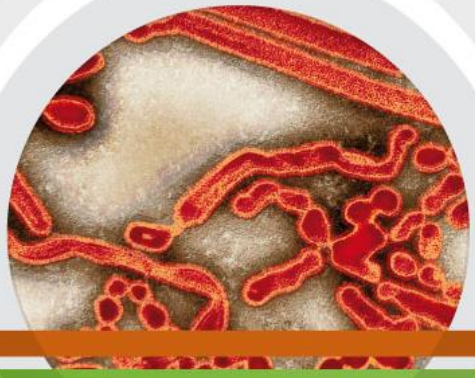


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, November 2015

Summary

For week 40/2015, the start of weekly reporting on influenza activity in the WHO European Region, to week 49/2015 only 1380 influenza detections across the Region have been reported. Though numbers of detections are low so far, 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 to represent ~50% of the type B detections.

To date, four EU/EEA countries have shared 47 influenza-positive specimens with the Francis Crick Institute, London, for detailed characterisation. So far, only 10 of these have been characterised antigenically, and genetic analyses are ongoing.

The six A(H1N1)pdm09 viruses characterised antigenically were similar to the vaccine virus A/California/07/2009. Worldwide a new sub-cluster of viruses defined by HA1 amino acid substitutions S162N and I216T in the 6B genetic group has emerged.

The three A(H3N2) test viruses characterised by haemagglutination inhibition (HI) assay, all falling in genetic subgroup 3C.2a, were poorly recognised (titres at least sixteenfold reduced compared with the homologous titre) 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 southern hemisphere 2016 influenza vaccines.

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

No B/Yamagata viruses were characterised, but worldwide recently collected viruses have fallen in genetic clade 3, represented by B/Phuket/3073/2013, the recommended vaccine virus for the northern hemisphere 2015–16 influenza season.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy for the first 10 weeks (weeks 40–49/2015) of reporting for the 2015–16 season. The percentage of sentinel specimens

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, November 2015. Stockholm: ECDC; 2015.

testing positive for influenza has not risen to 10% in any week. A total of 1380 detections had been made with type A viruses prevailing over type B at a ratio of 3.7:1. So far, of the type A viruses subtyped (n = 557) and the type B viruses ascribed to lineage (n = 44), A(H1N1)pdm09 have prevailed over A(H3N2) and B/Victoria over B/Yamagata by ratios of 3.8:1 and 1.2:1, respectively.

Since the start of weekly reporting for the 2015–16 influenza season (week 40/2015) only four shipments of specimens from countries in the EU/EEA (England, Germany, Norway and Slovenia) have been received at the Crick Worldwide Influenza Centre (WIC). Of the 47 specimens received, a mix of clinical samples and virus isolates, the majority (91.5%) were type A viruses, and A(H1N1)pdm09 outnumbered A(H3N2) at a ratio of approximately 3.8:1 (Table 2). Of the four type B specimens received (8.5% of the specimens), there were two each falling in B/Victoria- and B/Yamagata-lineages. The majority of specimens, those from Germany, Norway and Slovenia, are still in the process of being characterised. The antigenic and genetic properties of influenza virus isolates characterised since the September 2015 report[1] are presented and discussed in this report.

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

Table 1. Influenza virus detections in the WHO European Region since the start of reporting for the 2015–16 season (weeks 40–49/2015)

Virus type/subtype	Cumulative number of detections			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**90**	**999**	**1089**	**78.9**	**3.7:1**
A(H1N1)pdm09	50	384	434	79.3	3.8:1
A(H3N2)	18	105	123	20.7	
A not subtyped	22	510	532		
Influenza B	**52**	**239**	**291**	**21.1**	
Victoria lineage	9	15	24	54.5	1.2:1
Yamagata lineage	3	17	20	45.5	
Lineage not ascribed	40	207	247		
Total detections (total tested)	**142 (6543)**	**1238 (174024)**	**1380 (180567)**		

*** 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.**

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	in progress	2	in progress						
SEPTEMBER													
United Kingdom	3					3	3 0						
OCTOBER													
Germany	2			1	in progress							1	in progress
Norway	10			7	in progress	2	in progress			1	in progress		
Slovenia	3	1	in progress	2	in progress								
United Kingdom	7			6	6					1	1		
NOVEMBER													
Germany	6			6	in progress								
Norway	7			6	in progress							1	in progress
Slovenia	4			4	in progress								
DECEMBER													
Slovenia	2			2	in progress								
	47	1		35	6	7	3 0	0		2	1	2	0
					74.5%		14.9%				4.3%		4.3%
4 Countries					91.5%						8.5%		

