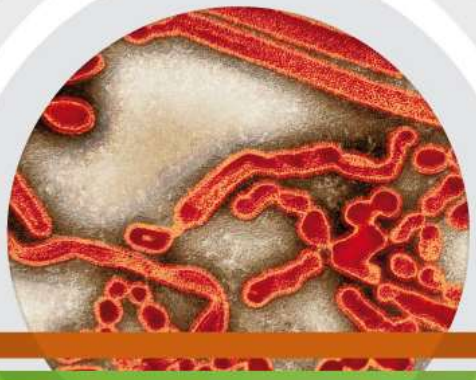


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, July 2017

Summary

In the course of the 2016–17 influenza season, nearly 146 000 influenza detections have been reported across the WHO European Region. 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 January 2017, EU/EEA countries have shared 592 influenza-positive specimens with collection dates after 31 December 2016. Since the June 2017 report 97 viruses have been characterised antigenically and 34 genetically. Many A(H3N2) viruses could only be characterised genetically as HA titres of these viruses were too low to allow antigenic characterisation by haemagglutination inhibition assay.

All nine 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. The subclade 6B.1 viruses, defined by HA1 amino acid substitutions S162N and I216T, became dominant worldwide and the 19 EU/EEA viruses characterised with 2017 collection dates were all within this subclade.

Fifty-seven A(H3N2) viruses had sufficient HA titre for characterisation by haemagglutination inhibition (HI) assay. Approximately half (25/57) were recognised well by antiserum raised against egg-propagated A/Hong Kong/4801/2014 (the current vaccine component). Of 147 A(H3N2) viruses characterised genetically with collection dates in 2017, 38 (26%) were subclade 3C.2a, 108 (73%) were subclade 3C.2a1, and one (1%) was 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. All 33 viruses characterised with collection dates in 2017, including viruses with the deletion in HA1, fell in genetic clade 1A, as do recently collected viruses worldwide.

Of the 18 B/Yamagata viruses characterised antigenically, 17 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 and for quadrivalent vaccines since 2016. Of the 65 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.

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

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 146 000 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 have been reported for weeks 21–29/2017, it is notable that the ratios for type A:type B and A(H3N2):A(H1N1)pdm09 have dropped to 0.2:1 and 3.8:1, respectively, while the B/Yamagata:B/Victoria ratio has increased to 10.6:1.

Since 1 January 2017, 53 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC), from 29 National Influenza Centres in the EU/EEA. These packages contained 592 specimens, a mix of clinical samples and virus isolates originating from 22 countries in EU/EEA, with specimen collection dates after 31 December 2016 (Table 2). The majority (75%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 11.3:1. Of the 149 type B specimens received (25% of the specimens), 58 were B/Victoria-lineage and 89 were B/Yamagata-lineage. Many specimens are still being characterised. The antigenic and genetic properties of influenza virus isolates characterised since the June 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 21-29/2017	Weeks 40/2016-20/2017	Weeks 21-29/2017	Weeks 40/2016-20/2017	Weeks 21-29/2017	Weeks 40/2016-20/2017	Weeks 21-29/2017	Weeks 40/2016-20/2017	Weeks 21-29/2017
Influenza A	**16 240**	**11**	**110 018**	**186**	**126 258**	**197**	**87.2**	**16.6**	**6.8:1**	**0.2:1**
A(H1N1)pdm09	187	6	370	13	557	19	1.0	20.7		
A(H3N2)	13 574	3	39 380	70	52 954	73	99.0	79.3	99.0:1	3.8:1
A not subtyped	2 479	2	70 268	103	72 747	105				
Influenza B	**1 961**	**23**	**16 557**	**965**	**18 518**	**988**	**12.8**	**83.4**		
Victoria lineage	386	5	346	11	732	16	28.5	8.6		
Yamagata lineage	481	1	1 358	169	1 839	170	71.5	91.4	2.5:1	10.6:1
Lineage not ascribed	1 094	17	14 853	785	15 947	802				
Total detections (total tested)	**18 201 (50 975)**	**34 (1 079)**	**126 575 (589 447)**	**1 151 (26 936)**	**144 776 (640 422)**	**1 185 (28 015)**				

* 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, June 2017. Stockholm: ECDC; 2017. Available from: https://ecdc.europa.eu/sites/portal/files/documents/influenza-virus-characterisation-jun-2017.pdf

Table 2. Summary of clinical samples and virus isolates, with collection dates after 31 December 2016, 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														
JANUARY														
Austria	1					1	0	1						
Belgium	43			1	1	41	4	37					1	0
Bulgaria	39			3	3	36	8	28						
Cyprus	18					18	2	16						
France	7					3	in process				4	4		
Germany	34			5	5	23	in process				1	1	5	5
Greece	36					27	8	16	1	0	8	4		
Ireland	3			1	1	2	1	1						
Italy	7					6	2	4					1	1
Latvia	5					4	1	2					1	1
Luxembourg	2					2	0	2						
Norway	7			2	2	3	1	2					2	1
Poland	28	1	0			27	3	13						
Portugal	17					15	in process				1	1	1	1
Romania	15					15	0	15						
Slovakia	15					13	8	5			1	1	1	1
Slovenia	18					10	3	6					8	8
Spain	6					5	0	5					1	1
Sweden	5					5	in process							
United Kingdom	1					1	in process							
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	in process				2	2	1	1
Germany	14			4	4	4	in process				2	2	4	4
Greece	7			1	0	5	0	0			1	0		
Iceland	13					10	7	3					3	3
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	in process							
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	in process				1	1		
United Kingdom	3					3	in process							
2017														
MARCH														
Austria	3					1	0	1			1	1	1	1
Bulgaria	1					1	0	1						
France	5			1	1	3	in process						1	1
Germany	13					8	in process				3	3	2	2
Iceland	6					4	2	2					2	2
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						
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
Latvia	2					1	1	0					1	1
Norway	24			3	3	4	1	3			9	8	8	8
Poland	1								1	0				
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
22 Countries	592	1	0	36	33	406	75	222	2	0	58	47	89	83
		0.2%		6.1%		68.6%			0.3%		9.8%		15.0%	
				74.7%							25.2%			

*** 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 June 2017 report are shown in Table 3. All nine 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, 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 within twofold of the antiserum titre for the homologous virus. All nine test viruses were recognised by the panel of antisera at titres within fourfold of the antisera titres with their respective homologous viruses. Furthermore, 90% of the individual titres of the test viruses were within twofold of the titres of the antisera for the homologous viruses.

