F01/13[*4]	F04/13[*2]	F41/13[*2]	F09/13[*2]	F15/16[*2]	F16/16[*2]
	Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A
REFERENCE VIRUSES													
B/Malaysia/2506/2004		2004-12-06	E3/E7	1280	320	160	40	80	40	80	10	<	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	2560	160	640	320	160	160	1280	80	40	20
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	160	640	320	160	80	640	40	20	20
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	320	1280	1280	1280	1280	1280	320	160	160
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	40	320	160	160	160	320	40	40	40
B/South Australia/81/2012	1A	2012-11-28	E4/E1	1280	160	320	160	160	160	640	40	20	20
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	2560	<	20	20	20	80	80	40	80	40
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK3	2560	10	20	20	<	80	40	40	80	80
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	2560	<	40	20	20	80	80	40	80	80
TEST VIRUSES													
B/England/36/2017	1A	2017-03-17	SIAT1/MDCK1	2560	<	40	20	20	80	80	40	80	40
B/England/46/2017	1A	2017-04-26	SIAT1/MDCK1	2560	<	20	20	20	80	80	40	80	40
						Vaccine							

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20

Sequences in phylogenetic trees

Table 5-2. 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	B/Mal	B/Bris	B/Malta	B/Jhb	B/For	B/Sth Aus	B/HK	B/Ireland	B/Nord-West	B/Maryland	NEW	B/Maryland	NEW	B/Nor	NEW						
	Ferret number			60/08	2506/04	60/08	636714/11	3964/12	V2367/12	81/12	514/09	3154/16	1/16	15/16		15/16		2409/16		B/Nor					
				Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK	MDCK		Egg		MDCK		MDCK					
				Sh 539, 540, 543,		NIB								CDC		CDC									
				544, 570, 571, 574[4,3]	F41/14[*2]	F52/16[*2]	F29/13[*2]	F01/13[-4]	F04/13[-2]	F41/13[*2]	F09/13[*2]	F15/16[*2]	F16/16[*2]	F2017-045[*2]		F2017-041[*2]		F20/17[*2]		F26/17[*2]					
	Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A	1A		1A		1A		1A					
REFERENCE VIRUSES																									
B/Malaysia/2506/2004		2004-12-06	E3/E7	2560	640	320	80	80	80	160	20	<	<	<		320		10		20					
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	2560	160	1280	320	160	160	640	40	40	20	<		320		10		20					
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	80	640	160	160	160	320	40	40	20	<		320		10		10					
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	640	1280	1280	1280	1280	1280	320	320	320	80		1280		80		80					
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	80	640	160	160	320	640	40	80	80	<		320		10		20					
B/South Australia/81/2012	1A	2012-11-28	E4/E1	1280	80	640	160	80	160	320	40	40	20	<		320		10		20					
B/Hong Kong/5114/2009	1B	2009-10-11	MDCK3	2560	<	80	20	20	80	80	40	80	80	<		20		<		20					
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK3	5120	<	80	20	20	80	80	40	160	80	<		40		10		20					
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	5120	10	80	40	20	80	80	40	160	160	<		80		10		20					
B/Maryland/15/2016	Δ 162-163 1A	2016-12-27	C3/MDCK1	160	<	10	<	<	20	<	<	10	<	640		320		640		640					
B/Maryland/15/2016	Δ 162-163 1A	2016-12-27	E4/E1	640	160	160	40	40	40	80	<	<	<	320		640		320		640					
B/Norway/2409/2017	Δ 162-163 1A	2017-04-27	MDCK1/MDCK1	80	<	<	<	<	10	<	<	<	<	320		320		640		320					
TEST VIRUSES																									
B/Bucuresti/209398/2017	1A	2017-03-10	MDCK1/MDCK1	5120	10	80	20	20	80	80	40	160	80	ND		ND		10		40					
B/Bucuresti/209401/2017	1A	2017-03-12	MDCK1/MDCK1	2560	<	80	20	<	40	80	40	80	80	ND		ND		10		40					
B/Bucuresti/209562/2017	1A	2017-03-15	MDCK1/MDCK1	5120	<	80	20	20	80	80	40	160	40	ND		ND		ND		ND					
B/Buzau/210450/2017	1A	2017-03-25	MDCK1/MDCK1	2560	20	160	40	40	160	160	40	80	80	<		10		10		20					
B/Olt/210464/2017	1A	2017-03-30	MDCK1/MDCK1	2560	<	80	20	20	80	80	40	160	80	<		10		10		20					
B/Bucuresti/210584/2017	1A	2017-04-03	MDCK1/MDCK1	2560	<	80	20	<	40	80	40	80	80	<		<		<		20					

