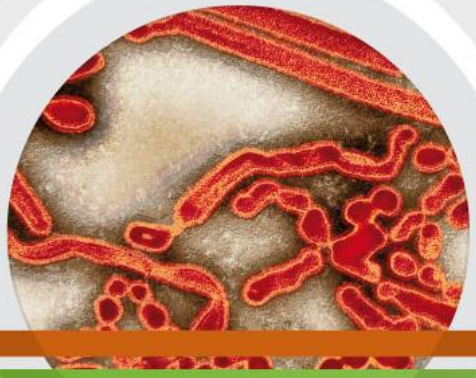


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, April 2016

Summary

From week 40/2015, the start of weekly reporting on influenza activity in the WHO European Region, to week 17/2016 over 160 000 influenza detections across the Region have been reported. Influenza type A viruses have prevailed over type B but, unlike the situation in the 2014–15 season, A(H1N1)pdm09 viruses greatly outnumbered A(H3N2), and the proportion of B/Victoria-lineage detections has risen substantially, representing ~92% of those assigned to a lineage.

To date, 25 EU/EEA countries have shared 600 influenza-positive specimens with the Francis Crick Institute, London, for detailed characterisation: one additional country and 128 specimens since the March 2016 report. Since the latter report, 70 viruses have been characterised antigenically and genetic analyses are ongoing.

Of 45 A(H1N1)pdm09 viruses characterised antigenically, 44 were similar to the vaccine virus A/California/7/2009. Worldwide new genetic subclusters 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 214 viruses characterised genetically for the 2015–2016 season, 25 (12%) were clade 6B, 182 (85%) were subclade 6B.1, and seven (3%) were subclade 6B.2.

The four 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. 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 65 A(H3N2) viruses characterised genetically for the 2015–2016 season: one (1%) was clade 3C.3, 40 (62%) were subclade 3C.2a and 24 (37%) were subclade 3C.3a.

The 15 B/Victoria-lineage viruses were antigenically similar to tissue culture-propagated surrogates of B/Brisbane/60/2008. All 63 viruses characterised genetically for the 2015–2016 season fell in genetic clade 1A, as do recently collected viruses worldwide.

Six B/Yamagata viruses have been characterised since the previous report; all 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 in the 2016 southern hemisphere and 2016–17 northern hemisphere seasons. All 10 viruses characterised genetically for the 2015–2016 season fell in genetic clade 3.

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).

Suggested citation: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, April 2016. Stockholm: ECDC; 2016.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy for the first 31 weeks (weeks 40/2015–17/2016) of reporting for the 2015–16 season. A total of over 160 000 detections had been made with type A viruses prevailing over type B at a ratio of 2.5:1; this compares to a ratio of 5.8:1 to week 7/2016 indicating a surge in influenza type B circulation over the last 10 weeks. So far, of the type A viruses subtyped (n = 80 261) and the type B viruses ascribed to lineage (n = 8 296), A(H1N1)pdm09 have prevailed over A(H3N2) and B/Victoria over B/Yamagata by ratios of 11.2:1 and 11.7:1, respectively.

Since the start of weekly reporting for the 2015–16 influenza season (week 40/2015), 46 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC), from 25 countries in the EU/EEA (Table 2). Of the 600 specimens received, a mix of clinical samples and virus isolates, the majority (80.3%) were type A viruses, and A(H1N1)pdm09 outnumbered A(H3N2) at a ratio of 5.1:1. Of the 118 type B specimens received (19.7% of the specimens), 97 were B/Victoria-lineage and 17 B/Yamagata-lineage. A number of specimens are still in the process of being characterised. The antigenic and genetic properties of influenza virus isolates characterised since the March 2016 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 40/2015–17/2016)

	Cumulative number of detections			Totals*	
Virus type/subtype	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**12909**	**102796**	**115705**	**71.5**	**2.5:1**
A(H1N1)pdm09	10820	62901	73721	91.8	11.2:1
A(H3N2)	1515	5025	6540	8.2	
A not subtyped	574	34870	35444		
Influenza B	**8917**	**37223**	**46140**	**28.5**	
Victoria lineage	3829	3809	7638	92.1	11.7:1
Yamagata lineage	110	548	658	7.9	
Lineage not ascribed	4978	32866	37844		
Total detections (total tested)	**21 826 (56 601)**	**140 019 (630 465)**	**161 845 (687 066)**		

*** 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, March 2016. Stockholm: ECDC; 2016. Available from: http://ecdc.europa.eu/en/publications/Publications/influenza-virus-characterisation-march-2016.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* / 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]
2015														
SEPTEMBER														
Iceland	1			1	1									
Poland	1					1	0	0						
Spain	1			1	1									
Sweden	1			1	1									
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	1								1	1
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	1									
Sweden	1					1	0	1						
United Kingdom	8			7	7						1	1		
NOVEMBER														
Austria	9			5	5	4	4	0						
Belgium	11			2	1	1	0	1			6	6	2	2
Denmark	1			1	1									
Estonia	3			3	0									
Finland	4			2	2	2	1	1						
France	5			1	1	1	1	0			3	3		
Germany	14			11	11	2	0	2			1	1		
Italy	2					1	1	0			1	1		
Netherlands	7			5	5						2	2		
Norway	11			7	6	1	1	0			1	1	2	2
Poland	1	1	0											
Portugal	8			8	7									
Slovenia	3					2	0	2	1	0				
Spain	5	2	0	2	1	1	1	0						
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	3		
Finland	8			7	6	1	1	0						
France	24			7	7	2	2	0			15	15		
Germany	21			17	17	3	3	0			1	1		
Greece	6			5	3	1	0	1						
Iceland	3			1	1	1	0	1			1	1		
Ireland	4			2	2	1	0	1			1	1		
Italy	8			3	3	5	2	3						
Latvia	4			3	3						1	1		
Netherlands	5			5	5									
Norway	5			3	3	2	1	1						
Poland	12	10	0	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														
Bulgaria	18			18	in process									
Cyprus	15			9	5	1	1	0			5	3		
Czech Republic	3			3	3									
Estonia	3			2	0						1	1		
Germany	26			11	11	5	5	0			8	8	2	2
Greece	27			27	17									
Hungary	7			4	4						3	3		
Iceland	6			5	5								1	1
Ireland	10			9	9						1	1		
Italy	1			1	1									
Latvia	8			6	6						2	2		
Netherlands	2			2	2									
Portugal	6			6	6									
Romania	8			7	7	1	0	1						
Slovenia	8			3	3	3	0	3	2	0				
Spain	19			16	15	1	0	1			2	2		
FEBRUARY														
Bulgaria	47			35	in process	1	0	1			11	in process		
Cyprus	9			8	8						1	1		
Germany	13			6	6	2	2	0					5	5
Greece	4			4	2									
Latvia	2			2	2									
Netherlands	1			1	1									
Romania	6			3	in process	2	in process				1	in process		
Spain	17			15	14						2	2		
MARCH														
Bulgaria	16			6	6	2	0	2			8	8		
Germany	9					1	0	1			7	7	1	1
Romania	9			6	in process	1	in process				1	in process	1	in process
	600	14	0	392	290	76	40	30	4	0	97	80	17	16
					65.3%		12.7%					16.2%		2.8%
25 Countries					80.3%							19.7%		

