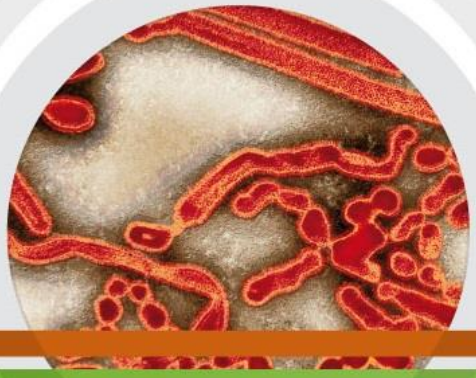

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2016

Summary

From week 40/2015, the start of weekly reporting on influenza activity in the WHO European Region, to week 07/2016 over 70 000 influenza detections across the Region have been reported. Influenza type A viruses are prevailing over type B but, unlike the situation in the 2014–15 season, A(H1N1)pdm09 viruses are prevailing over A(H3N2), and the proportion of B/Victoria-lineage detections has risen substantially, representing ~92% of those ascribed to a B virus lineage.

To date, 23 EU/EEA countries have shared 424 influenza-positive specimens with the Francis Crick Institute, London, for detailed characterisation: 16 additional countries and 330 specimens since the December 2015 report. Since the latter report, 230 viruses have been characterised antigenically and genetic analyses are ongoing.

The 166 A(H1N1)pdm09 viruses characterised antigenically were similar to the vaccine virus A/California/7/2009. Worldwide new genetic sub-clusters of viruses within the 6B clade have emerged, with two being designated as subclades: 6B.1 defined by HA1 amino acid substitutions S162N and I216T and 6B.2 defined by HA1 amino acid substitutions V152T and V173I. Of the 123 viruses characterised genetically, 18 (14%) were clade 6B, 98 (80%) were subclade 6B.1 and seven (6%) were subclade 6B.2.

The 26 A(H3N2) test viruses characterised by haemagglutination inhibition (HI) assay were poorly recognised by reference antiserum raised against egg-propagated A/Switzerland/9715293/2013, the vaccine virus recommended for use in the 2015–2016 northern hemisphere influenza season, despite over 75% of the test viruses falling in the same genetic subclade (3C.3a) as the vaccine virus. The test viruses were recognised somewhat better by antisera raised against egg-propagated A/Hong Kong/4801/2014, the virus recommended for use in 2016 southern hemisphere and 2016–2017 northern hemisphere influenza vaccines. Of 40 A(H3N2) viruses characterised genetically: one (2%) was clade 3C.3, 23 (58%) were subclade 3C.2a and 16 (40%) were subclade 3C.3a.

The 33 B/Victoria-lineage viruses were antigenically similar to B/Brisbane/60/2008 and fell in genetic clade 1A as do recently collected viruses worldwide.

The five B/Yamagata viruses characterised fell in genetic clade 3 and 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 use in quadrivalent vaccines in the 2016 southern hemisphere and 2016–17 northern hemisphere influenza seasons.

This report was prepared by Rod Daniels, Vicki Gregory, Burcu Ermetal, Aine Rattigan and John McCauley on behalf of the European Reference Laboratory Network for Human Influenza (ERLI-Net), under contract to the European Centre for Disease Prevention and Control (ECDC).

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Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy for the first 21 weeks (weeks 40/2015–07/2016) of reporting for the 2015–16 season. A total of over 70 000 detections had been made with type A viruses prevailing over type B at a ratio of 5.8:1. So far, of the type A viruses subtyped (n = 42594) and the type B viruses ascribed to lineage (n = 1587), A(H1N1)pdm09 have prevailed over A(H3N2) and B/Victoria over B/Yamagata by ratios of 10:1 and 12:1, respectively.

Since the start of weekly reporting for the 2015–16 influenza season (week 40/2015) 40 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC), from 23 countries in the EU/EEA (Table 2). Of the 424 specimens received, a mix of clinical samples and virus isolates, the majority (83.5%) were type A viruses, and A(H1N1)pdm09 outnumbered A(H3N2) at a ratio of approximately 4.2:1. Of the 70 type B specimens received (16.5% of the specimens), 55 were B/Victoria-lineage and 10 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 December 2015 report[1] are presented and discussed in this report.

Table 1. Influenza virus detections in the WHO European Region since the start of reporting for the 2015–16 season (weeks 40/2015-07/2016)

	Cumulative number of detections			Totals*	
Virus type/subtype	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**6574**	**53778**	**60352**	**85.3**	**5.8:1**
A(H1N1)pdm09	5417	33307	38724	90.9	10.0:1
A(H3N2)	867	3003	3870	9.1	
A not subtyped	290	17468	17758		
Influenza B	**2769**	**7651**	**10420**	**14.7**	
Victoria lineage	920	543	1463	92.2	11.8:1
Yamagata lineage	36	88	124	7.8	
Lineage not ascribed	1813	7020	8833		
Total detections (total tested)	**9343 (30548)**	**61429 (318245)**	**70772 (348793)**		

*** Percentages are shown for total detections (types A & B, and for viruses ascribed to subtype/lineage). Ratios are given for type A:B, A(H1N1)pdm09: A(H3N2) and Victoria:Yamagata lineages.**

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, December 2015. Stockholm: ECDC; 2015. Available from: http://ecdc.europa.eu/en/publications/Publications/influenza-virus-characterisation-december-2015.pdf

Table 2. Summary of clinical samples and virus isolates received from EU/EEA Member States: packages received since the start of the 2015–16 reporting period (week 40/2015)

MONTH*	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country		Number received	Number propagated	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated	Number received	Number propagated[1]	Number received	Number propagated[1]
2015														
AUGUST														
Norway	3			1	1	2	1	1						
Sweden	1					1	0	1						
SEPTEMBER														
Iceland	1			1	1									
Poland	1					1	in process							
Spain	1			1	1									
Sweden	1			1	in process									
United Kingdom	3					3	3	0						
OCTOBER														
Austria	1			1	1									
Belgium	1			1	1									
France	2			2	2									
Germany	2			1	1								1	1
Italy	2			1	in process								1	in process
Latvia	1			1	1									
Netherlands	1			1	1									
Norway	11			8	6	2	2	0			1	1		
Portugal	1			1	1									
Romania	1			1	1									
Slovenia	2	1	0	1	1									
Spain	2			2	in process									
Sweden	1					1	0	1						
United Kingdom	8			7	7						1	1		
NOVEMBER														
Austria	9			5	5	4	4	0						
Belgium	11			2	in process	1	0	1			6	in process	2	2
Denmark	1			1	1									
Estonia	3			3	in process									
Finland	4			2	2	2	1	1						
France	5			1	in process	1	1	0			3	in process		
Germany	14			11	11	2	0	2			1	1		
Italy	2					1	in process		1	in process				
Netherlands	7			5	in process						2	in process		
Norway	11			7	6	1	1	0			1	1	2	2
Poland	1	1	in process											
Portugal	8			8	7									
Slovenia	3					2	0	2	1	in process				
Spain	5	3	0	2	1									
Sweden	11			7	7	4	4	0						
United Kingdom	7			7	5									
DECEMBER														
Austria	3					3	2	1						
Czech Republic	2			2	2									
Denmark	7			7	7									
Estonia	6			1	0				1	0	4	in process		
Finland	8			7	6	1	1	0						
France	24			7	in process	2	2	0			15	in process		
Germany	21			17	17	3	3	0			1	1		
Greece	6			5	in process	1	0	1						
Iceland	3			1	1	1	0	1			1	1		
Ireland	4			2	2	1	0	1			1	1		
Italy	8			3	in process	5	2	3						
Latvia	3			3	3									
Netherlands	5			5	in process									
Norway	5			3	3	2	1	1						
Poland	12	10	in process	1	1						1	0		
Portugal	14			10	7	3	2	1					1	1
Romania	1					1	0	1						
Slovenia	5					5	1	3						
Spain	14			8	7	2	0	1			4	4		
United Kingdom	3			3	3									
2016														
JANUARY														
Czech Republic	3			3	3									
Estonia	3			2	0						1	1		
Germany	24			11	in process	3	in process				8	in process	2	in process
Greece	25			25	in process									
Hungary	7			4	in process						3	in process		
Iceland	6			5	5								1	1
Ireland	10			9	9						1	1		
Italy	1			1	1									
Netherlands	2			2	in process									
Portugal	6			6	6									
Romania	8			7	7	1	0	1						
Slovenia	8			3	3	3	0	3	2	0				
Spain	10			10	in process									
FEBRUARY														
Netherlands	1			1	in process									
Spain	7			7	in process									
	424	15	0	274	164	65	31	27	5	0	55	13	10	7
				64.6%		15.3%					13.0%		2.4%	
23 Countries				83.5%							16.5%			

*** 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

Haemagglutination inhibition (HI) analyses of viruses that have been performed since the December 2015 report are shown in Tables 3-1 to 3-6. The 166 A(H1N1)pdm09 viruses from EU/EEA countries were antigenically similar to the vaccine virus, A/California/7/2009. Generally, the test viruses were recognised by the panel of antisera at titres within fourfold of the titres for the homologous viruses, with the exception of the antiserum raised against A/Christchurch/16/2010. This antiserum recognised 96/166 (58%) test viruses at a titre within fourfold of the titre for the homologous virus. Reference viruses carrying HA1 G155E amino acid substitutions, A/Bayern/69/2009 and A/Lviv/N6/2009, showed reduced activity with the antisera raised against A/California/7/2009 and reference viruses in genetic clades 4, 5, 6, 7 and subclades 6A, 6B and 6B.1.

All test viruses for which HA sequences were available fell in subclade 6B (Tables 3-1 to 3-4 and Figure 1). Sequencing is still in process for test viruses indicated in Tables 3-5 and 3-6. Since 2009, the HA genes have evolved, and nine clades have been designated. For well over a year 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 subclades emerging. All EU/EEA viruses characterised since the September 2014 report[2] carry HA genes in subclade 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 clade 6B and two of these have been designated as subclades: viruses in subclade 6B.1 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**, while those in subclade 6B.2 are defined by **HA1** amino acid substitutions **V152T** and **V173I** (Figure 1). Of the 103 test viruses for which HA sequencing was performed nine (8.9%) were designated clade 6B, 89 (86.4%) subclade 6B.1 and five (4.9%) subclade 6B.2 viruses (Tables 3-1 to 3-4). All but one test virus, A/Netherlands/2905/2015 (subclade 6B.1: Table 3-1), yielded HI titres within twofold of the homologous titre with the ferret antisera raised against A/California/7/2009.