Vaccine

* 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

Table 5-3. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				B/Bris 60/08 Egg Sh 539, 540, 543, 544, 570, 571, 574[a1,3] 1A	B/Mal 2506/04 Egg F41/14[*2]	B/Bris 60/08 Egg NIB F52/16[*2] 1A	B/Malta 636714/11 Egg F29/13[*2] 1A	B/Jhb 3964/12 Egg F01/13[*4] 1A	B/For V2367/12 MDCK F04/13[*2] 1A	B/Sth Aus 81/12 Egg F41/13[*2] 1A	B/HK 514/09 MDCK F09/13[*2] 1B	B/Ireland 3154/16 MDCK F15/16[*2] 1A	B/Nord-West 1/16 MDCK F16/16[*2] 1A
Passage history															
Ferret number															
Genetic group															
REFERENCE VIRUSES															
B/Malaysia/2506/2004		2004-12-06	E3/E7	2560	640	160	40	80	40	80	20	<	<		
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	1280	160	640	160	160	160	640	80	40	20		
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	160	640	160	160	160	640	80	40	20		
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	320	1280	640	640	640	1280	160	160	80		
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	2560	80	640	160	160	320	320	80	80	40		
B/South Australia/81/2012	1A	2012-11-28	E4/E1	2560	160	640	160	80	160	320	80	40	20		
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	2560	<	80	20	<	40	80	160	80	80		
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	80	10	<	40	40	80	80	80		
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK3	5120	<	80	20	<	80	80	80	80	80		
TEST VIRUSES															
B/Ireland/02932/2017		2017-02-24	C1/MDCK1	2560	<	40	20	<	40	80	80	80	80		
B/Bucuresti/210480/2017	1A	2017-04-04	MDCK1	2560	10	80	20	20	80	80	80	80	80		
B/Bucuresti/931-C8857/2017	1A	2017-04-05	MDCK1	5120	80	640	80	80	160	640	160	160	80		
B/Olt/210799/2017	1A	2017-04-08	MDCK1	2560	10	80	20	20	80	80	80	80	80		
B/Bucuresti/210885/2017	1A	2017-04-09	MDCK1	2560	10	80	20	<	80	80	80	80	80		