* 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 March 2016 report are shown in Tables 3-1 to 3-3. Of the 45 A(H1N1)pdm09 viruses from EU/EEA countries that were antigenically characterised 44 were 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 only 6/45 (13%) test viruses at a titre within fourfold of the titre for the homologous virus. In addition, antiserum raised against A/Lviv/N6/2009 showed eightfold reduced titres with two of the test viruses, compared to the homologous titre. Reference viruses carrying HA1 G155E amino acid substitutions, A/Bayern/69/2009 and A/Lviv/N6/2009, showed reduced recognition by the antisera raised against A/California/7/2009 and reference viruses in genetic clades 4, 5, 6, 7 and subclades 6A, 6B, 6B.1 and 6B.2.

While sequencing is ongoing for the majority of test viruses indicated in Tables 3-1 to 3-3, the seven viruses from Latvia characterised genetically all fell in subclade 6B.1 (Table 3-1). 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).

[2] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2014. Stockholm: ECDC; 2014. Available from: http://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												
				A/Cal	A/Bayern	A/Lviv	A/Chch	A/Astrak	A/St. P	A/St. P	A/HK	A/Sth Afr	A/Slov	A/Israel		
				7/09	69/09	N6/09	16/10	1/11	27/11	100/11	5659/12	3626/13	2903/15	Q-504/15		
	Passage history			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	Egg	Egg	MDCK		
	Ferret number			F06/16[-1]	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]	F08/16[-2]		
	Genetic group						4	5	6	7	6A	6B	6B.1	6B.2		
REFERENCE VIRUSES																
A/California/7/2009	clone 38-32	2009-04-09	E3/E2	1280	640	640	320	1280	640	2560	1280	640	1280	1280		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	80	640	320	160	80	80	80	80	80	80	40	G155E	
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	160	1280	1280	320	160	160	160	320	160	320	160	G155E>G, D222G	
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	2560	1280	2560	1280		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK6	1280	640	320	640	1280	640	2560	1280	640	1280	1280		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	2560	2560	1280	2560	2560		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	640	640	640	1280	640	2560	2560	1280	2560	1280		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	160	640	320	640	640	640	640	320		
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	1280	640	640	640	1280	640	2560	1280	1280	1280	1280		
A/Slovenia/2903/2015	clone 37 6B.1	2015-10-26	E4/E1	1280	640	640	640	1280	640	2560	2560	1280	2560	1280		
A/Israel/Q-504/2015	6B.2	2015-12-15	C1/MDCK2	1280	640	640	640	1280	1280	2560	2560	1280	2560	2560		
TEST VIRUSES																
A/Latvia/01-006305/2016	6B.1	2016-01-04	C1/MDCK1	640	320	320	320	640	320	1280	640	640	1280	640		
A/Latvia/01-019811/2016		2016-01-10	Cx/MDCK1	640	320	160	320	640	320	640	640	640	1280	640		
A/Latvia/01-069507/2016	6B.1	2016-01-18	C1/MDCK1	160	320	320	160	320	160	640	320	320	640	640		
A/Latvia/01-045064/2016	6B.1	2016-01-19	C2/MDCK1	640	640	320	320	640	640	1280	1280	640	1280	1280		
A/Latvia/01-049333/2016	6B.1	2016-01-21	C2/MDCK1	640	640	320	320	640	320	1280	1280	640	1280	1280		
A/Latvia/01-074070/2016	6B.1	2016-01-30	C1/MDCK1	640	640	320	320	640	320	1280	1280	640	1280	1280		
A/Latvia/03-011553/2016	6B.1	2016-02-29	Cx/MDCK1	640	320	160	320	640	320	1280	640	640	1280	640		
A/Latvia/02-072980/2016	6B.1	2016-02-29	Cx/MDCK1	1280	1280	640	640	1280	640	2560	1280	1280	2560	1280		
				Vaccine												