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

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

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
		Passage history			A/Cal	A/Bayern	A/Lviv	A/Chch	A/Astrak	A/St. P	A/St. P	A/HK	A/Sth Afr	
					7/09	69/09	N6/09	16/10	1/11	27/11	100/11	5659/12	3626/13	
		Ferret number			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	Egg	
		Genetic group			F01/15*1	F09/15*1	F14/13*1	F15/14*1	F22/13*1	F26/14*1	F24/11*1	F30/12*1	F3/14*1	
								4	5	6	7	6A	6B	
REFERENCE VIRUSES														
A/California/7/2009			2009-04-09	E1/E3	640	640	640	160	160	160	160	160	160	
A/Bayern/69/2009			2009-07-01	MDCK5/MDCK1	80	160	160	80	40	<	40	40	40	G155E
A/Lviv/N6/2009			2009-10-27	MDCK4/SIAT1/MDCK3	640	1280	640	160	80	80	80	160	80	G155E>G, D222G
A/Christchurch/16/2010		4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	1280	2560	2560	2560	
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	640	640	640	640	2560	640	2560	2560	1280	
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	2560	2560	1280	
A/St. Petersburg/100/2011		7	2011-03-14	E1/E2	1280	640	640	640	2560	640	2560	2560	1280	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK1	160	320	160	160	640	320	640	1280	640	
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	320	320	320	320	640	320	640	640	640	
TEST VIRUSES														
A/Lisboa/29/20015		6B.1	2015-10-03	MDCK1/MDCK1	640	1280	640	640	1280	640	2560	2560	1280	S162N, I216T
A/Belgium/2015G0741/2015		6B.1	2015-10-20	SIAT1/MDCK1	320	640	320	320	640	320	2560	1280	640	S162N, I216T
A/England/357/2015		6B.2	2015-10-26	SIAT1/MDCK1	320	640	160	640	1280	640	2560	1280	1280	V152T, V173I
A/Latvia/11-044910/2015		6B.1	2015-10-26	C2/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Netherlands/2905/2015		6B.1	2015-10-28	MDCK1/MDCK1	160	320	160	320	640	320	1280	1280	640	S162N, I216T
A/Lisboa/30/20015		6B	2015-11-08	MDCK1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	
A/Finland/541/2015		6B.1	2015-11-09	MDCK1/MDCK1	320	640	640	640	1280	640	2560	1280	1280	S162N, I216T
A/Netherlands/2915/2015		6B.1	2015-11-10	MDCK1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Netherlands/2917/2015		6B.1	2015-11-12	MDCK1/MDCK1	320	640	320	640	1280	640	2560	2560	1280	S162N, I216T
A/England/358/2015		6B	2015-11-16	SIAT1/MDCK1	320	640	320	640	640	320	1280	1280	1280	
A/England/364/2015		6B.1	2015-11-17	SIAT1/MDCK1	320	640	160	640	640	640	2560	1280	1280	S162N, I216T
A/England/365/2015		6B.1	2015-11-17	SIAT1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Lisboa/31/20015		6B	2015-11-18	MDCK1/MDCK1	320	320	160	320	640	320	1280	1280	1280	
A/Lisboa/32/20015		6B.1	2015-11-19	SIAT2/MDCK1	320	640	640	640	1280	640	2560	2560	1280	S162N, I216T
A/England/370/2015		6B.1	2015-11-20	SIAT1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Lisboa/33/20015		6B	2015-11-25	SIAT1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	
A/Finland/546/2015		6B.1	2015-11-26	MDCK1/MDCK1	320	640	640	640	1280	640	2560	1280	1280	S162N, I216T
A/Lisboa/34/20015		6B	2015-11-27	SIAT2/MDCK1	640	1280	640	640	1280	640	5120	2560	1280	
A/Netherlands/2925/2015		6B.1	2015-11-29	MDCK1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Finland/550/2015		6B.1	2015-12-04	MDCK1/MDCK1	320	640	640	640	1280	640	2560	2560	1280	S162N, I216T
A/England/375/2015		6B.2	2015-12-04	MDCK1/MDCK1	320	640	640	640	1280	640	2560	1280	1280	V152T, V173I
A/Finland/553/2015		6B.1	2015-12-06	MDCK1/MDCK1	320	640	640	640	1280	640	2560	1280	1280	S162N, I216T
A/England/372/2015		6B.1	2015-12-07	SIAT1/MDCK1	320	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/England/377/2015		6B.2	2015-12-10	SIAT1/MDCK1	320	640	640	640	1280	640	2560	2560	1280	V152T, V173I
A/Latvia/12-037196/2015		6B.1	2015-12-15	C2/MDCK1	320	640	320	640	640	640	2560	1280	640	S162N, I216T
A/Latvia/12-042353/2015		6B.1	2015-12-16	SIAT1/MDCK1	320	640	320	640	640	640	2560	1280	1280	S162N, I216T
A/Latvia/12-063862/2015		6B.1	2015-12-29	SIAT1/MDCK1	320	640	320	640	640	320	2560	1280	640	S162N, I216T

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

Vaccine

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera									
					A/Cal 7/09 Egg NIB F05/14*1	A/Bayern 69/09 MDCK F09/15*1	A/Lviv N6/09 MDCK F14/13*1	A/Chch 16/10 Egg F15/14*1 4	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 F3/14*1 6B	
REFERENCE VIRUSES														
A/California/7/2009	NIBSC		2009-04-09	E4/E1	640	320	320	320	640	320	1280	640	640	
A/Bayern/69/2009			2009-07-01	MDCK5/MDCK1	<	320	160	40	40	<	40	40	40	G155E
A/Lviv/N6/2009			2009-10-27	MDCK4/SIAT1/MDCK3	80	1280	1280	160	80	80	160	160	80	G155E>G, D222G
A/Christchurch/16/2010		4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	2560	1280	
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	1280	1280	640	640	1280	640	2560	2560	1280	
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	2560	2560	1280	
A/St. Petersburg/100/2011		7	2011-03-14	E1/E3	1280	640	640	640	1280	640	2560	2560	1280	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK1	320	160	160	160	320	160	640	640	320	
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	640	640	320	640	640	1280	640	1280	
TEST VIRUSES														
A/Desgenettes/2318/2015		6B.1	2015-10-02	MDCK2/MDCK1	1280	320	320	320	640	320	1280	1280	640	S162N, I216T
A/Grenoble/2322/2015		6B.1	2015-10-02	MDCK2/MDCK1	1280	640	640	640	1280	640	2560	2560	1280	S162N, I216T
A/Austria/883648/2015		6B.1	2015-10-08	SIAT1/MDCK1	640	320	160	320	640	320	1280	640	640	S162N, I216T
A/Slovenia/2903/2015		6B.1	2015-10-26	E2	1280	1280	640	640	1280	1280	2560	2560	1280	S162N, I216T
A/Slovenia/2903/2015	clone 56	6B.1	2015-10-26	E3	1280	640	320	640	1280	640	2560	2560	1280	S162N, I216T
A/Austria/888727/2015		6B.1	2015-11-08	SIAT1/MDCK1	640	320	160	320	640	320	1280	1280	640	S162N, I216T
A/Austria/888621/2015		6B.1	2015-11-09	SIAT1/MDCK1	640	320	320	320	640	320	1280	1280	640	S162N, I216T
A/Austria/889649/2015		6B.1	2015-11-13	SIAT1/MDCK1	640	320	320	320	640	320	1280	1280	640	S162N, I216T
A/Austria/889721/2015		6B.1	2015-11-16	SIAT1/MDCK1	640	320	160	320	320	320	1280	640	640	S162N, I216T
A/Bayern/148/2015		6B	2015-11-24	C2/MDCK1	1280	640	320	320	1280	320	1280	1280	1280	
A/Austria/891161/2015		6B.1	2015-11-24	SIAT1/MDCK1	1280	640	320	320	640	320	1280	1280	1280	S162N, I216T
A/Baden-Wurttemberg/253/2015		6B.1	2015-12-01	C2/MDCK1	640	640	320	320	1280	640	1280	1280	640	S162N, I216T
A/Sachsen-Anhalt/91/2015		6B.1	2015-12-05	C2/MDCK1	640	320	320	320	640	320	1280	1280	640	S162N, I216T
A/Berlin/171/2015		6B.1	2015-12-07	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Bremen/26/2015		6B.1	2015-12-07	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Berlin/172/2015			2015-12-08	C2/MDCK1	1280	640	320	320	1280	640	1280	1280	1280	
A/Lyon/9.12.R09/2015		6B.1	2015-12-09	MDCK2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Baden-Wurttemberg/254/2015		6B.1	2015-12-09	C2/MDCK1	640	320	320	320	640	320	1280	1280	640	S162N, I216T
A/Clermont Ferrand/2611/2015		6B.1	2015-12-12	MDCK2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Bremen/27/2015		6B.1	2015-12-14	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Mecklenburg-Vorpommern/21/2015			2015-12-15	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	
A/Berlin/174/2015			2015-12-16	C2/MDCK1	1280	640	320	320	1280	640	1280	1280	1280	
A/Berlin/175/2015			2015-12-18	C2/MDCK1	1280	640	320	640	1280	640	2560	2560	1280	
A/Sachsen/104/2015		6B.1	2015-12-18	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T
A/Mecklenburg-Vorpommern/20/2015			2015-12-20	C2/MDCK1	1280	640	320	640	1280	640	2560	2560	1280	
A/Mecklenburg-Vorpommern/19/2015		6B.1	2015-12-21	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	640	S162N, I216T
A/Berlin/176/2015		6B.1	2015-12-22	C2/MDCK1	640	320	160	320	640	320	1280	1280	640	S162N, I216T