* 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 September 2015 report are shown in Table 3. The six A(H1N1)pdm09 viruses from England 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 only 1/6 (17%) test viruses at a titre within fourfold of the titre for the homologous virus. All antisera raised against viruses falling outside of genetic group 1, the A/California/7/2009 group, recognised the egg-propagated vaccine virus at titres fourfold to sixteenfold reduced compared with the titres of the antisera with their homologous viruses. Fold reductions were greater for MDCK-isolated viruses from 2009 that carried amino acid substitution at HA1 position 155 (G155E).

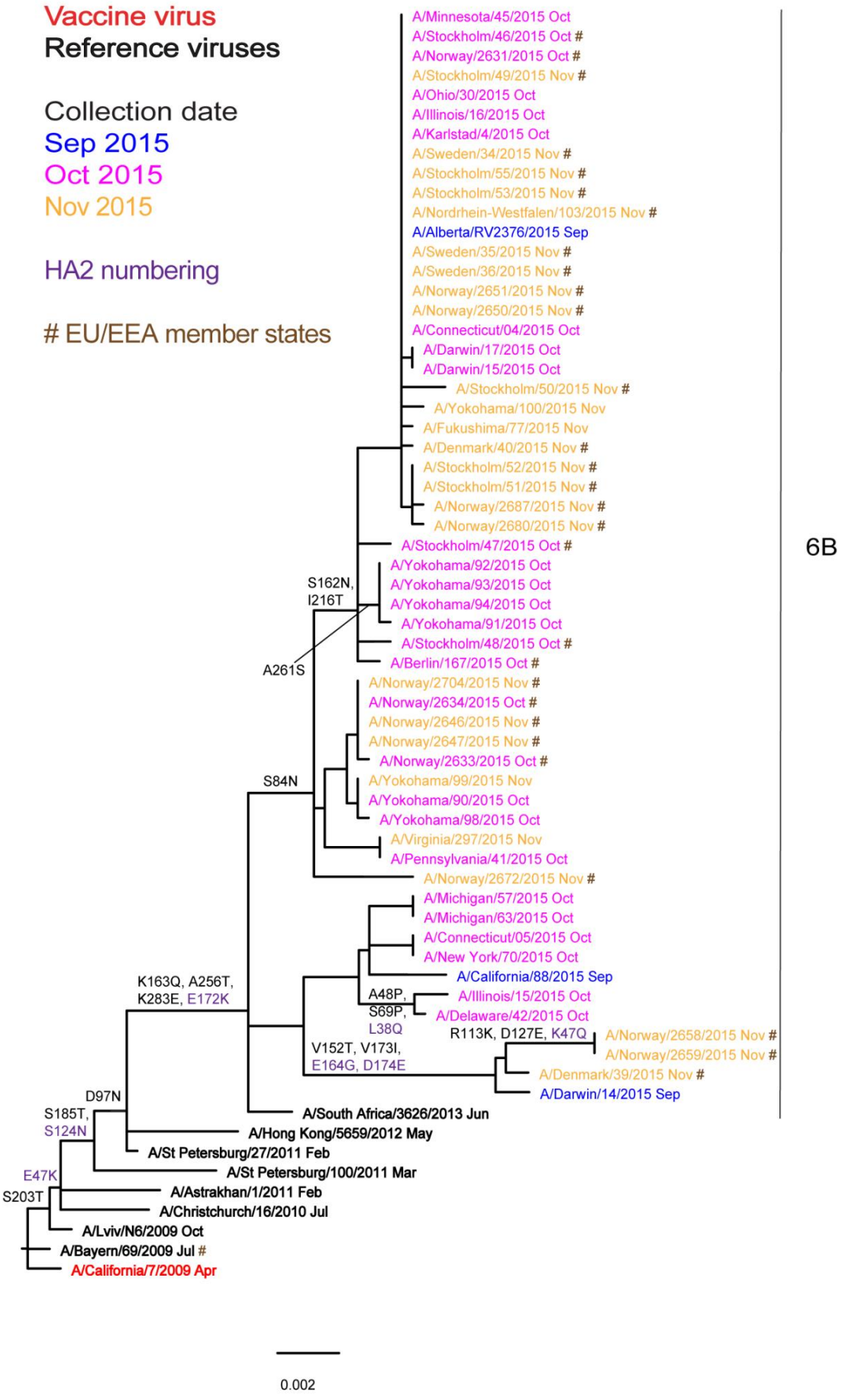
Test viruses from England were ascribed to genetic group 6B, based on HA sequences shared with the WIC by NIC England (Table 3). As genetic characterisation is ongoing at the WIC, a phylogenetic tree for full-length HA genes of A(H1N1)pdm09 viruses with collection dates since the beginning of week 40/2015 deposited in GISAID was constructed (Figure 1). Since 2009, the HA genes have evolved, and eight genetic groups have been designated. For over a year, viruses in genetic group 6 – represented by A/St Petersburg/27/2011 and carrying amino acid substitutions of **D97N**, **S185T** and **S203T** in **HA1** and **E47K** and **S124N** in **HA2** compared with A/California/7/2009 – have predominated worldwide, with a number of subgroups emerging. All EU/EEA viruses characterised since the September 2014 report[2] carry HA genes in genetic subgroup 6B, which is characterised by additional amino acid substitutions of **K163Q**, **A256T** and **K283E** in **HA1** and **E172K** in **HA2** compared with A/California/7/2009, e.g. A/South Africa/3626/2013. Notably, a new sub-cluster of viruses, defined by HA1 amino acid substitutions **S162N** and **I216T** in **HA1**, in the 6B genetic group has emerged worldwide and, based on HA sequences available to the WIC at the time of preparing this report, is present in Denmark, England, Germany, Norway and Sweden. The **S162N** substitution results in the formation of a new potential glycosylation site at residues 162–164 of HA1.

