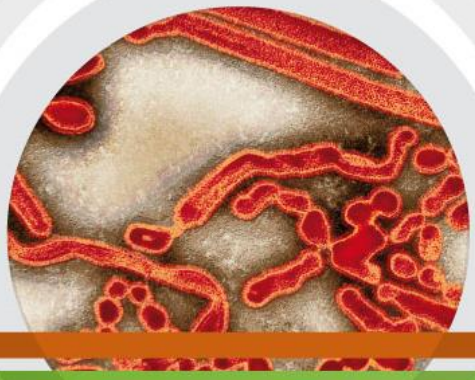

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, June 2015

Summary

Over the course of the 2014–15 influenza season influenza A(H3N2), A(H1N1)pdm09 and type B viruses have co-circulated in EU/EEA countries. To date, 23 EU/EEA countries have shared 878 influenza-positive specimens with the WHO Collaborating Centre in London for detailed characterisation. Since the May 2015 report[1], 73 viruses have been characterised antigenically and 53 genetically.

The 16 A(H1N1)pdm09 viruses characterised antigenically were similar to the vaccine virus A/California/07/2009; all 11 characterised genetically had HA genes belonging to genetic subgroup 6B, as observed worldwide.

All 31 A(H3N2) viruses characterised by haemagglutination inhibition (HI) assay were poorly recognised by the reference antiserum raised against the A/Texas/50/2012 vaccine virus but relatively well recognised by antisera raised against some cell-propagated genetic subgroup 3C.3a viruses. The 318 (24 since the May 2015 report) viruses, with collection dates after 31 August 2014, characterised genetically this season fell in genetic group/subgroups 3C.3 (39), 3C.3b (66), 3C.3a (39) and 3C.2a (174). Viruses in genetic group 3C.3, excluding those in subgroup 3C.3a, were antigenically similar to reference viruses closely related to A/Texas/50/2012, while those in subgroups 3C.3a and 3C.2a were antigenically distinct.

The five B/Victoria-lineage viruses were antigenically similar to B/Brisbane/60/2008, and the four for which HA sequencing has been completed all fell in genetic clade 1A. All 21 B/Yamagata-lineage test viruses characterised antigenically showed good reactivity with antisera raised against B/Phuket/3073/2013 (the clade 3 virus recommended for the southern hemisphere 2015 and northern hemisphere 2015–16 vaccines). Antisera raised against B/Massachusetts/02/2012 (the clade 2 virus recommended for the 2014–15 northern hemisphere season vaccine) did not recognise test viruses as well as antisera raised against B/Phuket/3073/2013. The 14 viruses characterised genetically all fell in clade 3, represented by B/Phuket/3073/2013.

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

This report was prepared by Rod Daniels, 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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Influenza-positive samples (897 viruses or clinical specimens: 87 being received since the May 2015 report) with collection dates after 31 August 2014 were received at the Crick Worldwide Influenza Centre, the Francis Crick Institute, Mill Hill Laboratory, from 23 countries in the EU/EEA. Overall, the majority (~78%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of > 3:1 (Table 1). Of the 194 type B specimens received (~22% of the specimens), 153 were of the B/Yamagata-lineage, 33 were not ascribed to a lineage, and only eight were of the B/Victoria lineage. Some of these samples, mostly received as clinical specimens, are still in the process of being characterised. The antigenic and genetic properties of influenza virus isolates characterised since the May 2015 report are presented and discussed in this report.

Table 1. Summary of clinical samples and virus isolates received from EU/EEA Member States, with collection dates after 31 August 2014

MONTH	TOTAL RECEIVED	A	H1N1pdm09		H3N2		B		B Victoria lineage		B Yamagata lineage	
Country		Number received	Number received	Number propagated[1]	Number received	Number propagated[2]	Number received	Number propagated	Number received	Number propagated[1]	Number received	Number propagated[1]
2014												
SEPTEMBER												
Belgium	1				1	1						
France	2				1	1					1	1
Spain	1				1	0 (1)						
Sweden	3				3	2 (1)						
OCTOBER												
Belgium	5				5	1 (4)						
Denmark	2				2	2						
Finland	3				1	1					2	2
France	6				5	1 (4)					1	1
Germany	6		3	3	2	2			1	1		
Malta	4				4	3 (1)						
Netherlands	6				5	3 (2)					1	1
Norway	8		5	3	3	1						
Slovenia	2				1	1					1	0
Spain	13				10	5 (1)					3	3
Sweden	2				2	1 (1)						
United Kingdom	2				1	1					1	1
NOVEMBER												
Belgium	4		1	1	1	0 (1)					2	1
Denmark	1				1	1						
Finland	2				2	0 (2)						
France	6		1	1	3	0 (3)					2	2
Germany	8		2	2	5	3 (2)					1	1
Latvia	1		1	1								
Luxembourg	1		1	1								
Netherlands	3				3	0 (3)						
Norway	11				3	2 (1)					8	3
Portugal	2										2	2
Slovenia	1		1	1								
Spain	10				9	6 (3)					1	1
Sweden	3				3	3						
United Kingdom	7				6	3 (2)					1	1
DECEMBER												
Austria	8				7	1 (6)					1	1
Belgium	5		3	3	1	1					1	1
Croatia	10		4	4	2	1	2	0			2	2
Czech Rep	7				7	1 (6)						
Denmark	5		2	2	3	0						
Estonia	1				1	0 (1)						
Finland	5		2	2	1	0 (1)					2	2
France	37		4	4	26	19 (7)					7	7
Germany	18		2	2	14	6 (6)			1	1	1	1
Greece	3				2	1 (1)					1	1
Italy	30		14	14	9	4 (5)					7	7
Latvia	8		1	1	5	3 (2)					2	2
Luxembourg	11		6	3	3	1 (2)	2	0				
Malta	4				4	1 (2)						
Netherlands	5		1	1	4	1 (3)						
Norway	26		4	4	15	7 (5)					7	4
Portugal	10				3	1 (2)					7	7
Slovenia	19		17	14	1	0	1	0				
Spain	48		2	2	40	9 (26)					6	6
Sweden	5				5	5						
United Kingdom	12		1	1	10	2 (5)					1	1
2015												
JANUARY												
Bulgaria	11				11	2 (9)						
Croatia	1				1	0						
Cyprus	8				8	6 (2)						
Denmark	2				2	2						
Estonia	24		1	0	22	2 (11)					1	0
Finland	1		1	1								
Germany	33		5	5	22	12 (10)					6	6
Greece	61		13	6	25	4 (14)	15	0	1	0	7	7
Italy	17		8	7	7	3 (4)					2	2
Latvia	2				2	0 (2)						
Luxembourg	1						1	0				
Malta	5				5	1 (1)						
Norway	8				7	4 (2)					1	1
Portugal	7		2	1	3	0 (2)					2	1
Romania	6		4	4	1	1					1	1
Slovenia	15		8	8	3	0 (3)	2	0			2	2
Spain	47		11	10	25	14 (11)	1	0			10	10
Sweden	4				4	3 (1)						
United Kingdom	27		2	2	25	7 (8)						
FEBRUARY												
Bulgaria	26		3	3	19	1 (15)					4	4
Cyprus	12				11	1 (9)					1	1
Finland	2				2	2						
Greece	13		3	0	4	0	4	0			2	1
Italy	41		12	12	15	5 (10)	1	0			13	13
Norway	1				1	1						
Romania	8		2	2	4	3 (1)					2	2
Spain	58	5	1	1	38	16 (16)	3	0			11	10
Sweden	6				6	6						
MARCH												
Bulgaria	3				2	0 (2)					1	1
Finland	1								1	1		
Italy	1						1	0				
Norway	8		3	2	4	2 (1)			1	1		
Romania	17		5	5	2	2					10	10
Sweden	1				1	1						
APRIL												
Finland	4				2	1 (1)			1	1	1	1
Norway	12		4	2	2	0 (1)			2	2	4	0
23 Countries	897	5	166	141	532	210 (248)	33		8	7	153	135
			18.5%		59.3%				0.9%		17.1%	
			78.4%				21.6%					