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

Table 3-2. 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	A/Israel		
				7/09	69/09	N6/09	16/10	1/11	27/11	100/11	5659/12	3626/13	2903/15	Q-504/15	G155E	
				Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	Egg	Egg	MDCK	G155E>G, D222G	
				F06/16[-1]	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]	F08/16[-2]		
Passage history							4	5	6	7	6A	6B	6B.1	6B.2		
Ferret number																
Genetic group																
REFERENCE VIRUSES																
A/California/7/2009	clone 38-32	2009-04-09	E3/E2	1280	640	640	640	1280	640	2560	2560	1280	2560	1280		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	40	640	320	80	80	40	80	80	80	80	80		
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	160	1280	1280	320	160	160	160	320	160	320	160		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	5120	2560	640	2560	2560	1280	2560	2560		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	1280	640	640	1280	640	2560	2560	1280	1280	2560		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E4	1280	1280	640	640	1280	640	2560	2560	1280	2560	1280		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E4	1280	640	640	640	1280	640	2560	1280	1280	2560	1280		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	640	320	160	320	640	320	1280	1280	640	1280	640		
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	640	1280	640	640	1280	640	1280	1280	1280	1280	1280		
A/Slovenia/2903/2015	clone 37 6B.1	2015-10-26	E4/E1	1280	640	640	640	1280	640	1280	2560	1280	2560	1280		
A/Israel/Q-504/2015	6B.2	2015-12-15	C1/MDCK2	1280	640	640	640	1280	1280	640	2560	1280	2560	2560		
TEST VIRUSES																
A/Spain/8740/2016		2016-01-25	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Spain/9134/2016		2016-01-26	MDCK1	1280	640	640	640	1280	640	2560	1280	1280	2560	2560		
A/Spain/9333/2016		2016-01-26	MDCK1	640	640	320	640	640	640	1280	1280	1280	1280	1280		
A/Cyprus/F66/2016		2016-01-26	MDCK1	1280	1280	640	640	1280	640	2560	2560	1280	2560	2560		
A/Spain/9779/2016		2016-01-27	MDCK1	1280	640	640	640	1280	640	2560	1280	1280	2560	1280		
A/Cyprus/F75/2016		2016-01-27	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Spain/10181/2016		2016-01-28	MDCK1	640	640	320	640	640	320	1280	1280	640	1280	1280		
A/Spain/12301/2016		2016-01-29	MDCK1	1280	640	320	640	1280	640	1280	1280	1280	2560	1280		
A/Cyprus/F116/2016		2016-02-01	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Spain/12109/2016		2016-02-03	MDCK1	640	640	320	320	640	320	1280	1280	1280	2560	1280		
A/Spain/12112/2016		2016-02-03	MDCK1	1280	640	640	640	1280	640	2560	2560	1280	2560	2560		
A/Spain/12113/2016		2016-02-03	MDCK1	1280	640	640	640	1280	640	2560	2560	1280	2560	2560		
A/Spain/12293/2016		2016-02-03	MDCK1	1280	640	320	640	640	640	1280	1280	640	1280	1280		
A/Cyprus/F142/2016		2016-02-03	MDCK1	2560	640	640	640	1280	640	2560	2560	1280	2560	2560		
A/Cyprus/F138/2016		2016-02-03	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	1280	1280		
A/Cyprus/F147/2016		2016-02-04	MDCK1	1280	640	320	640	640	640	1280	1280	1280	1280	1280		
A/Niedersachsen/6/2016		2016-02-04	C2/MDCK1	2560	1280	640	1280	2560	1280	2560	2560	1280	2560	2560		
A/Cyprus/F152/2016		2016-02-05	MDCK1	1280	640	320	640	1280	640	1280	1280	1280	1280	1280		
A/Cyprus/F179/2016		2016-02-07	MDCK1	640	640	320	640	640	640	1280	1280	640	1280	1280		
A/Cyprus/F176/2016		2016-02-07	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	2560		
A/Sachsen/20/2016		2016-02-08	C2/MDCK1	1280	640	320	320	640	640	1280	1280	1280	2560	1280		
A/Hessen/6/2016		2016-02-10	C2/MDCK1	1280	640	640	640	1280	640	2560	1280	1280	2560	2560		
A/Baden-Wurttemberg/18/2016		2016-02-10	C1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Cyprus/F220/2016		2016-02-12	MDCK1	640	640	320	640	1280	640	1280	1280	640	1280	1280		
A/Thuringen/17/2016		2016-02-22	C2/MDCK1	2560	640	640	1280	1280	1280	2560	2560	2560	2560	2560		
A/Serbia-NS/1583/2016		2016-02-23	MDCK1	1280	1280	640	640	1280	1280	2560	2560	1280	2560	2560		
A/Bayern/28/2016		2016-02-26	C1/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	2560		
				Vaccine												

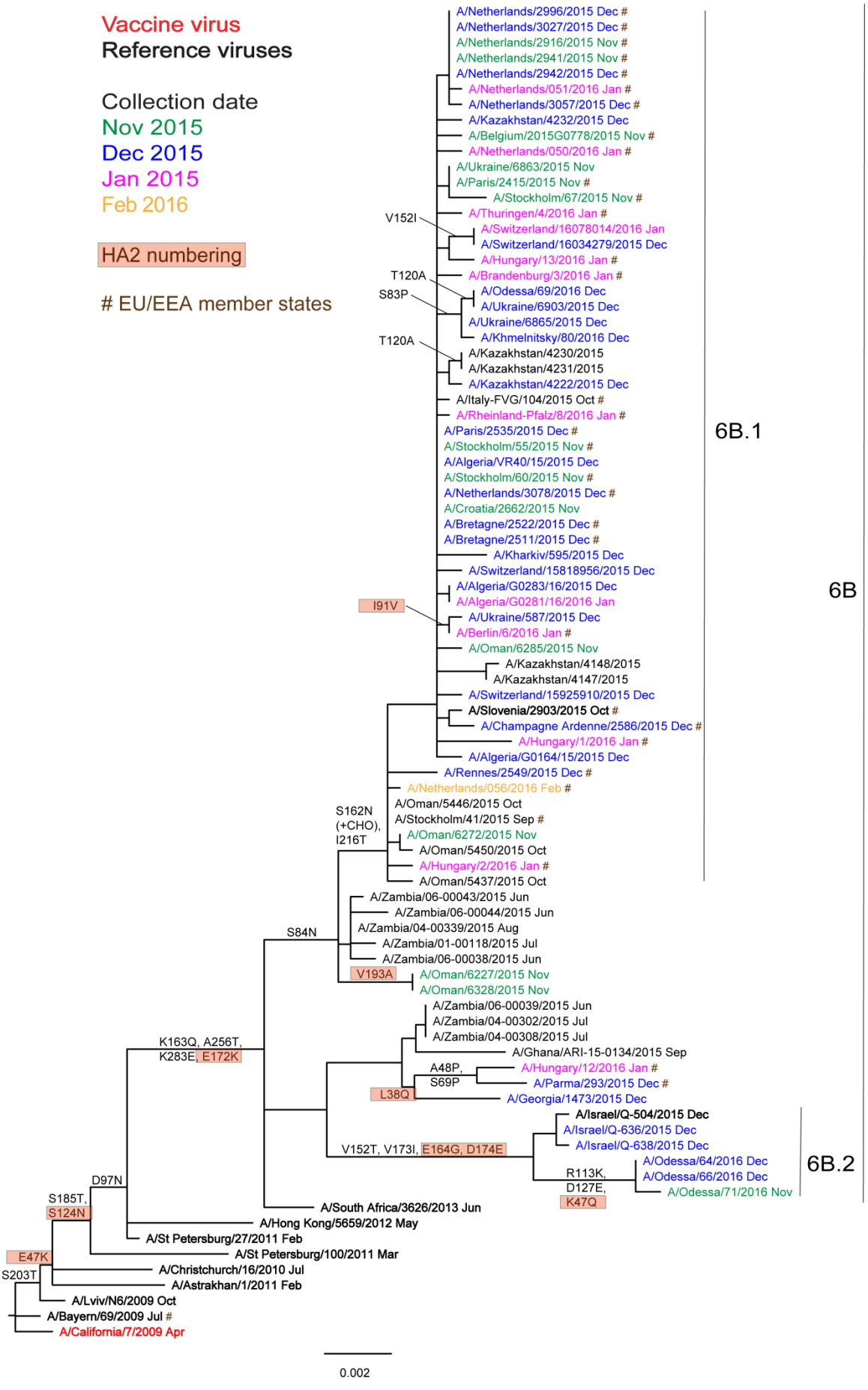
* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
[1] < = <40; [2] < = <80; ND = Not done