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

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre									
				Post infection ferret antisera									
				A/Cal 7/09 F01/15	A/Bayern 69/09 F09/15	A/Lviv N6/09 F14/13	A/Chch 16/10 F15/14 4	A/Astrak 1/11 F22/13 5	A/St. P 27/11 F26/14 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	A/Sth Afr 3626/13 F3/14 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	320	320	80	40	40	40	40	40	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	1280	160	80	80	80	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	640	640	640	640	1280	640	2560	2560	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	640	640	640	320	1280	640	2560	1280	640	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	640	640	1280	640	2560	1280	640	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK1	80	160	80	80	320	160	640	640	320	
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	320	320	640	320	640	320	640	640	640	
TEST VIRUSES													
A/England/336/2015	6B	2015-10-03	SIAT1/MDCK1	320	320	320	320	640	320	1280	1280	640	S162N (+CHO), I216T
A/England/341/2015	6B	2015-10-05	SIAT1/MDCK1	640	1280	640	640	1280	640	2560	2560	1280	
A/England/343/2015	6B	2015-10-05	MDCK1/MDCK1	320	640	320	320	640	640	1280	1280	1280	S162N (+CHO), I216T
A/England/350/2015	6B	2015-10-06	SIAT1/MDCK1	1280	320	320	320	640	320	1280	640	640	
A/England/353/2015	6B	2015-10-16	SIAT1/MDCK1	320	320	320	320	1280	640	2560	1280	1280	S162N (+CHO), I216T
A/England/351/2015	6B	2015-10-19	SIAT1/MDCK1	320	320	320	320	640	320	1280	1280	640	S162N (+CHO), I216T
				Vaccine									

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 any NA-mediated binding of A(H3N2) viruses to the RBCs, are shown in Table 4. The three test viruses from England retained sufficient HA titre to be analysed by HI assay and all fell in genetic subgroup 3C.2a, based on HA sequences shared by NIC England.

The three 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, in terms of absolute titres antisera raised against cell-propagated A/Samara/73/2013 (3C.3), A/Stockholm/6/2014 (3C.3a: cell- and egg-propagated), cell-propagated A/Hong Kong/5738/2014 (3C.2a) and the vaccine virus recommended for the southern hemisphere 2016 influenza season, egg-propagated A/Hong Kong/4801/2014 (3C.2a), gave consistent reactivity with all three test viruses. The antiserum raised against the northern hemisphere 2015–16 vaccine component, egg-propagated A/Switzerland/9715293/2013 (3C.3a), reacted with only one test virus at a titre of 40 (the cut-off for the HI assay). An additional antiserum raised against cell-propagated A/Hong Kong/4801/2014 (3C.2a) showed reactivity with only two of the test viruses.