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 parentheses 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 May 2015 report are shown in Table 2. All 16 A(H1N1)pdm09 viruses, from Finland, Norway and Romania, were antigenically similar to the vaccine virus, A/California/7/2009, showing no more than twofold reduction in HI titre compared to that for the homologous virus. All 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 56% (9/16) of the test viruses at a titre within fourfold of the titre for the homologous virus. As reported previously, 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 at least eightfold reduced compared to the titres of the antisera with their homologous viruses.

Figure 1 shows a phylogenetic tree for the HA genes of representative, recently circulating A(H1N1)pdm09 viruses. Since 2009, the HA genes have evolved, and eight genetic groups have been designated. Over the last twelve months, 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.

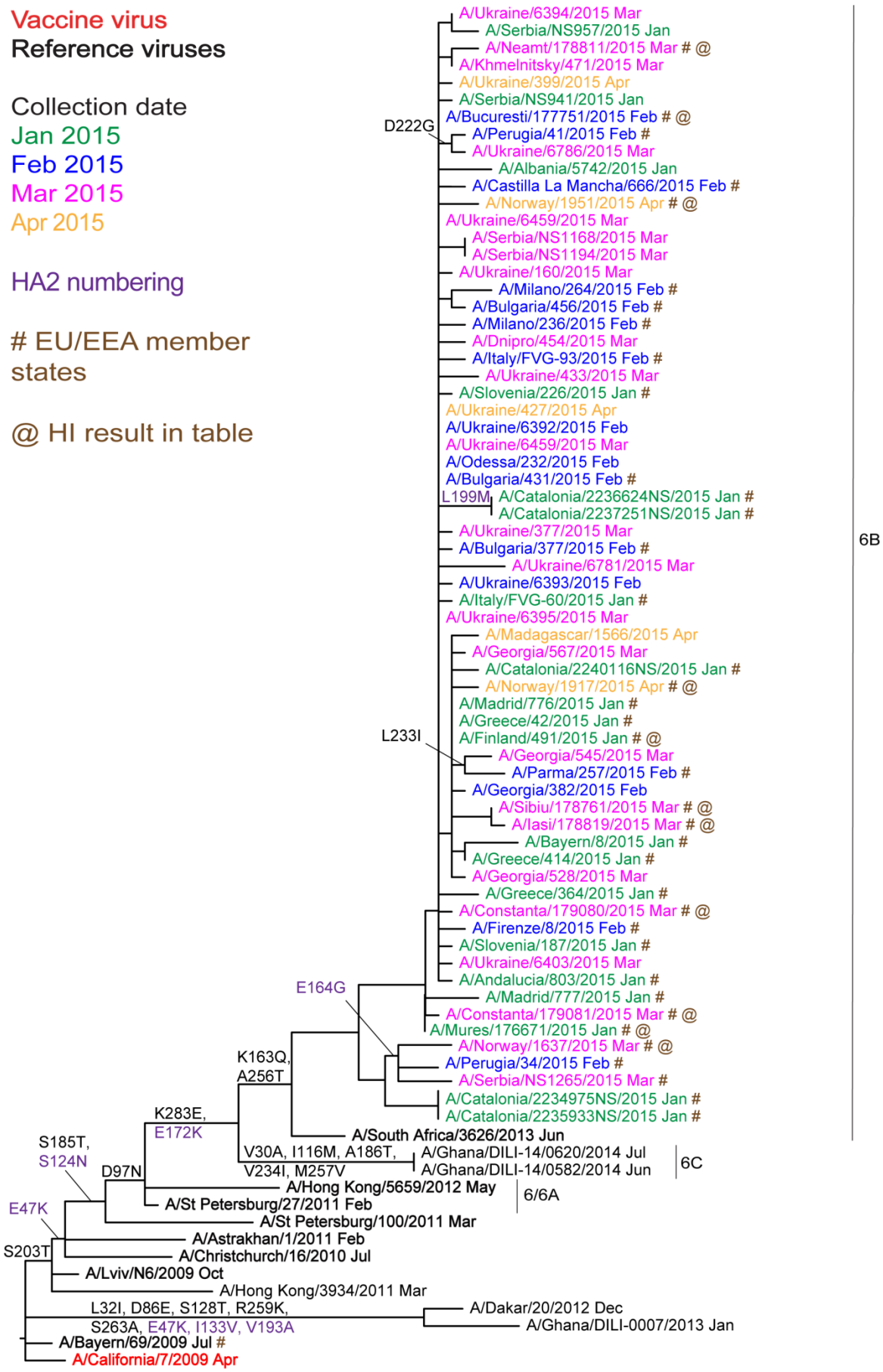
These results are compatible with those that contributed to the World Health Organization recommendation [1] to retain the A/California/7/2009 vaccine virus for the northern hemisphere 2015–16 influenza season.