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

[1] < = <40

Vaccine

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
	Passage history			A/Cal 7/09 Egg NIB F05/14 [-1]	A/Bayern 69/09 MDCK F09/15 [-1]	A/Lviv N6/09 MDCK F14/13 [-1]	A/Chch 16/10 Egg F15/14 [-1]	A/Astrak 1/11 MDCK F22/13 [-1]	A/St. P 27/11 Egg F26/14 [-1]	A/St. P 100/11 Egg F24/11 [-1]	A/HK 5659/12 MDCK F30/12 [-1]	A/Sth Afr 3626/13 Egg F3/14 [-1]		
	Ferret number			4	5	6	7	6A	6B						
	Genetic group														
REFERENCE VIRUSES															
A/California7/2009		2009-04-09	E4/E2	640	320	320	320	640	320	1280	640	640			
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	<	320	160	80	40	<	40	40	40			
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	80	640	640	160	80	80	80	160	80	G155E		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	1280	1280	G155E>G, D222G		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	640	320	640	1280	640	1280	2560	1280			
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	640	640	1280	640	1280	1280	1280			
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	640	640	640	1280	640	2560	1280	1280			
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK1	320	160	80	160	320	160	640	640	320			
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	640	320	320	320	640	320	640	640	640			
TEST VIRUSES															
A/Iceland/53/2015	6B.1	2015-09-30	MDCK0/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	S162N, I216T		
A/Scotland/P2/2015	6B.1	2015-11-19	MDCK1	640	320	320	640	640	320	1280	1280	640	S162N, I216T		
A/Denmark/62/2015	6B.1	2015-12-04	SIAT1/MDCK2//MDCK1	640	320	160	320	640	320	1280	640	640	S162N, I216T		
A/Denmark/46/2015		2015-12-07	SIAT1/MDCK2//MDCK1	320	160	80	160	320	160	640	320	320			
A/Denmark/49/2015	6B.1	2015-12-09	SIAT2/MDCK2/MDCK1	640	320	160	320	320	320	640	640	640	S162N, I216T		
A/Denmark/50/2015	6B.1	2015-12-10	SIAT1/MDCK2//MDCK1	640	160	160	320	640	320	640	640	640	S162N, I216T		
A/Denmark/51/2015		2015-12-10	SIAT1/MDCK2//MDCK1	640	640	320	640	1280	640	1280	1280	1280			
A/Navarra/1850/2015		2015-12-17	SIAT1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280			
A/Madrid/1859/2015	6B.1	2015-12-24	SIAT1/MDCK1	1280	640	320	640	1280	640	1280	1280	1280	S162N, I216T		
A/Iceland/55/2015	6B.1	2015-12-28	MDCK0/MDCK1	1280	640	320	640	1280	640	1280	1280	1280	S162N, I216T		
A/Baleares/16036/2015		2015-12-30	SIAT1/MDCK1	1280	640	320	640	1280	640	1280	1280	1280			
A/Poland/7474/2015	6B.1	2015-12-31	MDCK4/MDCK1	640	640	320	640	1280	640	2560	1280	1280	S162N, I216T		
A/Poland/7474/2015	6B.1	2015-12-31	SIAT4/MDCK1	2560	1280	640	1280	1280	640	2560	2560	2560	S162N, I216T		
A/Navarra/26/2016	6B.1	2016-01-03	SIAT1/MDCK1	1280	640	320	640	1280	640	1280	1280	1280	S162N, I216T		
A/Baleares/35/2016	6B.1	2016-01-05	SIAT1/MDCK1	640	320	320	320	1280	320	1280	1280	640	S162N, I216T		
A/Iceland/1/2016	6B.1	2016-01-08	MDCK0/MDCK1	640	640	320	640	1280	640	1280	1280	1280	S162N, I216T		
A/Iceland/2/2016		2016-01-08	MDCK0/MDCK1	1280	640	320	640	1280	320	1280	1280	1280			
A/Iceland/4/2016	6B.1	2016-01-12	MDCK0/MDCK1	640	640	320	640	1280	640	2560	1280	1280	S162N, I216T		
A/Iceland/5/2016	6B.1	2016-01-13	MDCK0/MDCK1	1280	640	640	1280	1280	640	2560	2560	1280	S162N, I216T		
A/Iceland/6/2016		2016-01-13	MDCK0/MDCK1	640	640	320	640	1280	640	1280	1280	1280			

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

Sequences in phylogenetic trees

Table 3-4. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre											
					Post-infection ferret antisera											
					A/Cal 7/09 Egg NIB FO5/14	A/Bayern 69/09 MDCK F09/15[1]	A/Lviv N6/09 MDCK F14/13[1]	A/Chch 16/10 Egg F15/14[1] 4	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 F3/14[1] 6B	A/Slov 2903/15 Egg F02/16[1] 6B.1	
REFERENCE VIRUSES																G155E
A/California/7/2009			2009-04-09	E4/E2	640	320	320	320	640	320	1280	1280	1280	1280	1280	G155E+G, D222G
A/Bayern/69/2009			2009-07-01	MDCK5/MDCK1	<	320	160	80	40	<	40	40	40	40	ND	
A/Lviv/N6/2009			2009-10-27	MDCK4/SIAT1/MDCK3	80	640	640	160	80	80	80	160	80	80	ND	
A/Christchurch/16/2010		4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	1280	1280	1280	ND	
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	1280	640	320	640	1280	640	1280	2560	1280	1280	ND	
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	640	640	640	1280	640	1280	1280	1280	1280	ND	
A/St. Petersburg/100/2011		7	2011-03-14	E1/E3	1280	640	640	640	1280	640	2560	1280	1280	1280	ND	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK1	320	160	80	160	320	160	640	640	640	320	ND	
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	640	640	320	640	640	1280	1280	1280	1280	1280	S162N, I216T
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4	2560	1280	640	1280	2560	1280	5120	2560	2560	5120	S162N, I216T	
TEST VIRUSES																
A/Norway/2647/2015		6B	2015-11-03	MDCK1	1280	320	320	640	1280	640	2560	1280	1280	1280	2560	
A/Stockholm/55/2015		6B.1	2015-11-10	MDCK0/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Stockholm/56/2015			2015-11-18	MDCK0/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	
A/Stockholm/57/2015			2015-11-18	MDCK0/MDCK1	1280	320	320	640	1280	320	1280	1280	1280	1280	2560	
A/Stockholm/59/2015			2015-11-19	MDCK0/MDCK1	2560	1280	640	640	2560	1280	2560	2560	2560	2560	5120	
A/Stockholm/67/2015		6B.1	2015-11-21	MDCK0/MDCK1	640	320	160	320	640	320	1280	640	640	640	1280	S162N, I216T
A/Stockholm/66/2015			2015-11-23	MDCK2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	
A/Stockholm/60/2015		6B.1	2015-11-25	MDCK0/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Portugal/SU66/2015			2015-11-26	MDCK2	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	
A/Portugal/SU63/2015		6B	2015-11-27	MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	
A/Norway/2774/2015		6B.2	2015-11-30	MDCK2	1280	640	640	640	1280	640	2560	2560	2560	2560	2560	V152T, V173I
A/Czech Republic/96/2015			2015-12-01	SIAT1/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	
A/Czech Republic/95/2015		6B.1	2015-12-01	SIAT1/MDCK1	1280	640	640	1280	1280	1280	2560	2560	2560	1280	2560	S162N, I216T
A/Portugal/SU81/2015		6B	2015-12-02	MDCK2	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	
A/Navarra/1801/2015		6B.1	2015-12-02	SIAT1/MDCK1	1280	640	160	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Norway/2844/2015			2015-12-04	MDCK1	640	640	320	320	640	1280	1280	1280	1280	640	2560	
A/Norway/2879/2015		6B.1	2015-12-05	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Norway/2946/2015		6B.1	2015-12-07	MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Denmark/48/2015		6B.2	2015-12-09	SIAT2/MDCK2/MDCK2	640	320	160	320	640	320	1280	640	640	640	1280	V152T, V173I
A/Finland/559/2015			2015-12-14	MDCK1	1280	640	320	640	640	640	2560	1280	1280	1280	2560	
A/Finland/555/2015			2015-12-15	MDCK2	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	
A/Finland/557/2015		6B.1	2015-12-15	MDCK1	640	320	160	320	640	320	1280	1280	1280	640	1280	S162N, I216T
A/Finland/556/2015		6B.1	2015-12-16	MDCK1	1280	320	320	640	1280	320	1280	1280	1280	1280	1280	S162N, I216T
A/Bretagne/2511/2015		6B.1	2015-12-16	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Paris/2535/2015		6B.1	2015-12-17	MDCK1/MDCK1	1280	320	320	320	640	320	1280	1280	1280	640	1280	S162N, I216T
A/Bayern/20150/2015			2015-12-21	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	
A/Spain/111793/2015		6B.1	2015-12-23	MDCK1	2560	1280	640	1280	2560	1280	2560	2560	2560	2560	5120	S162N, I216T
A/Parma/295/2015		6B.1	2015-12-25	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Bayern/20151/2015			2015-12-26	C2/MDCK1	640	640	320	640	1280	320	1280	1280	1280	640	1280	
A/Spain/112307/2015		6B.1	2015-12-28	MDCK1	1280	640	160	640	1280	640	2560	2560	1280	1280	2560	S162N, I216T
A/Thuringen/101/2015			2015-12-28	C2/MDCK1	1280	640	640	1280	1280	640	2560	2560	1280	1280	2560	
A/Champagne Ardenne/2586/2015		6B.1	2015-12-28	MDCK1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Parma/296/2015		6B.1	2015-12-29	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Poland/7474/2015		6B.1	2015-12-31	SIAT1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Czech Republic/3/2016		6B.1	2016-01-01	SIAT1/MDCK1	1280	1280	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Czech Republic/2/2016			2016-01-01	SIAT2/MDCK1	1280	320	320	640	640	640	1280	1280	1280	1280	2560	
A/Czech Republic/1/2016		6B.1	2016-01-01	SIAT2/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Athens/12/2016		6B.1	2016-01-04	MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Thuringen/1/2016			2016-01-04	C2/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	
A/Thuringen/2/2016			2016-01-04	C2/MDCK1	1280	640	640	640	1280	640	5120	2560	2560	1280	5120	
A/Hamburg/1/2016		6B.1	2016-01-04	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Baden-Wurttemberg/1/2016		6B.1	2016-01-05	C2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Slovenia/121/2016		6B.1	2016-01-06	MDCKx/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Thuringen/3/2016		6B.1	2016-01-07	C2/MDCK1	1280	640	320	640	1280	640	2560	2560	1280	1280	2560	S162N, I216T
A/Slovenia/77/2016		6B.1	2016-01-08	MDCKx/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Ireland/1750/2016		6B.1	2016-01-08	MDCK1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Athens/67/2016		6B.1	2016-01-10	MDCK1	640	320	320	640	1280	640	2560	1280	1280	1280	2560	S162N, I216T
A/Slovenia/126/2016		6B.1	2016-01-10	MDCKx/MDCK1	1280	640	320	640	1280	320	1280	1280	1280	1280	2560	S162N, I216T
A/Ireland/2142/2016		6B.1	2016-01-11	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Ireland/2229/2016			2016-01-11	MDCK1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	
A/Berlin/1/2016		6B.1	2016-01-11	C2/MDCK1	640	640	320	320	1280	640	2560	2560	1280	1280	2560	S162N, I216T
A/Berlin/2/2016			2016-01-11	C2/MDCK1	640	320	320	320	1280	640	1280	1280	1280	640	2560	
A/Parma/1/2016		6B.1	2016-01-11	MDCK1/MDCK1	1280	640	640	1280	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Athens/123/2016		6B.1	2016-01-12	MDCK1	640	320	160	320	640	320	1280	1280	1280	640	1280	S162N, I216T
A/Athens/140/2016		6B.1	2016-01-12	MDCK1	1280	640	320	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T
A/Athens/135/2016			2016-01-13	MDCK1	640	320	160	320	640	320	1280	1280	1280	640	1280	S162N, I216T
A/Ireland/263/2016			2016-01-14	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	2560	
A/Ireland/280/2016		6B.1	2016-01-17	MDCK1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	1280	2560	S162N, I216T