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, available from GISAID, is shown in Figure 2. The HA genes fall within genetic group 3C. This group 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 have been antigenically similar. In 2014 three new genetic subgroups emerged, one in subdivision 3C.2, 3C.2a, and two in 3C.3, 3C.3a and 3C.3b (Figure 2). While viruses in genetic subgroups 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 subgroups compared with A/Texas/50/2012 are:

- (3C.2) N145S and V186G[5] 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, N145S and V186G 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.

Figure 2 shows that genetic subgroup 3C.2a viruses have dominated in recent months, and viruses from Denmark, England and Sweden have been characterised. Sequence of a 3C.3b genetic subgroup virus has also been reported (A/Norway/2605/2015).

Based on results available at the time of the February 2015 vaccine composition meeting – which showed cross-reactivity of antisera raised against genetic subgroup 3C.3a and 3C.2a viruses, but with issues of antigenic changes on egg-adaptation of genetic subgroup 3C.2a viruses at that time, and 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. After February 2015, 3C.2a viruses became prevalent, and a new genetic subgroup designated 3C.3b emerged, with these three subgroups being antigenically distinguishable. While ferret antisera raised against 3C.3a and 3C.2a viruses showed some cross-reactivity with viruses in all three genetic subgroups, antisera raised against 3C.3b

[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

[5] Note: The G186V substitution in HA1 occurred during adaptation of A/Texas/50/2012 to propagation in hens' eggs.

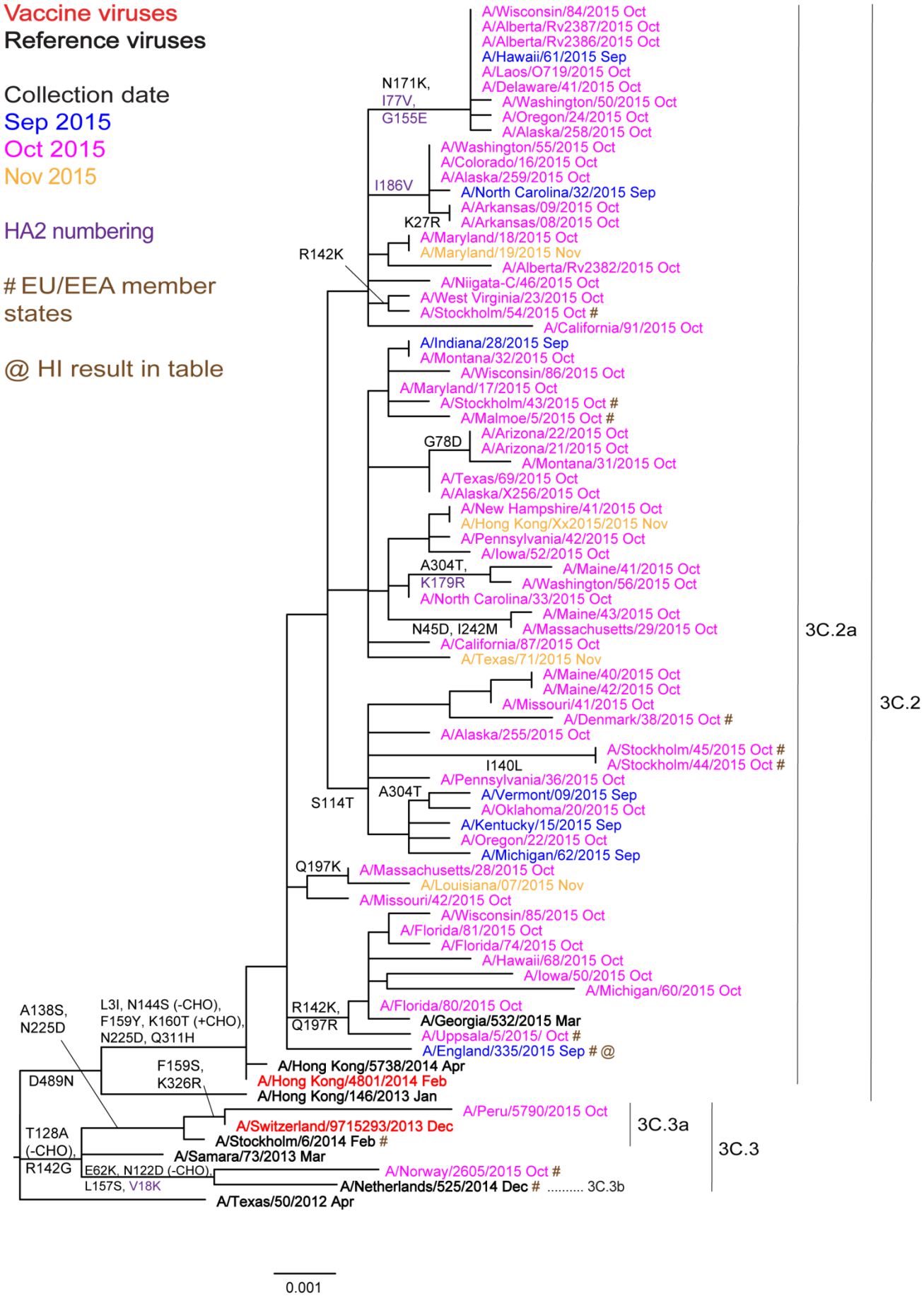
viruses were subgroup specific. Therefore, with the availability of new genetic subgroup 3C.2a vaccine candidates and the continued cross-reactivity of antisera raised against genetic subgroup 3C.3a and 3C.2a viruses, in September 2015 the World Health Organization recommendation for the A(H3N2) component of influenza vaccines for the southern hemisphere 2016 influenza season was for an A/Hong Kong/4801/2014-like (3C.2a) virus.