Vaccine

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20

Sequences in phylogenetic trees

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

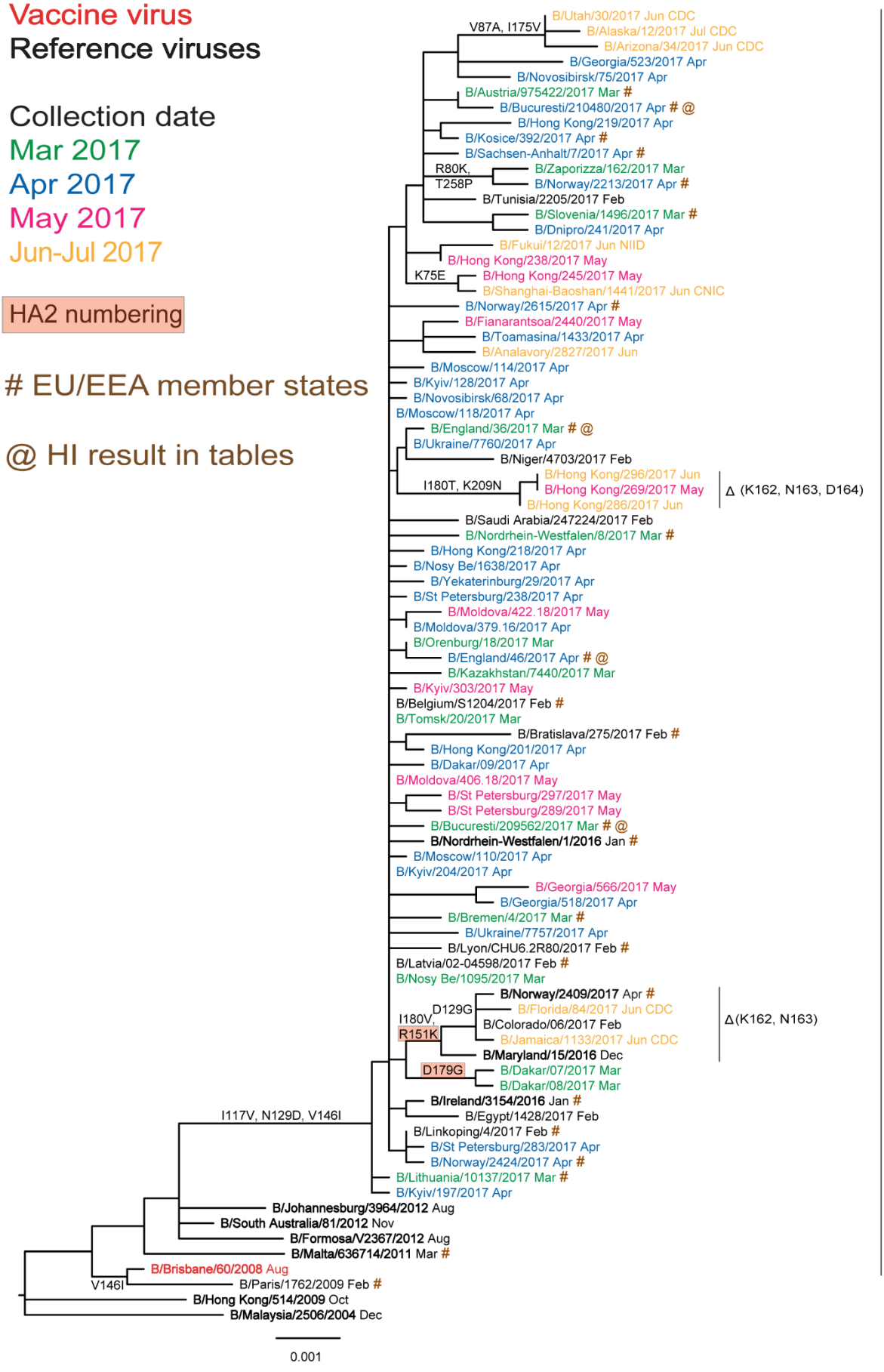


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

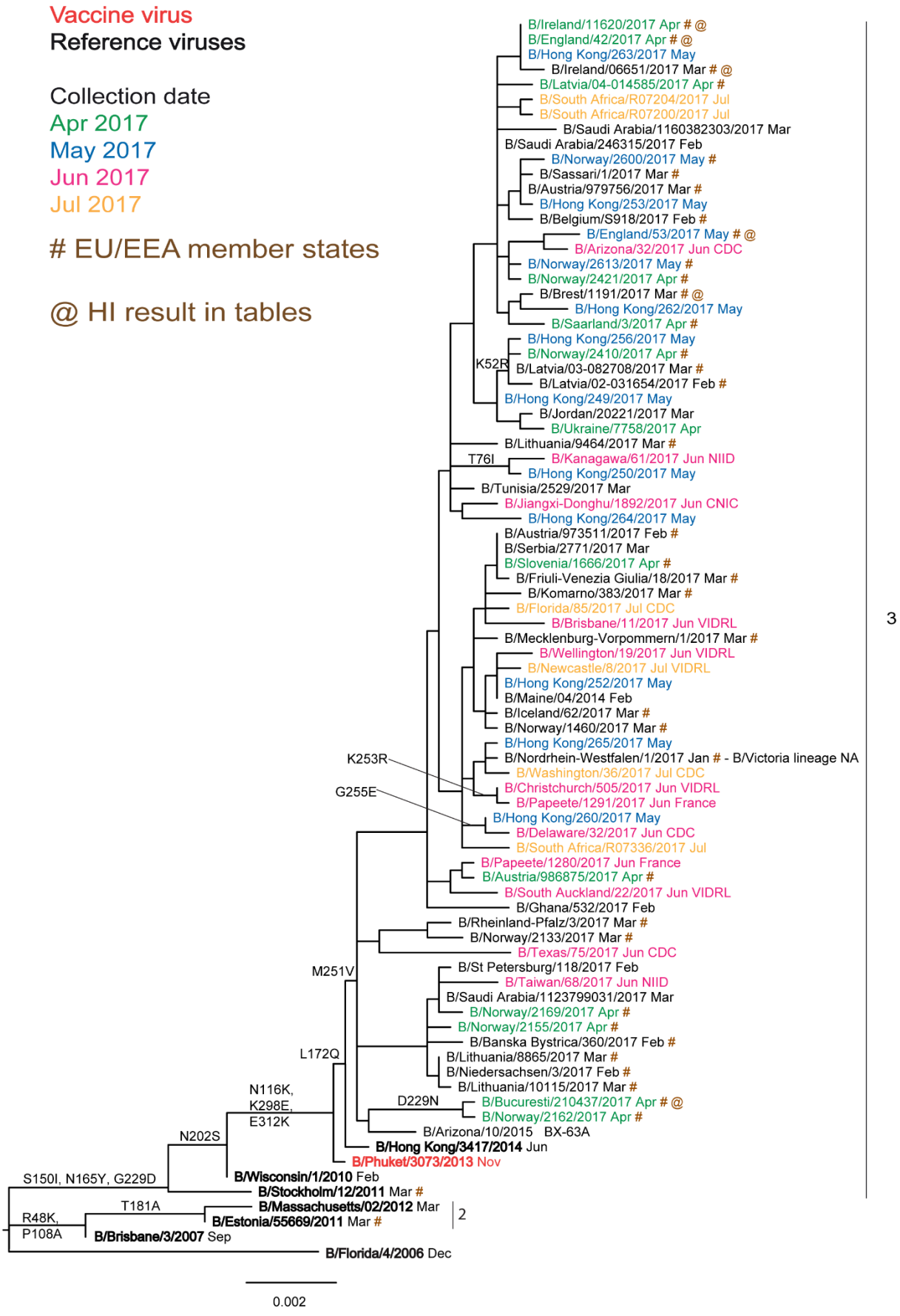
Viruses	Other information	Passage history / Ferret number / Genetic Group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera										
					B/Phuket 3073/13 Egg SH614[*1,3] 3	B/Fl 4/06 Egg F17/13[*1] 1	B/Bris 3/07 Egg F38/14[*2] 2	B/Estonia 55669/11 MDCK F27/13[*2] 2	B/Mass 02/12 MDCK F05/15[*2] 2	B/Mass 02/12 Egg F42/14[*2] 2	B/Wis 1/10 Egg F36/15[*2] 3	B/Stock 12/11 Egg F06/15[*2] 3	B/Phuket 3073/13 MDCK F27/15[*4] 3	B/Phuket 3073/13 Egg NIB F51/16*2 3	B/HK 3417/14 Egg St Judes F715/14[*2,4] 3
REFERENCE VIRUSES															
B/Florida/4/2006		1	2006-12-15	E7	5120	1280	1280	320	160	1280	320	320	40	1280	320
B/Brisbane/3/2007		2	2007-09-03	E2/E3	2560	1280	1280	160	160	1280	160	320	20	1280	320
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	2560	80	160	640	640	160	160	20	10	80	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK4	2560	640	320	640	640	640	320	160	80	640	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	640	640	80	80	640	80	80	10	320	160
B/Wisconsin/1/2010		3	2010-02-20	E3/E3	2560	160	160	20	20	160	80	80	20	640	160
B/Stockholm/12/2011		3	2011-03-28	EX/E2	1280	160	80	20	<	80	80	80	10	160	80
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK2	5120	160	160	160	160	320	160	80	160	320	160
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	160	160	10	<	80	80	40	10	320	80