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

Vaccine

Sequences in phylogenetic trees

Table 3-5. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				A/Cal 7/09 Egg NIB F05/14	A/Bayern 69/09 MDCK F09/15[-1]	A/Lviv N6/09 MDCK F14/13[-1]	A/Chch 16/10 Egg F15/14[-1]	A/Astrak 1/11 MDCK F22/13[-1]	A/St. P 27/11 Egg F26/14[-1]	A/St. P 100/11 Egg F24/11[-1]	A/HK 5659/12 MDCK F30/12[-1]	A/Sth Afr 3626/13 Egg F03/14[-1]	A/Slov 2903/2015 Egg F02/16[-2]
	Passage history						4	5	6	7	6A	6B	6B.1
	Ferret number												
	Genetic group												
REFERENCE VIRUSES													
A/California/7/2009		2009-04-09	NIBSC E4/E2	640	320	320	320	640	320	1280	1280	640	640
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	<	320	320	160	80	40	80	80	80	<
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	80	1280	640	320	80	80	80	160	80	80
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	5120	2560	640	2560	2560	1280	2560
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	640	640	1280	1280	640	2560	2560	1280	2560
A/St. Petersburg/27/2011	6	2011-02-14	E1/E4	1280	640	640	640	1280	640	2560	1280	1280	1280
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	640	1280	1280	640	2560	2560	2560	2560
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	320	320	320	1280	1280	640	640
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	640	640	640	640	640	640	2560	1280	1280	1280
A/Slovenia/2903/2015	clone 37 6B.1	2015-10-26	E4	1280	640	640	2560	2560	1280	5120	2560	1280	2560
TEST VIRUSES													
A/Iasi/187166/2015	in process	2015-10-13	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Denmark/41/2015	in process	2015-11-27	SIAT3/MDCK2/MDCK1	640	640	320	640	1280	640	1280	1280	1280	2560
A/Denmark/43/2015	in process	2015-12-03	MDCK3/MDCK1	320	320	160	320	640	320	1280	640	640	1280
A/Ireland/72156/2015	in process	2015-12-17	MDCK1/MDCK1	1280	640	640	1280	1280	640	2560	2560	1280	5120
A/Lisboa/51/2015	in process	2015-12-17	SIAT1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	5120
A/Lisboa/49/2015		2015-12-18	SIAT3/MDCK1	2560	1280	640	1280	2560	1280	2560	2560	2560	5120
A/Lisboa/65/2015		2015-12-21	SIAT2/MDCK1	1280	640	640	640	1280	640	2560	2560	1280	5120
A/Lisboa/53/2015	in process	2015-12-22	SIAT1/MDCK1	1280	1280	640	1280	1280	640	2560	2560	1280	2560
A/Ireland/169/2015	in process	2015-12-29	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Lisboa/66/2015		2015-12-29	SIAT1/MDCK1	2560	1280	640	640	1280	640	2560	2560	1280	5120
A/Lisboa/68/2016	in process	2015-12-29	SIAT1/MDCK1	2560	1280	640	1280	2560	1280	2560	2560	2560	5120
A/Lisboa/2/2016	in process	2016-01-02	SIAT2/MDCK2	1280	640	320	640	1280	640	1280	1280	1280	2560
A/Lisboa/5/2016	in process	2016-01-03	SIAT1/MDCK1	1280	640	640	1280	1280	1280	2560	2560	1280	2560
A/Ireland/767/2016	in process	2016-01-04	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Lisboa/1/2016	in process	2016-01-04	SIAT1/MDCK1	1280	1280	640	1280	1280	1280	2560	1280	1280	2560
A/Lisboa/7/2016		2016-01-04	SIAT1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Ireland/768/2016		2016-01-05	MDCK1/MDCK1	1280	640	640	1280	1280	640	2560	2560	1280	2560
A/Ireland/2133/2016	in process	2016-01-06	MDCK1/MDCK1	1280	640	640	640	1280	640	2560	2560	2560	5120
A/Galati/190006/2016		2016-01-06	MDCK1/MDCK1	1280	1280	1280	1280	2560	1280	5120	2560	1280	5120
A/Iisboa/4/2016		2016-01-06	SIAT1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	5120
A/Ireland/179/2016		2016-01-07	MDCK1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Lisboa/3/2016	in process	2016-01-07	SIAT1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560
A/Dambovita/190170/2016		2016-01-18	MDCK1/MDCK1	1280	640	320	640	1280	640	1280	1280	1280	2560
A/Dambovita/190171/2016		2016-01-18	MDCK2/MDCK1	1280	1280	640	1280	1280	640	2560	2560	1280	5120
A/Bucuresti/190324/2016	in process	2016-01-19	MDCK1/MDCK1	2560	1280	1280	1280	2560	1280	5120	2560	2560	5120
A/Dambovita/190341/2016	in process	2016-01-21	MDCK1/MDCK1	1280	640	640	1280	1280	640	2560	2560	1280	2560
				Vaccine									

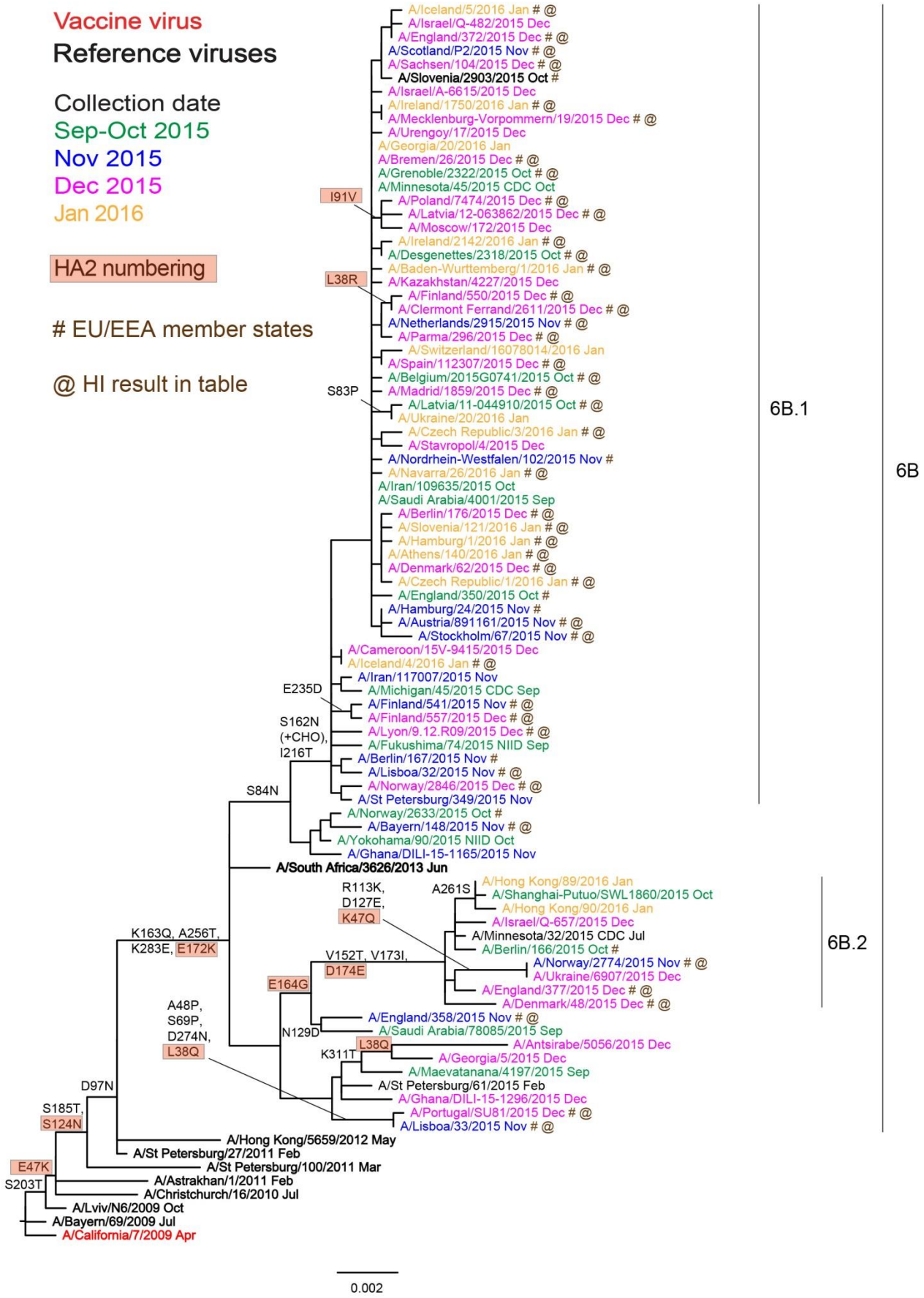
* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) [1] < = <40; [2] < = <80

Table 3-6. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				A/Cal	A/Bayern	A/Lviv	A/Chch	A/Astrak	A/St. P	A/St. P	A/HK	A/Sth Afr	A/Slov		
				7/09	69/09	N6/09	16/10	1/11	27/11	100/11	5659/12	3626/13	2903/2015	G155E	
	Passage history			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	Egg	Egg	G155E>G, D222G	
	Ferret number			F05/14	F09/15^{-1}	F14/13^{-1}	F15/14^{-1}	F22/13^{-1}	F26/14^{-1}	F24/11^{-1}	F30/12^{-1}	F03/14^{-1}	F02/16^{-2}		
	Genetic group						4	5	6	7	6A	6B	6B.1		
REFERENCE VIRUSES															
A/California/7/2009	NIBSC	2009-04-09	E4/E3	2560	1280	1280	640	2560	1280	5120	2560	2560	2560		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	40	320	320	80	80	40	80	80	80	80		
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	80	1280	1280	320	160	160	160	320	160	320		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	2560	1280	2560		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	1280	640	1280	2560	1280	5120	2560	1280	2560		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E4	1280	640	640	640	1280	640	2560	1280	1280	1280		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	2560	1280	1280	1280	2560	1280	5120	5120	2560	5120		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK1	1280	320	320	320	1280	640	2560	1280	1280	640		
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	12580	640	1280	640	1280	640	2560	1280	1280	1280		
A/Slovenia/2903/2015	clone 37	2015-10-26	E4	1280	640	640	640	1280	640	2560	2560	1280	1280		
TEST VIRUSES															
A/Aragon/1615/2015	in process	2015-09-29	SIAT3/SIAT1	1280	1280	640	1280	1280	1280	2560	2560	1280	2560		
A/Madrid/SO13656/2015	in process	2015-10-29	SIAT1/SIAT1	1280	640	320	640	1280	640	2560	1280	1280	2560		
A/Navarra/1736/2015	in process	2015-11-14	SIAT1/SIAT1	2560	640	640	640	2560	1280	5120	2560	1280	5120		
A/Castilla La Mancha/16013/2015	in process	2015-12-30	SIAT1/SIAT1	1280	640	320	640	1280	640	2560	2560	1280	2560		
A/Greece/39/2016	in process	2016-01-15	MDCK2	1280	640	320	640	1280	640	2560	2560	1280	2560		
A/Greece/41/2016	in process	2016-01-16	MDCK2	1280	640	320	1280	1280	640	2560	2560	1280	2560		
A/Greece/50/2016	in process	2016-01-18	MDCK1	640	320	320	640	640	320	1280	1280	1280	2560		
A/Greece/65/2016	in process	2016-01-22	MDCK1	1280	640	640	640	1280	640	2560	2560	1280	2560		
				Vaccine											

*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[3], 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 or the loss of the ability of viruses to agglutinate any of the RBCs. This is a particular problem for most viruses that fall in genetic subgroup 3C.2a as was highlighted first in the November 2014 report[4].

