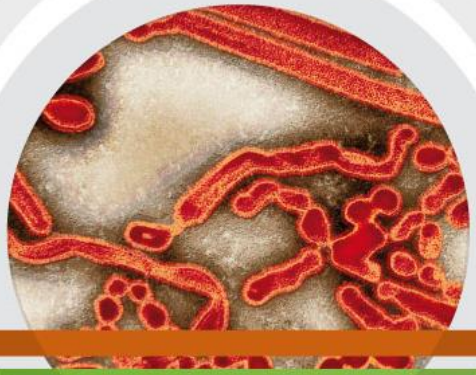

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, June 2017

Summary

In the course of the 2016–2017 influenza season, nearly 146 000 influenza detections across the EU/EAA 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 January 2017 EU/EEA countries have shared 1039 influenza-positive specimens with the WHO Collaborating Centre (CC), London, for detailed characterisation: 518 of these had collection dates after 31 December 2016. Subsequent to the WHO CC's Vaccine Composition Meeting (VCM) report for February 2017, 217 viruses were characterised antigenically and 525 genetically, many with collection dates prior to 1 January 2017. Many A(H3N2) viruses could only be characterised genetically as HA titres were too low to allow antigenic characterisation by haemagglutination inhibition assay. Post-VCM report results are presented and discussed in this ECDC virus characterisation report.

All 22 A(H1N1)pdm09 viruses characterised antigenically were similar to the 2016–17 vaccine virus, A/California/7/2009, but showed somewhat better 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, became dominant worldwide and all 16 EU/EEA viruses characterised with 2017 collection dates, were within this subclade.

The 105 A(H3N2) test viruses able to be characterised by haemagglutination inhibition (HI) assay were recognised well by antisera raised against egg-propagated A/Hong Kong/4801/2014 (the current vaccine component) and several cell culture-propagated viruses in the 3C.2a clade. 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 1 (1%) was subclade 3C.3a.

Of the 32 B/Victoria-lineage viruses tested, 31 were antigenically similar to tissue culture-propagated surrogates of B/Brisbane/60/2008. One virus, B/Norway/2409/2017, gave no reactivity with any of the ferret antisera used and was shown to have a deletion of two amino acids in HA1 at positions 162 and 163. All 23 viruses characterised with collection dates in 2017, including the viruses with the deletion in the HA, fell in genetic clade 1A, as do recently collected viruses worldwide.

Of the 58 B/Yamagata viruses characterised antigenically, 42 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 44 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 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, 50 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC), from countries in the EU/EEA. These packages contained 518 specimens, a mix of clinical samples and virus isolates originating from 21 countries in EU/EAA, with collection dates after 31 December 2016 (Table 2). The majority (73%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 10.5:1. Of the 137 type B specimens received (26% of the specimens), 52 were B/Victoria-lineage and 82 were B/Yamagata-lineage. Many specimens are still in the process of being characterised. The antigenic and genetic properties of influenza virus isolates, characterised since the February 2017 Crick Worldwide Influenza Centre Vaccine Composition Meeting (VCM) 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] Worldwide Influenza Centre at the Francis Crick Institute, a WHO Collaborating Centre for Reference and Research on Influenza. Report prepared for the WHO annual consultation on the composition of influenza vaccines for use in the northern hemisphere 2017–2018 [14].

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	in process							
Belgium	20					20	2	16						
Bulgaria	39			4	in process	35	in process							
Cyprus	18					18	in process							
Germany	33			5	5	22	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	in process						1	in process
Latvia	5					4	1	2					1	1
Luxembourg	2					2	0	2						
Norway	7			2	2	3	in process						2	in process
Poland	28	1	in process			27	in process							
Portugal	1										1	1		
Romania	15					15	0	15						
Slovakia	15					13	in process				1	in process	1	in process
Slovenia	18					10	in process						8	in process
Spain	6					5	in process						1	1
2017 FEBRUARY														
Austria	16			3	in process	7	in process						6	in process
Belgium	9					7	in process				1	in process	1	in process
Bulgaria	12			2	2	7	1	6			3	2		
France	2										2	in process		
Germany	15			5	in process	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	in process							
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						
Slovakia	9			2	2	3	in process				3	3	1	1
Slovenia	7					5	in process						2	2
Spain	1					1	1	0						
Sweden	4					3	in process				1	in process		
2017 MARCH														
Austria	3					1	in process		1	in process	1	in process		
Bulgaria	1					1	0	1						
Germany	13					8	in process				3	in process	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	in process				1	0	4	3
Poland	6					6	0	2						
Slovakia	1												1	1
Slovenia	7					2	in process				1	1	4	4
2017 APRIL														
Austria	2												2	in process
Germany	4					2	in process				1	1	1	1
Latvia	2					1	1	0					1	1
Norway	24			3	3	4	1	3			9	in process	8	8
Poland	1								1	0				
Slovakia	1										1	1		
Slovenia	1												1	1
2017 MAY														
Norway	5					3	1	1					2	2
21 Countries	518	1	0	33	18	347	35	91	3	0	52	24	82	57
		0.2%		6.4%		67.0%			0.6%		10.0%		15.8%	
				73.4%					26.4%					

*** 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 February 2017 VCM report [14] are shown in Table 3. All 22 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, recognised all but two of the test viruses gave titres at within twofold of the titre of the antiserum for the homologous virus. Generally, test viruses were recognised by the panel of antisera at titres within fourfold of the titres of the antisera with their respective homologous viruses.

Exceptions were observed with antisera raised against A/Lviv/N6/2009, A/St. Petersburg/100/2011 and A/Israel/Q-504/2015. These antisera recognised 4/22 (18%), 9/22 (41%) and 18/22 (82%) test viruses at titres within fourfold of titres for the homologous viruses, respectively. Reference viruses carrying HA1 G155E amino acid substitutions, A/Bayern/69/2009 and A/Lviv/N6/2009, showed reduced recognition (fourfold or greater) by the antisera raised against both vaccine viruses and reference viruses in genetic clades 5, 6, 7, 6B, 6B.1 and 6B.2.

All test viruses sequenced after the report for the February 2017 WHO VCM belong to genetic subclade 6B.1 (Table 1 and Figure 1). Since 2009, the HA genes have evolved, and nine clades have been designated. For approximately three years, viruses in clade 6 represented by A/St Petersburg/27/2011 and carrying amino acid substitutions of **D97N**, **S185T** and **S203T** in **HA1** and **E47K** and **S124N** in **HA2,** compared with A/California/7/2009, have predominated worldwide with a number of subgroups emerging. All EU/EEA viruses characterised since the September 2014 report[2] carry HA genes in subgroup 6B, which is characterised by additional amino acid substitutions of **K163Q, A256T** and **K283E** in **HA1** and **E172K** in **HA2** compared with A/California/7/2009, e.g. A/South Africa/3626/2013. A number of virus clusters have emerged within subgroup 6B, and two of these have been designated as subclades. Viruses in subclade 6B.1, represented by A/Michigan/45/2015, are defined by **HA1** amino acid substitutions **S84N, S162N** (which results in the formation of a new potential glycosylation motif at residues 162-164 of HA1) and **I216T**. Those in subclade 6B.2 are defined by **HA1** amino acid substitutions **V152T** and **V173I,** represented by A/Israel/Q-504/2015. All viruses examined fell into subclade 6B.1.

During the 2016–2017 influenza season, A(H1N1)pdm09 activity has been low compared to the previous season, and the viruses involved remained antigenically indistinguishable by post-infection ferret antisera raised against the A/California/7/2009 vaccine virus. The basis for the change of the A(H1N1)pdm09 component in the vaccine was described in the September 2016 ECDC characterisation report[3]. To summarise, studies with post-vaccination and post-infection human sera showed that a significant proportion could distinguish representative viruses of subclades 6B.1 and 6B.2 from the vaccine virus. Moreover, the reports of high levels of infection associated with A(H1N1)pdm09 in many countries, and the great dominance of subclade 6B.1 viruses among the H1N1pdm09 viruses in circulation led to the recommendation made by WHO to include an A/Michigan/45/2015–like virus in vaccines for the 2017 southern hemisphere and 2017–18 northern hemisphere influenza seasons [1,2].

[2] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2014. Stockholm: ECDC; 2014. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Influenza-ERLI-Net-report-Sept-2014.pdf

[3] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2016. Stockholm: ECDC; 2016. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/influenza-virus-characterisation-september-2016.pdf