B/Hong Kong/3417/2014		3	2014-06-04	E4/E3	1280	80	40	20	<	40	40	20	<	80	160
TEST VIRUSES															
B/Lisboa/2/2017		3	2017-01-24	SIAT1/MDCK1	5120	160	320	320	640	320	320	160	320	640	320
B/Ireland/94721/2017		3	2017-01-31	C1/MDCK1	5120	160	160	80	80	160	160	40	160	320	160
B/Austria/971742/2017		3	2017-02-17	C1/MDCK1	5120	320	320	320	1280	320	320	160	160	640	160
B/Austria/971746/2017		3	2017-02-18	C1/MDCK1	5120	320	640	640	1280	640	640	320	320	640	320
B/Austria/972293/2017		3	2017-02-20	C1/MDCK2	5120	160	160	160	320	160	320	80	160	320	320
B/Austria/972415/2017		3	2017-02-20	C1/MDCK1	2560	80	80	80	40	80	80	20	40	160	160
B/Austria/972769/2017		3	2017-02-20	C1/MDCK1	2560	80	80	40	20	40	40	20	40	80	160
B/Lorraine/1080/2017		3	2017-02-22	MDCK1/MDCK1	1280	40	40	80	20	40	40	20	20	80	160
B/Brest/1191/2017		3	2017-03-05	MDCK1/MDCK1	2560	40	40	40	20	40	40	20	20	80	160
B/Ireland/06651/2017		3	2017-03-13	C1/MDCK1	5120	80	80	80	40	80	80	40	160	160	160
B/England/42/2017		3	2017-04-01	SIAT1/MDCK1	1280	40	40	20	10	20	40	10	40	40	80
B/Ireland/11620/2017		3	2017-04-02	C1/MDCK1	2560	80	80	40	40	40	80	20	80	80	160
B/Bucuresti/210437/2017		3	2017-04-04	MDCK1/MDCK1	5120	160	160	80	80	160	160	40	160	160	160
B/Ireland/12497/2017		3	2017-04-06	C1/MDCK1	2560	80	80	80	80	160	160	40	160	160	160
B/England/53/2017		3	2017-05-31	MDCK1/MDCK1	2560	160	160	80	80	160	160	40	80	320	160
														Vaccine[#]	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
1 < = <40; 2 < = <10; 3 hyperimmune sheep serum; 4 RDE serum pre-adsorbed with TRBC