Results of HI tests performed with guinea pig RBCs in the presence of 20nM oseltamivir, added to circumvent NA-mediated binding of A(H3N2) viruses to the RBCs, are shown in Tables 4-1 and 4-2. Of the 26 test viruses that retained sufficient HA titre to be analysed by HI assay, 22 were analysed genetically with 17 falling in subclade 3C.3a and five in subclade 3C.2a.

The test viruses, propagated in MDCK-SIAT1 cells, reacted poorly in HI assays with the panel of post-infection ferret antisera relative to the titres of the antisera with their respective homologous viruses (shown in red: Tables 4-1 and 4-2). However, in terms of absolute titres antisera raised against A/Stockholm/6/2014 (3C.3a: cell- and egg-propagated), cell-propagated A/Hong Kong/5738/2014 (3C.2a) and A/Hong Kong/4801/2014 (3C.2a: cell- and egg-propagated), gave consistent reactivity with all but one test virus: A/Padova/1/2015 (for which sequencing is in progress: Table 4-2) showed reactivity with antiserum raised against tissue culture-propagated A/Switzerland/9715293/2013 only. In terms of absolute titre, the antiserum raised against the northern hemisphere 2015–16 vaccine component, egg-propagated A/Switzerland/9715293/2013 (3C.3a) reacted with all test viruses at titres equivalent to (50% of viruses) or twofold reduced compared to titres achieved with egg-propagated A/Hong Kong/4801/2014, the virus recommended for use in vaccines for the southern hemisphere 2016 and northern hemisphere 2016–17 influenza seasons.

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. In 2014 three new subclades emerged, one in subdivision 3C.2, 3C.2a, and two in 3C.3, 3C.3a and 3C.3b, with subclade 3C.2a viruses dominating in recent months (Figure 2). While viruses in subclades 3C.2a and 3C.3a are antigenic drift variants, those in 3C.3b have remained antigenically similar to previously circulating viruses in the 3C.3 subdivision. Amino acid substitutions that define these subdivisions and subclades are:

- (3C.2) **N145S** in **HA1**, and **D160N** in **HA2**, e.g. A/Hong Kong/146/2013
- (3C.2a) Those in 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/5738/2014
- (3C.3) **T128A** (resulting in the loss of a potential glycosylation site), **R142G** and **N145S** in **HA1**, e.g. A/Samara/73/2013
- (3C.3a) those in 3C.3 plus **A138S**, **F159S** and **N225D** in **HA1**, many with **K326R**, e.g. A/Switzerland/9715293/2013
- (3C.3b) those in 3C.3 plus **E62K, K83R, N122D** (resulting in the loss of a potential glycosylation site), **L157S** and **R261Q** in **HA1** with **M18K** in **HA2**, e.g. A/Stockholm/28/2014

Based on results available at the time of the February 2015 vaccine composition meeting, that showed cross-reactivity of antisera raised against subclade 3C.3a and 3C.2a viruses, but changes acquired on egg-adaptation of genetic subgroup 3C.2a viruses and, at that time, the lack of a suitable 3C.2a vaccine candidate, the World Health Organization recommendation was to use an A/Switzerland/9715293/2013-like virus as the A(H3N2) component of vaccines for the northern hemisphere 2015–16 influenza season [1]. After February 2015, a new subclade designated 3C.3b emerged, these three subclades being antigenically distinguishable, but subclade 3C.2a viruses became prevalent and have remained so. While ferret antisera raised against 3C.3a and 3C.2a subclade viruses showed some cross-reactivity with viruses in all three subclades, antisera raised against 3C.3b viruses were subclade specific. With the availability of new subclade 3C.2a vaccine candidates and the continued cross-reactivity of antisera raised against viruses in subclades 3C.3a and 3C.2a viruses, the World Health Organization recommendation for the A(H3N2) component of influenza vaccines for the southern hemisphere 2016 [2] and northern hemisphere 2016–17 [3] influenza seasons was for an A/Hong Kong/4801/2014-like (3C.2a) virus.

[3] For example, the September 2013 report: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2013. Stockholm: ECDC; 2013. Available from: http://www.ecdc.europa.eu/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf

[4] 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/Neth	A/HK	A/HK	A/HK	A/HK	A/HK	A/HK	A/Georgia
				50/12	73/13	6/14	6/14	9715293/13	9715293/13	525/14	146/13	5738/14	4801/14	4801/14	4801/14	4801/14	532/15
	Passage history			Egg	SIAT	SIAT	Egg	SIAT	Egg	SIAT	Egg	MDCK	MDCK	MDCK	Egg	Egg	SIAT
	Ferret number			F36/12^{-1}	F35/15^{-1}	F14/14^{-1}	F20/14^{-1}	F18/15^{1}	F32/14^{-1}	F23/15^{-1}	F10/15^{-1}	F30/14^{-1}	F43/15^{-1}	F43/15^{-1}	F43/15^{-1}	F12/15^{-1}	F33/15^{-1}
	Genetic group			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.3b	3C.2	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a	3C.2a
REFERENCE VIRUSES																	
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	2560	1280	160	640	80	640	320	320	160	320	80	160	80	160
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	1280	640	640	640	80	320	320	320	320	640	160	320	160	320
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	160	80	640	320	160	160	80	160	160	160	160	160	160	160
A/Stockholm/6/2014	3C.3a isolate 2	2014-02-06	E4/E1	640	80	160	320	80	640	80	40	160	320	40	160	40	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	40	40	320	160	80	80	40	40	80	80	40	80	40	40
A/Switzerland/9715293/2013	3C.3a clone 123	2013-12-06	E4/E1	640	160	160	320	40	640	40	80	160	320	80	160	80	160
A/Netherlands/525/2014	3C.3b	2014-12-17	SIAT2/SIAT2	320	160	160	160	40	80	640	80	80	80	80	80	80	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	2560	640	80	640	40	320	160	640	160	320	80	320	80	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK3	80	40	320	160	80	80	40	80	160	320	160	320	160	160
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1	80	40	320	160	40	80	40	80	160	320	160	320	160	160
A/Hong Kong/4801/2014	3C.2a isolate 1	2014-02-26	E6/E2	40	80	80	40	40	40	40	<	160	640	320	640	320	320
A/Georgia/532/2015	3C.2a plaque 20	2015-03-09	SIAT2	160	80	320	160	40	40	40	80	160	320	160	320	80	640
TEST VIRUSES																	
A/Austria/890287/2015	3C.3a	2015-11-18	SIAT1/SIAT6	80	40	320	160	80	80	40	80	160	160	160	160	160	80
A/Aix-en-Provence/2474/2015	3C.2a	2015-11-20	MDCK3/SIAT1	40	<	80	40	<	<	<	<	40	80	40	80	40	40
A/Austria/890744/2015	3C.3a	2015-11-20	SIAT1/SIAT5	80	40	320	160	80	80	40	80	80	80	80	80	80	80
A/Austria/891959/2015	3C.3a	2015-11-30	SIAT1/SIAT3	40	<	160	80	<	40	<	<	40	40	40	40	40	<
A/Austria/892085/2015	3C.3a	2015-11-30	SIAT1/SIAT4	160	80	640	320	160	160	80	160	160	160	160	160	160	160
A/Finland/547/2015	3C.3a	2015-11-30	SIAT1/SIAT1	80	40	320	160	40	80	40	40	160	80	160	80	160	40
A/Finland/547/2015	3C.3a	2015-11-30	SIAT1/SIAT2	80	40	320	160	80	80	40	80	80	160	80	160	80	80
A/Nordrhein-Westfalen/104/2015	3C.3a	2015-12-03	C2/SIAT1	160	40	320	160	80	80	40	80	160	160	160	160	160	40
A/Finland/552/2015	3C.2a	2015-12-03	SIAT1/SIAT2	40	<	80	40	<	<	<	40	40	80	40	80	40	<
A/Austria/893502/2015	3C.3a	2015-12-07	SIAT1/SIAT2	40	<	160	80	<	40	<	<	40	40	40	40	40	<
A/Berlin/173/2015	3C.3a	2015-12-09	C2/SIAT1	40	<	160	80	<	<	<	<	40	40	40	40	40	<
A/Austria/893755/2015	3C.3a	2015-12-09	SIAT1/SIAT1	40	<	160	80	<	40	<	<	40	40	40	40	40	<
A/Lyon/2608/2015	3C.2a	2015-12-14	MDCK2/SIAT1	40	<	80	40	40	<	<	40	80	80	80	80	80	80
									Vaccine NH 2015-16							Vaccine SH 2016	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) ^{1} < = <40