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

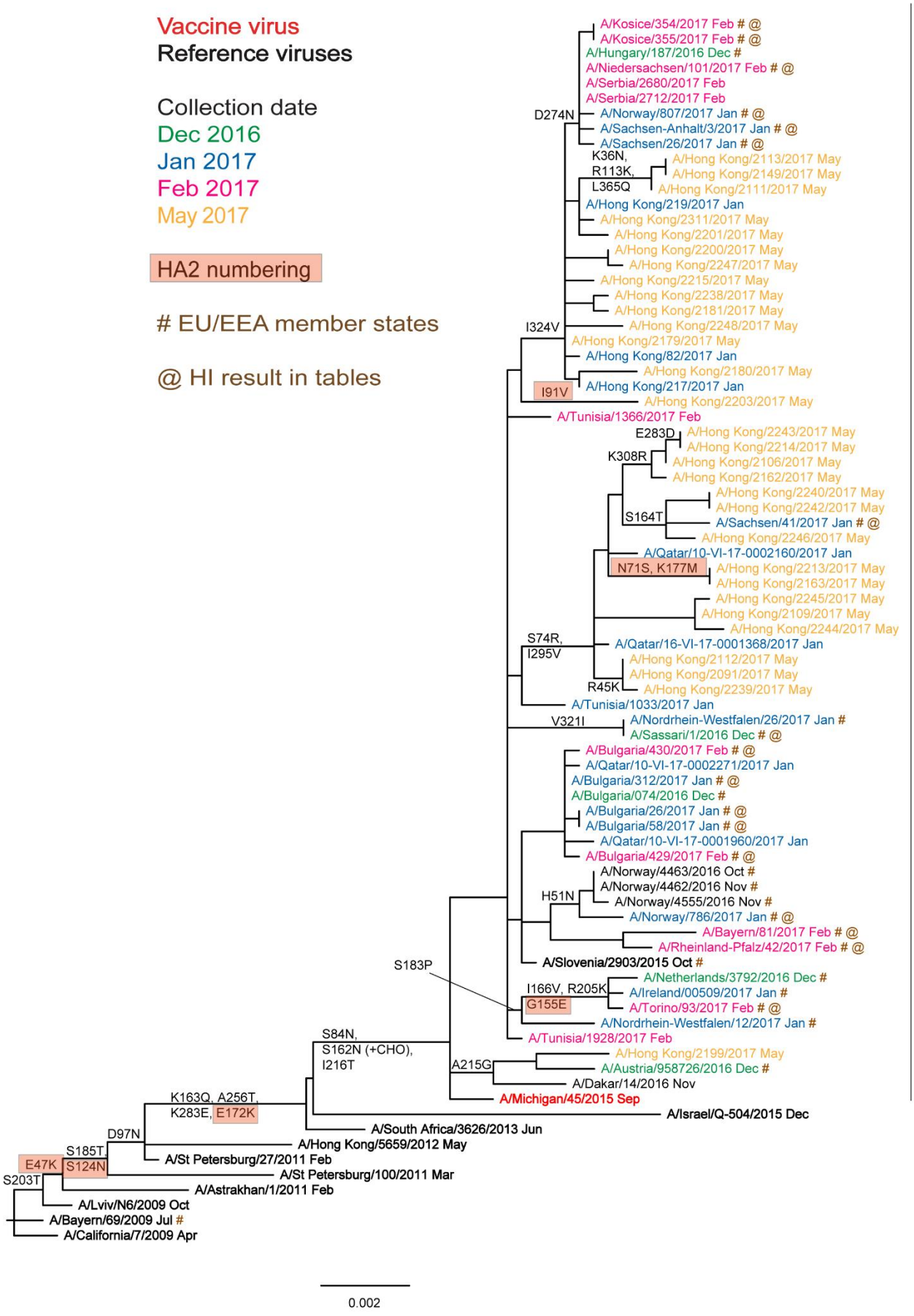
Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre											
					Post-infection ferret antisera											
					A/Mich	A/Cal	A/Bayern	A/Lviv	A/Astrak	A/St. P	A/St. P	A/HK	A/Sth Afr	A/Slov	A/Israel	
					45/15	7/09	69/09	N6/09	1/11	27/11	100/11	5659/12	3626/13	2903/2015	Q-504/15	
		Passage history			Egg	Egg	MDCK	MDCK	MDCK	Egg	Egg	MDCK	Egg	Egg	MDCK	
		Ferret number			NIB F42/16[*1]	F06/16[*1]	F09/15[*1]	F14/13[*1]	F22/13[*1]	F26/14[*1]	F24/11[*1]	F30/12[*1]	F03/14[*1]	F02/16[*2]	F08/16[*2]	
		Genetic group			6B.1				5	6	7	6A	6B	6B.1	6B.2	
REFERENCE VIRUSES																
A/Michigan/45/2015		6B.1	2015-09-07	E3/E2	640	640	320	160	640	320	1280	1280	640	1280	640	
A/California/7/2009	clone 38-32		2009-04-09	E3/E4	640	640	320	160	640	320	1280	640	640	1280	640	
A/Bayern/69/2009			2009-07-01	MDCK5/MDCK1	40	40	320	160	80	40	40	80	80	80	40	G155E
A/Lviv/N6/2009			2009-10-27	MDCK4/SIAT1/MDCK3	160	160	1280	1280	80	80	160	320	80	160	160	G155E>G, D222G
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	2560	1280	1280	640	1280	640	2560	2560	1280	2560	1280	
A/St. Petersburg/27/2011		6	2011-02-14	E1/E4	2560	1280	1280	640	2560	640	2560	2560	1280	2560	1280	
A/St. Petersburg/100/2011		7	2011-03-14	E1/E4	5120	5120	2560	1280	5120	1280	5120	5120	5120	5120	5120	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	160	160	80	160	320	320	640	160	320	320	
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	1280	640	640	640	640	640	1280	1280	1280	1280	640	
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E1	2560	2560	640	640	1280	640	2560	2560	1280	2560	2560	
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	2560	1280	640	320	1280	640	2560	2560	1280	2560	2560	
TEST VIRUSES																
A/Sassari/1/2016		6B.1	2016-12-30	MDCK3/MDCK1	640	640	320	160	640	320	1280	1280	640	2560	1280	
A/Bulgaria/58/2017		6B.1	2017-01-02	SIAT2/MDCK1	640	320	160	80	320	160	640	320	320	640	320	
A/Bulgaria/26/2017		6B.1	2017-01-02	SIAT2/MDCK1	640	320	160	80	320	160	640	640	320	640	640	
A/Bulgaria/312/2017		6B.1	2017-01-11	SIAT2/MDCK1	640	320	160	80	320	160	640	640	320	640	320	
A/Sachsen/26/2017		6B.1	2017-01-26	C2/MDCK1	640	320	160	80	320	320	640	640	640	1280	640	
A/Norway/786/2017		6B.1	2017-01-27	MDCK1/MDCK1	640	320	160	160	640	160	640	640	640	1280	640	
A/Norway/807/2017		6B.1	2017-01-27	MDCK1/MDCK1	640	320	160	80	320	160	640	640	640	1280	320	
A/Sachsen-Anhalt/3/2017		6B.1	2017-01-27	C1/MDCK1	320	320	80	40	320	160	640	640	320	640	640	
A/Sachsen/41/2017		6B.1	2017-01-27	C1/MDCK1	1280	160	320	320	320	160	640	320	320	640	640	
A/Niedersachsen/101/2017		6B.1	2017-02-01	C1/MDCK1	320	320	160	80	320	160	640	320	320	640	320	
A/Bulgaria/430/2017		6B.1	2017-02-01	SIAT2/MDCK1	640	320	160	160	320	160	640	640	320	1280	640	
A/Bulgaria/429/2017		6B.1	2017-02-01	SIAT2/MDCK1	640	320	320	160	320	160	1280	640	640	1280	640	
A/Norway/1019/2017			2017-02-06	MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	
A/Kosice/355/2017		6B.1	2017-02-15	MDCKx/MDCK1	640	160	320	160	320	160	640	640	640	1280	640	
A/Kosice/354/2017		6B.1	2017-02-16	MDCKx/MDCK1	640	320	320	160	640	320	1280	640	640	1280	640	
A/Torino/93/2017		6B.1	2017-02-17	MDCK3/MDCK1	640	640	320	160	640	320	1280	640	640	1280	640	
A/Rheinland-Pfalz/42/2017		6B.1	2017-02-17	C2/MDCK1	640	320	160	80	320	160	640	640	640	1280	640	
A/Bayern/81/2017		6B.1	2017-02-27	C1/MDCK1	640	640	160	80	320	320	640	640	640	1280	640	
A/Norway/1888/2017		6B.1	2017-03-20	MDCK1/MDCK1	1280	640	640	320	640	320	1280	640	1280	2560	1280	
A/Norway/2146/2017		6B.1	2017-04-03	MDCK1/MDCK1	640	640	640	160	1280	320	1280	640	1280	2560	1280	
A/Norway/2147/2017		6B.1	2017-04-04	MDCK1	1280	1280	640	320	1280	320	2560	1280	1280	2560	1280	
A/Norway/2339/2017		6B.1	2017-04-19	MDCK1	640	1280	640	320	640	320	2560	1280	1280	2560	1280	
					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

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[4] 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 highlighted first in the November 2014 report[5], 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 4-4. Since the February 2017 VCM report, 105 EU/EAA viruses retained sufficient HA titre to be analysed by HI assay. A further 140 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.

The antiserum raised against egg-propagated A/Switzerland/9715293/2013 (3C.3a), the northern hemisphere 2015–16 vaccine component, reacted poorly with all but 10 (10%) test viruses at titres ≥eightfold reduced compared to the homologous titre. Eight of the ten viruses have been characterised genetically to date and all eight fall within the 3C.3a subclade. However, the antiserum raised against the cell culture-propagated cultivar of A/Switzerland/9715293/2013 was able to recognise 98 (93%) test viruses at titres similar to the homologous titre of the antiserum but this antiserum had a very low titre for the homologous virus. 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 102/105 (97%) test viruses at titres within fourfold compared to the titre of the antiserum for the homologous virus. Antiserum raised against the cell-propagated cultivar of A/Hong Kong/4801/2014 was slightly less effective with 90/105 (86%) giving titres within fourfold of that for the homologous virus. Similarly, an antiserum raised against another cell culture-propagated virus in clade 3C.2a, A/Hong Kong/5738/2014, recognised the test viruses well, with 103/105 (98%) of viruses recognised at a titre within fourfold of the homologous titre, 79% at a titre within twofold of the homologous titre of the antiserum. However, an antiserum raised against A/Georgia/2565/2016, another 3C.2a virus, recognised the test viruses poorly. Antisera have been raised against two reference viruses in the 3C.2a1 subclade, A/Oman/2565/2016 and A/Norway/4436/2016, but these reference viruses are unable to agglutinate red blood cells. Nevertheless, all the test viruses but two were recognised by these antisera at a range of titres within fourfold of the highest titre. The exceptions were A/Ireland/72703/2016, which was less well recognised by the antiserum raised against A/Norway/4436/2016, and A/Catalonia/93065/2016, which was less well recognised by the antisera raised against both A/Norway/4436/2016 and A/Catalonia/93065/2016 than were the other test viruses. Of the 72 viruses analysed by HI and characterised genetically, to date, 10, 23 and 39 fell within genetic subclades 3C.3a, 3C.2a and 3C.2a1 respectively.