[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 2. 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 F29/11	A/Bayern 69/09 F11/11	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 F23/11 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	1280	640	1280	160	160	160	320	160	160		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	80	320	320	80	40	80	40	80	40	G155E	
A/Lviv/N6/2009		2009-10-27	MDCK4/SIAT1/MDCK3	320	1280	1280	160	80	160	160	320	80	G155E>G, D222G	
A/Christchurch/16/2010	4	2010-07-12	E1/E3	2560	1280	1280	5120	1280	1280	5120	2560	1280		
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	640	640	640	1280	1280	2560	2560	1280		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	640	640	1280	1280	2560	1280	1280		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	640	640	1280	1280	2560	1280	640		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	160	320	640	1280	1280	320		
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	320	640	320	640	640	1280	1280	1280		
TEST VIRUSES														
A/Iasi/175973/2015		2015-01-13	MDCK2/MDCK 1	1280	640	640	1280	2560	1280	5120	2560	1280		
A/Iasi/176380/2015	6B	2015-01-21	MDCK1/MDCK 1	1280	320	640	640	1280	1280	2560	1280	1280		
A/Mures/176671/2015	6B	2015-01-26	SIAT1/MDCK 1	640	320	320	320	640	1280	2560	1280	640		
A/Iasi/176656/2015	6B	2015-01-27	MDCK1/MDCK 1	1280	640	640	1280	2560	2560	2560	2560	1280		
A/Finland/491/2015	6B	2015-01-28	MDCK1/MDCK1	1280	320	640	640	1280	1280	2560	1280	1280		
A/Bucuresti/177751/2015	6B	2015-02-17	MDCK1/MDCK 1	1280	640	640	1280	2560	2560	5120	2560	2560		
A/Valcea/178103/2015		2015-02-23	SIAT1/MDCK 1	640	320	320	320	1280	1280	2560	1280	1280		
A/Neamt/178811/2015	6B	2015-03-04	MDCK1/MDCK 1	2560	1280	1280	1280	2560	2560	5120	2560	2560		
A/Sibiu/178761/2015	6B	2015-03-05	MDCK1/MDCK 1	2560	640	1280	1280	2560	2560	5120	2560	2560		
A/Iasi/178819/2015	6B	2015-03-06	MDCK1/MDCK 1	2560	640	640	1280	2560	2560	5120	2560	2560		
A/Constanta/179080/2015	6B	2015-03-11	MDCK2/MDCK 1	2560	640	1280	1280	2560	2560	5120	2560	2560		
A/Constanta/179081/2015	6B	2015-03-11	MDCK1/MDCK 1	2560	640	1280	1280	2560	2560	5120	2560	2560		
A/Norway/1690/2015		2015-03-17	MDCK1/MDCK3	2560	640	640	1280	2560	1280	5120	2560	2560		
A/Norway/1637/2015	6B	2015-03-22	MDCK1	640	320	320	320	640	640	1280	640	640		
A/Norway/1951/2015	6B	2015-04-10	MDCK1	1280	640	640	640	1280	1280	2560	1280	1280		
A/Norway/1917/2015	6B	2015-04-13	MDCK1	1280	320	640	640	1280	640	2560	1280	1280		
Sequences in phylogenetic tree			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 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, conducted since the May 2015 report are shown in Tables 3-1 and 3-2. The viruses were received from Finland, Norway, Romania and Sweden, and the HA genetic group is indicated for those viruses that have been sequenced, and those included in the HA phylogenetic tree (Figure 2) are highlighted. Of the 37 successfully propagated viruses, 31 (84%) retained sufficient HA titre to be analysed by HI assay, a proportion significantly higher than that in the May 2015 report. The remainder (n = 6) were either unable to agglutinate guinea pig RBCs at all or were unable to agglutinate RBCs in the presence of 20nM oseltamivir. The majority of viruses unable to be titred by HI that were subjected to genetic analysis belonged to genetic subgroup 3C.2a.

All 31 test viruses, propagated in MDCK-SIAT1 cells, reacted poorly in HI assays (≥ eightfold decrease) with post-infection ferret antiserum raised against the egg-propagated vaccine virus, A/Texas/50/2012, compared to the titre of the antiserum with the homologous virus. Similarly, low levels of reactivity were seen with antisera raised against the egg-propagated reference virus A/Hong Kong/146/2013: no test virus reacted within fourfold of the titre with the homologous egg-propagated virus. Better reactivity was seen with test viruses when analysed with an antiserum raised against the exclusively egg-propagated A/Stockholm/6/2014 isolate 2, a virus belonging to genetic subgroup 3C.3a. This antiserum showed a low titre for the homologous virus but recognised 20 of the test viruses at titres within fourfold of the homologous titre. Antiserum raised against egg-propagated A/Switzerland/9715293/2013, the virus in genetic subgroup 3C.3a recommended for the southern hemisphere 2015 and northern hemisphere 2015–16 vaccines, gave a homologous titre of 640 and did not recognise any of the test viruses at titres within fourfold of the homologous titre. Similarly, antiserum raised against egg-propagated A/Hong Kong/5738/2014 clone 121, a virus in genetic subgroup 3C.2a, failed to recognise any of the test viruses at titres within fourfold of the homologous titre.

Ferret antisera raised against reference viruses propagated in tissue culture cells, A/Victoria/361/2011 and A/Samara/73/2013, recognised the test viruses somewhat more effectively. The antiserum raised against A/Victoria/361/2011 recognised 11/14 (79%) of the test viruses at titres within fourfold of the titre with the homologous virus, but the antiserum raised against A/Samara/73/2013 recognised only ~35% of test viruses at a titre within fourfold of the titre for the homologous virus. These reference viruses have HA genes from genetic groups 3C.1 and 3C.3, respectively. Of the antisera raised against 3C.3a reference viruses propagated exclusively in cell culture, the antiserum raised against A/Stockholm/6/2014 recognised 30/31 (97%) test viruses at titres within fourfold of that with the homologous virus, while fold-drop comparisons for the antiserum raised against A/Switzerland/9715293/2013 could not be made due to the low homologous titre and the 1/40 cut-off used in the assays. An antiserum raised against a reference virus belonging to genetic subgroup 3C.2a that had been exclusively propagated in cell culture, A/Hong Kong/5738/2014, recognised 20/31 (65%) test viruses at titres within fourfold of that for the homologous virus. Antiserum raised against A/Netherlands/525/2014, a 3C.3b virus, did not react with test viruses in the 3C.2a and 3C.3a genetic subgroups.

[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

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, recently circulating A(H3N2) viruses is shown in Figure 2. The HA genes fall within genetic group 3C. This group has three subdivisions: 3C.1 (to which the recommended vaccine virus for the 2014–15 northern hemisphere season, A/Texas/50/2012, belongs), 3C.2 and 3C.3. Viruses in these three subdivisions have been antigenically similar. However, 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/Newcastle/22/2014.

Of the A(H3N2) viruses received from EU/EEA countries, with collection dates since 31 August 2014, 318 have been characterised genetically. These have fallen in HA genetic subgroups 3C.2a (n = 174; 55%), 3C.3a (n = 39; 12%) and 3C.3b (n = 66; 21%), with the remainder (n = 39; 12%) being in subdivision 3C.3. This is indicative of 67% of recently circulating A(H3N2) viruses being antigenic drift variants compared to A/Texas/50/2012, the virus recommended for use in northern hemisphere 2014–15 vaccines.

Based on results available at the time of the February 2015 vaccine composition meeting, that 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, 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.