HA gene sequencing is still in progress for all the test viruses shown in Table 3. To date, all of the EU/EEA viruses characterised genetically for the 2016–17 season fell within subclade 6B.1. A representative phylogenetic tree is shown in Figure 1. The HA genes of some viruses from EU/EEA countries cluster into a genetic subgroup defined by the amino acid substitutions D274N and I324V in HA1.

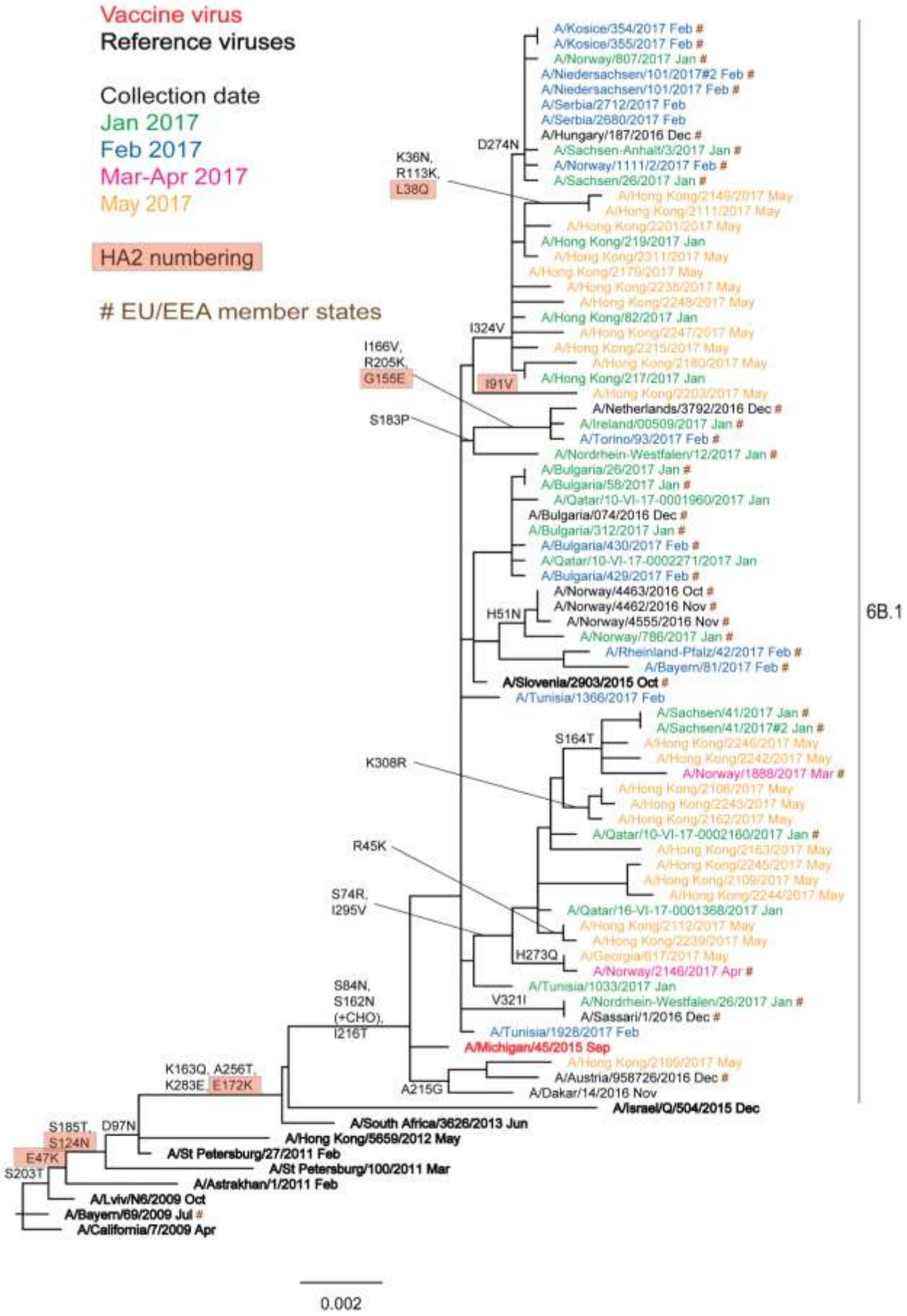
Table 3. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre												
				Post-infection ferret antisera												
				A/Mich 45/15 Egg 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		
		Passage history													G155E	
		Ferret number														G155E>G, D222G
		Genetic group														
REFERENCE VIRUSES																
A/Michigan/45/2015		2015-09-07	E3/E4	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		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	<	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		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	640	640	320	320	1280	320	2560	1280	640	1280	640		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E4	640	640	640	320	640	320	2560	1280	640	2560	640		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E5	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/Belgium/G198/2017		2017-01-23	SIATx/MDCK1	640	640	320	160	320	160	640	640	640	1280	640		
A/Austria/971917/2017		2017-02-13	C2/MDCK1	640	640	320	160	640	320	1280	1280	1280	1280	1280		
A/Austria/971919/2017		2017-02-13	C1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640		
A/Thuringen/130/2017		2017-02-18	C1/MDCK1	1280	640	640	320	640	320	1280	1280	1280	2560	1280		
A/Austria/971790/2017		2017-02-20	C2/MDCK1	1280	640	640	320	640	640	1280	1280	1280	2560	1280		
A/Bretagne/1184/2017		2017-03-22	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	1280		
A/England/41/2017		2017-04-12	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640		
A/Paris/1226/2017		2017-05-03	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640		
A/Paris/1227/2017		2017-05-03	MDCK1/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640		
				Vaccine NH 2017-18	Vaccine NH 2016-17											