Since 2009, seven genetic groups based on the HA gene have been defined for A(H3N2) viruses. Phylogenetic analysis of the HA genes of representative A(H3N2) viruses with recent collection dates is shown in Figure 2. The HA genes fall within clade 3C. This clade has three subdivisions: 3C.1 (represented by A/Texas/50/2012, the vaccine virus recommended for use in the 2014–15 northern hemisphere season), 3C.2 and 3C.3. Viruses in these three subdivisions had been antigenically similar. Following further diversification, in 2014 three new subclades were designated, one in subdivision 3C.2, 3C.2a, and two in 3C.3, 3C.3a and 3C.3b. Viruses in subclades 3C.2a and 3C.3a are antigenic drift variants and have circulated widely, with subclade 3C.2a viruses dominating 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 defining subclade 3C3a.

A total of 147 A(H3N2) viruses with collection dates since 1 January 2017 have been analysed genetically. One belonged to subclade 3C.3a and 146 fell within subclade 3C.2a. Of the latter, 108 were further differentiated as subclade 3C.2a1 viruses.

[4] 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

[5] 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

The World Health Organization recommendations for the A(H3N2) component of influenza vaccines for the northern hemisphere 2016–17 [2], southern hemisphere 2017 [3] and northern hemisphere 2017–18 [4] influenza seasons was for an A/Hong Kong/4801/2014-like (3C.2a) virus.

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/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
	Passage history			Egg	SIAT	SIAT	Egg	SIAT	Egg	MDCK	MDCK	Egg	SIAT	SIAT	SIAT
	Ferret number			F36/12-1	F35/15-1	F14/14-1	F20/14-1	F18/15-1	F32/14-1	F30/14-1	F43/15-1	F12/15-1	F33/15-1	NIB F50/16-1	F03/17-1
	Genetic group			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a1	3C.2a1
REFERENCE VIRUSES															
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	5120	640	160	640	80	640	160	640	80	160	160	320
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	1280	640	320	320	80	320	320	640	80	320	320	640
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	40	40	320	160	80	80	160	160	40	80	160	160
A/Stockholm/6/2014 isolate 2	3C.3a	2014-02-06	E4/E1	640	80	160	320	40	640	160	320	40	80	160	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	40	40	160	160	160	80	80	160	40	80	160	160
A/Switzerland/9715293/2013 clone 123	3C.3a	2013-12-06	E4/E1	320	160	160	320	40	640	160	320	160	160	160	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	80	80	160	160	80	80	160	320	160	160	320	320
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK2	160	80	320	160	160	160	320	640	160	320	640	320
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	40	80	40	40	40	40	160	320	160	320	640	160
A/Georgia/532/2015 plaq 20	3C.2a	2015-03-09	SIAT1/SIAT5	160	80	320	160	80	80	320	320	160	1280	320	320
TEST VIRUSES															
A/Stockholm/48/2016	3C.2a	unknown	MDCK1/SIAT1	40	40	160	80	40	40	80	320	80	80	160	160
A/Czech Republic/178/2017	3C.2a1	unknown	MDCKx/SIAT1	<	<	40	40	40	<	40	80	40	40	160	80
A/Lyon/22077/2016	3C.2a1	2016-10-24	MDCK3/SIAT1	40	40	160	80	80	40	80	320	80	160	160	160
A/Poitiers/22382/2016	3C.2a1	2016-11-01	MDCK3/SIAT1	80	80	320	160	160	80	160	320	160	160	320	320
A/Clermont Ferrand/2227/2016	3C.2a1	2016-11-02	MDCK2/SIAT1	<	40	160	80	40	40	80	160	40	80	80	160
A/Poitiers/2239/2016	3C.2a	2016-11-02	MDCK3/SIAT1	40	40	160	80	40	40	80	160	80	160	160	160
A/Sachsen/74/2016	3C.2a1	2016-11-07	C1/SIAT1	40	<	160	80	80	<	80	160	80	40	160	160
A/Stockholm/42/2016	3C.2a1	2016-11-10	MDCK1/SIAT1	40	40	160	80	40	40	80	320	80	80	160	160
A/Latvia/11-072125/2016	3C.2a1	2016-11-28	C2/SIAT1	40	40	80	80	40	80	80	160	80	80	80	80
A/Austria/956928/2016	3C.2a1	2016-11-30	C1/SIAT1	80	80	160	160	80	80	80	320	80	160	160	160
A/Hungary/175/2016	3C.2a	2016-12-02	MDCK1/SIAT1	40	<	80	80	40	<	<	80	40	40	160	160
A/Austria/957344/2016	3C.2a1	2016-12-04	C1/SIAT1	<	<	160	40	40	<	<	160	40	40	80	160
A/Austria/957860/2016	3C.2a1	2016-12-06	C2/SIAT1	40	40	160	80	80	40	80	160	80	80	160	160
A/Latvia/12-020474/2016	3C.2a1	2016-12-08	C2/SIAT1	40	40	80	80	40	40	80	320	80	80	160	80
A/Bayern/76/2016	3C.2a	2016-12-13	C1/SIAT1	40	40	160	80	160	40	160	160	80	80	320	320
A/Hungary/188/2016	3C.2a1	2016-12-13	MDCK1/SIAT1	40	<	40	40	40	<	40	40	<	40	80	80
A/Hungary/191/2016	3C.2a1	2016-12-13	MDCK1/SIAT1	40	40	160	80	40	40	80	160	80	80	160	160
A/Hungary/202/2016	3C.2a	2016-12-14	MDCK1/SIAT1	40	<	80	40	40	<	80	80	<	40	80	80
A/Czech Republic/169/2016	3C.2a1	2016-12-14	MDCK2/SIAT1	40	<	160	80	40	40	160	160	80	80	160	160
A/Sweden/153/2016	3C.2a	2016-12-16	MDCK1/SIAT1	<	<	160	40	40	<	40	160	40	80	160	80
A/Luxembourg/637222/2016	3C.2a1	2016-12-16	SIAT2	80	40	320	80	160	40	160	160	80	160	320	320
A/Sweden/157/2016	3C.2a1	2016-12-17	MDCK1/SIAT1	40	<	160	80	80	<	80	160	40	40	160	160
A/Czech Republic/176/2016	3C.2a	2016-12-19	MDCK2/SIAT1	40	<	160	40	40	40	160	160	40	160	160	160
A/Greece/726/2016	3C.2a	2016-12-19	SIAT1	40	40	160	80	40	<	160	160	80	80	160	160
A/Ireland/000098/2016	3C.3a	2016-12-29	C1/SIAT1	40	40	320	160	80	80	80	80	40	80	80	80
A/Ireland/86110/2016	3C.2a1	2016-12-29	C1/SIAT1	<	<	40	40	<	<	40	160	40	40	80	80
A/Ireland/00492/2017	3C.2a1	2017-01-02	C1/SIAT1	40	40	80	80	40	40	80	160	80	160	160	160
A/Slovenia/53/2017	3C.2a	2017-01-04	MDCK1/SIAT1	40	40	160	80	40	40	80	160	40	80	80	160
A/Greece/35/2017	3C.2a1	2017-01-10	SIAT2	40	<	80	40	40	<	80	160	80	40	160	160
A/Athens GR/496/2017	3C.2a	2017-01-17	SIAT1	40	40	160	80	80	40	160	160	80	80	160	320
A/Athens GR/499/2017	3C.2a1	2017-01-17	SIAT1	40	40	160	80	80	40	160	320	80	80	160	160
A/Athens GR/510/2017	3C.2a1	2017-01-18	SIAT1	80	40	320	160	160	80	160	320	80	160	320	320
A/Athens GR/566/2017	3C.2a1	2017-01-19	SIAT1	40	40	160	80	40	40	80	160	80	80	160	160

Vaccine

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

Sequence in phylogenetic tree

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/Texas 50/12 Egg F08/14-1	A/Samara 73/13 SIAT F35/15-1	A/Stock 6/14 SIAT F14/14-1	A/Stock 6/14 Egg F20/14-1	A/Switz 9715293/13 SIAT F18/15-1	A/Switz 9715293/13 Egg F32/14-1	A/HK 5738/14 MDCK F30/14-1	A/HK 4801/14 MDCK F43/15-1	A/HK 4801/14 Egg F12/15-1	A/Georgia 532/15 SIAT F33/15-1	A/Oman 2585/16 SIAT NB F50/16-1	A/Nor 4436/16 SIAT F03/17-1
	Passage history			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	640	160	640	40	640	160	320	80	320	160	320
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	1280	1280	640	640	160	640	320	1280	160	640	640	1280
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	80	80	320	320	160	160	160	320	80	160	320	320
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1	160	80	80	320	40	640	80	320	40	80	160	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	40	40	320	160	160	80	80	160	40	160	160	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1	160	160	160	320	80	640	160	320	40	160	320	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	40	40	320	80	160	80	320	640	160	160	320	640
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK2	80	80	160	160	80	80	160	320	160	160	160	320
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	40	80	40	40	40	40	160	640	160	640	320	160
A/Georgia/532/2015 plaq 20	3C.2a	2015-03-09	SIAT1/SIAT5	40	80	320	320	160	160	320	640	80	1280	320	640
A/Norway/4465/2016 isolate 2 clone 27			E6	<	<	<	40	40	<	160	160	80	1280	320	160
TEST VIRUSES															
A/Luxembourg/62062/2016	3C.2a1	2016-12-06	MDCK1/SIAT1	40	40	160	80	40	80	80	320	80	160	160	160
A/Luxembourg/63257/2016		2016-12-12	MDCK1/SIAT1	40	40	160	160	40	40	80	320	80	160	160	160
A/Iceland/65/2016	3C.2a1	2016-12-12	MDCK1/SIAT1	40	40	160	80	40	40	160	160	80	160	160	160
A/Iceland/66/2016	3C.2a	2016-12-14	MDCK1/SIAT1	40	40	160	80	40	40	160	160	80	160	160	160
A/Iceland/68/2016	3C.3a	2016-12-15	MDCK1/SIAT1	80	80	640	320	160	160	160	320	160	160	320	320
A/Iceland/70/2016	3C.2a	2016-12-19	MDCK1/SIAT1	40	40	160	80	40	40	160	160	80	320	160	160
A/Iceland/72/2016	3C.2a	2016-12-19	MDCK1/SIAT1	40	40	160	80	40	40	160	320	80	160	160	160
A/Iceland/74/2016	3C.3a	2016-12-21	MDCK1/SIAT1	40	40	320	160	80	80	160	160	80	160	160	160
A/Iceland/76/2016	3C.2a1	2016-12-24	MDCK1/SIAT1	40	40	160	80	40	40	80	160	80	160	160	160
A/Iceland/78/2016	3C.2a	2016-12-26	MDCK1/SIAT1	40	40	160	80	40	40	160	160	80	160	160	320
A/Poland/30484/2016	3C.2a	2016-12-28	SIAT2	40	40	160	80	80	40	80	160	40	80	160	160