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

Table 3-1. 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 antisera												
			A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12 Egg	A/Texas 50/12 F05/13	A/Samara 73/13 F24/13	A/HK 146/13 F10/15	A/Stock 6/14 T/C F14/14 Egg	A/Stock 6/14 F20/14 Egg	A/Switz 9715293/13 T/C NIB F13/14	A/Switz 9715293/13 Egg F32/14	A/HK 5738/14 T/C F30/14 NIB	A/HK 5738/14 F53/14
Genetic group				3C.1	3C.1	3C.3	3C.2	3C.3a	3C.3a isolate 2	3C.3a	3C.3a cl123	3C.2a	3C.2a cl 121
REFERENCE VIRUSES													
A/Perth/16/2009	2009-07-04	E3/E3	640	80	320	80	80	40	80	<	40	<	<
A/Victoria/361/2011	2011-10-24	MDCK2/MDCK2/SIAT1	80	160	640	320	160	320	160	40	80	80	40
A/Texas/50/2012	2012-04-15	E5/E2	320	640	2560	640	320	160	640	40	320	160	80
A/Samara/73/2013	2013-03-12	C1/SIAT4	160	320	640	640	320	320	320	80	320	320	40
A/Hong Kong/146/2013	2013-01-11	E3/E3	320	320	1280	640	1280	80	640	40	640	320	40
A/Stockholm/6/2014	2014-02-06	SIAT1/SIAT3	<	40	80	160	80	320	160	80	80	80	40
A/Stockholm/6/2014	2014-02-06	E4/E1 isolate 2	80	320	320	80	80	160	320	80	640	160	40
A/Switzerland/9715293/2013	2013-12-06	SIAT1/SIAT3	<	40	80	160	40	320	160	80	80	160	40
A/Switzerland/9715293/2013	2013-12-06	E4/E1 clone 123	40	160	320	160	80	160	320	80	640	320	40
A/Hong Kong/5738/2014	2014-04-30	MDCK1/MDCK3	40	40	160	160	80	320	80	40	80	320	40
A/Hong Kong/5738/2014	2014-04-30	E5/E1 clone121	40	40	160	160	40	160	80	40	40	320	640
TEST VIRUSES													
A/Norway/3172/2014	2014-12-09	MDCK2	<	40	160	80	80	160	80	<	40	160	<
A/Norway/353/2015	2015-01-04	MDCK1	40	80	320	160	160	160	80	<	40	80	<
A/Norway/217/2015	2015-01-12	MDCK1	40	80	320	160	80	160	80	<	<	40	<
A/Norway/923/2015	2015-01-20	SIAT2	40	80	160	160	80	160	80	<	<	40	<
A/Iasi/176654/2015	2015-01-27	MDCK1/SIAT1	<	<	<	<	<	80	40	40	40	40	<
A/Finland/506/2015	2015-02-02	SIAT1	80	80	160	160	80	160	80	<	40	80	<
A/Iasi/177049/2015	2015-02-04	MDCK1/SIAT1	<	<	<	<	<	80	40	40	40	40	<
A/Iasi/177050/2015	2015-02-04	MDCK1/SIAT1	<	<	<	<	<	80	40	40	40	<	<
A/Finland/494/2015	2015-02-11	SIAT2/SIAT1	40	40	160	80	40	160	40	<	<	40	<
A/Timis/177582/2015	2015-02-12	MDCK1/SIAT1	40	80	160	80	80	80	40	<	40	<	<
A/Norway/1151/2015	2015-02-25	SIAT1	<	40	160	80	40	80	40	<	<	40	<
A/Bucuresti/179471/2015	2015-03-18	SIAT1/SIAT1	80	80	160	160	80	160	80	<	<	40	<
A/Norway/1656/2015	2015-03-21	SIAT1	80	80	160	160	80	160	80	<	40	80	<
A/Finland/525/2015	2015-04-13	SIAT1/SIAT1	40	80	160	80	80	160	40	<	<	40	<
					Vaccine NH2014-15						Vaccine SH2015 NH2015-16		