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

Viruses	Collection Date	Passage History	Haemagglutination inhibition titre[1]											
			Post-infection ferret antiserum											
			A/Texas 50/12 Egg F36/12	A/Samara 73/13 F35/15	A/HK 146/13 F10/15	A/Stock 6/14 T/C F14/14	A/Stock 6/14 Egg F20/14	A/Switz 9715293/13 T/C F18/15	A/Switz 9715293/13 Egg F32/14	A/HK 5738/14 T/C F30/14	A/Neth 525/14 F23/15	A/HK 4801/14 T/C F43/15	A/HK 4801/14 Egg F12/15
	Genetic group		3C.1	3C.3	3C.2	3C.3a	3C.3a isolate 2	3C.3a	3C.3a cl123	3C.2a	3c.3b	3C.2a	3C.2a
REFERENCE VIRUSES													
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	5120	640	320	160	640	40	640	80	320	320	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT3	2560	1280	320	640	640	80	640	320	320	640	320
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	2560	640	640	80	640	80	640	320	320	640	160
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	160	80	160	640	320	160	160	160	80	320	160
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1 isolate 2	640	80	40	160	320	80	640	160	80	320	40
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT4	160	40	80	320	320	80	160	160	40	160	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1 clone 123	640	160	80	160	320	80	640	160	40	160	80
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK3	160	40	80	320	160	80	80	160	40	320	160
A/Netherlands/525/2014	3C.3b	2014-12-17	SIAT2/SIAT2	640	160	80	320	320	80	160	160	1280	160	80
A/Hong Kong/4801/2014	3C.2a	2014-02-26	MDCK4/MDCK2/SIAT1	80	40	80	320	160	80	80	160	40	320	160
A/Hong Kong/4801/2014	3C.2a	2014-02-26	E6/E2 isolate 1	40	80	<	80	40	40	40	160	40	320	320
TEST VIRUSES														
A/England/333/2015	3C.2a	2015-09-04	MDCK2/SIAT1	<	40	<	40	40	<	<	40	<	80	40
A/England/334/2015	3C.2a	2015-09-06	MDCK2/SIAT1	40	80	40	80	80	40	40	80	<	160	80
A/England/335/2015	3C.2a	2015-09-29	SIAT1/SIAT1	<	40	<	80	80	<	<	40	<	<	40
										Vaccine NH 2015-16				Vaccine SH 2016

1. < = <40; ND= Not Done

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



Influenza B virus analyses

Only four influenza type B viruses have been received from EU/EEA countries, two each of the B/Victoria- and B/Yamagata-lineages (Table 1).

Influenza B – Victoria lineage

Since the September 2015 report only one virus of this lineage from an EU/EEA country has been characterised antigenically. HI results are shown in Table 5 and, as observed throughout the previous season, the test virus carried HA genes of genetic group 1A.