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

1 < = <40; 2 < = <80

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 continue 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 initially highlighted 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 to 4-2. Since the June 2017 report, 57 EU/EEA viruses retained sufficient HA titre to be analysed by HI assay. A further 80 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 35/57 (61%) test viruses at titres within fourfold compared to the titre of the antiserum for the homologous virus. Antiserum raised against the cell culture-propagated cultivar of A/Hong Kong/4801/2014 was somewhat more effective, with 46/57 (81%) giving titres within fourfold of that for the homologous virus. Antisera have been raised against two reference viruses in the 3C.2a1 subclade, cell culture-propagated A/Oman/2565/2016 and A/Norway/4436/2016, but these reference viruses are unable to agglutinate RBCs. Nevertheless, a similar number of test viruses, 46/57 (81%) and 44/57 (77%) were recognised by these antisera respectively, at a range of titres within fourfold of the highest titre. An antiserum raised against egg-propagated A/Switzerland/9715293/2013 (3C.3a), the northern hemisphere 2015–16 vaccine component, reacted well with all but eight (14%) test viruses at titres within fourfold of the homologous titre. Genetic analysis is ongoing.

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.

[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	Collection date	Passage history	Haemagglutination inhibition titre															
				Post-infection ferret antisera															
				A/Texas	A/Samara	A/Stock	A/Stock	A/Switz	A/Switz	A/HK	A/HK	A/HK	A/HK	A/Georgia	A/Oman	A/Nor
				50/12	73/13	6/14	6/14	9715293/13	9715293/13	5738/14	4801/14	4801/14	532/15	2585/16	4436/16	
				Egg	SIAT	SIAT	Egg	SIAT	Egg	MDCK	MDCK	Egg	SIAT	SIAT	SIAT	
	Passage history			F08/14[1]	F35/15[1]	F14/14[1]	F20/14[1]	F18/15[1]	F73/16[1]	F30/14[1]	F43/15[1]	F12/15[1]	F33/15[1]	NIB F50/16[1]	F03/17[1]	
	Ferret number			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a1	3C.2a1	
	Genetic group															
REFERENCE VIRUSES																
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	2560	1280	160	1280	80	640	320	640	80	160	160	160	640
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	640	640	320	640	160	320	640	1280	160	320	640	640	640
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	80	40	320	160	160	160	160	320	80	160	320	320	320
A/Stockholm/6/2014 isolate 2	3C.3a	2014-02-06	E4/E1	160	80	160	320	40	640	160	320	40	40	160	160	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	40	40	320	160	80	80	80	80	40	80	160	160	160
A/Switzerland/9715293/2013 clone 123	3C.3a	2013-12-06	E4/E1	160	320	320	640	80	1280	320	320	80	160	320	320	640
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	160	160	320	320	160	80	160	640	160	160	320	320	640
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1	160	80	160	160	160	80	160	640	160	160	160	160	320
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	80	160	80	80	80	40	320	640	320	640	640	640	320
A/Georgia/532/2015 plaq 20	3C.2a	2015-03-09	SIAT1/SIAT5	160	160	320	320	160	160	320	640	320	1280	640	640	640
TEST VIRUSES																
A/Trencin/46/2016		2016-12-01	MDCK1/SIAT1	80	80	160	160	80	80	160	320	80	80	160	160	160
A/Piestany/80/2016		2016-12-12	MDCK1/SIAT1	40	40	160	80	80	40	160	160	80	80	160	160	160