1. < = <40

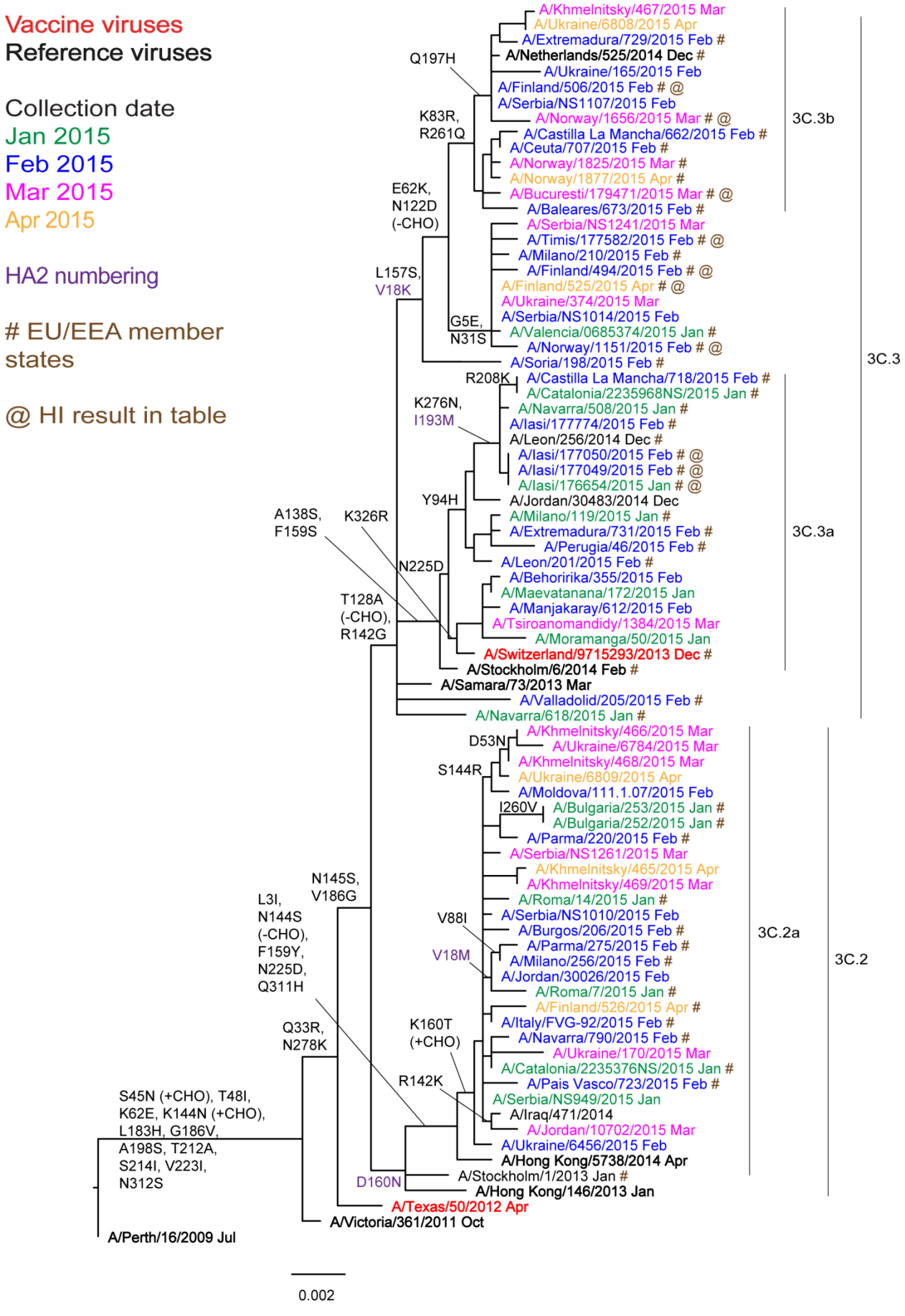
Sequences in phylogenetic tree

Table 3-2. 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 antisera											
			A/Perth 16/09 F18/11	A/Texas 50/12 Egg F05/13	A/Samara 73/13 F24/13	A/HK 146/13 F10/15	A/Stock 6/14 T/C F14/14	A/Stock 6/14 9715293/13 Egg F20/14	A/Switz T/C NIB F13/14	A/Switz 9715293/13 Egg F32/14	A/HK 5738/14 T/C F30/14	A/HK 5738/14 NIB F53/14	A/Neth 525/14 F23/15
	Genetic group			3C.1	3C.3	3C.2	3C.3a	3C.3a isolate 2	3C.3a	3C.3a cl123	3C.2a	3C.2a cl 121	3c.3b
REFERENCE VIRUSES													
A/Perth/16/2009	2009-07-04	E3/E3	640	320	160	160	40	160	<	40	<	40	80
A/Texas/50/2012	2012-04-15	E5/E2	320	2560	640	320	160	640	40	320	160	80	320
A/Samara/73/2013	2013-03-12	C1/SIAT4	160	1280	640	640	640	640	80	320	320	80	320
A/Hong Kong/146/2013	2013-01-11	E3/E3	320	1280	640	1280	80	640	40	320	320	80	320
A/Stockholm/6/2014	2014-02-06	SIAT1/SIAT2	<	80	160	80	320	160	80	80	80	80	80
A/Stockholm/6/2014	2014-02-06	E4/E1 isolate 2	80	160	80	80	160	320	80	640	160	80	80
A/Switzerland/9715293/2013	2013-12-06	SIAT1/SIAT2	<	40	160	40	320	160	80	80	80	40	40
A/Switzerland/9715293/2013	2013-12-06	E4/E1 clone 123	40	160	160	80	160	320	80	640	320	40	80
A/Hong Kong/5738/2014	2014-04-30	MDCK1/MDCK3	<	160	160	80	320	160	40	80	160	40	40
A/Hong Kong/5738/2014	2014-04-30	E5/E1 clone121	40	160	80	40	80	80	40	40	320	640	80
A/Netherlands/525/2014		SIAT2/SIAT2	80	320	320	80	320	160	40	80	80	<	640
TEST VIRUSES													
A/Stockholm/31/2014	3C.2a	2014-11-26	MDCK1/SIAT1	<	40	<	<	80	40	<	<	40	<	<
A/Stockholm/28/2014	3C.3b	2014-12-02	MDCK1/SIAT1	80	320	320	80	160	80	40	40	80	<	640
A/Stockholm/36/2014	3C.2a	2014-12-02	MDCK2/SIAT1	<	80	40	<	160	80	<	<	80	<	<
A/Stockholm/30/2014	3C.2a	2014-12-04	MDCK1/SIAT1	<	80	80	40	160	80	<	<	80	<	<
A/Stockholm/32/2014	3C.3a	2014-12-09	MDCK1/SIAT1	<	80	80	40	320	160	40	40	80	<	<
A/Stockholm/38/2014	3C.2a	2014-12-27	MDCK1/SIAT1	<	80	80	<	80	80	<	<	80	<	<
A/Stockholm/1/2015	3C.2a	2015-01-12	MDCK1/SIAT1	<	160	80	40	160	80	<	<	160	40	<
A/Stockholm/7/2015	3C.2a	2015-01-13	MDCK1/SIAT1	<	80	80	<	160	80	<	<	80	<	<
A/Stockholm/8/2015	3C.2a	2015-01-25	MDCK1/SIAT1	<	80	80	40	160	80	<	<	80	<	<
A/Stockholm/12/2015	3C.3	2015-02-10	MDCK1/SIAT1	<	80	40	<	<	<	<	<	<	<	160
A/Stockholm/13/2015	3C.2a	2015-02-10	MDCK0/SIAT1	<	80	80	40	160	80	<	<	80	<	<
A/Stockholm/18/2015	3C.3b	2015-02-11	MDCK0/SIAT1	80	320	320	80	320	160	80	40	80	40	320
A/Stockholm/20/2015	3C.3b	2015-02-24	MDCK0/SIAT1	80	320	320	80	320	160	160	40	80	<	640
A/Stockholm/19/2015	3C.3b	2015-02-25	MDCK0/SIAT1	80	320	160	80	320	80	80	40	80	<	320
A/Sweden/15/2015	3C.2a	2015-02-27	MDCK2/SIAT3	<	40	40	<	80	40	<	<	40	<	<
A/Sweden/16/2015	3C.3b	2015-03-05	MDCK1/SIAT1	80	320	320	80	320	160	80	40	80	<	320
A/Norway/1800/2015		2015-03-25	SIAT3	<	80	80	40	80	40	<	<	40	<	160
				Vaccine NH2014-15						Vaccine SH2015 NH2015-16				

1. < = <40

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



Influenza B virus analyses

Influenza B viruses represented approximately 22% of samples received from EU/EEA countries with collection dates after 31 August 2014 (Table 1). Of the 161 viruses ascribed to a lineage, B/Yamagata viruses predominated over those of B/Victoria at a ratio of 19:1.

Influenza B – Victoria lineage

Since the May 2015 report, five viruses of this lineage have been received, three from Norway and two from Finland. HI results are shown in Table 4 and the four viruses sequenced at the time of writing this report all carried HA genes of genetic group 1A.

The five test viruses showed 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, 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, all test viruses showed reactivity within twofold of the titres for the corresponding homologous viruses with antisera raised against viruses genetically closely related to B/Brisbane/60/2008 but propagated in cell culture; these antisera were raised against B/Paris/1762/2009, B/Hong Kong/514/2009 and B/Odessa/3886/2010, viruses that are considered to be surrogate cell-propagated antigens representing the egg-propagated prototype virus. Similarly, all but one of the test viruses reacted at titres within fourfold of the homologous titre with antiserum raised against cell-propagated B/Formosa/V2367/2012; sequencing of the poor reactor, B/Norway/1570/2015, is in progress.

Phylogenetic analysis of the HA gene of representative B/Victoria lineage viruses, based on sequences available in GISAID with collection dates since 1 January 2015, is shown in Figure 3. 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. Compared to the phylogenetic analysis presented in the April 2015 report[6], containing viruses with collection dates up to the end of December 2014, there has been a change in prevalence of genetic subgroup from that defined by HA1 amino acid substitution K209N (e.g. B/Baden-Württemberg/3/2014) to that defined by N129D substitution (e.g. B/Iceland/63/2014) based on viruses collected in the USA and Japan. Of the four test viruses in this report with available HA sequences, one (B/Norway/2179/2015) fell in the group defined by N129D substitution and one (B/Norway/2102/2015) in the group defined by K209N substitution; the two viruses from Finland fell in a separate group defined by amino acid substitutions K56N and V124A in HA1 with D179E in HA2.

Influenza B – Yamagata lineage

HI results for the 21 B/Yamagata-lineage test viruses, from Finland, Greece, Norway, Romania and Spain, analysed since the May 2015 report are shown in Tables 5-1 and 5-2. All 14 test viruses for which HA gene sequencing was performed fell in genetic clade 3 and these sequences are included in the phylogenetic tree (Figure 4).

Post-infection ferret antiserum raised against the egg-propagated vaccine virus B/Massachusetts/02/2012, recommended for use in the 2014–15 northern hemisphere influenza season, recognised 24% (5/21) of test viruses at titres within fourfold of the titre with the homologous virus. A ferret antiserum raised against a cell culture-propagated cultivar of B/Massachusetts/02/2012 recognised 67% (14/21) of test viruses at titres within fourfold of its titre with the homologous virus. Antisera raised against cell culture-propagated B/Estonia/55669/2011 and belonging to the B/Massachusetts/02/2012 clade (clade 2) recognised all test viruses at titres within fourfold of the titres of the antisera with the homologous virus.