Sequences in phylogenetic trees

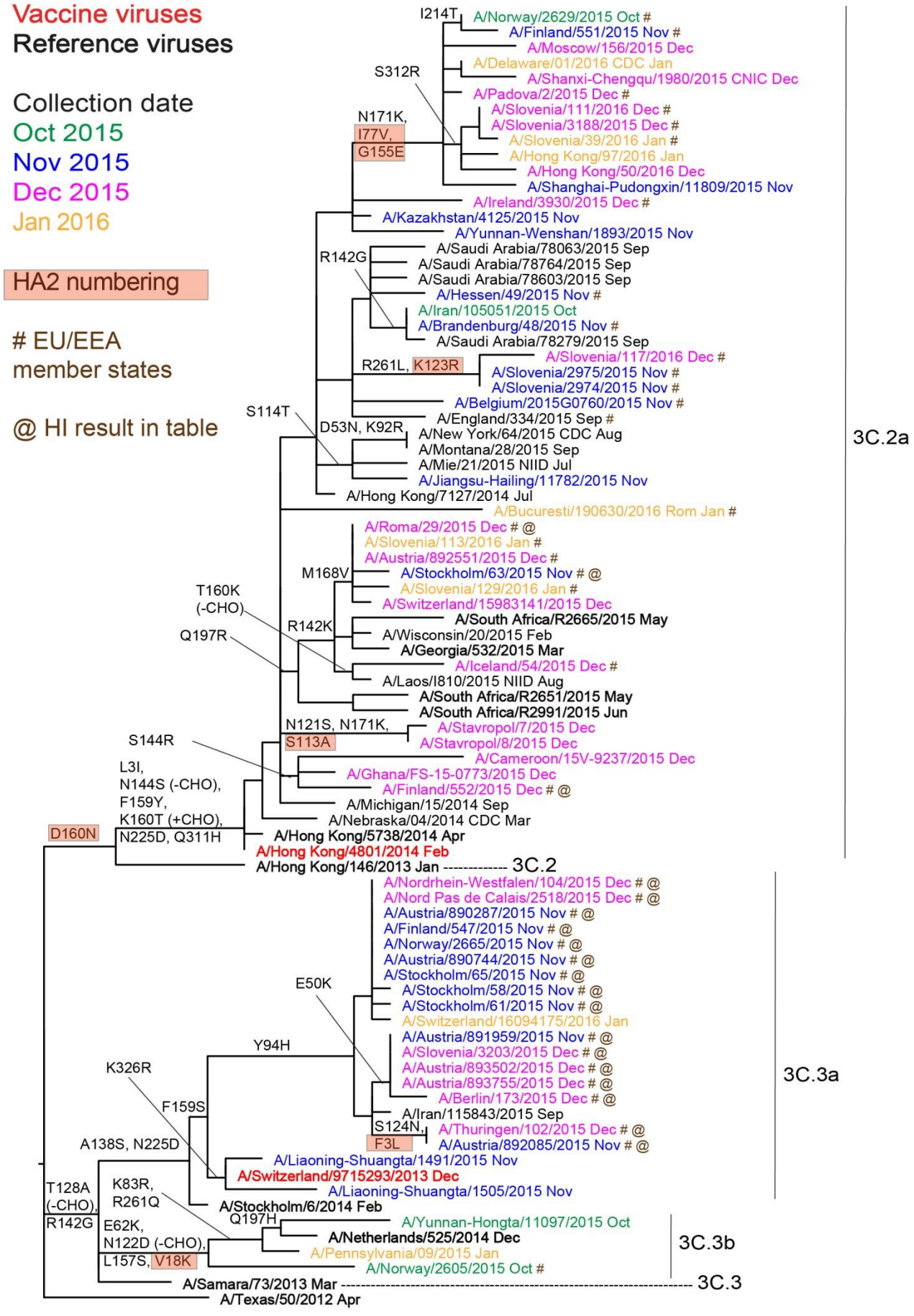
Table 4-2. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				A/Texas/50/2012	A/Samara/73/2013	A/Stock/6/14	A/Switz/9715293/13	A/Stock/6/14	A/Switz/9715293/13	A/Neth/525/14	A/HK/146/13	A/HK/5738/14	A/HK/4801/14	A/HK/4801/14	A/Georgia/532/15
				50/12	73/13	6/14	9715293/13	Egg	Egg	SIAT	Egg	MDCK	MDCK	Egg	SIAT
	Passage history			Egg	SIAT	SIAT	SIAT	Egg	Egg	SIAT	Egg	MDCK	MDCK	Egg	SIAT
	Ferret number			F36/12[1]	F35/15[1]	F14/14[1]	F18/15[1]	F20/14[1]	F32/14[1]	F23/15[1]	F10/15[1]	F30/14[1]	F43/15[1]	F12/15[1]	F33/15[1]
	Genetic group			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.3b	3C.2	3C.2a	3C.2a	3C.2a	3C.2a
REFERENCE VIRUSES															
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	2560	640	160	640	320	640	320	320	160	320	80	160
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT3	1280	640	640	320	320	320	320	320	320	640	160	320
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	160	80	640	160	320	160	80	160	160	320	160	160
A/Stockholm/6/2014 isolate 2	3C.3a	2014-02-06	E4/E1	640	80	160	640	320	640	80	80	160	320	40	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	80	40	320	80	160	80	40	40	160	160	80	80
A/Switzerland/9715293/2013 clone 123	3C.3a	2013-12-06	E4/E1	640	160	160	640	320	640	80	80	320	320	80	160
A/Netherlands/525/2014	3C.3b	2014-12-17	SIAT2/SIAT2	640	160	320	160	160	160	640	160	80	160	80	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	2560	640	80	640	640	640	320	640	320	640	160	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2	160	40	320	80	160	80	40	80	160	320	160	160
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK2	80	40	160	80	80	40	40	80	80	320	80	80
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	80	80	80	80	80	40	80	40	320	640	320	320
A/Georgia/532/2015 plaq 20	3C.2a	2015-03-09	SIAT1/SIAT3	160	80	160	160	40	80	40	80	160	320	160	320
TEST VIRUSES															
A/Norway/2665/2015	3C.3a	2015-11-09	SIAT1	80	80	640	320	80	80	40	80	160	160	160	80
A/Stockholm/58/2015	3C.3a	2015-11-17	MDCK0/SIAT1	80	40	320	320	80	160	40	80	160	160	160	80
A/Stockholm/65/2015	3C.3a	2015-11-20	MDCK0/SIAT1	160	80	640	320	160	160	80	160	160	320	160	160
A/Stockholm/63/2015	3C.2a	2015-11-23	MDCK0/SIAT2	80	40	160	80	40	40	<	80	80	160	80	160
A/Stockholm/61/2015	3C.3a	2015-11-23	MDCK0/SIAT1	160	80	640	320	160	160	80	160	160	640	160	80
A/Thuringen/102/2015	3C.3a	2015-12-04	C1/SIAT1	80	40	320	320	80	80	40	80	160	160	160	80
A/Norway/2877/2015	in process	2015-12-08	SIAT1	80	<	320	160	80	40	40	40	80	80	80	80
A/Nord Pas de Calais/2518/2015	3C.3a	2015-12-18	MDCK1/SIAT1	80	40	320	320	80	80	40	80	160	160	160	80
A/Lisboa/75/2015	in process	2015-12-25	SIAT2/SIAT1	40	<	320	160	40	80	40	<	80	80	80	40
A/Lisboa/76/2015	in process	2015-12-25	SIAT1/SIAT1	40	<	160	80	<	40	<	<	40	40	40	<
A/Padova/1/2015	in process	2015-12-28	SIAT1/SIAT2	<	<	<	<	640	<	<	<	<	<	<	<
A/Slovenia/3203/2015	3C.3a	2015-12-29	SIATx/SIAT2	40	<	160	80	<	40	40	<	40	40	80	40
A/Roma/29/2015	3C.2a	2015-12-30	SIAT1/SIAT2	40	<	160	40	40	<	<	40	80	80	40	160
									Vaccine NH 2015-16					Vaccine SH 2016	

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

Sequences in phylogenetic trees

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



Influenza B virus analyses

Seventy influenza type B viruses have been received from EU/EEA countries, of which 65 were ascribed to a lineage: 55 B/Victoria-lineage and 10 B/Yamagata-lineage (Table 2).

Influenza B – Victoria lineage

Since the December 2015 report, 33 viruses of this lineage from EU/EEA countries have been characterised antigenically. HI results are shown in Tables 5-1 and 5-2, as observed throughout the previous season, the test viruses carried HA genes of clade 1A.

The test viruses showed similar HI reactivity patterns to those from the 2014–15 influenza season: greater than eightfold reductions in HI titres compared with the titre for the homologous virus with post-infection ferret antisera raised against the recommended vaccine virus for quadrivalent live and inactivated vaccines for the northern hemisphere 2015–2016 influenza season, B/Brisbane/60/2008. Similarly, they were poorly recognised by post-infection ferret antisera raised against the egg-propagated reference viruses B/Malta/636714/2011, B/Johannesburg/3964/2013 and B/South Australia/81/2012. In contrast, they showed reactivity 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 B/Paris/1762/2009, B/Hong Kong/514/2009 and B/Odessa/3886/2010.

Phylogenetic analysis of the HA gene of representative B/Victoria lineage viruses is shown in Figure 3. Worldwide, recent viruses have HA genes that fall into the B/Brisbane/60/2008 clade (clade 1A) and remain antigenically similar to the recommended vaccine virus, B/Brisbane/60/2008, for use in quadrivalent vaccines. The great majority of viruses, with collection dates since October 2015, fall in a major sub-cluster defined by amino acid substitutions N129D, V146I and I117V within clade 1A.

These results, linked with the rise in the proportion of B/Victoria-lineage viruses seen in the 2015 southern hemisphere and 2015–2016 northern hemisphere influenza seasons, support the recommendations made in to include B/Brisbane/60/2008 in trivalent influenza vaccines for the southern hemisphere 2016 [2] and northern hemisphere 2016–2017 influenza seasons.

Influenza B – Yamagata lineage

HI results for five B/Yamagata-lineage test viruses analysed since the December 2015 report are shown in Table 6. Those viruses characterised genetically fell in clade 3.

The homologous titres of the ten post-infection ferret antisera, shown in red, ranged from 80 to 640, and the test viruses show similar reactivity patterns with the exception of B/Lisboa/151/2015. B/Lisboa/151/2015 showed good reactivity with all antisera but for that raised against egg-propagated B/Stockholm/12/2011 (Table 6). Compared with the homologous titre of the antisera raised against the four viruses from clade 2, test viruses were generally less well recognised, notably so for the antiserum raised against egg-propagated B/Massachusetts/02/2012, the vaccine virus recommended for use in the 2014–15 northern hemisphere influenza season, than they were by the five antisera raised against clade 3 viruses compared to the titres for the homologous viruses.

Antisera raised against egg-propagated clade 3 viruses B/Phuket/3073/2013 (the virus recommended for inclusion in trivalent influenza vaccines for the northern hemisphere 2014–2015 season) and B/Hong Kong/3417/2014 recognised all test viruses at titres within twofold of their respective homologous titres, as did that raised against egg-propagated B/Wisconsin/1/2010 (a previous vaccine virus). However, the antisera raised against tissue culture-propagated B/Phuket/3073/2013 and egg-propagated B/Stockholm/12/2011 showed somewhat reduced reactivity (fourfold or greater) with some of the test viruses.