Vaccine

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

Table 4-3. 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												
	Passage history			A/Texas	A/Samara	A/Stock	A/Switz	A/Switz	A/HK	A/HK	A/HK	A/Georgia	A/Oman	A/Nor		
	Ferret number			50/12	73/13	6/14	9715293/13	9715293/13	5738/14	4801/14	4801/14	532/15	2585/16	4436/16		
	Genetic group			Egg	SIAT	SIAT	Egg	SIAT	MDCK	MDCK	Egg	SIAT	SIAT	SIAT		
				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]		
				3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a1	3C.2a1		
REFERENCE VIRUSES																
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	2560	640	160	640	80	320	160	320	80	320	160	640	
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	640	640	320	320	160	320	320	640	160	640	320	640	
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	40	40	320	160	160	80	160	160	80	160	160	160	
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1	160	160	160	320	80	320	160	320	40	80	160	320	
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	<	40	160	80	160	80	80	80	40	80	160	160	
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1	80	160	160	320	80	640	160	320	40	160	160	320	
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	80	40	160	160	80	40	160	640	160	320	320	320	
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1	80	80	160	160	80	80	160	640	160	320	320	320	
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	40	80	80	80	40	<	320	640	160	640	640	320	
A/Georgia/532/2015 plaq 20	3C.2a	2015-03-09	SIAT1/SIAT5	80	80	160	160	80	80	160	320	80	640	320	320	
TEST VIRUSES																
A/Ireland/72254/2016	3C.3a	2016-11-12	C1/SIAT1	40	40	320	160	160	160	80	160	80	80	160	160	
A/Ireland/72703/2016	3C.2a1	2016-11-14	C1/SIAT1	<	<	<	<	<	<	40	160	40	40	80	40	
A/Catalonia/9305S/2016	3C.2a1	2016-11-24	C0/SIAT1	40	<	160	80	40	40	80	160	80	40	160	160	
A/Ireland/76255/2016	3C.2a1	2016-11-29	C2/SIAT1	<	<	<	<	<	<	<	40	<	<	40	40	
A/Belgium/G0687/2016	3C.2a	2016-11-30	SIAT1	40	40	160	80	40	40	160	160	80	80	320	320	
A/Ireland/78717/2016	3C.3a	2016-12-06	C1/SIAT1	80	80	640	320	160	160	160	160	80	80	160	160	
A/Ireland/80971/2016	3C.2a1	2016-12-15	C1/SIAT1	40	40	80	160	40	80	160	160	80	80	160	160	
A/Ireland/81104/2016	3C.3a	2016-12-15	C1/SIAT1	80	80	320	640	160	320	160	320	160	160	320	320	
A/Ireland/81354/2016	3C.2a	2016-12-17	C2/SIAT1	40	<	80	160	40	40	80	160	80	160	160	160	
A/Ireland/81180/2016	3C.2a1	2016-12-19	C1/SIAT1	40	<	80	160	40	40	80	320	40	80	160	160	
A/Ireland/81920/2016	3C.3a	2016-12-21	C1/SIAT1	40	40	320	640	160	160	160	160	80	80	160	160	
A/Ireland/82326/2016	3C.3a	2016-12-21	C1/SIAT1	40	40	320	640	160	160	160	160	80	80	160	160	
A/Catalonia/9415S/2017	3C.2a	2016-12-21	C0/SIAT1	40	40	160	80	40	40	80	160	80	40	160	160	
A/Ireland/82745/2016	3C.3a	2016-12-22	C1/SIAT1	80	80	640	320	160	160	160	160	80	80	160	160	
A/Belgium/G0024/2017	3C.2a1	2017-01-03	SIAT1	40	40	160	80	80	40	160	320	80	160	160	160	
A/Belgium/G0042/2017	3C.2a1	2017-01-05	SIAT1	40	<	160	80	40	40	160	160	80	80	160	160	
A/Latvia/01-024575/2017	3C.2a	2017-01-10	C2/SIAT1	80	80	160	320	160	80	160	320	80	160	320	320	
A/Cyprus/F49/2017	3C.2a1	2017-01-12	SIAT1	40	<	160	80	40	40	80	160	80	40	160	160	
A/Athens GR/563/2017	3C.2a1	2017-01-19	SIAT1	40	<	160	40	80	40	80	160	80	80	160	160	
A/Norway/484/2017	3C.2a	2017-01-22	SIAT1/SIAT1	<	<	160	80	<	<	40	80	40	160	160	160	
A/Cyprus/F148/2017	3C.2a1	2017-01-26	SIAT1	40	40	80	80	40	40	80	320	80	80	160	160	
A/Catalonia/3509691NS/2017	3C.2a	2017-02-02	C0/SIAT1	40	40	160	80	40	40	80	160	80	80	160	160	
A/Norway/1120/2017	3C.2a	2017-02-11	SIAT1/SIAT1	<	<	160	80	40	40	80	160	40	160	160	160	
A/Latvia/02-057392/2017	3C.2a1	2017-02-17	C1/SIAT1	80	40	160	320	160	80	160	320	160	80	320	320	
A/Latvia/02-056748/2017	3C.2a	2017-02-20	C2/SIAT1	80	40	160	160	80	80	160	320	80	320	160	160	
A/Latvia/02-062187/2017		2017-02-22	C2/SIAT1	80	80	160	320	80	80	160	320	80	160	320	320	
A/Iceland/40/2017	3C.2a1	2017-02-22	MDCK1/SIAT1	<	<	160	40	40	<	160	80	40	80	80	160	
A/Iceland/64/2017	3C.2a1	2017-03-08	MDCK1/SIAT1	<	<	160	40	40	<	40	160	40	40	80	160	
A/Iceland/69/2017	3C.3a	2017-03-09	MDCK1/SIAT1	40	40	320	160	80	160	80	160	80	80	160	160	
A/Latvia/04-003626/2017	3C.2a1	2017-04-03	C1/SIAT1	80	40	160	160	80	80	160	320	80	80	160	160	