Antisera raised against a previously recommended vaccine virus (B/Wisconsin/1/2010) and an egg-propagated reference virus (B/Stockholm/12/2011), both belonging to clade 3 represented by B/Wisconsin/1/2010 and B/Phuket/3073/2013, recognised all test viruses at titres within fourfold of the titres with the homologous viruses. Similarly, test viruses were recognised well by antisera raised against recent egg-propagated viruses compared to their respective homologous titres: all test viruses reacted within twofold with antiserum raised against B/Phuket/3073/2013 (the virus recommended as a vaccine virus for the southern hemisphere 2015 and northern hemisphere 2015–16 influenza seasons) and antiserum raised against the B/Hong Kong/3417/2014 reference virus. Antiserum raised against a cell culture-propagated cultivar of B/Phuket/3073/2013 recognised 95% (20/21) of test viruses at titres within fourfold of the titre for the homologous virus. Based on HI titre fold-drop, antisera raised against the egg-propagated clade 3 viruses, which include previous (A/Wisconsin/1/2010) and recently recommended (A/Phuket/3073/2013) vaccine viruses, are more reactive with currently circulating clade 3 viruses

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

than antisera raised against the egg-propagated clade 2 B/Massachusetts/02/2012 vaccine virus used in the northern hemisphere 2014–15 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 small proportion of viruses, detected in many parts of the world, have HA genes of clade 3 of the B/Yamagata lineage combined with NA genes of the B/Victoria lineage: B/Finland/489/2014 also carries an NA gene of the B/Victoria lineage, but the HA gene of B/Finland/489/2014 falls within the subgroup defined by HA1 L172Q amino acid substitution. A small group of viruses that are antigenically distinguishable from the great majority of clade 3 viruses, designated as clade 3a, have been detected in Australia but seemingly not elsewhere.

Table 4. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre: Post-infection ferret antisera									
				B/Bris[1,3] 60/08 Sh 522 1A	B/Mal[2] 2506/04 F37/11	B/Bris[2] 60/08 F22/12 1A	B/Paris[2] 1762/09 F07/11 1A	B/HK[2] 514/09 F19/13 1B	B/Odessa[2] 3886/10 F13/15 1B	B/Malta[2] 636714/11 F33/11 1A	B/Jhb[2] 3964/12 F01/13 1A	B/For[4] V2367/12 F04/13 1A	B/Sth Aus[2] 81/12 F41/13 1A
REFERENCE VIRUSES													
B/Malaysia/2506/2004		2004-12-06	E3/E7	640	640	80	<	20	10	80	160	80	160
B/Brisbane/60/2008	1A	2008-08-04	E4/E5	1280	160	640	80	160	160	640	640	320	1280
B/Paris/1762/2009	1A	2009-02-09	C2/MDCK2	1280	10	20	80	160	160	20	40	80	160
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	640	<	20	80	80	160	10	40	40	80
B/Odessa/3886/2010	1B	2010-03-19	C2/MDCK2	1280	10	20	80	80	160	20	40	80	160
B/Malta/636714/2011	1A	2011-03-07	E4/E1	640	80	160	40	80	80	320	320	160	640
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	640	1280	160	320	160	1280	1280	1280	1280
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	1280	80	320	80	80	160	160	160	320	1280
B/South Australia/81/2012	1A	2012-11-28	E4/E2	1280	80	640	80	160	160	320	320	320	1280
TEST VIRUSES													
B/Norway/1570/2015		2015-03-06	MDCK1/MDCK3	1280	<	<	80	80	80	<	<	<	40
B/Finland/507/2015	1A	2015-03-31	MDCK2/MDCK1	1280	20	20	80	80	320	20	40	80	80
B/Finland/530/2015	1A	2015-04-20	MDCK1/MDCK1	1280	10	20	160	160	320	20	40	80	80
B/Norway/2102/2015	1A	2015-04-20	MDCK1	640	<	20	80	80	80	10	<	80	80
B/Norway/2179/2015	1A	2015-04-30	MDCK1	1280	20	40	160	320	160	40	80	80	160
									Vaccine*				