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												
				A/Cal	A/Bayern	A/Lviv	A/Chch	A/Astrak	A/St. P	A/St. P	A/HK	A/Sth Afr	A/Slov	A/Israel		
				7/09	69/09	N6/09	16/10	1/11	27/11	100/11	5659/12	3626/13	2903/15	Q-504/15		
				Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	Egg	Egg	MDCK		
	Passage history			F06/16[1]	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]	F08/16[2]		
	Ferret number						4	5	6	7	6A	6B	6B.1	6B.2		
	Genetic group														G155E	G155E>G, D222G
REFERENCE VIRUSES																
A/California/7/2009	clone 38-32	2009-04-09	E3/E2	640	640	640	320	1280	640	1280	1280	640	1280	640		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	40	320	320	80	40	40	80	40	40	40	40		
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	80	1280	640	160	80	80	80	160	80	160	160		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	640	2560	1280	1280	1280	1280		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	1280	640	640	1280	640	2560	1280	1280	1280	1280		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E4	640	640	320	320	1280	320	1280	1280	640	1280	640		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E4	640	640	320	320	640	320	1280	1280	640	1280	640		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	80	160	320	160	640	640	320	640	320		
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	640	640	320	320	640	320	640	640	640	640	640		
A/Slovenia/2903/2015	clone 37	6B.1	E4/E1	1280	640	640	640	1280	640	2560	1280	1280	2560	1280		
A/Israel/Q-504/2015		6B.2	C1/MDCK2	1280	640	320	640	1280	640	1280	1280	1280	1280	1280		
TEST VIRUSES																
A/Cyprus/F40/2016		2016-01-15	MDCK2	640	640	320	320	640	640	1280	1280	640	1280	1280		
A/Cyprus/F56/2016		2016-01-23	MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Spain/9785/2016		2016-01-26	MDCK3	1280	640	320	640	1280	640	2560	2560	1280	2560	1280		
A/Cyprus/F51/2016		2016-01-26	MDCK1	640	640	320	320	640	320	1280	1280	640	1280	1280		
A/Spain/11403/2016		2016-02-02	MDCK2	640	640	320	320	640	320	1280	1280	640	1280	1280		
A/Spain/11878/2016		2016-02-04	MDCK2	640	320	320	320	640	320	1280	1280	640	1280	1280		
A/Bulgaria/857/2016		2016-03-14	SIAT2/MDCK1	640	320	320	320	640	320	1280	1280	640	1280	1280		
A/Bulgaria/855/2016		2016-03-14	SIAT2/MDCK1	640	320	160	320	640	320	1280	640	640	640	640		
A/Bulgaria/865/2016		2016-03-15	SIAT2/MDCK1	1280	640	320	640	1280	640	2560	1280	1280	2560	1280		
A/Bulgaria/897/2016		2016-03-21	SIAT1/MDCK1	1280	640	320	320	640	640	1280	1280	1280	1280	1280		
				Vaccine												

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
[1] < = <40; [2] < = <80; ND = Not Done

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 Table 4. Four test viruses, from Germany, retained sufficient HA titre to be analysed by HI assay, and of the three analysed genetically, two fell in subclade 3C.3a and one 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: Table 4). However, the antisera raised against A/Stockholm/6/2014 (3C.3a: tissue culture- and egg-propagated), tissue culture-propagated A/Hong Kong/5738/2014 (3C.2a), tissue culture-propagated A/Georgia/532/2015 and A/Hong Kong/4801/2014 (3C.2a: tissue culture- and egg-propagated), gave reactivity with all test viruses. The antiserum raised against egg-propagated A/Switzerland/9715293/2013 (3C.3a), the northern hemisphere 2015–16 vaccine component, reacted with test viruses at titres reduced at least eightfold compared with the homologous titre, while antiserum raised against 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, yielded titres reduced by four-to-eightfold compared to the homologous titre and gave absolute titres of 40 or greater.

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/Netherlands/525/2014

Based on results available at the time of the February 2015 vaccine composition meeting which showed cross-reactivity of antisera raised against subclade 3C.3a and 3C.2a viruses, but with 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 are 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