Vaccine

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

Sequences in phylogenetic tree

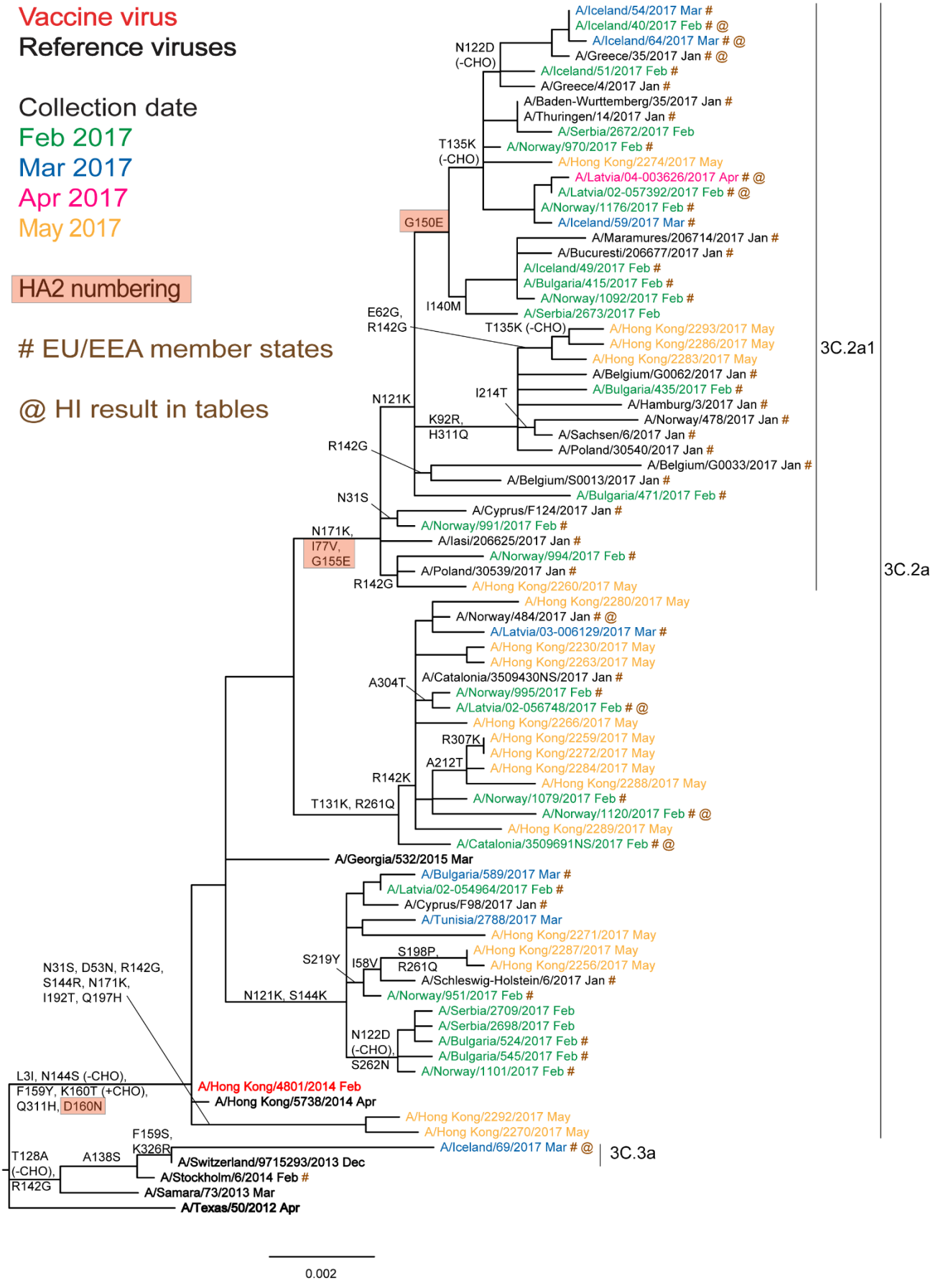
Table 4-4. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre											
					Post-infection ferret antisera											
		Passage history			A/Texas	A/Samara	A/Stock	A/Stock	A/Switz	A/Switz	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
		Ferret number			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
		Genetic group			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a1	3C.2a1
REFERENCE VIRUSES																
A/Texas/50/2012		3C.1	2012-04-15	E5/E2	1280	640	160	640	40	320	160	320	80	160	160	320
A/Samara/73/2013		3C.3	2013-03-12	C1/SIAT4	640	640	640	640	160	320	320	1280	160	320	320	640
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT2	80	40	320	160	160	160	160	160	80	80	160	160
A/Stockholm/6/2014	isolate 2	3C.3a	2014-02-06	E4/E1	160	80	160	320	80	320	160	320	40	40	160	320
A/Switzerland/9715293/2013		3C.3a	2013-12-06	SIAT1/SIAT3	<	<	320	80	80	80	80	80	40	40	80	160
A/Switzerland/9715293/2013	clone 123	3C.3a	2013-12-06	E4/E1	160	160	160	320	40	640	160	320	40	80	160	320
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	80	160	320	160	80	80	320	640	160	160	320	320
A/Hong Kong/4801/2014		3C.2a	2014-02-26	MDCK4/MDCK1	80	80	160	160	80	80	160	640	160	160	160	160
A/Hong Kong/4801/2014	isolate 1	3C.2a	2014-02-26	E6/E2	40	80	40	40	40	40	320	640	160	320	640	160
A/Georgia/532/2015	plaq 20	3C.2a	2015-03-09	SIAT1/SIAT5	80	80	160	160	80	80	160	320	160	640	320	320
TEST VIRUSES																
A/Lithuania/6735/2017			unknown	MDCK2/SIAT1	<	<	160	40	<	<	40	40	40	40	80	160
A/Lithuania/7612/2017			unknown	MDCK2/SIAT1	<	<	80	40	40	<	80	160	40	40	80	80
A/Bulgaria/2/2017			2017-01-02	SIAT2/SIAT1	40	40	320	80	80	80	160	160	160	80	320	320
A/Bulgaria/56/2017			2017-01-04	SIAT2/SIAT1	40	<	160	80	<	<	160	160	40	40	80	160
A/Bulgaria/132/2017			2017-01-06	SIAT2/SIAT1	40	80	320	160	80	80	160	320	160	80	320	320
A/Bulgaria/301/2017			2017-01-09	SIAT2/SIAT1	40	80	320	160	80	80	160	320	160	80	320	320
A/Bulgaria/182/2017			2017-01-10	SIAT2/SIAT1	80	40	320	160	80	80	160	320	160	80	320	320
A/Sachsen/4/2017			2017-01-10	C1/SIAT1	40	40	80	80	40	40	160	160	80	80	160	160
A/Bulgaria/252/2017			2017-01-12	SIAT2/SIAT1	40	40	320	80	80	40	160	160	80	80	320	320
A/Berlin/9/2017			2017-01-16	C1/SIAT1	<	<	160	40	<	<	80	80	80	<	160	160
A/Poland/412/2017			2017-01-18	SIAT1	40	40	160	80	40	40	160	320	80	80	160	160
A/Poland/555/2017			2017-01-24	SIAT1	40	40	80	80	40	40	160	160	80	160	160	160
A/Bulgaria/373/2017			2017-01-24	SIAT2/SIAT1	40	40	320	160	80	80	320	160	80	80	320	320
A/Hessen/14/2017			2017-01-26	C1/SIAT1	40	40	320	80	40	80	160	160	80	40	160	160
A/Bulgaria/427/2017			2017-01-30	SIAT2/SIAT1	<	<	160	80	40	<	80	80	40	40	160	160
A/Bulgaria/414/2017			2017-02-01	SIAT2/SIAT1	<	<	80	80	40	<	80	80	40	80	80	160
A/Iceland/18/2017			2017-02-13	MDCK1/MDCK2	40	80	640	320	160	160	160	160	80	80	160	160
A/Iceland/27/2017			2017-02-16	MDCK1/SIAT1	<	40	160	160	40	80	80	80	40	40	80	80
A/Iceland/23/2017			2017-02-16	MDCK1/SIAT1	40	40	320	160	80	80	80	80	40	40	80	80
A/Iceland/31/2017			2017-02-19	MDCK1/SIAT1	<	40	160	160	40	80	80	80	40	40	80	80
A/Lithuania/6165/2017			2017-02-20	MDCK2/SIAT1	80	80	160	80	80	80	160	320	80	640	320	320
A/Lithuania/6583/2017			2017-02-21	MDCK2/SIAT1	40	80	80	80	40	40	160	320	80	160	160	320
A/Iceland/37/2017			2017-02-21	MDCK1/SIAT1	40	40	320	160	80	160	80	160	80	80	160	160
A/Iceland/36/2017			2017-02-21	MDCK1/SIAT1	40	<	160	80	40	40	160	160	80	40	160	160
A/Norway/1481/2017			2017-02-27	SIAT1	40	40	160	80	40	40	160	160	80	80	160	160
A/Lithuania/7703/2017			2017-02-27	MDCK2/SIAT1	40	40	80	80	80	<	80	160	80	40	80	160
A/Norway/1477/2017			2017-03-04	SIAT1	40	<	160	80	40	40	80	160	40	80	160	160
A/Lithuania/7906/2017			2017-03-06	MDCK2/SIAT1	40	40	160	80	80	80	160	160	160	320	320	320
A/Norway/2400/2017			2017-04-28	SIAT1/SIAT1	80	80	320	160	80	80	160	640	160	80	160	160
A/Jordan/20157/2017			2017-04-22	SIAT2	80	80	160	160	80	80	80	160	80	80	320	320
A/Norway/2629/2017			2017-05-04	SIAT1	160	80	640	160	160	80	320	320	320	160	320	320

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 137 influenza type B-positive specimens with collection dates after 31 December 2016: 134 were ascribed to a lineage, 52 B/Victoria-lineage and 82 B/Yamagata-lineage (Table 2).

Influenza B – Victoria lineage

Since the February VCM [14] report 32 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 Tables 5-1 to 5-3.

Most of the test viruses showed similar HI reactivity patterns to those observed throughout the 2014–15 and 2015–16 influenza seasons. All but one of the test viruses were recognised poorly by antisera raised against the egg-propagated vaccine virus, B/Brisbane/60/2008, recommended for use in both trivalent and quadrivalent vaccines. B/Rheinland-Pfalz/43/2016 was recognised well by the antiserum raised against B/Brisbane/60/2008 and was shown to be identical in sequence to the B-Victoria lineage vaccine component and is most likely to be as a result of the recovery of the influenza B component of the live attenuated influenza vaccine. The remaining 31 test viruses were generally not recognised well by post-infection ferret antisera raised against reference viruses propagated in eggs (B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012) although the antiserum raised against B/South Australia/81/2012 recognised 24/31 (77%) test viruses at a titre within fourfold of the homologous titre of the antiserum. By contrast, 31 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). Notably, B/Norway/2409/2017 showed no reactivity with post-infection ferret antisera raised against egg-propagated or cell-propagated viruses and a very low reaction with the hyperimmune sheep antiserum pool raised against B/Brisbane/60/2008. B/Norway/2409/2017 has a deletion of two amino acids at residues 162 and 163 in the HA1 glycoprotein; several other examples of this variant have been seen elsewhere, most notably in North America.

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 into the B/Brisbane/60/2008 clade (clade 1A) and the majority remain antigenically similar to the vaccine virus B/Brisbane/60/2008. 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. The viruses with the 162-163 HA1 deletion have additional substitutions **D129G, I180V** in **HA1** and **R151K** in **HA2**.

These results, linked with the rise in the proportion of B/Victoria-lineage viruses seen since 2015, supported the continued recommendation to include B/Brisbane/60/2008 in trivalent and quadrivalent influenza vaccines for the southern hemisphere 2017 [3] and northern hemisphere 2017–2018 [4].

Influenza B – Yamagata lineage

HI results for 58 B/Yamagata-lineage test virus analysed since the February VCM [14] report are shown in Tables 6-1 to 6-3. All the viruses sequenced 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 42/58 (72%) test viruses at titres within fourfold of the titre of the virus for the homologous virus. However, an antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 recognised only 57% of viruses at titres within fourfold of the homologous titre of the antiserum. An antiserum raised against the former vaccine virus egg-propagated B/Wisconsin/1/2010 recognised a higher proportion of the test viruses, 77% (45 of 58), at a titre within fourfold of the homologous titre of the antiserum, and, similarly, antisera raised against egg-propagated B/Stockholm/12/2011 and egg-propagated B/Hong Kong/3417/2014 recognised 91% (53 of 58) and 100% (all 58), respectively, of the test virus at titres within fourfold of the respective homologous titres of the antisera.