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

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

Sequences in phylogenetic tree

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

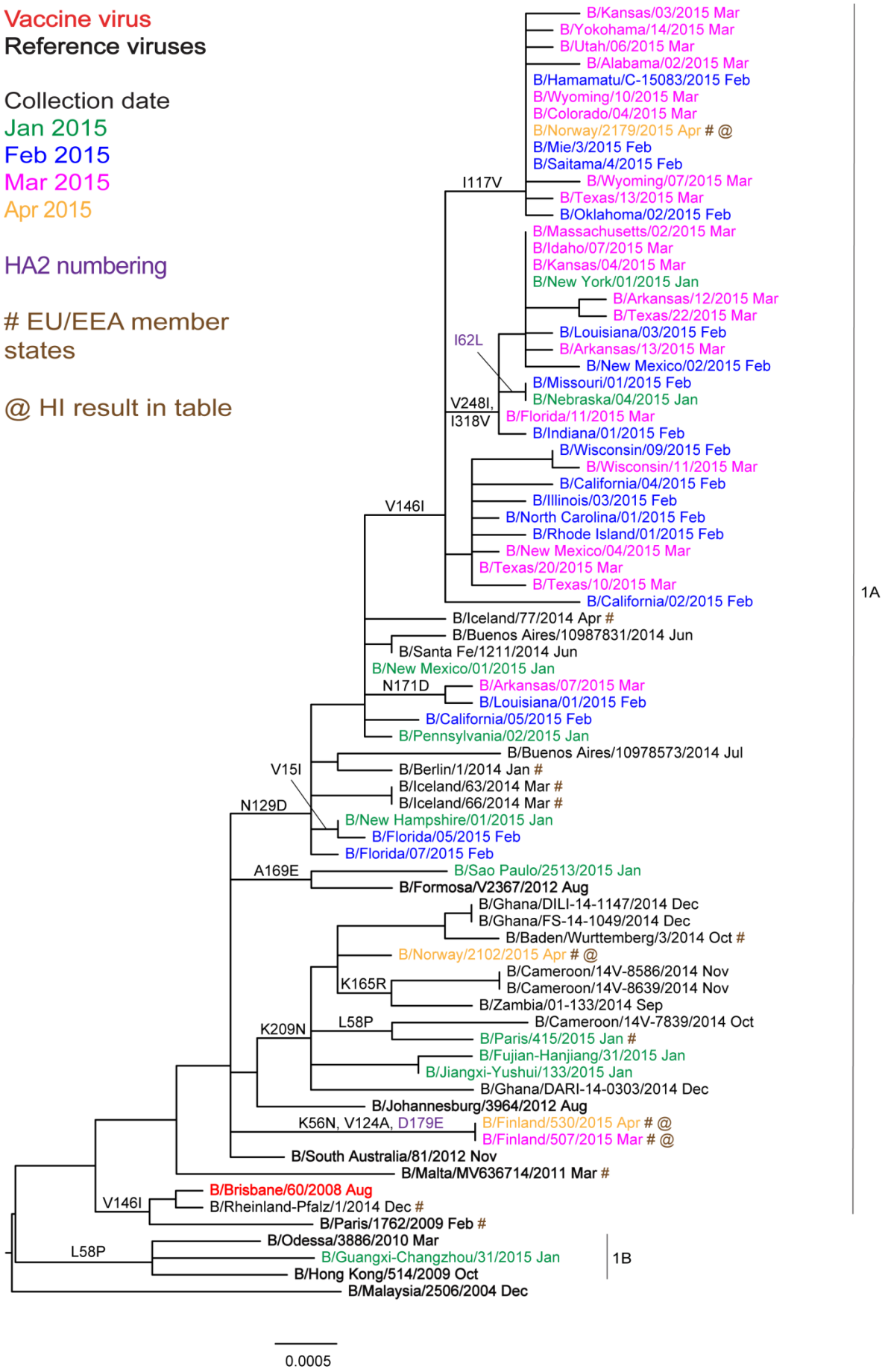


Table 5-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre: Post-infection ferret antisera										
				B/Fl[1,3] 4/06 SH479	B/Fl[1] 4/06 F1/10	B/Bris[1] 3/07 F38/14	B/Wis[2] 1/10 F10/13	B/Stock[2] 12/11 F12/12	B/Estonia2 55669/11 F32/12	B/Mass[2] 02/12 Egg F42/14	B/Mass[2] 02/12 T/C F15/13	B/Phuket[2] 3073/13 Egg F36/14	B/Phuket[2] 3073/13 T/C F35/14	B/HK[4] 3417/14 Egg St Judes F715/14
	1			1	1	2	3	3	2	2	2	3	3	3
REFERENCE VIRUSES														
B/Florida/4/2006	1	2006-12-15	E7/E1	2560	640	640	160	320	40	1280	320	160	20	160
B/Brisbane/3/2007	2	2007-09-03	E2/E3	1280	320	320	80	160	40	640	160	80	10	160
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	640	160	160	160	320	10	160	40	80	40	160
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	160	80	80	320	10	160	40	80	40	160
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	80	80	40	40	80	80	640	40	80	320
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	2560	640	640	160	320	80	1280	320	160	40	320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	320	320	160	640	640	160	80	640
B/Phuket/3073/2013	3	2013-11-21	E4/E3	640	160	160	160	320	10	160	40	80	40	160
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK2	1280	320	320	320	320	320	320	640	320	640	320
B/Hong Kong/3417/2014	3	2014-06-04	E4/E1	80	80	40	40	40	160	40	40	20	20	160
TEST VIRUSES														
B/Valladolid/137/2015		2015-01-28	MDCK1/MDCK1	320	80	80	160	160	40	160	160	80	320	160
B/Valladolid/138/2015	3	2015-01-28	MDCK1/MDCK1	640	80	160	160	160	160	160	320	160	640	160
B/Iasi/176858/2015		2015-01-30	MDCK1/MDCK1	160	160	160	320	320	160	320	320	320	640	160
B/Bucuresti/177398/2015	3	2015-02-09	MDCK1/MDCK1	80	80	80	160	160	80	160	160	160	320	160
B/Iasi/178240/2015		2015-02-25	MDCK1/MDCK1	80	80	80	320	320	80	320	640	320	640	320
B/Calarasi/178283/2015		2015-02-25	MDCK2/MDCK1	160	160	80	320	320	80	320	640	160	1280	320
B/Galati/178448/2015		2015-03-02	MDCK2/MDCK1	320	80	80	160	160	80	160	160	160	320	80
B/Dolj/178771/2015		2015-03-05	MDCK2/MDCK1	640	80	160	160	160	80	160	160	160	320	160
B/Dolj/179263/2015	3	2015-03-07	MDCK2/MDCK1	320	80	80	80	80	80	80	160	160	320	80
B/Constanta/179082/2015	3	2015-03-11	MDCK1/MDCK1	320	80	80	160	80	40	80	80	80	160	160
B/Teleorman/179501/2015	3	2015-03-18	MDCK1/MDCK1	320	80	80	160	160	40	160	160	80	160	160
B/Bucuresti/179506/2015		2015-03-18	MDCK1/MDCK1	640	80	160	320	160	160	320	320	160	640	320
B/Calarasi/179521/2015	3	2015-03-19	MDCK1/MDCK1	320	80	80	160	160	80	160	160	160	320	160
B/Tulcea/179584/2015	3	2015-03-19	MDCK2/MDCK1	320	80	80	160	160	80	160	160	160	320	160
B/Bucuresti/179677/2015	3	2015-03-21	MDCK1/MDCK1	320	80	80	160	80	40	80	80	80	160	160
B/Iasi/179780/2015	3	2015-03-25	MDCK1/MDCK1	320	80	80	160	160	40	80	80	80	160	160
										Vaccine NH2014-15		Vaccine SH2015 NH2015-16		

1. < = <40; 2. < = <10; 3. hyperimmune sheep serum; 4. RDE serum pre-absorbed with TRBC; 5. < = <20