A/Prievidza/77/2016		2016-12-19	MDCK1/SIAT1	80	80	160	160	80	80	160	640	160	160	320	320	320
A/Komarno/93/2016		2016-12-20	MDCK1/SIAT1	80	80	320	160	160	80	320	320	160	160	320	320	320
A/Trnava/97/2016		2016-12-21	MDCK1/SIAT1	80	80	320	160	160	80	160	320	160	320	320	320	320
A/Trnava/90/2016		2016-12-21	MDCK2/SIAT1	40	40	160	160	80	40	320	320	160	160	160	160	320
A/Trencin/94/2016		2016-12-22	MDCK1/SIAT1	160	160	320	160	160	160	320	320	160	640	640	640	640
A/Stockholm/59/2016		2016-12-25	MDCK2/SIAT1	40	<	160	80	40	40	160	160	40	40	160	160	160
A/Bratislava/112/2016		2016-12-30	MDCKx/SIAT1	80	80	160	160	80	80	160	320	160	80	160	160	160
A/Lubic ai/132/2017		2017-01-03	MDCKx/SIAT1	<	<	<	<	<	<	40	80	<	80	80	80	80
A/Levice/133/2017		2017-01-04	MDCKx/SIAT1	160	80	320	160	160	80	160	640	160	160	160	320	320
A/Kosice/182/2017		2017-01-05	MDCKx/SIAT1	80	80	160	160	80	40	160	320	160	80	160	160	160
A/Povazska Bystrica/151/2017		2017-01-10	MDCKx/SIAT1	80	40	160	80	80	80	160	320	160	80	320	320	320
A/Nitra/157/2017		2017-01-11	MDCKx/SIAT1	80	80	320	160	80	80	160	320	160	160	320	320	320
A/Stockholm/8/2017		2017-01-12	MDCK0/SIAT1	40	<	80	40	40	<	80	160	40	40	80	80	80
A/Nove Zamky/184/2017		2017-01-17	MDCKx/SIAT1	80	80	320	160	160	80	160	320	160	320	320	320	320
A/Piestany/205/2017		2017-01-18	MDCKx/SIAT1	80	80	320	160	160	80	160	320	160	160	320	320	320
A/Poitiers/767/2017		2017-01-18	MDCK2/SIAT1	80	80	320	160	80	80	160	320	80	320	320	320	320
A/Perugia/26/2017		2017-01-20	SIAT3/SIAT2	80	80	320	160	160	80	160	320	160	160	320	320	320
A/Stockholm/26/2017		2017-01-21	MDCK0/SIAT1	40	40	40	40	<	<	80	160	40	40	40	40	80
A/Dunajska Streda/232/2017		2017-01-24	MDCKx/SIAT1	80	80	320	160	80	80	160	320	80	160	320	320	320
A/Slovenia/625/2017		2017-01-25	MDCKx/SIAT1	80	80	320	160	160	80	320	320	160	80	640	640	320
A/Sassari/9/2017		2017-01-30	SIAT1/SIAT1	80	80	320	160	160	80	320	320	160	80	320	320	320
A/Friuli-Venezia Giulia/59/2017		2017-02-01	SIAT1/SIAT1	40	40	80	80	40	<	80	160	40	40	80	80	80
A/Sachsen/107/2017		2017-02-07	C1/SIAT1	<	<	160	<	<	<	40	80	<	<	<	80	40
A/Perugia/30/2017		2017-02-07	SIAT1/SIAT1	<	<	80	40	<	<	80	80	<	<	<	80	80
A/Slovenia/1159/2017		2017-02-15	MDCKx/SIAT1	160	40	320	160	160	80	160	320	160	80	320	320	320
A/Bratislava/322/2017		2017-02-15	MDCKx/SIAT1	80	80	160	160	80	40	160	320	160	320	160	160	320
A/Sachsen/99/2017		2017-02-23	C2/SIAT1	80	40	80	80	40	40	80	160	80	40	80	80	80
A/Slovenia/1391/2017		2017-03-08	MDCKx/SIAT1	40	40	320	80	80	80	160	160	80	80	320	320	320
A/Slovenia/1406/2017		2017-03-08	MDCKx/SIAT1	<	<	<	<	<	<	40	40	<	<	<	80	40
A/Mecklenburg-Vorpommern/17/2017		2017-03-08	C1/SIAT1	40	<	160	40	40	<	160	80	40	<	<	160	80
A/Brandenburg/40/2017		2017-03-10	C1/SIAT1	40	<	160	40	40	<	80	80	40	<	<	160	160
A/Thuringen/52/2017		2017-03-13	C1/SIAT1	40	<	160	40	40	<	160	80	40	<	<	160	80
A/Nordrhein-Westfalen/106/2017		2017-03-17	C1/SIAT1	40	<	160	<	40	<	160	80	40	<	<	160	160
A/Sachsen/71/2017		2017-03-20	C1/SIAT1	40	<	160	40	40	<	80	80	40	<	<	40	80
A/Niedersachsen/185/2017		2017-03-20	C2/SIAT1	40	<	160	40	40	40	80	80	40	40	40	160	160
A/Norway/1940/2017	3C.2a1	2017-03-20	SIAT1/SIAT1	80	80	320	160	160	80	160	320	160	160	160	320	80
A/Norway/1934/2017	3C.2a	2017-03-21	SIAT1/SIAT1	40	40	160	80	40	<	160	160	40	40	40	160	160
A/Norway/2113/2017	3C.2a1	2017-03-30	SIAT1/SIAT1	40	<	160	80	80	<	160	160	40	<	<	160	160
A/Bremen/27/2017		2017-04-19	C1/SIAT1	40	<	160	80	40	<	80	80	40	<	<	40	160