[#] B/Yamagata-lineage virus recommended for use in quadravalent vaccines

Sequences in phylogenetic trees

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



Summary of genetic data submitted to TESSy

For the 2016–17 season beginning week 40/2016 until week 39/2017, 4 364 viruses have been characterised genetically:

17 viruses were defined as A(H1N1)pdm09 clade 6B, represented by A/South Africa/3626/2013, and 62 were subclade 6B.1 as represented by A/Michigan/45/2015.

1 127 viruses were A(H3N2) subclade 3C.2a, represented by A/Hong Kong/4801/2014; 2 656 were subclade 3C.2a1, represented by A/Bolzano/7/2016; 43 were subclade 3C.3a, represented by A/Switzerland/9715293/2013; one was subclade 3C.3, represented by A/Samara/73/2013; and five belonged to a group that was unlisted.

145 viruses were B/Victoria-lineage clade 1A, represented by B/Brisbane/60/2008, and one was clade 1B, represented by B/Hong Kong/514/2009.

294 viruses were B/Yamagata-lineage clade 3, represented by B/Phuket/3073/2013, with 13 that were not attributed to a clade.

Antiviral susceptibility

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 999 viruses from EU/EAA countries with collection dates after week 40/2016 at the WIC: 43 A(H1N1)pdm09, 795 A(H3N2), 59 B/Victoria-lineage and 102 B/Yamagata-lineage viruses. Since the July 2017 report one A(H1N1)pdm09 virus (A/Paris/1227/2017: NA H275Y) has shown HRI by oseltamivir and four A(H3N2) viruses have shown RI to oseltamivir and zanamivir (A/Bremen/27/2017 NA N329K, A/Austria/971753/2017 NA S331R, A/Belgium/G108/2017 NA S331R, A/Belgium/G448/2017 NA S331R).

For weeks 40/2016–39/2017 of the 2016–17 influenza season, countries reported on the antiviral susceptibility of 78 A(H1N1)pdm09 viruses, 3 167 A(H3N2) viruses and 360 influenza type B viruses from sentinel and non-sentinel sources to TESSy. All but four showed no molecular or phenotypic evidence of RI by neuraminidase inhibitors (oseltamivir and zanamivir); three A(H3N2) isolates showed RI by both oseltamivir and zanamivir, and one type B isolate showed RI with oseltamivir only.

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 ECDC rapid risk assessment [6] for these A(H7N9) viruses was 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 29 September 2017 [9], with the latest cases being reported on 13 September 2017 [5].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 29 September 2017 [9]. ECDC published an updated rapid risk assessment 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].

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 WHO CC Melbourne (The Peter Doherty Institute) 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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