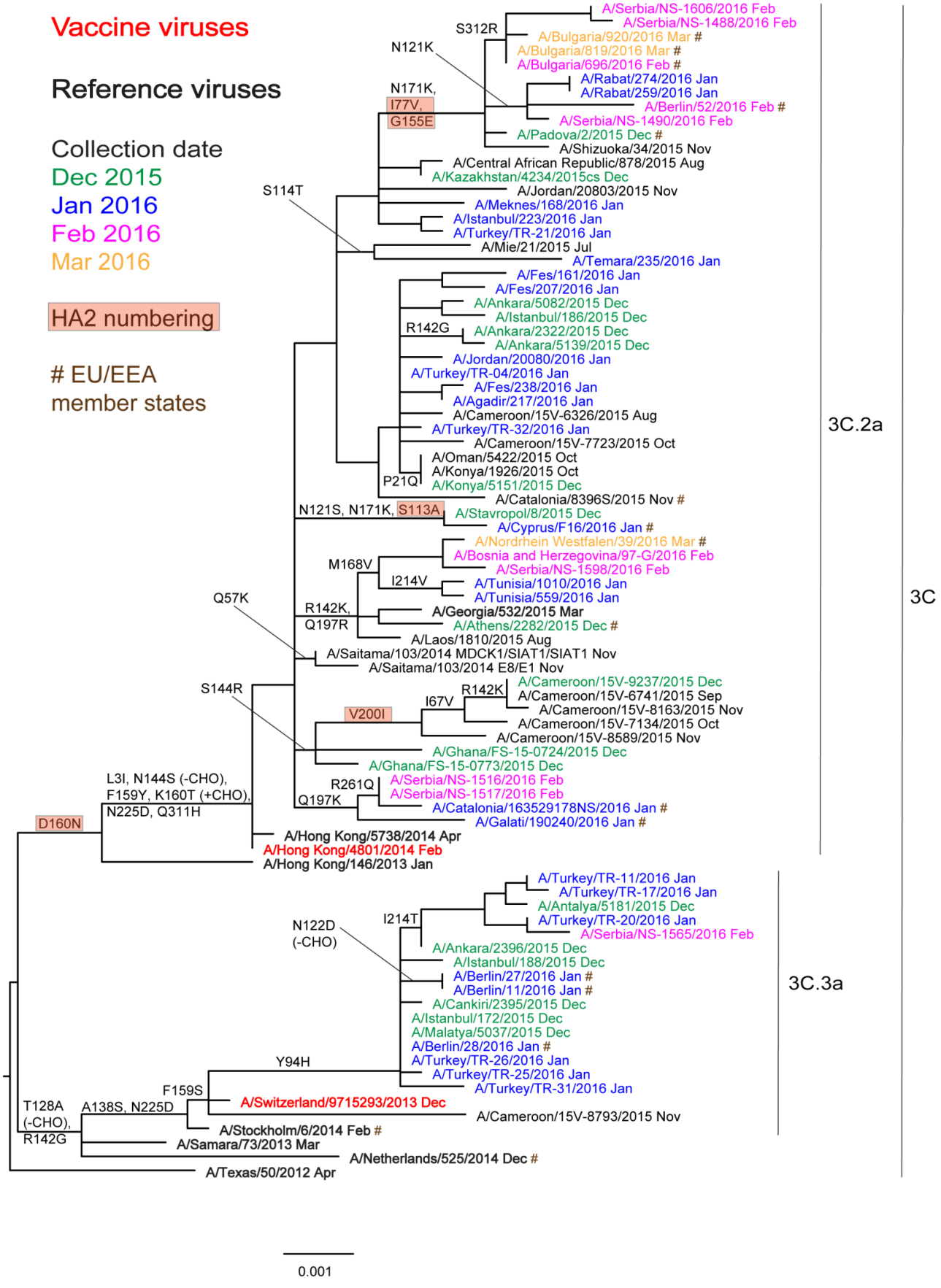
[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2014. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/ERLI-Net report November 2014.pdf

Table 4. 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	A/Samara/73/13	A/Stock/6/14	A/Stock/6/14	A/Switz/9715293/13	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
				Egg	SIAT	SIAT	Egg	SIAT	Egg	SIAT	Egg	MDCK	MDCK	Egg	SIAT
	Passage history			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}	F12/15^{-1}	F33/15^{-1}
	Ferret number			3C.1	3C.3	3C.3a	3C.3a	3C.3a	3C.3a	3C.3b	3C.2	3C.2a	3C.2a	3C.2a	3C.2a
	Genetic group														
REFERENCE VIRUSES															
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	2560	640	160	640	40	640	320	320	160	320	80	160
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT3	640	640	320	320	80	320	320	320	320	640	160	320
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	40	40	320	160	160	80	40	80	80	160	80	80
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1	320	80	160	320	80	640	80	80	160	320	40	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	<	<	160	80	80	40	<	40	80	80	40	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1	160	160	160	320	40	640	40	80	160	160	80	160
A/Netherlands/525/2014	3C.3b	2014-12-17	SIAT2/SIAT4	320	160	160	160	80	80	1280	160	80	160	80	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	1280	320	80	320	80	320	160	640	160	320	80	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	40	40	160	80	40	40	<	40	160	160	80	80
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK1/SIAT1	40	40	160	80	80	40	<	40	80	160	80	80
A/Hong Kong/4801/2014	3C.2a	2014-02-26	E6/E2	40	80	80	80	40	40	40	<	160	320	320	320
A/Georgia/532/2015	3C.2a	2015-03-09	SIAT1/SIAT3	80	40	160	80	80	40	<	80	160	160	80	320
TEST VIRUSES															
A/Berlin/27/2016	3C.3a	2016-01-23	C3/SIAT1	<	40	320	160	80	80	40	40	80	80	80	80
A/Berlin/28/2016	3C.3a	2016-01-28	C2/SIAT1	40	40	320	160	80	80	40	80	160	160	80	160
A/Baden-Wurttemberg/36/2016		2016-02-08	C2/SIAT1	<	<	320	160	40	40	<	40	80	80	80	80
A/Berlin/52/2016	3C.2a	2016-02-10	C3/SIAT1	<	<	160	40	<	<	<	40	80	80	40	40
								Vaccine NH 2015-16						Vaccine SH 2016 NH 2016-17	

* 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 118 influenza type B viruses of which 114 were ascribed to a lineage: 97 B/Victoria-lineage and 17 B/Yamagata-lineage (Table 2).

Influenza B – Victoria lineage

Since the March 2016 report 15 viruses of this lineage from EU/EEA countries have been characterised antigenically. HI results are shown in Table 5; while genetic characterisation is ongoing, it is anticipated that test viruses will carry genes of clade 1A, as observed throughout the previous season and this season to date.

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 reference viruses propagated in eggs B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012. In contrast, all 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 B/Paris/1762/2009, B/Odessa/3886/2010 and B/Hong Kong/514/2009. Similar results were observed with antisera raised against recently circulating clade 1A viruses propagated in tissue culture: B/Iceland/56/2015, B/Ireland/3154/2015 and B/Nordrhein-Westfalen/1/2016.