Sequences in phylogenetic tree

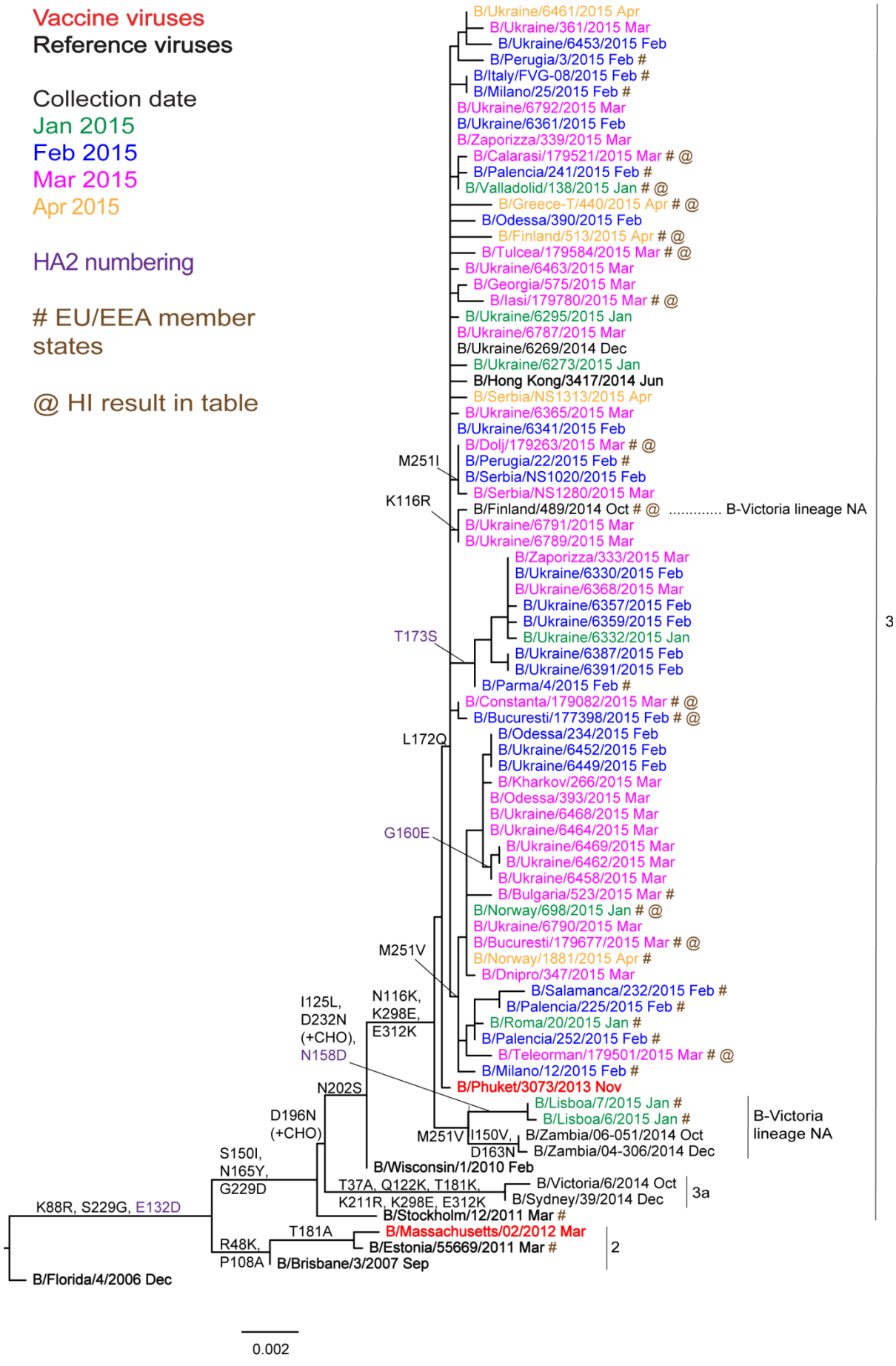
Table 5-2. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				B/Fl[1,3]	B/Fl[1]	B/Bris[1]	B/Wis[2]	B/Stock[2]	B/Estonia2	B/Mass[2]	B/Mass[2]	B/Phuket[2]	B/Phuket[2]	B/Phuket[2]	B/HK[4]
				4/06	4/06	3/07	1/10	12/11	55669/11	02/12	02/12	3073/13	3073/13	3073/13	3417/14
				SH479	F1/10	F38/14	F10/13	F12/12	F32/12	Egg F42/14	T/C F15/13	Egg F36/14	T/C F35/14	Egg St Judes F715/14	
				1	1	2	3	3	2	2	2	3	3		3
REFERENCE VIRUSES															
B/Florida/4/2006	1	2006-12-15	E7/E1	2560	640	640	160	320	80	640	320	320	40		320
B/Brisbane/3/2007	2	2007-09-03	E2/E3	1280	320	320	80	160	40	640	160	80	10		160
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	640	320	160	320	320	20	160	80	160	40		320
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	160	80	80	160	20	160	40	160	40		160
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	160	80	80	80	160	80	640	160	80		320
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	2560	640	640	160	320	80	1280	160	320	20		320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	320	320	160	640	640	320	160		640
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	320	320	320	320	20	160	80	320	80		320
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK2	2560	320	320	640	640	320	640	640	640	640		640
B/Hong Kong/3417/2014	3	2014-06-04	E4/E1	160	80	40	80	80	10	40	40	40	20		160
TEST VIRUSES															
B/Finland/489/2014	3	2014-10-31	MDCKx/MDCK1/MDCK1	320	80	40	160	80	40	40	80	160	80		160
B/Finland/527/2014	3	2014-10-31	MDCKx/MDCK1/MDCK1	320	160	80	160	160	40	80	80	160	160		320
B/Norway/698/2015	3	2015-01-29	MDCK1/MDCK1	320	160	160	160	320	40	320	80	160	160		320
B/Finland/513/2015	3	2015-04-02	MDCK1/MDCK1	320	80	80	160	80	40	40	80	160	160		320
B/Greece-T/440/2015	3	2015-04-17	MDCK1	320	80	80	160	160	40	80	160	160	160		320
										Vaccine NH2014-15		Vaccine SH2015 NH2015-16			

1. < = <40; 2. < = <10; 3. hyperimmune sheep serum; 4. RDE serum pre-absorbed with TRBC; 5. < = <20

Sequences in phylogenetic tree

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



Summary of genetic data submitted to TESSy

As of 17 May 2015 (to week 20/2015), the majority of influenza viruses identified genetically since week 40/2014 were A(H3N2) viruses (60%), with lower numbers of influenza B viruses (23%) and A(H1N1)pdm09 viruses (17%) being reported. All influenza A(H1N1)pdm09 viruses fell into genetic clade 6 with the great majority (98%) falling in genetic subgroup 6B, represented by A/South Africa/3626/2013. Influenza B viruses of the B/Yamagata lineage outnumbered those of the B/Victoria lineage by 41 to 1. The majority of influenza A(H3N2) viruses belonged to genetic subgroup 3C.2a (62%), represented by A/Hong Kong/5738/2014; smaller proportions were in genetic group 3C.3 (30%), represented by A/Samara/73/2013, genetic subgroup 3C.3a (< 7%), represented by A/Switzerland/9715293/2013, genetic group 3C.2, represented by A/Stockholm/1/2013 (< 1%), and genetic subgroup 3C.1 (1%), represented by A/Texas/50/2012, the vaccine virus for the 2014–15 northern hemisphere influenza season. For EU/EEA countries, similar proportions have been observed among the influenza-positive samples shared with the WHO CC, except for the small number of A(H3N2) subgroup 3C.1 detections.

Over the period of weeks 21–26/2015, influenza B has dominated with 434 detections (92 B/Yamagata, 1 B/Victoria and 341 not ascribed to lineage) with 195 influenza detections (66 H3N2, 34 H1N1pdm09 and 95 not subtyped). Of these 14 have been characterised genetically: three H1N1pdm09 (all subgroup 6B), 14 H3N2 (12 3C.2a, one 3C.3 and one 3C.3b) and five influenza B viruses (all B/Yamagata clade 3).

Antiviral susceptibility

Between weeks 40/2014–20/2015, based on reports to TESSy, 2616 influenza viruses (1535 A(H3N2), 566 A(H1N1)pdm09 and 515 type B) were subjected to phenotypic or genotypic testing for neuraminidase inhibitor (NAI) susceptibility. Four A(H3N2) viruses showed reduced susceptibility to oseltamivir with three viruses carrying NA E119V amino acid substitution and one carrying NA R292K substitution. The latter virus showed reduced susceptibility to zanamivir. Two A(H1N1)pdm09 viruses showed reduced susceptibility to oseltamivir.

A total of 715 viruses, with collection dates after 31 August 2014, from EU/EEA countries have been assessed phenotypically for NAI susceptibility at the London WHO CC: 149 influenza B, 137 A(H1N1)pdm09 and 429 A(H3N2) inclusive of many 3C.2a genetic subgroup viruses that could not be analysed by HI assay. All but one influenza B/Yamagata-lineage virus were susceptible to oseltamivir and zanamivir. The B/Yamagata-lineage virus showed reduced inhibition by oseltamivir and zanamivir, and carried NA amino acid substitution D197G.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [2] 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 [3]. Increased numbers of cases were reported over the course of the 2013–14 and 2013–14 seasons. 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 23 June 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 15 June 2015 [9].

Influenza A(H5N1) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 23 June 2015 [6]. The assessment included a description of a further two new laboratory-confirmed human cases of avian influenza A(H5N1) virus infection in Egypt. This represents a further reduced number of new cases compared to earlier recent reports. ECDC published an updated rapid risk assessment on the situation in Egypt on 13 March 2015 [10] and an epidemiological update 10 April 2015 [11]. On 14 July 2015 the WHO reported on a recent fatal case of human infection with avian A(H5N6) virus in China [12].

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 in London, and used at the WHO Vaccine Composition Meetings held at WHO Geneva on 22–24 September 2014 and 23–25 February 2015, can be found at:

http://crick.ac.uk/media/221823/nimr-vcm-report-sep-14-web.pdf
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 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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