This test virus showed a similar HI reactivity pattern 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, B/Brisbane/60/2008. Similarly, it was 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, it showed reactivity within twofold of the titres for the corresponding homologous viruses with antisera raised against viruses that are considered to be surrogate cell-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, based on sequences available in GISAID with collection dates from July 2015, is shown in Figure 3. There are five sequences available for viruses collected in Norway during November 2015. Worldwide, recent viruses have HA genes that fall into the B/Brisbane/60/2008 genetic clade (clade 1A) and remain antigenically similar to the recommended vaccine virus, B/Brisbane/60/2008, for use in quadrivalent vaccines. Viruses with collection dates in October and November of 2015 all fall in a major sub-cluster defined by amino acid substitutions N129D, V146I and I117V within genetic clade 1A.

These results, linked with the rise in the proportion of B/Victoria-lineage viruses, support the recommendation made in September 2015 to include B/Brisbane/60/2008 in trivalent influenza vaccines for the southern hemisphere 2016 influenza season.

Influenza B – Yamagata lineage

No B/Yamagata-lineage viruses have yet been characterised antigenically or genetically.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses with collection dates from July 2015. Worldwide, the 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 are reassortants carrying NA genes normally associated with the B/Victoria-lineage.

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

Viruses	Collection date	Passage History	Haemagglutination inhibition titre										
			Post-infection ferret antisera										
			B/Bris[1,3] 60/08 Sh 539 / 540 / 543 / 544	B/Mal[2] 2506/04 F37/11	B/Bris[2] 60/08 F22/12	B/Paris[2] 1762/09 F07/11	B/HK[2] 514/09 F19/13	B/Odessa[2] 3886/10 F19/11	B/Malta[2] 636714/11 F29/13	B/Jhb[2] 3964/12 F01/13	B/For[4] V2367/12 F04/13	B/Sth Aus[2] 81/12 F41/13
	Genetic group		1A	1A	1A	1A	1B	1B	1A	1A	1A	1A
REFERENCE VIRUSES												
B/Malaysia/2506/2004		2004-12-06	E3/E6	640	640	80	<	20	<	160	160	80	160
B/Brisbane/60/2008	1A	2008-08-04	E4/E5	640	40	160	20	40	40	320	160	160	320
B/Paris/1762/2009	1A	2009-02-09	C2/MDCK2	1280	10	10	80	80	80	40	20	80	40
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	640	<	10	40	80	80	40	10	40	40
B/Odessa/3886/2010	1B	2010-03-19	C2/MDCK2	1280	40	40	80	80	80	40	80	160	160
B/Malta/636714/2011	1A	2011-03-07	E4/E1	640	80	320	40	80	40	640	320	320	640
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	2560	320	1280	160	320	160	1280	1280	1280	1280
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	1280	40	160	40	40	40	320	160	320	320
B/South Australia/81/2012	1A	2012-11-28	E4/E1	640	40	160	40	40	80	320	160	160	640
TEST VIRUSES													
B/England/345/2015	1A	08/10/2015	SIAT1/MDCK1	640	10	<	40	40	80	40	<	40	40
						Vaccine*							

1. < = <40; 2. < = <10; 3. hyperimmune sheep serum; 4. <=<20

* B/Victoria-lineage virus recommended for use in quadravalent vaccines (Northern Hemisphere 2015-16)