Vaccine

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

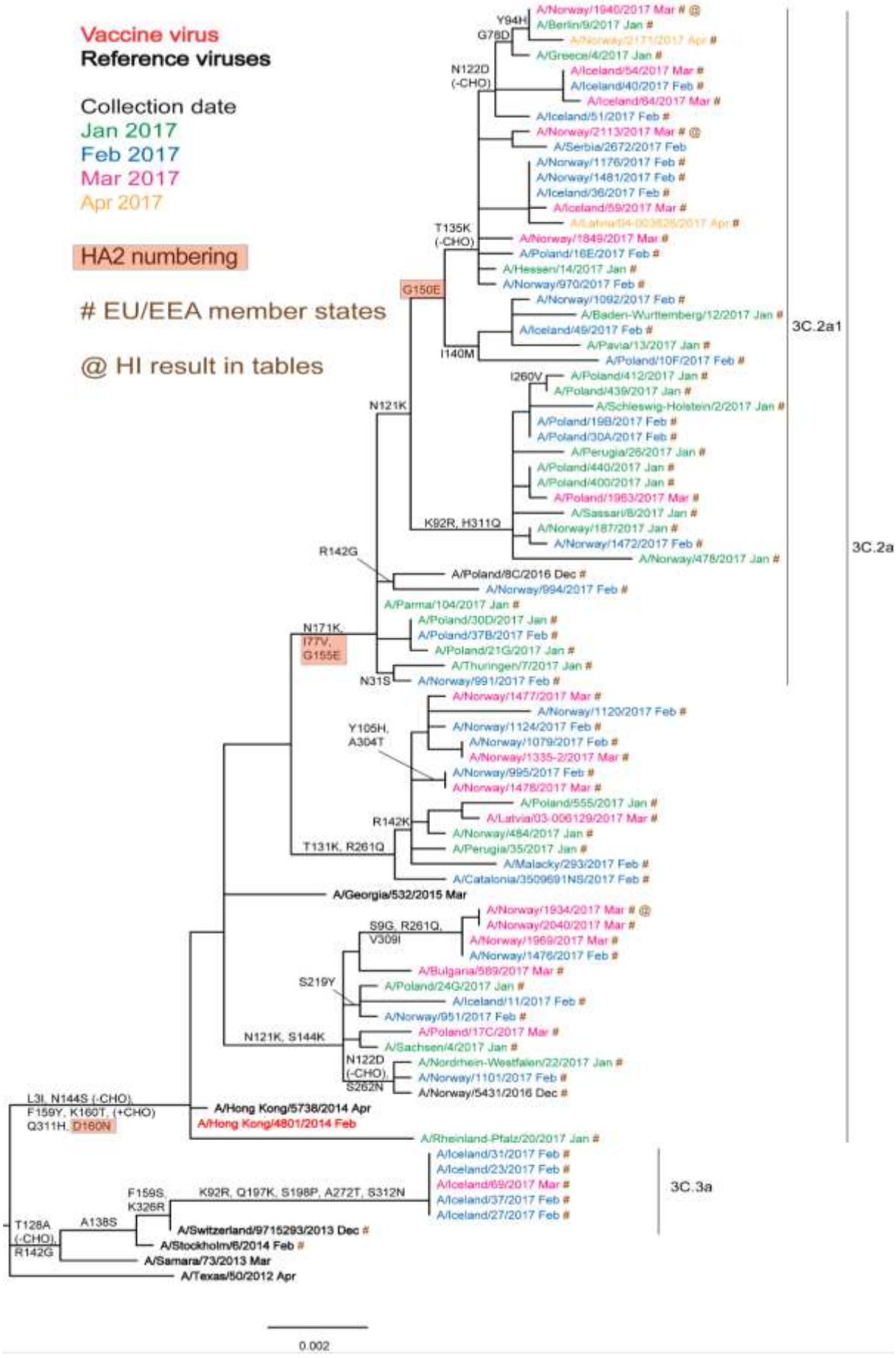
Sequences in phylogenetic trees

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	A/Switz	A/HK	A/HK	A/Oman	A/Nor	
				6/14	9715293/13	4801/14	4801/14	2585/16	4436/16	
	Passage history			SIAT	SIAT	MDCK	Egg	SIAT	SIAT	
	Ferret number			F14/14[-1]	F18/15[+1]	F43/15[-1]	F12/15[-1]	NIB F50/16[-1]	F03/17[-1]	
	Genetic group			3C.3a	3C.3a	3C.2a	3C.2a	3C.2a1	3C.2a1	
REFERENCE VIRUSES										
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	320	160	320	80	320	320	
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	320	80	160	40	160	160	
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1	160	80	320	80	160	160	
A/Hong Kong/4801/2014	isolate 1 3C.2a	2014-02-26	E6/E2	80	40	640	320	320	320	
TEST VIRUSES										
A/Stockholm/58/2016		2016-12-28	MDCK0/SIAT1	160	40	160	80	160	160	
A/Stockholm/60/2016		2016-12-28	MDCK1/SIAT2	160	40	160	80	160	160	
A/Thuringen/165/2017		2017-01-13	C1/SIAT2	320	80	320	80	160	320	
A/Stockholm/11/2017		2017-01-14	MDCK0/SIAT2	160	40	160	80	160	160	
A/Sundsvall/1/2017		2017-01-17	MDCK1/SIAT1	320	80	320	80	160	160	
A/Belgium/H25/2017		2017-01-25	SIATx/SIAT1	160	40	320	80	160	160	
A/Belgium/H23/2017		2017-01-29	SIATx/SIAT1	40	<	80	40	40	80	
A/England/19/2017		2017-01-31	SIAT1/SIAT1	160	80	320	80	80	160	
A/Paris/1023/2017		2017-02-16	MDCK1/SIAT1	80	40	80	40	80	160	
A/Linkoping/3/2017		2017-02-17	MDCK1/SIAT1	160	80	320	80	160	160	
A/Linkoping/1/2017		2017-02-17	MDCK2/SIAT2	320	80	320	80	320	320	
A/Basse Normandie/1055/2017		2017-02-20	MDCK1/SIAT1	80	40	160	40	160	160	
A/Linkoping/2/2017		2017-02-27	MDCK3/SIAT1	160	40	160	80	80	80	
A/Niedersachsen/186/2017		2017-03-21	C2/SIAT2	320	80	160	80	320	320	
A/Dijon/1176/2017		2017-03-14	MDCK1/SIAT1	80	<	80	40	80	40	
A/Paris/1145/2017		2017-03-06	MDCK1/SIAT1	160	<	80	40	80	160	
										Vaccine

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

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



Influenza B virus analyses

EU/EEA countries have provided 149 influenza type B-positive specimens with collection dates after 31 December 2016: 147 were ascribed to a lineage, 58 B/Victoria-lineage and 89 B/Yamagata-lineage (Table 2).

Influenza B – Victoria lineage

Since the June 2017 report, 13 viruses of the B/Victoria lineage have been characterised antigenically. All viruses sequenced to date belonged to genetic clade 1A and HI results are shown in Table 5.

All 13 test viruses showed similar HI reactivity patterns to those observed throughout the 2014–15 and 2015–16 influenza seasons. None of the test viruses gave titres within fourfold of the titre for the homologous virus with an antiserum raised against the egg-propagated vaccine virus, B/Brisbane/60/2008, recommended for use in both trivalent and quadrivalent vaccines. These 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 all test viruses at a titre within fourfold of the homologous titre 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).

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. In one group the HA gene encodes an HA with deletions of residues 162 and 163 of HA1 (exemplified by B/Norway/2409/2017) while the other group encodes an HA with deletions of residues 162, 163 and 164 of HA1 (exemplified by B/Hong Kong/269/2017). Viruses with the 162-163 HA1 deletion have additional substitutions **D129G, I180V** in **HA1** and **R151K** in **HA2** and viruses with the 162-164 HA1 deletion have additional substitutions **I180T** and **K209N** in **HA1**.