An antiserum raised against another formerly recommended vaccine virus egg-propagated B/Massachusetts/02/2012, a clade 2 virus, recognised the test viruses less well, with only 20 of the 58 viruses (34%) being recognised at titres within fourfold of the homologous titre of the antiserum. However, the test viruses were recognised better by the cell culture-propagated cultivar of B/Massachusetts/02/2012 with 38 of 58 test viruses (66%) of test viruses being recognised at titres within fourfold of the homologous titre of the antiserum. An antiserum raised against another cell culture-propagated clade 2 virus B/Estonia/55669/2011 recognised 27 of 58 test viruses (47%) of test viruses at titres within fourfold of the homologous titre of the antiserum.

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 the great majority falling in a subgroup defined by HA1 L172Q and

M251V amino acid substitutions. Two viruses, annotated in the phylogenetic tree, are reassortants carrying NA genes normally associated with the B/Victoria-lineage.

Based on such results, a B/Phuket/3073/2013-like virus was recommended for inclusion in quadrivalent vaccines for the 2017–2018 northern hemisphere [4] season.

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	B/Mal	B/Bris	B/Malta	B/Jhb	B/For	B/Sth Aus	B/HK	B/Ireland	B/Nord-West		
				60/08	2506/04	60/08	636714/11	3964/12	V2367/12	81/12	514/09	3154/16	1/16		
				Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK		
				Sh 539, 540, 543, 544, 570, 571, 574[1,3]											
	Ferret number				F41/14[*2]	F26/13[*2]	F29/13[*4]	F01/13[*4]	F04/13[*2]	F41/13[*2]	F09/13[*2]	F15/16[*4]	F16/16[*4]		
	Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A		
REFERENCE VIRUSES															
B/Malaysia/2506/2004		2004-12-06	E3/E7	1280	160	40	40	80	40	80	10	<	<		
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	80	640	320	320	160	640	80	40	20		
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	80	640	320	320	160	640	40	40	20		
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	160	1280	1280	1280	1280	1280	160	80	80		
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	2560	20	640	160	160	160	320	40	20	20		
B/South Australia/81/2012	1A	2012-11-28	E4/E1	1280	20	320	160	80	80	320	20	<	10		
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	1280	<	40	<	<	20	20	20	40	20		
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	40	<	<	40	20	20	40	20		
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK1	2560	10	80	<	20	40	40	40	40	40		
TEST VIRUSES															
B/Rheinland-Pfalz/43/2016	1A	2016-11-21	C2/MDCK1	2560	40	640	<	160	160	640	40	20	20		
B/Portugal/SU275/2017	1A	2017-01-02	MDCK1	2560	<	80	<	<	40	40	20	40	20		
B/Athens GR/78/2017	1A	2017-01-03	MDCK1	2560	20	80	<	20	40	40	20	40	40		

Vaccine

Vaccine breakthrough

* 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		
	Ferret number			60/08	2506/04	60/08	636714/11	3964/12	V2367/12	81/12	514/09	3154/16	1/16		
				Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK		
				Sh 539, 540, 543, 544, 570, 571, 574[a,3]	F41/14[-2]	F37/14[-2]	F29/13[-4]	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	40	40	40	40	80	10	<	<		
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	1280	80	160	160	160	80	320	40	20	20		
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	80	320	320	160	160	640	40	20	20		
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	160	640	640	640	640	640	160	80	80		
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	2560	20	160	80	160	160	160	40	20	10		
B/South Australia/81/2012	1A	2012-11-28	E4/E1	1280	40	160	80	80	80	160	20	<	10		
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	1280	<	<	<	<	20	20	20	40	20		
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	<	<	<	20	20	20	40	20		
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK3	2560	<	<	<	<	40	40	40	40	40		
TEST VIRUSES															
B/Niedersachsen/4/2017	1A	2017-01-30	C1/MDCK1	2560	<	<	<	<	40	20	20	40	10		
B/Bayern/10/2017	1A	2017-02-02	C1/MDCK1	2560	<	<	<	<	40	40	20	40	20		
B/Hessen/1/2017	1A	2017-02-02	C1/MDCK1	2560	<	<	<	<	40	40	20	40	20		
B/Norway/998/2017	1A	2017-02-08	MDCK1/MDCK1	2560	<	<	<	<	20	40	20	40	20		
B/Norway/1102/2017	1A	2017-02-13	MDCK1/MDCK1	2560	<	<	<	<	40	40	20	20	20		
B/Norway/1040/2017	1A	2017-02-15	MDCK1/MDCK1	2560	<	<	<	<	40	40	20	40	40		
B/Norway/1076/2017	1A	2017-02-16	MDCK1/MDCK1	5120	<	<	<	<	40	80	40	40	40		
B/Bulgaria/513/2017	1A	2017-02-23	SIAT2/MDCK1	1280	<	<	<	<	20	40	20	20	20		
B/Bulgaria/516/2017	1A	2017-02-24	SIAT2/MDCK1	2560	<	<	<	<	40	40	20	40	20		
B/Nordrhein-Westfalen/8/2017	1A	2017-03-07	C1/MDCK1	2560	<	<	<	<	40	40	40	40	20		
B/Bremen/4/2017	1A	2017-03-13	C1/MDCK1	2560	<	<	<	<	40	40	20	40	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

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										
	Passage history			B/Bris	B/Mal	B/Bris	B/Malta	B/Jhb	B/For	B/Sth Aus	B/HK	B/Ireland	B/Nord-West	
				60/08	2506/04	60/08	636714/11	3964/12	V2367/12	81/12	514/09	3154/16	1/16	
				Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK	
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[4,3]	F41/14[-2]	NIB F52/16[-4]	F29/13[-4]	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	1A	1B	1A	1A	
REFERENCE VIRUSES														
B/Malaysia/2506/2004		2004-12-06	E3/E7	1280	320	80	40	80	40	80	<	<	<	
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	80	640	160	160	80	320	40	40	20	
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	80	640	320	160	160	320	40	40	40	
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	320	1280	1280	1280	640	1280	160	160	160	
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	40	320	80	160	160	320	40	40	40	
B/South Australia/81/2012	1A	2012-11-28	E4/E1	1280	80	320	80	80	80	320	20	20	20	
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	2560	<	20	20	<	20	40	40	80	80	
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	20	20	<	40	40	40	80	80	
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK3	5120	<	20	20	<	80	40	40	80	160	
TEST VIRUSES														
B/Povazska Bystrica/175/2017	1A	2017-01-16	MDCKx/MDCK1	2560	<	40	10	<	80	80	20	80	40	
B/Bratislava/275/2017	1A	2017-02-01	MDCKx/MDCK1	2560	<	40	10	<	80	80	20	80	40	
B/Latvia/02-04598/2017	1A	2017-02-02	C2/MDCK1	5120	<	20	10	<	40	40	40	80	80	
B/Sastin-Straze/332/2017	1A	2017-02-13	MDCKx/MDCK1	2560	<	40	10	<	80	80	20	80	40	
B/Poprad/324/2017	1A	2017-02-13	MDCKx/MDCK1	5120	<	40	20	<	160	160	40	80	80	
B/Norway/1167/2017	1A	2017-02-16	MDCK2	5120	<	80	20	20	80	80	40	160	80	
B/Lithuania/6295/2017	1A	2017-02-20	MDCK2/MDCK1	2560	20	20	10	<	40	40	20	80	80	
B/Slovenia/1496/2017	1A	2017-03-20	MDCK1	5120	<	40	20	20	40	80	40	160	80	
B/Lithuania/10137/2017	1A	2017-03-22	MDCK2/MDCK1	2560	<	20	20	20	40	40	40	80	80	
B/Norway/2077/2017		2017-04-01	MDCK1/MDCK1	2560	<	40	10	<	80	80	40	80	40	
B/Kosice/392/2017	1A	2017-04-06	MDCKx/MDCK1	5120	<	40	10	<	80	80	40	80	80	
B/Norway/2213/2017		2017-04-10	MDCK1	5120	<	40	20	20	80	80	40	80	80	
B/Sachsen-Anhalt/7/2017		2017-04-18	C2/MDCK1	5120	<	40	20	20	80	80	40	80	80	
B/Norway/2309/2017		2017-04-21	MDCK1/MDCK1	2560	<	40	10	<	40	80	20	80	40	
B/Norway/2302/2017	1A	2017-04-21	MDCK1/MDCK1	2560	<	40	20	<	80	80	40	80	80	
B/Norway/2424/2017	1A	2017-04-26	MDCK1/MDCK1	2560	<	20	20	<	80	80	20	80	40	
B/Norway/2409/2017	1A	2017-04-27	MDCK1/MDCK1	80	<	<	<	<	<	<	<	<	<	
B/Norway/2615/2017		2017-04-30	MDCK1	2560	<	40	20	20	80	80	20	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