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

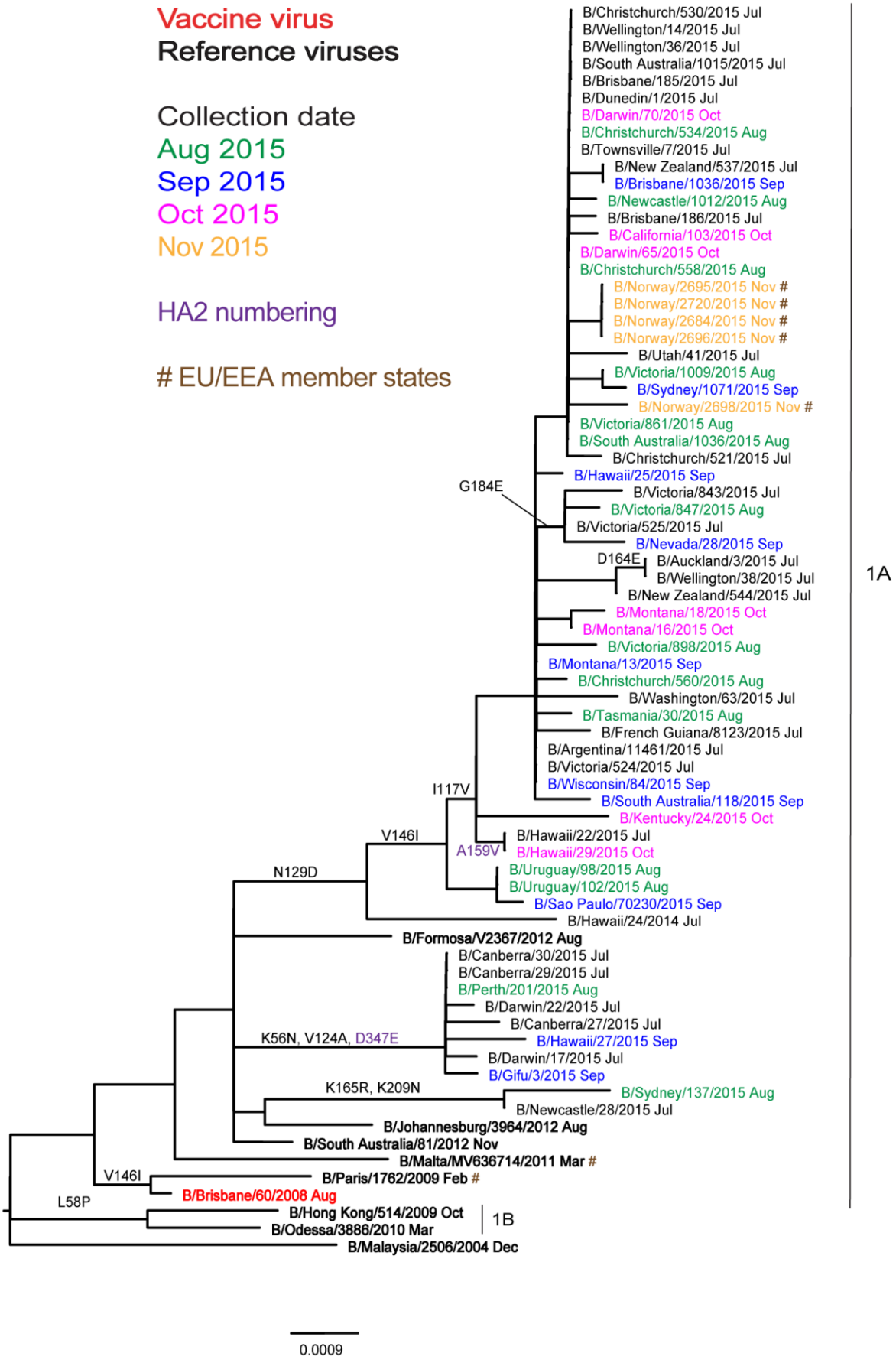
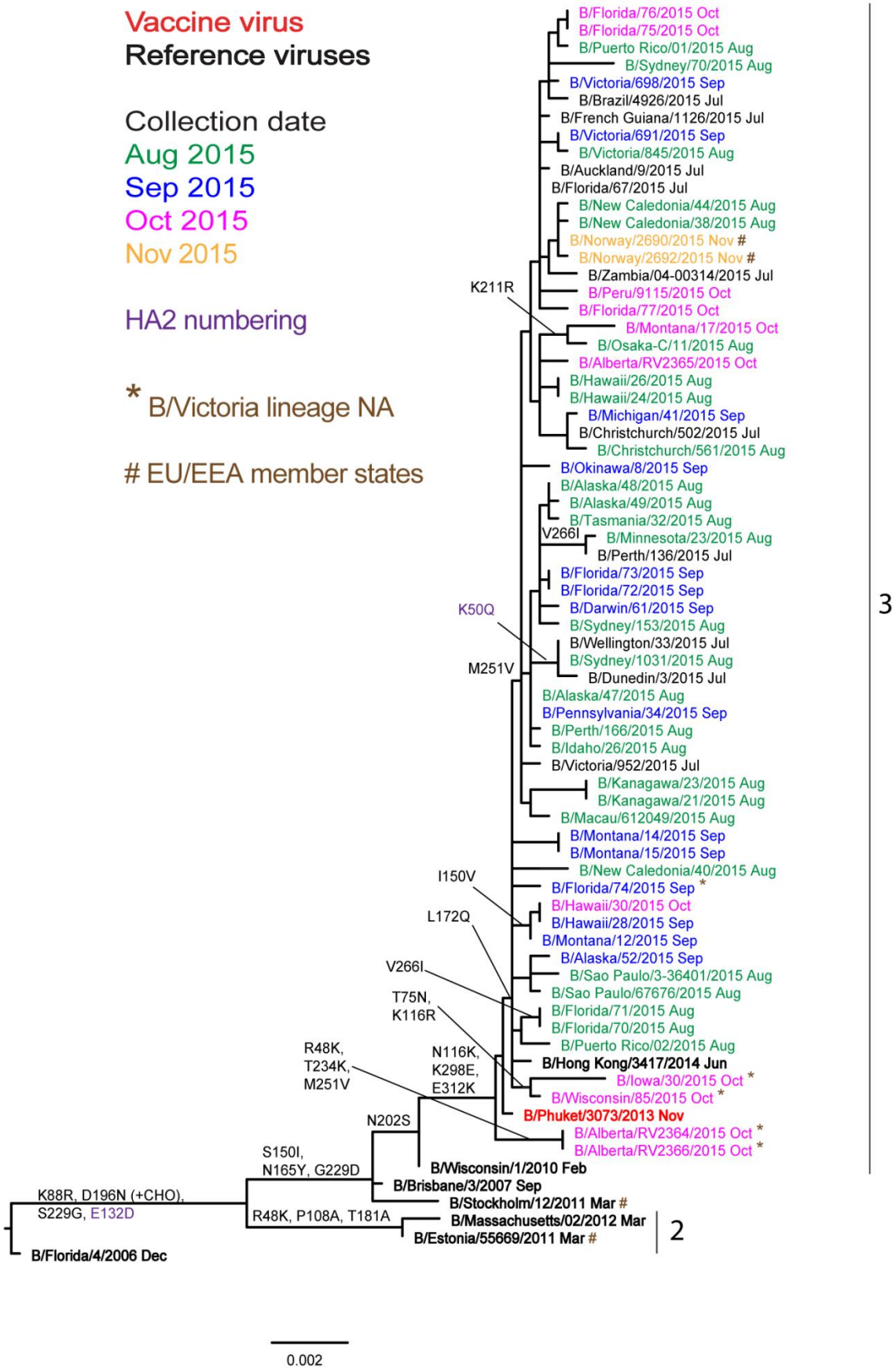