Influenza B – Yamagata lineage

HI results for 18 B/Yamagata-lineage test virus analysed since the June 2017 report are shown in Table 6. The two viruses sequenced both belonged to genetic clade 3.

Antisera raised against egg-propagated B/Phuket/3073/2013, recommended for inclusion in quadrivalent influenza vaccines since the southern hemisphere 2016 season, recognised 17/18 (94%) test viruses at titres within fourfold of the titre of the virus for the homologous virus. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised 89% of 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, recognised all of the test viruses at a titre within fourfold of the homologous titre of the antiserum. Similarly, antisera raised against clade 3 egg-propagated viruses B/Stockholm/12/2011 and B/Hong Kong/3417/2014 recognised all of the test virus at titres within fourfold of the respective homologous titres of the antisera.

Antisera raised against both egg and cell-propagated clade 2 viruses recognised the test viruses less well, with seven to nine of the 18 viruses (39-50%) being recognised at titres within fourfold of the homologous titres of the antisera. Genetic analysis of the most recently received viruses is ongoing.

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 the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade (clade 3), with most of them 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 the B/Victoria-lineage viruses.

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			Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK
		Ferret number			Sh 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/E6	5120	320	80	40	80	40	80	10	<	<
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	5120	160	640	320	320	160	1280	80	40	40
B/Malta/636714/2011		1A	2011-03-07	E4/E1	5120	80	320	160	160	80	320	40	20	20
B/Johannesburg/3964/2012		1A	2012-08-03	E1/E2	5120	320	1280	640	640	640	1280	160	80	80
B/Formosa/V2367/2012		1A	2012-08-06	MDCK1/MDCK3	5120	40	320	160	80	160	320	40	40	40
B/South Australia/81/2012		1A	2012-11-28	E4/E1	5120	80	160	80	80	80	320	20	20	10
B/Hong Kong/514/2009		1B	2009-10-11	MDCK3	5120	<	20	20	20	40	80	40	40	40
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	5120	<	20	40	<	40	40	20	40	80
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK3	5120	<	40	80	<	80	80	40	80	80
TEST VIRUSES														
B/Lyon/CHU/12.1R308/2017		1A	2017-01-12	MDCK2/MDCK1	5120	40	20	10	20	40	80	40	40	40
B/St Etienne/931/2017		1A	2017-01-22	MDCK2/MDCK1	5120	10	40	20	40	80	80	40	80	40
B/St Etienne/932/2017		1A	2017-01-22	MDCK2/MDCK1	5120	40	40	20	40	80	80	40	80	40
B/Lyon/CHU/25.1R258/2017		1A	2017-01-25	MDCK2/MDCK1	5120	<	20	10	<	40	80	40	80	40
B/Lyon/CHU6.2R80/2017		1A	2017-02-05	MDCK2/MDCK1	5120	<	20	10	<	40	80	40	80	40
B/Lyon/1010/2017		1A	2017-02-17	MDCK2/MDCK1	5120	<	20	40	20	80	80	40	40	40
B/Linkoping/4/2017		1A	2017-02-18	MDCK1/MDCK1	5120	<	20	80	20	80	40	40	40	40
B/Belgium/S1204/2017			2017-02-28	SIATx/MDCK1	5120	<	20	10	<	40	80	20	40	40
B/Austria/975422/2017			2017-03-07	C1/MDCK1	5120	<	40	20	20	80	80	40	80	320
B/Niedersachsen/20/2017			2017-03-10	C1/MDCK1	2560	<	40	10	<	80	80	40	80	80
B/England/36/2017			2017-03-17	SIAT1/MDCK1	2560	<	40	20	20	80	80	40	80	40
B/Norway/2076/2017			2017-04-01	MDCK2	2560	<	40	20	<	80	80	40	80	40
B/England/46/2017			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