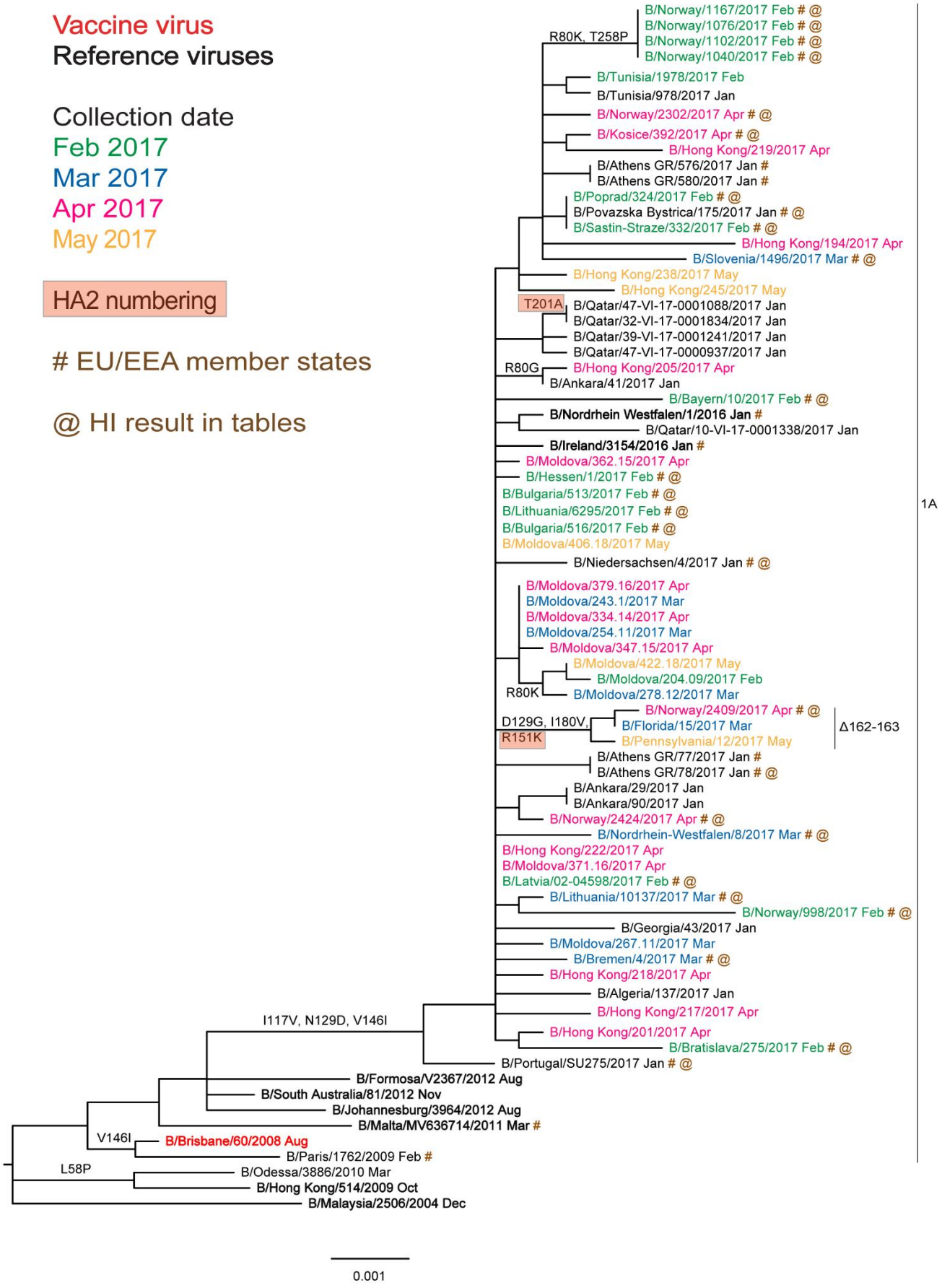


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					B/Phuket	B/Fl	B/Bris	B/Estonia	B/Mass	B/Mass	B/Wis	B/Stock	B/Phuket	B/Phuket	B/HK
					3073/13	4/06	3/07	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13	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[*1]	F05/15[*1]	F42/14[*2]	F10/13[*2]	F06/15[*2]	F35/14[*2]	F37/14[*2]	St Judes F715/14[*1,4]
		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	2560	640	640	320	160	640	160	160	20	160	160
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	1280	1280	320	160	1280	320	320	20	320	320
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	1280	80	80	640	160	40	40	20	40	40	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	640	320	320	160	80	40	160	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	640	320	320	160	80	320	40	80	<	80	160
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	5120	640	320	320	40	640	640	320	80	640	640
B/Stockholm/12/2011		3	2011-03-28	Ex/E2	1280	160	80	40	<	80	80	160	20	80	80
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK2	5120	320	320	320	640	320	320	160	640	320	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	160	160	40	10	160	160	80	20	160	160
B/Hong Kong/3417/2014		3	2014-06-04	E4/E1	1280	80	40	40	10	80	80	40	10	80	160
TEST VIRUSES															
A/Denmark/48/2016		3	2016-10-06	SIAT2/MDCK1/SIAT1	2560	80	160	80	80	80	160	40	80	80	160
B/Sachsen/74/2016		3	2016-11-21	C1/MDCK1	1280	40	20	80	40	20	40	20	80	40	160
B/Luxembourg/63550/2016		3	2016-12-15	MDCK1	1280	40	20	40	20	20	40	20	40	40	80
B/Catalonia/2134258NS/2017		3	2017-01-04	C0/MDCK1	2560	160	160	80	320	160	160	40	160	160	160
B/Norway/877/2017		3	2017-01-25	MDCK1/MDCK1	1280	40	40	40	20	40	40	20	40	40	80
B/Rheinland-Pfalz/1/2017		3	2017-01-31	C1/MDCK1	1280	40	80	40	20	40	80	20	40	40	80
														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 quadrivalent vaccines

Sequences in phylogenetic trees

Table 6-2. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

					Haemagglutination inhibition titre										
					Post-infection ferret antisera										
Viruses	Other information		Collection date	Passage history	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[*5]	F05/15[*2]	F42/14[*2]	F10/13[*2]	F06/15[*2]	F35/14[*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	10	160	160
B/Brisbane/3/2007		2	2007-09-03	E2/E2	1280	640	640	160	160	640	160	160	<	320	160
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	640	40	40	320	160	20	10	<	<	40	80
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	320	160	320	80	80	10	80	160
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	320	640	160	80	640	80	80	<	320	160
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	320	320	80	<	320	320	160	40	320	160
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	80	80	<	<	80	40	80	<	40	80
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK2	5120	160	320	160	320	320	320	80	320	320	160
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	320	160	40	10	160	160	80	20	320	160
B/Hong Kong/3417/2014		3	2014-06-04	E4/E1	1280	40	40	<	<	40	40	20	<	40	160
TEST VIRUSES															
B/Slovenia/741/2017		3	2017-01-30	MDCKx/MDCK1	2560	80	160	80	80	80	160	40	80	80	160
B/Slovenia/739/2017		3	2017-01-30	MDCK1/MDCK1	5120	320	320	160	160	320	160	80	320	160	320
B/Slovenia/816/2017		3	2017-02-01	MDCKx/MDCK1	5120	160	160	160	80	160	160	40	160	160	160
B/Niedersachsen/3/2017		3	2017-02-06	C1/MDCK1	1280	40	40	40	20	40	80	20	40	40	80
B/Iceland/09/2017		3	2017-02-07	MDCK1/MDCK1	1280	80	80	80	40	80	80	20	80	40	80
B/Latvia/02-018885/2017		3	2017-02-07	C2/MDCK1	5120	320	320	320	640	320	320	160	640	320	320
B/Norway/1073/2017		3	2017-02-13	MDCK1/MDCK1	2560	40	80	80	40	80	80	20	80	40	160
B/Latvia/02-031654/2017		3	2017-02-13	C2/MDCK1	2560	80	160	160	160	160	160	40	160	80	320
B/Norway/1014/2017		3	2017-02-14	MDCK1/MDCK1	2560	40	40	80	40	40	80	20	40	40	80
B/Nordrhein-Westfalen/5/2017		3	2017-02-14	C1/MDCK1	1280	80	80	40	20	40	80	20	40	40	160
B/Norway/1152/2017		3	2017-02-15	MDCK1/MDCK1	2560	40	80	80	40	80	80	20	40	40	160
B/Bremen/2/2017		3	2017-02-15	C1/MDCK1	1280	40	40	40	20	40	40	20	40	40	80
B/Latvia/02-058113/2017		3	2017-02-21	C2/MDCK1	2560	80	80	80	80	80	80	20	80	80	160
B/Iceland/46/2017		3	2017-02-24	MDCK1/MDCK1	2560	160	160	160	320	160	160	80	640	160	160
B/Iceland/45/2017		3	2017-02-24	MDCK1/MDCK1	1280	40	80	40	20	80	80	20	40	80	80
B/Norway/1473/2017		3	2017-02-25	MDCK2	5120	160	160	80	80	160	160	40	160	160	160
B/Slovenia/1321/2017		3	2017-02-27	MDCK1/MDCK1	5120	80	160	80	80	160	160	40	160	80	320
B/Norway/1484/2017		3	2017-02-28	MDCK1	5120	80	80	80	80	80	160	40	80	80	160
B/Iceland/58/2017		3	2017-03-03	MDCK1/MDCK1	1280	40	80	80	40	80	40	20	40	40	80
B/Norway/1471/2017		3	2017-03-03	MDCK1	2560	80	80	80	80	40	80	40	80	80	160
B/Iceland/62/2017		3	2017-03-06	MDCKx/MDCK1	2560	160	160	320	640	320	160	80	640	320	160
B/Lithuania/8622/2017		3	2017-03-10	MDCK2/MDCK1	5120	160	160	160	320	320	160	80	160	160	160
B/Lithuania/8865/2017		3	2017-03-14	MDCK2/MDCK1	2560	40	80	80	40	40	80	20	40	40	160
B/Slovenia/1427/2017		3	2017-03-14	MDCK1/MDCK1	2560	80	80	80	40	40	80	20	40	80	160
B/Slovenia/1458/2017			2017-03-16	SIATx/MDCK1	5120	160	160	160	160	160	160	40	160	160	320
B/Slovenia/1467/2017		3	2017-03-20	SIATx/MDCK1	2560	40	80	80	40	40	80	20	80	40	160
B/Lithuania/9464/2017		3	2017-03-20	MDCK2/MDCK1	5120	320	320	640	1280	320	320	160	1280	320	320
B/Lithuania/10115/2017		3	2017-03-23	MDCK2/MDCK1	2560	80	80	80	40	80	80	40	80	80	160
B/Slovenia/1560/2017		3	2017-03-27	MDCKx/MDCK1	2560	40	80	40	40	40	80	20	40	40	160
B/Latvia/03-082708/2017		3	2017-03-30	C2/MDCK1	2560	80	80	160	160	80	80	40	160	80	160
B/Latvia/04-014585/2017		3	2017-04-05	C1/MDCK1	1280	40	80	40	80	40	40	20	40	40	160
B/Slovenia/1666/2017		3	2017-04-11	MDCKx/MDCK1	2560	40	80	80	40	40	80	20	40	40	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; 5 < = <20