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 L172Q amino acid substitution in HA1. A number of viruses, including the four test viruses characterised genetically here, form a sub-cluster defined by HA1 M251V amino acid substitution. A few viruses illustrated in the phylogenetic trees are reassortants carrying NA genes normally associated with the B/Victoria-lineage – none was from an EU-EAA country.

Based on such results, a B/Phuket/3073/2013-like virus has been recommended for inclusion in quadrivalent vaccines for the 2016 southern hemisphere [2] and 2016–2017 northern hemisphere [3] influenza seasons.

Table 5-1. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses		Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				B/Bris 60/08	B/Mal 2506/04	B/Bris 60/08	B/Paris 1762/09	B/Malta 636714/11	B/Jhb 3964/12	B/For V2367/12	B/Sth Aus 81/12	B/HK 514/09	B/Odessa 3886/10
	Passage history			Egg	Egg	Egg	MDCK	Egg	Egg	MDCK	Egg	MDCK	MDCK
	Ferret number			Sh 539/540 /543/544[*1,3]	F37/11[*2]	F22/12[*2]	F07/11[*2]	F29/13[*2]	F01/13[*2]	F04/13[*4]	F41/13[*2]	F09/13[*2]	F19/11[*2]
	Genetic group			1A		1A	1A	1A	1A	1A	1A	1B	1B
REFERENCE VIRUSES													
B/Malaysia/2506/2004		2004-12-06	E3/E7	320	320	20	<	80	80	40	80	10	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E5	640	40	160	40	320	320	160	640	40	40
B/Paris/1762/2009	1A	2009-02-09	C2/MDCK2	640	<	<	40	40	40	40	40	20	40
B/Malta/636714/2011	1A	2011-03-07	E4/E1	640	40	160	40	320	320	160	640	40	40
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	2560	160	640	80	1280	1280	640	1280	80	40
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	640	20	80	40	160	160	160	320	20	20
B/South Australia/81/2012	1A	2012-11-28	E4/E2	640	40	160	40	160	320	160	640	40	20
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	640	<	<	40	40	20	20	40	80	40
B/Odessa/3886/2010	1B	2010-03-19	MDCK2/MDCK4	640	<	<	40	40	40	40	40	40	80
TEST VIRUSES													
B/Belgium/2015G0748/2015	1A	2015-11-03	SIAT1/MDCK1	320	<	<	20	20	20	40	40	20	20
B/Belgium/2015G0753/2015	1A	2015-11-03	SIAT1/MDCK1	640	<	<	20	20	20	40	40	20	20
B/Belgium/2015G0762/2015	1A	2015-11-10	SIAT1/MDCK1	640	<	<	40	40	40	40	40	20	40
B/Belgium/2015G0764/2015	1A	2015-11-10	SIAT1/MDCK1	640	<	<	40	40	40	40	40	20	40
B/Netherlands/2914/2015	1A	2015-11-10	MDCK1/MDCK1	640	<	<	40	20	20	40	40	20	20
B/Belgium/2015G0769/2015	1A	2015-11-18	SIAT1/MDCK1	640	<	<	20	40	40	40	40	20	20
B/Sachsen/37/2015	1A	2015-11-25	C2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Marseille/2589/2015	1A	2015-12-03	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Marseille/2590/2015	1A	2015-12-09	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Lyon/2583/2015	1A	2015-12-11	MDCK2/MDCK1	640	<	<	40	40	20	40	40	20	20
B/Lyon/14.12.R13/2015	1A	2015-12-13	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Marseille/2643/2015	1A	2015-12-13	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Marseille/2645/2015	1A	2015-12-13	MDCK2/MDCK1	640	<	<	40	80	80	80	160	40	40
B/Thuringen/43/2015	1A	2015-12-14	C2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Lyon/2585/2015	1A	2015-12-15	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Lyon/17.12.R76/2015	1A	2015-12-17	MDCK2/MDCK1	640	<	<	40	40	40	40	80	40	40
B/Lyon/2658/2015	1A	2015-12-22	MDCK2/MDCK1	640	<	<	40	40	40	40	40	40	40
						Vaccine NH 2015-16[#] SH 2016							

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

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

Sequences in phylogenetic trees

Table 5-2. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses		Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				B/Bris 60/08	B/Mal 2506/04	B/Bris 60/08	B/Paris 1762/09	B/Malta 636714/11	B/Jhb 3964/12	B/For V2367/12	B/Sth Aus 81/12	B/HK 514/09	B/Odessa 3886/10
	Passage history			Egg	Egg	Egg	MDCK	Egg	Egg	MDCK	Egg	MDCK	MDCK
	Ferret number			Sh 539/540 /543/544 [*1,3]	F37/11 [*2]	F22/12 [*2]	F07/11 [*2]	F29/13 [*2]	F01/13 [*2]	F04/13 [*4]	F41/13 [*2]	F09/13 [*2]	F19/11 [*2]
	Genetic group			1A		1A	1A	1A	1A	1A	1A	1B	1B
REFERENCE VIRUSES													
B/Malaysia/2506/2004		2004-12-06	E3/E7	640	320	20	<	40	160	40	80	10	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E5	640	40	160	40	320	320	160	640	40	40
B/Paris/1762/2009	1A	2009-02-09	C2/MDCK2	640	<	<	40	20	40	40	40	20	40
B/Malta/636714/2011	1A	2011-03-07	E4/E1	640	40	80	40	320	320	160	640	40	20
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	2560	320	640	160	1280	1280	1280	1280	160	80
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	1280	20	80	40	160	160	160	320	40	20
B/South Australia/81/2012	1A	2012-11-28	E4/E2	640	40	80	20	160	320	160	640	40	40
B/Hong Kong/514/2009	1B	2009-10-11	MDCK3	640	<	<	40	40	20	40	40	40	80
B/Odessa/3886/2010	1B	2010-03-19	C2/MDCK2	1280	<	<	40	80	40	80	80	40	80
TEST VIRUSES													
B/Norway/2726/2015	1A	2015-11-14	MDCK1	1280	<	<	80	80	80	80	80	40	40
B/Castilla La Mancha/1807/2015	1A	2015-12-03	SIAT1/MDCK1	1280	<	<	80	40	40	80	40	40	80
B/Castilla La Mancha/1808/2015	1A	2015-12-14	SIAT1/MDCK1	1280	<	<	40	40	40	80	40	20	40
B/Castilla La Mancha/1809/2015	1A	2015-12-14	SIAT1/MDCK1	640	10	<	80	40	40	80	80	40	80
B/Castilla La Mancha/1820/2015	1A	2015-12-14	SIAT1/MDCK1	1280	<	<	80	40	40	80	40	40	40
B/Ireland/71062/2015	in process	2015-12-15	MDCK1/MDCK1	1280	<	<	80	40	40	80	80	40	40
B/Bretagne/2531/2015	1A	2015-12-16	MDCK1/MDCK1	640	<	<	80	40	<	40	80	20	40
B/Nord Pas de Calais/2578/2015	1A	2015-12-23	MDCK1/MDCK1	640	<	<	80	40	<	40	80	20	40
B/Bretagne/2597/2015	1A	2015-12-29	MDCK1/MDCK1	640	<	<	80	40	<	40	80	20	40
B/Estonia/97395/2015	1A	2015-12-30	MDCK2	640	<	<	40	40	40	40	80	40	40
B/Iceland/56/2015	1A	2015-12-30	MDCK0/MDCK1	640	<	<	40	20	20	40	40	20	40
B/Estonia/97415/2016	1A	2016-01-04	MDCK1	640	<	<	40	40	40	40	80	40	40
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK1	640	<	<	80	40	40	40	80	20	40
B/Schleswig-Holstein/1/2016	1A	2016-01-05	C2/MDCK1	1280	<	<	80	40	40	80	80	40	40
B/Thuringen/1/2016	1A	2016-01-11	C2/MDCK1	1280	<	<	80	40	40	80	80	40	40
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK1	640	<	<	80	40	40	80	40	40	40
						Vaccine NH 2015-16[#] SH 2016							