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 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.

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 to include B/Brisbane/60/2008 in trivalent influenza vaccines for the southern hemisphere 2016 [2] and northern hemisphere 2016–2017 [3] influenza seasons and in the quadrivalent vaccines.

Influenza B – Yamagata lineage

HI results for six B/Yamagata-lineage test viruses analysed since the March 2016 report are shown in Table 6. While genetic characterisation is ongoing, it is anticipated that test viruses will carry genes of clade 3, as observed throughout the previous season and this season to date.

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 (Table 6).

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 fourfold of their respective homologous titres, as did that raised against egg-propagated B/Wisconsin/1/2010 (a previous vaccine virus). Antisera raised against egg-propagated B/Stockholm/12/2011 and tissue culture-propagated B/Phuket/3073/2013 showed fourfold reduced reactivity with greater numbers of the test viruses. The test viruses consistently showed fourfold or greater reductions in HI titres, compared to the homologous titre, with the antiserum raised against egg-propagated B/Massachusetts/02/2012, the clade 2 vaccine virus recommended for use in the 2014–15 northern hemisphere influenza season.

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 amino acid substitution. A few viruses, annotated in the phylogenetic tree (e.g. B/Italy/FVG-19/2015), are reassortants carrying NA genes normally associated with the B/Victoria-lineage.

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

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre											
					Post-infection ferret antisera											
		Passage history			B/Bris 60/08 Egg	B/Mal 2506/04 Egg	B/Bris 60/08 Egg	B/Paris 1762/09 MDCK	B/Malta 636714/11 Egg	B/Jhb 3964/12 Egg	B/For V2367/12 MDCK	B/Sth Aus 81/12 Egg	B/HK 514/09 MDCK	B/Odessa 3886/10 MDCK	B/Iceland 56/15 MDCK	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK
		Ferret number			Sh 630*1	F37/11*2	F22/12*2	F07/11*2	F29/13*2	F01/13*4	F04/13*4	F41/13*2	F09/13*2	F19/11*2	F14/16*2	F15/16*2	F16/16*2
		Genetic group			1A		1A	1A	1A	1A	1A	1A	1B	1B	1A	1A	1A
REFERENCE VIRUSES																	
B/Malaysia/2506/2004			2004-12-06	E3/E7	2560	320	20	<	80	160	40	160	40	<	<	<	<
B/Brisbane/60/2008	Sh = NIB-58	1A	2008-08-04	E4/E4	2560	40	160	40	320	320	160	640	80	40	80	40	40
B/Paris/1762/2009		1A	2009-02-09	C2/MDCK2	160	<	<	80	40	40	40	80	80	80	80	40	80
B/Malta/636714/2011		1A	2011-03-07	E4/E1	1280	40	80	40	320	320	160	640	80	20	80	40	40
B/Johannesburg/3964/2012		1A	2012-08-03	E1/E2	2560	160	320	80	640	640	640	1280	160	40	80	80	80
B/Formosa/V2367/2012		1A	2012-08-06	MDCK1/MDCK3	2560	40	80	40	160	160	160	320	80	20	80	40	40
B/South Australia/81/2012		1A	2012-11-28	E4/E2	1280	40	80	40	160	320	160	640	80	40	80	40	40
B/Hong Kong/514/2009		1B	2009-10-11	MDCK3	40	<	<	20	10	<	10	20	40	40	40	<	20
B/Odessa/3886/2010		1B	2010-03-19	C2/MDCK1	320	<	<	40	40	40	40	80	80	40	40	20	40
B/Iceland/56/2015		1A	2015-12-30	MDCK0/MDCK1	160	<	<	40	40	40	40	80	80	40	80	40	80
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK1	320	<	<	80	40	40	80	80	80	40	160	40	80
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK1	320	<	<	80	80	80	80	160	160	80	160	40	80
TEST VIRUSES																	
B/Cyprus/F82/2016			2016-01-29	MDCK2	160	<	<	80	40	40	40	80	80	40	40	80	80
B/Cyprus/F85/2016			2016-01-28	MDCK1	2560	40	<	40	80	160	80	320	80	20	20	40	40
B/Cyprus/F84/2016			2016-01-28	MDCK1	640	10	<	40	80	80	80	160	80	40	40	80	40
B/Cyprus/F174/2016			2016-02-05	MDCK2	320	<	<	80	40	40	40	80	80	40	40	80	80
B/Sachsen/26/2016			2016-03-07	C1/MDCK1	40	<	<	20	10	<	20	20	40	10	<	40	40
B/Mecklenburg-Vorpommern/4/2016			2016-03-07	C1/MDCK1	160	<	<	40	40	20	40	80	80	40	40	80	40
B/Bayern/14/2016			2016-03-09	C1/MDCK1	160	<	<	40	40	40	40	80	80	40	40	80	80
B/Baden-Wurttemberg/56/2016			2016-03-10	C1/MDCK1	160	<	<	40	40	20	40	80	80	40	40	80	40
B/Bulgaria/849/2016			2016-03-12	SIAT2/SIAT1	160	<	<	ND	40	40	40	80	80	ND	40	80	80
B/Berlin/54/2016			2016-03-14	C1/MDCK1	320	<	<	80	40	40	40	80	80	40	40	80	80
B/Hessen/16/2016			2016-03-14	C1/MDCK1	320	<	<	80	40	40	40	80	80	40	40	80	80
B/Thuringen/62/2016			2016-03-14	C1/MDCK1	80	<	<	20	10	<	40	10	40	40	20	40	20
B/Bulgaria/881/2016			2016-03-16	SIAT2/SIAT1	160	<	<	ND	20	20	40	80	80	ND	40	80	80
B/Bulgaria/905/2016			2016-03-18	SIAT1/SIAT1	160	<	<	ND	20	20	40	40	40	ND	20	40	40
B/Bulgaria/896/2016			2016-03-21	SIAT1/SIAT1	320	<	<	ND	40	20	40	80	80	ND	40	80	80
							Vaccine NH 2015-16# SH 2016 NH 2016-17										