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

Sequences in phylogenetic trees

Table 6-3. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

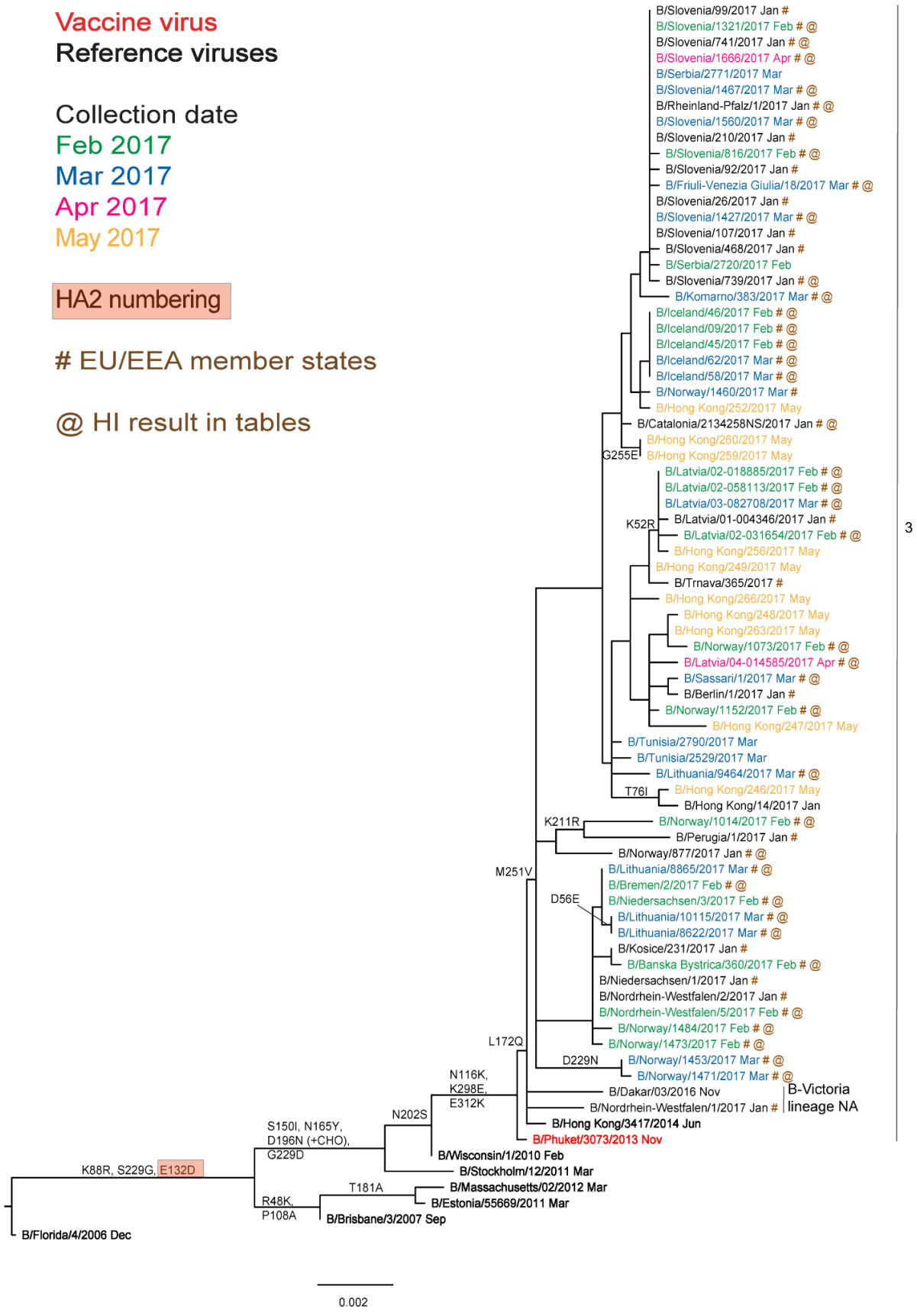
Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre														
				Post-infection ferret antisera														
				B/Phuket	B/Fl	B/Bris	B/Estonia	B/Mass	B/Mass	B/Wis	B/Stock	B/Phuket	B/Phuket		B/HK	
				3073/13	4/06	3/07	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13		3417/14	
				Egg	Egg	Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg		Egg	
				SH614[1,3]	F17/13[-1]	F38/14[-2]	F27/13[-2]	F05/15[-2]	F42/14[-2]	F36/15[-2]	F06/15[-2]	F35/14[-2]	NIB F51/16*2		St Judes F715/14[2,4]	
	Passage history			3	1	2	2	2	2	3	3	3	3		3	
	Ferret number															
	Genetic Group															
REFERENCE VIRUSES																
B/Florida/4/2006	1	2006-12-15	E7/E1	2560	640	640	160	80	640	160	160	20	320		160	
B/Brisbane/3/2007	2	2007-09-03	E2/E2	2560	640	640	160	80	640	160	160	20	320		160	
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	1280	80	160	640	160	80	40	20	20	40		160	
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	640	320	640	160	80	40	320		320	
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	1280	640	640	160	80	640	80	80	<	320		80	
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	5120	320	640	80	20	320	320	160	40	320		320	
B/Stockholm/12/2011	3	2011-03-28	EX/E2	1280	160	160	40	10	80	40	80	20	160		80	
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK2	5120	320	320	160	320	320	320	160	320	320		320	
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	160	40	20	160	80	80	20	320		80	
B/Hong Kong/3417/2014	3	2014-06-04	E4/E1	1280	80	80	20	10	40	80	20	10	80		160	
TEST VIRUSES																
B/Thuringen/2/2017		2017-02-15	C1/MDCK1	1280	40	40	40	10	40	40	20	40	80		80	
B/Banska Bystrica/360/2017	3	2017-02-20	MDCKx/MDCK1	1280	40	40	40	20	20	20	20	20	20		80	
B/Norway/1453/2017	3	2017-03-03	MDCK3	1280	40	40	40	20	20	20	10	20	20		80	
B/Friuli-Venezia Giulia/18/2017	3	2017-03-06	MDCK1/MDCK1	2560	80	40	40	40	40	40	20	40	40		80	
B/Sassari/1/2017	3	2017-03-10	MDCK3/MDCK1	2560	80	160	80	80	40	40	40	80	80		160	
B/Mecklenburg-Vorpommern/1/2017		2017-03-13	C1/MDCK1	2560	80	80	80	80	80	80	40	160	160		160	
B/Rheinland-Pfalz/3/2017		2017-03-22	C1/MDCK1	2560	80	80	80	40	160	80	40	80	160		160	
B/Komarno/383/2017	3	2017-03-23	MDCKx/MDCK1	2560	80	80	80	40	40	80	20	80	80		160	
B/Norway/2133/2017		2017-03-28	MDCK1/MDCK1	2560	80	160	80	40	80	80	40	40	160		160	
B/Norway/2162/2017		2017-04-03	MDCK1/MDCK1	2560	160	160	80	80	160	80	80	80	320		160	
B/Norway/2155/2017		2017-04-04	MDCK1	2560	80	160	80	40	80	80	40	40	160		160	
B/Norway/2169/2017		2017-04-04	MDCK1/MDCK1	5120	160	160	80	80	160	160	80	80	320		320	
B/Saarland/3/2017		2017-04-06	C1/MDCK1	2560	160	160	80	80	160	80	40	160	320		160	
B/Norway/2363/2017		2017-04-21	MDCK1	2560	160	160	80	40	80	80	40	40	160		160	
B/Norway/2431/2017		2017-04-21	MDCK2	2560	80	80	40	10	40	40	20	80	160		160	
B/Norway/2387/2017		2017-04-24	MDCK1	2560	160	160	80	80	160	80	40	80	320		160	
B/Norway/2410/2017		2017-04-26	MDCK1	2560	80	160	80	80	160	80	40	80	320		160	
B/Norway/2421/2017		2017-04-28	MDCK2	2560	80	160	80	40	80	80	40	80	160		160	
B/Norway/2613/2017		2017-05-02	MDCK1	5120	160	160	160	80	320	160	160	320	320		160	
B/Norway/2600/2017		2017-05-02	MDCK1	2560	80	80	80	20	80	80	20	80	160		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 quadrivalent 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 2016–2017 season beginning week 40/2016 until week 31/2017, 4483 viruses have been characterised genetically: 17 were defined as A(H1N1)pdm09 clade 6B represented by A/South Africa/3626/2013 and 55 were subclade 6B.1 as represented by A/Michigan/45/2015; 1178 were A(H3N2) subclade 3C.2a represented by A/Hong Kong/4801/2014, 2653 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; 171 were B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008 and one clade 1B was represented by B/Hong Kong/514/2009; 346 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 800 viruses at the WIC: 35 A(H1N1)pdm09, 652 A(H3N2), 38 B/Victoria-lineage and 75 B/Yamagata-lineage viruses. All A(H1N1)pdm09 and B viruses showed normal inhibition (NI) by these neuraminidase inhibitors. Four A(H3N2) viruses showed reduced inhibition with oseltamivir: A/Poland/30484/2016, A/Poland/17C/2017, A/Poland/12186/2016, and A/Luxembourg/61798/2016, the latter two also showing reduced inhibition with zanamivir.

For weeks 40/2016–26/2017 of the 2016–2017 influenza season, countries reported on the antiviral susceptibility of 61 A(H1N1)pdm09 viruses, 3086 A(H3N2) viruses and 325 influenza type B viruses from sentinel and non-sentinel sources to TESSy. All but four showed no molecular or phenotypic evidence of reduced inhibition by neuraminidase inhibitors (oseltamivir and zanamivir); three A(H3N2) isolates showed reduced inhibition by both oseltamivir and zanamivir, and one B isolate gave reduced inhibition 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 [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 15 June 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 15 June 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 the 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 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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