Figure 4. Phylogenetic comparison of influenza B/Yamagata-lineage HA genes



Summary of genetic data submitted to TESSy

For the period covering weeks 40–49/2015, 73 viruses have been characterised genetically: 41 A(H1N1)pdm09 subgroup 6B represented by A/South Africa/3626/2013; A(H3N2) 15 subgroup 3C.2a represented by A/Hong Kong/4801/2014, 1 subgroup 3C.3a represented by A/Switzerland/9715293/2013 and 1 subgroup 3C.3 represented by A/Samara/73/2013; 10 B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008; and 5 B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013.

Antiviral susceptibility

For weeks 40–49/2015 of the 2015–2016 influenza season, countries reported on the antiviral susceptibility of 12 A(H3N2) viruses, 52 A(H1N1)pdm09 viruses and two B/Victoria-lineage viruses from sentinel and non-sentinel sources. None showed molecular or phenotypic evidence of reduced inhibition by neuraminidase inhibitors.

Antiviral susceptibility testing on specimens received at the WIC has yet to be performed.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [1] 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 [2]. Increased numbers of cases were reported over the course of the 2013–14 and 2014–15 seasons and cases have been reported recently [3].
A revised Rapid Risk Assessment [4] 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 [5], updated on 13 November 2015 [6], and conducted a new risk assessment on 23 February 2015 [7]. 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 [8] and has provided subsequent situation updates, with the latest being on 13 November 2015 [3].

Influenza A(H5N1) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 13 November 2015 [6]. No new laboratory-confirmed human cases of H5Nx infection had been reported to WHO since the update on 17 July 2015. ECDC published an updated rapid risk assessment on the situation in Egypt on 13 March 2015 [9] and an epidemiological update 10 April 2015 [10]. On 14 July 2015 the WHO reported on a fatal case of human infection with avian A(H5N6) virus in China [11].

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 Meeting held at WHO Geneva 23–25 February 2015, can be found at:

http://crick.ac.uk/media/221813/nimr-report-feb2015-web.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 (#) as are those viruses for which data are 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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