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; ND = Not Done

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

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

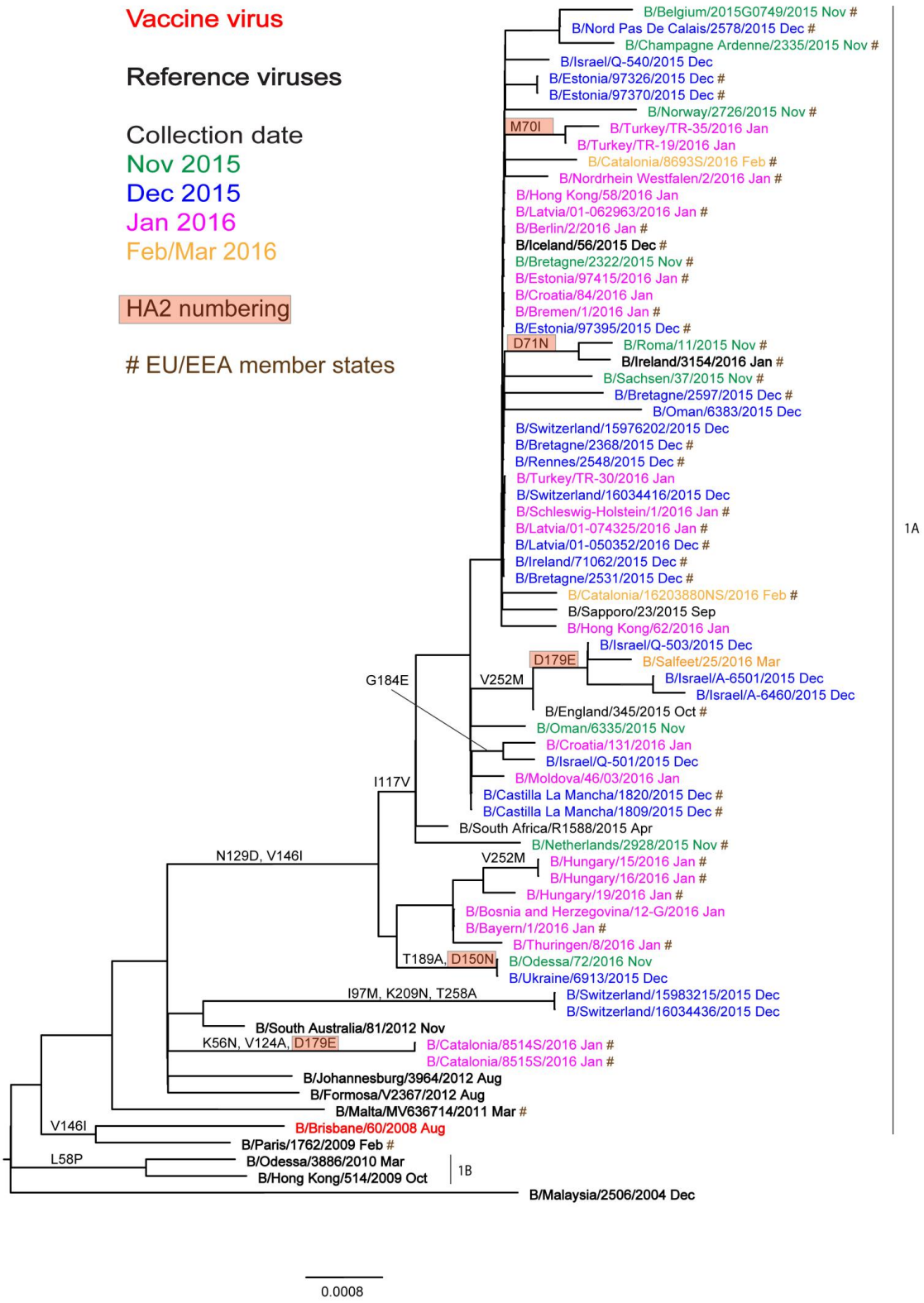


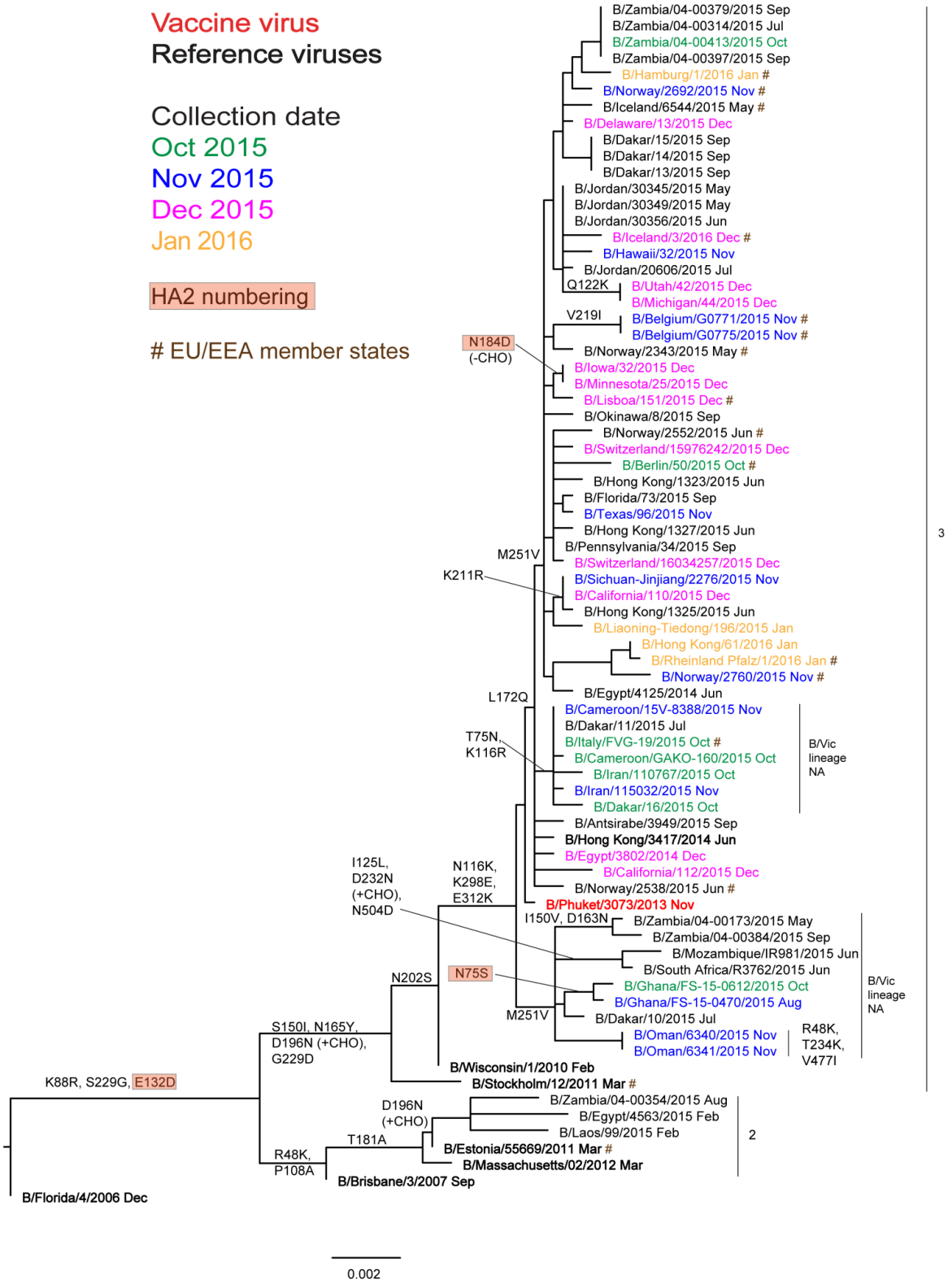
Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses		Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
	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]	F1/10[*1]	F38/14[*2]	F32/12[*2]	F05/15[*1]	F42/14[*2]	F10/13[*2]	F06/15[*1]	F35/14[*2]	F36/14[*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	640	320	320	40	80	640	80	80	20	80	80
B/Brisbane/3/2007	2	2007-09-03	E2/E3	640	160	320	40	40	320	40	80	10	80	80
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	40	40	80	80	40	40	20	20	40	80
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	640	320	320	160	320	320	160	80	80	160	320
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	640	320	320	40	80	640	80	80	10	80	80
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	80	80	10	10	160	160	80	20	80	80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	80	80	10	<	80	40	80	20	40	80
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK2	2560	80	160	80	160	160	160	80	320	160	160
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	320	20	10	320	320	160	40	160	160
B/Hong Kong/3417/2014	3	2014-06-04	E4/E3	640	40	40	<	<	40	40	20	10	20	80
TEST VIRUSES														
B/Rheinland-Pfalz/4/2016		2016-02-15	C2/MDCK1	1280	80	40	40	40	40	80	20	80	80	160
B/Berlin/16/2016		2016-02-22	C2/MDCK1	1280	80	40	40	20	80	80	20	80	80	80
B/Nordrhein-Westfalen/26/2016		2016-02-22	C1/MDCK1	1280	80	40	20	20	40	40	20	80	40	160
B/Berlin/25/2016		2016-02-22	C1/MDCK1	1280	80	40	20	20	40	40	20	80	40	160
B/Bayern/5/2016		2016-02-29	C2/MDCK1	1280	80	80	40	20	160	80	40	80	80	160
B/Brandenburg/17/2016		2016-03-08	C2/MDCK1	1280	80	80	40	40	80	80	40	160	80	160
													Vaccine NH 2015-16 SH2016[#] NH 2016-17[#]	

* 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

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



Summary of genetic data submitted to TESSy

For the period covering weeks 40/2015–17/2016, 5022 viruses have been characterised genetically: 3 480 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 2015–2016 influenza season); 381 A(H3N2) subclade 3C.2a represented by A/Hong Kong/4801/2014, 159 subclade 3C.3a represented by A/Switzerland/9715293/2013, six subclade 3C.3b represented by A/Stockholm/28/2014, and six subclade 3C.3 represented by A/Samara/73/2013; 864 B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008; and 126 B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013.