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

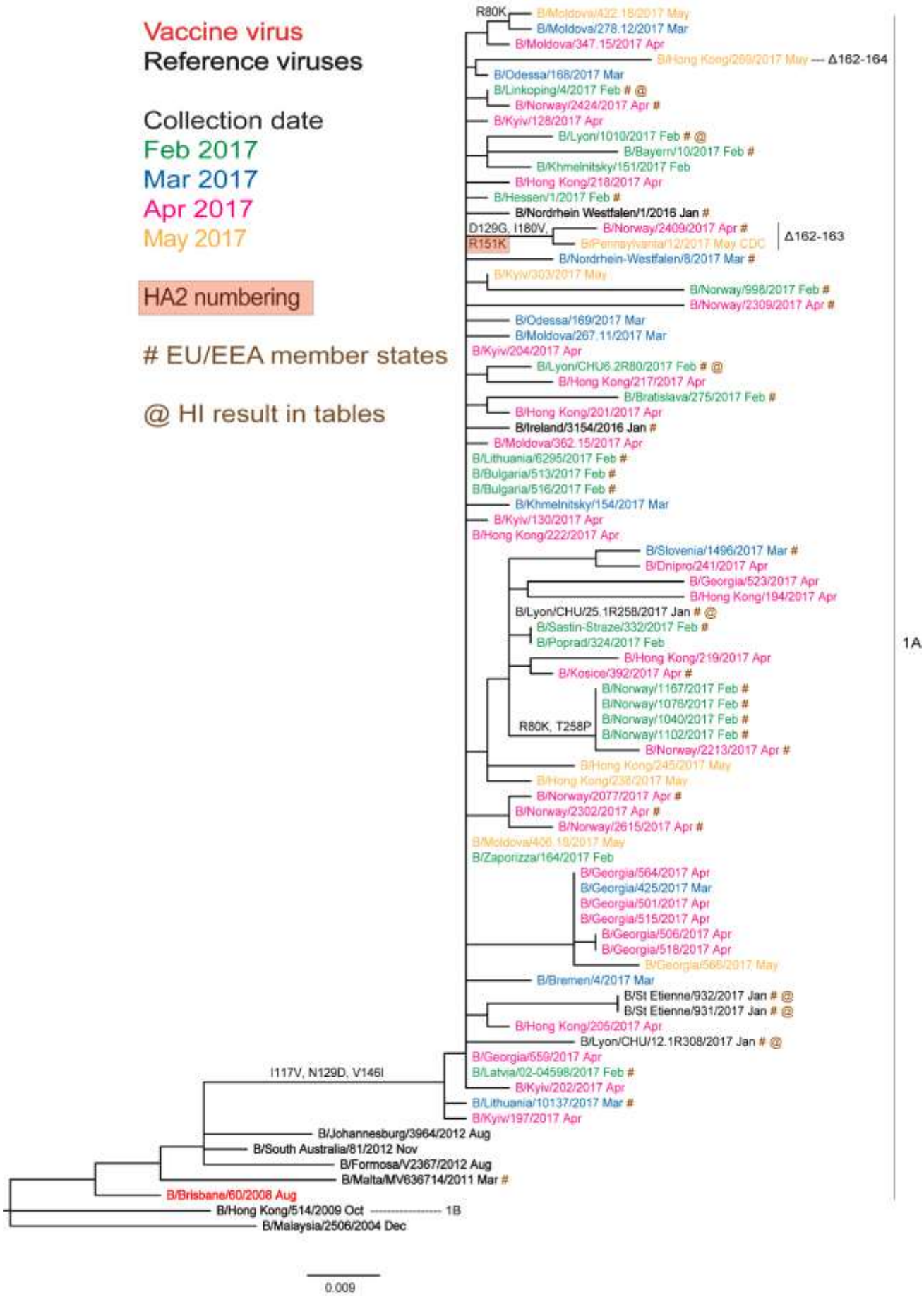


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

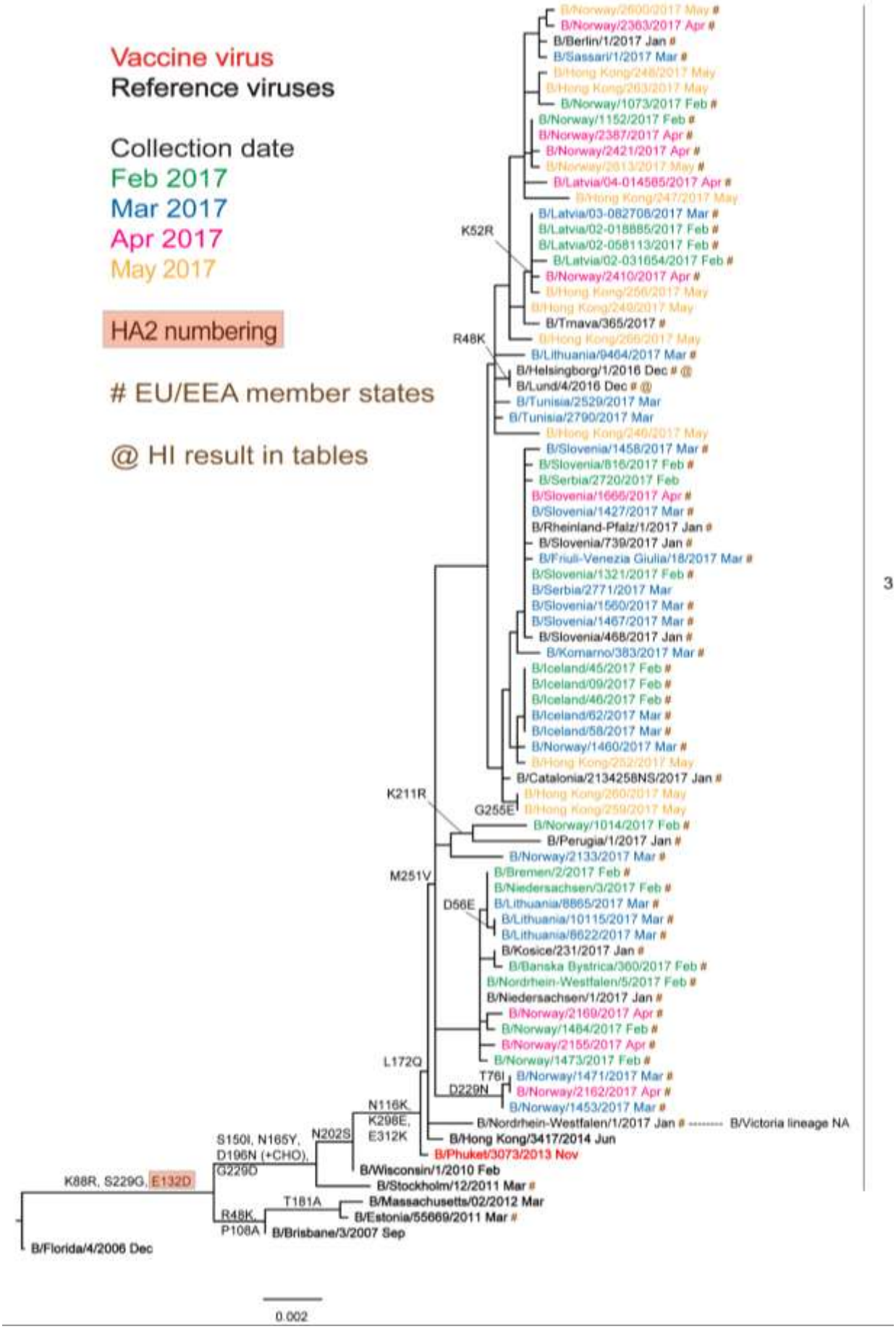
Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					B/Phuket 3073/13	B/Fl 4/06	B/Bris 3/07	B/Estonia 55669/11	B/Mass 02/12	B/Mass 02/12	B/Wis 1/10	B/Stock 12/11	B/Phuket 3073/13	B/Phuket 3073/13	B/HK 3417/14
		Passage history			Egg	Egg	Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	Egg
		Ferret number			SH614*1,3	F17/13*1	F38/14*2	F27/13*2	F05/15*2	F42/14*2	F36/15*2	F06/15*2	F27/15*2	NIB F51/16*2	St Judes F715/14*2,4
		Genetic Group			3	1	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES															
B/Florida/4/2006		1	2006-12-15	E7/E1	1280	640	640	160	80	640	160	160	<	640	160
B/Brisbane/3/2007		2	2007-09-03	E2/E3	1280	640	640	160	80	640	160	160	<	640	160
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	2560	160	160	640	640	160	320	20	80	160	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	320	320	320	160	40	<	320	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	640	640	160	80	640	80	80	<	320	160
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	160	160	40	20	320	160	160	<	320	160
B/Stockholm/12/2011		3	2011-03-28	EX/E2	1280	160	80	20	<	80	80	80	<	160	80
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK2	5120	160	160	160	160	160	320	80	160	320	160
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	160	160	20	10	80	80	80	<	320	80
B/Hong Kong/3417/2014		3	2014-06-04	E4/E1	640	40	40	10	<	40	40	20	<	80	80
TEST VIRUSES															
B/Helsingborg/1/2016		3	2016-12-08	MDCK0/MDCK1	2560	80	80	80	80	40	80	20	40	80	80
B/Lund/4/2016		3	2016-12-10	MDCK0/MDCK1	2560	80	80	40	40	40	80	20	40	80	80
B/Lisboa/2/2017			2017-01-24	SIAT1/MDCK1	5120	160	320	320	640	320	320	160	320	640	320
B/Belgium/S918/2017			2017-02-11	SIATx/MDCK1	1280	40	40	40	20	20	40	10	<	40	80
B/Thuringen/2/2017			2017-02-15	C1/MDCK1	1280	40	40	40	10	40	40	20	40	80	80
B/Austria/971742/2017			2017-02-17	C1/MDCK1	5120	320	320	320	1280	320	320	160	160	640	160
B/Austria/971746/2017			2017-02-18	C1/MDCK1	5120	320	640	640	1280	640	640	320	320	640	320
B/Austria/972293/2017			2017-02-20	C1/MDCK2	5120	160	160	160	320	160	320	80	160	320	320
B/Austria/972415/2017			2017-02-20	C1/MDCK1	2560	80	80	80	40	80	80	20	40	160	160
B/Austria/972769/2017			2017-02-20	C1/MDCK1	2560	80	80	40	20	40	40	20	40	80	160
B/Lorraine/1080/2017			2017-02-22	MDCK1/MDCK1	1280	40	40	80	20	40	40	20	20	80	160
B/Austria/973511/2017			2017-02-27	C1/MDCK1	5120	320	160	160	320	320	320	160	160	320	160
B/Brest/1191/2017			2017-03-05	MDCK1/MDCK1	2560	40	40	40	20	40	40	20	20	80	160
B/Austria/979756/2017			2017-03-27	C2/MDCK1	2560	80	80	80	40	20	80	20	<	80	160
B/Norway/2431/2017			2017-04-21	MDCK2	2560	80	80	40	10	40	40	20	80	160	160
B/Austria/986609/2017			2017-04-24	C1/MDCK1	5120	160	160	160	320	160	160	80	80	320	160