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

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

Sequences in phylogenetic trees

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

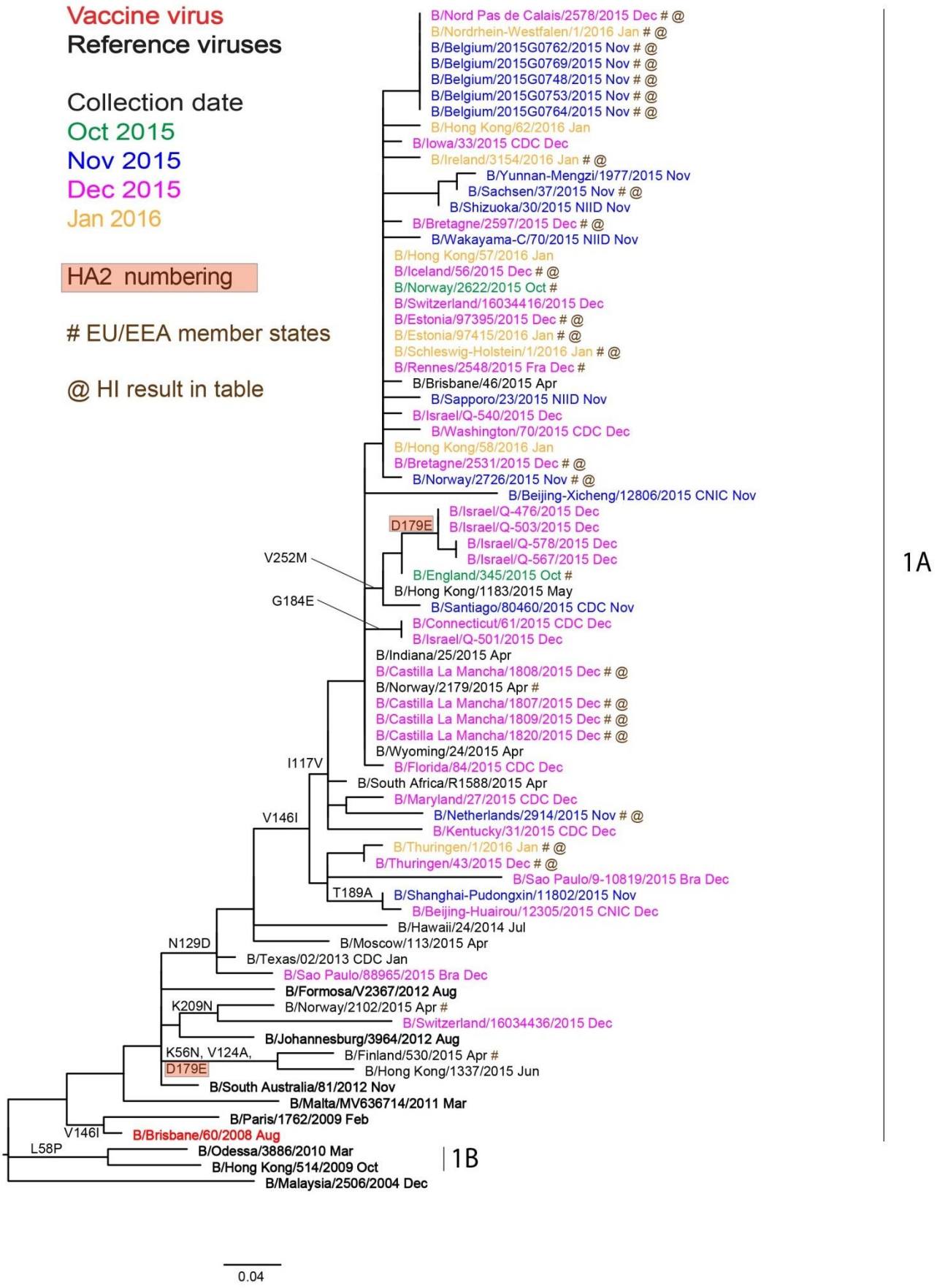


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses				Haemagglutination inhibition titre												
				Post-infection ferret antisera												
	Collection date	Passage History		B/Phuket[1,3]	B/Fl[1]	B/Bris[2]	B/Estonia[2]	B/Mass[2]	B/Mass[2]	B/Wis[2]	B/Stock[1]	B/Phuket[2]	B/Phuket[2]	B/HK[4]
Passage history														
Ferret number				3073/13	4/06	3/07	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13	3417/14
Genetic Group				Egg	Egg	Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	Egg
				SH614	F1/10	F38/14	F32/12	F05/15	F42/14	F10/13	F06/15	F35/14	F36/14	St Judes F715/14
				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	80	160	1280	160	320	40	320	320
B/Brisbane/3/2007	2	2007-09-03	E2/E3	640	160	320	20	40	320	40	80	10	80	80
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	80	80	80	160	40	40	20	40	40	160
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	80	320	640	160	80	40	160	320
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	640	160	320	20	80	640	80	80	10	80	80
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	80	80	10	<	80	80	80	20	160	80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	80	80	10	<	80	40	80	20	80	80
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK2	2560	160	160	80	160	320	160	80	320	320	160
B/Phuket/3073/2013	3	2013-11-21	E4/E2	2560	160	160	10	<	160	160	80	20	160	160
B/Hong Kong/3417/2014	3	2014-06-04	E4/E1	640	80	40	<	<	40	40	20	10	40	160
TEST VIRUSES														
B/Belgium/2015G0771/2015	3	2015-11-18	SIAT1/MDCK1	1280	80	80	20	40	40	80	40	80	80	160
B/Belgium/2015G0775 /2015	3	2015-11-20	SIAT1/MDCK1	1280	80	40	20	20	40	40	20	40	80	160
B/Norway/2760/2015	3	2015-11-23	MDCK1	2560	80	80	40	<	80	80	<	80	80	160
B/Lisboa/151/2015	in process	2015-12-17	SIAT1/MDCK1	5120	80	160	160	160	160	160	<	320	320	160
B/Iceland/3/2016	3	2016-01-11	MDCK0/MDCK1	2560	80	80	40	40	160	160	40	160	160	160

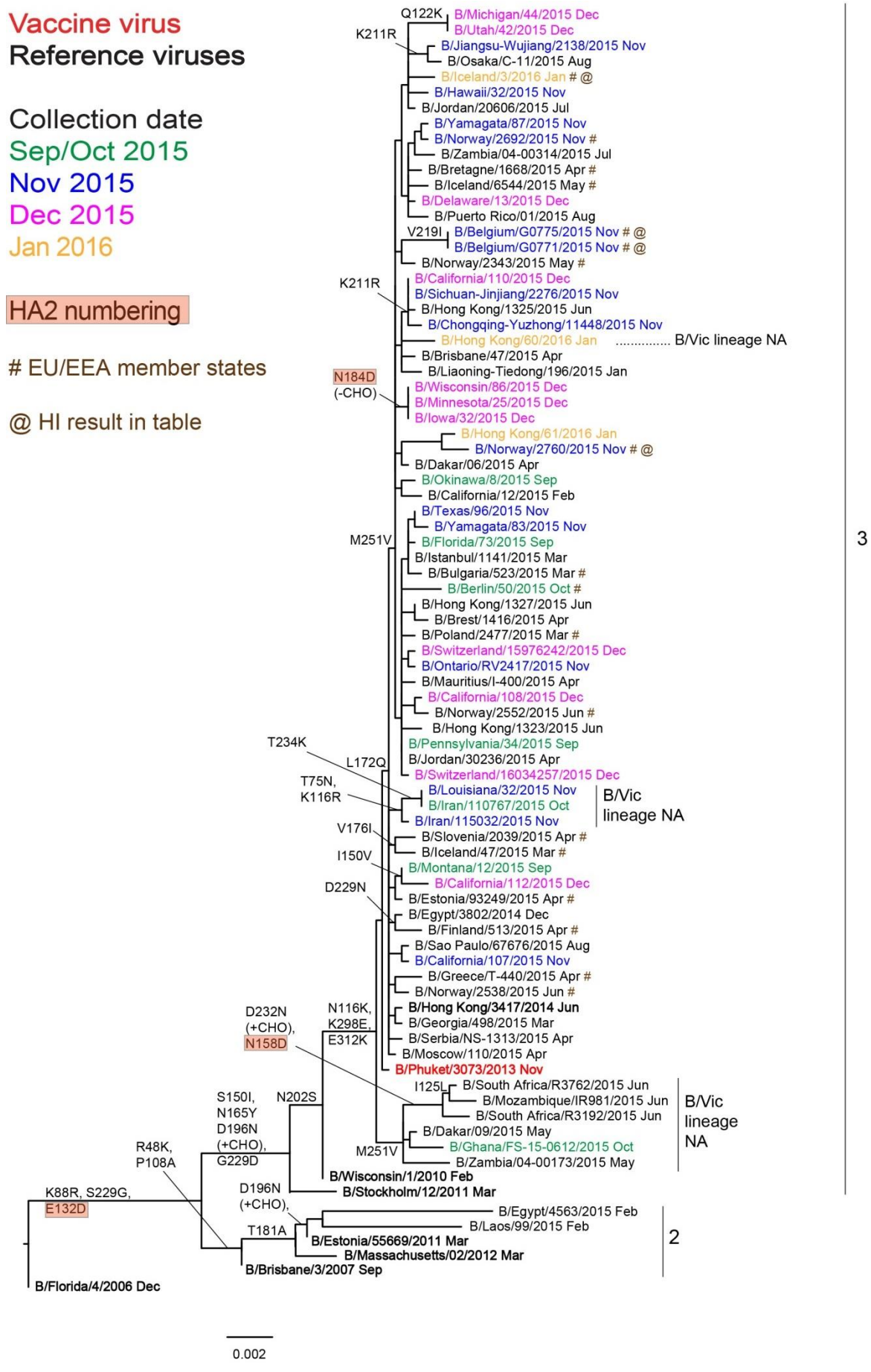
Vaccine NH 2015-16 SH 2016[#]

* 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-absorbed 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 period covering weeks 40/2015-07/2016, 2576 viruses have been characterised genetically: 1952 A(H1N1)pdm09 clade 6B represented by A/South Africa/3626/2013 (6B.1 and 6B.2 subclade designations were not available as reporting categories at the start of the 2014–2015 influenza season); A(H3N2) 195 subclade 3C.2a represented by A/Hong Kong/4801/2014, 87 subclade 3C.3a represented by A/Switzerland/9715293/2013 and six subclade 3C.3 represented by A/Samara/73/2013; 273 B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008; and 63 B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013.

Antiviral susceptibility

For weeks 40/2015–07/2016 of the 2015–2016 influenza season, countries reported on the antiviral susceptibility of 69 A(H3N2) viruses, 803 A(H1N1)pdm09 viruses and 93 influenza type B viruses from sentinel and non-sentinel sources. All but six showed no molecular or phenotypic evidence of reduced inhibition (RI) by neuraminidase inhibitors. Five A(H1N1)pdm09 viruses carried NA H275Y amino acid substitution associated with highly reduced inhibition (HRI) by oseltamivir and one A(H3N2) virus showed RI by oseltamivir associated with NA-E119V amino acid substitution.

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 312 viruses at the WIC: 193 A(H1N1)pdm09, 55 A(H3N2), 54 B/Victoria-lineage and 10 B/Yamagata-lineage viruses. All showed normal inhibition (NI) by these neuraminidase inhibitors.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [4] reported that the China Health and Family Planning Commission notified the WHO of three cases of human infection with influenza A(H7N9). The cases were confirmed by laboratory testing on 29 March 2013 by the Chinese CDC. A description of the characteristics of H7N9 viruses can be found on the WHO website [5]. Increased numbers of cases were reported over the course of the 2013–14, 2014–15 and 2015–16 seasons and cases have been reported recently [6]. A revised Rapid Risk Assessment [7] for these A(H7N9) viruses was carried out by ECDC and posted on 2 February 2015. WHO posted a summary of human infection on 31 January 2014 [8], updated on 20 January 2016 [9] with 10 new cases since 14 December 2015, and conducted a risk assessment on 23 February 2015 [10]. In light of the assessment, WHO advised that countries continue to strengthen influenza surveillance. WHO last summarised the numbers of cases of human infection related to their geographic location on 14 July 2014 [11] and has provided subsequent situation updates, with the latest being on 17 December 2015 [6].

Influenza A(H5N1) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 20 January 2016 [9]. Since the last WHO Influenza update on 14 December 2015, two new laboratory-confirmed human cases of avian influenza A(H5N1) virus infection were reported to WHO: one each by Bangladesh and China, with both individuals having been exposed to poultry. Over the same time period China reported five human cases of A(H5N6) infection. ECDC published an updated rapid risk assessment on the situation in Egypt on 13 March 2015 [12] and an epidemiological update 10 April 2015 [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, the Francis Crick Institute, Mill Hill Laboratory (formerly the MRC National Institute for Medical Research) and used at the WHO Vaccine Composition Meetings held at WHO Geneva 23–25 February 2015, and in Memphis, USA, 21–23 September 2015 can be found, respectively at:

https://www.crick.ac.uk/media/221813/nimr-report-feb2015-web.pdf and
https://www.crick.ac.uk/media/273950/crick_sep2015_vcm_report_to_post.pdf

A report for the WHO Vaccine Composition Meetings held at WHO Geneva 22–24 February 2016 will be made available shortly.

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 (#) as are those viruses for which data is presented in the HI tables (@). 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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