Antiviral susceptibility

For weeks 40/2015–17/2016 of the 2015–2016 influenza season, countries reported on the antiviral susceptibility of 2 240 A(H1N1)pdm09 viruses, 134 A(H3N2) viruses and 324 influenza type B viruses from sentinel and non-sentinel sources. All but 21 showed no molecular or phenotypic evidence of reduced inhibition (RI) by neuraminidase inhibitors (oseltamivir and zanamivir). Twenty 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 466 viruses at the WIC: 296 A(H1N1)pdm09, 66 A(H3N2), 88 B/Victoria-lineage and 16 B/Yamagata-lineage viruses. All but one A(H1N1)pdm09 virus showed normal inhibition (NI) by these neuraminidase inhibitors: A/Bayern/20151/2015 showed reduced inhibition (RI) by zanamivir and carried NA I117R amino acid substitution.

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 4 April 2016 [9] with 30 new cases since the report of 25 February 2016, 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 03 May 2016 [6].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 4 April 2016 [9]. Since the last WHO Influenza update on 25 February 2016, five laboratory-confirmed human cases of avian influenza A(H5) virus infection have been reported to WHO: four A(H5N1) cases by Egypt and one A(H5N6) case by China. 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]. On 2 December 2015, ECDC published a rapid risk assessment related to identification highly pathogenic H5 viruses in poultry in France [14].

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 and used at the WHO Vaccine Composition Meetings held in Memphis, USA 21-23 September 2015 and at WHO Geneva 22–24 February 2016 can be found, respectively, at:

https://www.crick.ac.uk/media/273950/crick_sep2015_vcm_report_to_post.pdf and
https://www.crick.ac.uk/media/286458/crick_feb2016_vcm_report_to_post.pdf

Note on the figures

The phylogenetic trees were constructed using RAxML, drawn using FigTree and annotated using Adobe Illustrator. The bars indicate the proportion of nucleotide changes between sequences. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the month of sample collection. Isolates from WHO NICs in EU/EEA countries are marked (#). Sequences for some viruses from non-EU/EEA countries were recovered from GISAID. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from GISAID's EpiFlu database which were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website), along with all laboratories who submitted sequences directly to the London WHO Collaborating Centre.

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