B/Austria/986875/2017			2017-04-24	C1/MDCK1	5120	320	160	160	320	320	320	80	160	320	160
B/England/53/2017			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 33/2017, 4489 viruses have been characterised genetically: 17 were defined as A(H1N1)pdm09 clade 6B represented by A/South Africa/3626/2013 and 56 were subclade 6B.1, as represented by A/Michigan/45/2015; 1179 were A(H3N2) subclade 3C.2a represented by A/Hong Kong/4801/2014, 2655 subclade 3C.2a1 represented by A/Bolzano/7/2016, 43 subclade 3C.3a represented by A/Switzerland/9715293/2013, one subclade 3C.3 represented by A/Samara/73/2013 and five belonged to a group that was unlisted; 172 were B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008 and one clade 1B represented by B/Hong Kong/514/2009; and 347 were B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013, with 13 unattributed.

Antiviral susceptibility

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 894 viruses from EU/EEA countries with collection dates after week 40/2016 at the Crick Worldwide Influenza Centre: 35 A(H1N1)pdm09, 720 A(H3N2), 51 B/Victoria-lineage and 88 B/Yamagata-lineage viruses. Since the June 2017 report, none of the viruses has shown reduced inhibition (RI) by either oseltamivir or zanamivir.

For weeks 40/2016-33/2017 of the 2016–17 influenza season, countries reported on the antiviral susceptibility of 62 A(H1N1)pdm09 viruses, 3108 A(H3N2) viruses and 343 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, World Health Organization (WHO) Global Alert and Response [3] 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 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 [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 25 July 2017 [9], with the latest cases being reported on 19 July 2017 [10].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 25 July 2017 [9]. ECDC published an updated rapid risk assessment on the situation in Egypt on 13 March 2015 [11] and an epidemiological update on 10 April 2015 [12]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [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 WHO vaccine composition meetings held at WHO Geneva 26–28 September 2016 and 27 February–1 March 2017 can be found at:

https://www.crick.ac.uk/media/326439/september_2016_interim_report.pdf and

https://www.crick.ac.uk/media/358671/crick_nh_vcm_report_feb_2017_v2.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 National Influenza Centres in EU/EEA countries are marked (#). Sequences for some viruses from non-EU/EEA countries were recovered from GISAID. We gratefully acknowledge the authors, the originating and submitting laboratories for 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), and all those laboratories that submitted sequences directly to the London WHO Collaborating Centre.

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