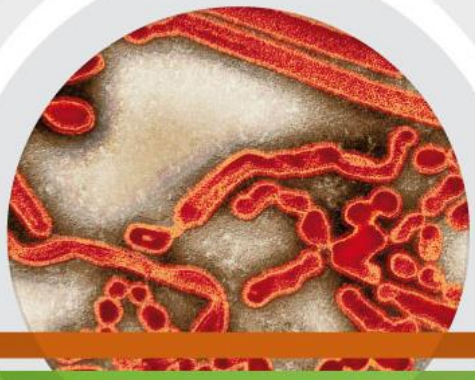

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, September 2014

Summary

During the 2013–14 season, A(H1N1)pdm09, A(H3N2), B/Victoria- and B/Yamagata-lineage influenza viruses co-circulated in EU/EEA Member States. The relative prevalence has varied between countries. The WHO Collaborating Centre in London received viruses with collection dates after 31 January 2014 from 21 EU/EEA countries.

Type A and type B viruses have been received at a ratio of approximately 10:1. A(H3N2) outnumbered A(H1N1)pdm09 viruses at a ratio of 1.4:1.

Recently circulating A(H1N1)pdm09 viruses, in Europe and worldwide, belonged to genetic subgroup 6B. Viruses in this subgroup are antigenically similar to the vaccine virus, A/California/07/2009.

Recently circulating A(H3N2) viruses have fallen within genetic group 3C represented by the recommended vaccine virus for the 2013–14 and 2014–15 seasons, A/Texas/50/2012. Antigenic analysis using antisera raised against cell-propagated H3N2 viruses indicates that the majority of circulating viruses are antigenically similar to those in circulation in the 2012–13 and 2013–14 influenza seasons, but those in a newly emerging genetic cluster, 3C.3a, are poorly recognised by some antisera.

Two genetic clades of B/Yamagata-lineage viruses continue to circulate: clade 3 represented by B/Phuket/3073/2013 and clade 2 represented by B/Massachusetts/02/2012 (the recommended vaccine component for the 2013–14 and 2014–15 influenza seasons). Viruses in clade 3 predominate in those samples collected since 31 January 2014.

Only two viruses of the B/Victoria-lineage were antigenically characterised since the July 2014 report. Neither was recognised well by the antiserum raised against the egg-propagated reference virus, A/Brisbane/60/2008, recommended as a component of quadrivalent influenza vaccines for 2013–14 and 2014–15 influenza seasons. Phylogenetic analysis revealed that all B/Victoria-lineage viruses received in 2014 were in genetic clade 1A, the B/Brisbane/60/2008 genetic clade.

In light of the emergence of antigenically distinct groups of influenza A(H3N2) and the altered prevalence of influenza B viruses, the WHO recommended composition of influenza vaccines for use in the 2015 southern hemisphere influenza season differed from that recommended for use in the 2014–15 northern hemisphere influenza season.

This report was prepared by Rod Daniels, Vicki Gregory 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, 386 viruses or clinical specimens, with collection dates after 31 January 2014 have been received at the MRC National Institute for Medical Research, WHO Collaborating Centre for Reference and Research on Influenza (WHO CC), from 21 countries in the EU/EEA region. The large majority (91.5%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 1.4:1 (Table 1). Of the small number of type B viruses received (~8.5% of the specimens), viruses of the B/Yamagata-lineage outnumbered those of the B/Victoria-lineage at a ratio of ~2.5:1.

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

MONTH	TOTAL RECEIVED	A	H1N1pdm09		H3N2		B	B Victoria lineage		B Yamagata lineage	
Country			Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]
FEBRUARY											
Austria	3				3	3					
Belgium	6		3	1	3	2					
Bulgaria	26		20	20	6	5					
Cyprus	12	1	11	11							
Finland	8		3	3	5	4					
Germany	11		4	4	3	3		2	2	2	2
Hungary	7		5	5	2	1					
Iceland	6		3	3	3	3					
Ireland	4		4	4							
Italy	28		12	11	14	14				2	2
Latvia	1		1	1							
Lithuania	4	1	1	1	2	2					
Norway	13		5	4	8	7					
Poland	9		2	1	7	5					
Portugal	6		4	4	1	1				1	1
Slovakia	5		3	3	2	2					
Slovenia	20		6	6	14	11					
Spain	1				1	0					
Sweden	7		1	1	4	4				2	2
United Kingdom	3				2	1		1	1		
MARCH											
Austria	10		2	2	5	5				3	3
Belgium	7		4	2	3	1					
Bulgaria	1		1	1							
Finland	3		1	1	2	2					
France	15		10	10	4	4				1	1
Iceland	7		4	4	1	1		2	2		
Ireland	2		2	2							
Italy	3		2	2	1	1					
Latvia	11		7	5	3	3				1	1
Lithuania	10				10	10					
Norway	7				6	4		1	1		
Poland	26	1	2	0	23	9					
Portugal	2		1	1	1	1					
Slovakia	3		1	1	1	1				1	1
Slovenia	3		2	2	1	1					
Spain	2		1	1						1	1
United Kingdom	8		4	4	2	2		1	1	1	1
APRIL											
Austria	3		1	1	2	2					
Belgium	10		2	1	7	4		1	1		
Finland	3				3	3					
France	8		3	3	5	4					
Iceland	3		2	2				1	1		
Ireland	7		1	1	6	6					
Latvia	2				2	2					
Lithuania	8				8	8					
Norway	1				1	1					
Poland	3		2	0	1	1					
Portugal	1				1	1					
Slovakia	3		1	1	2	2					
Slovenia	2		1	1	1	1					
Spain	7				7	7					
MAY											
France	1									1	1
Iceland	3				2	2				1	1
Lithuania	1				1	1					
Norway	5		2	1	1	1				2	2
Portugal	1									1	1
United Kingdom	1				1	1					
JUNE											
France	1		1	1							
Iceland	1				1	1					
Norway	4				3	2				1	1
Spain	1				1	1					
United Kingdom	1				1	1					
JULY											
Spain	4				1	1	1			2	2
AUGUST											
France	1				1	1					
	386	3	148	133	202	167	1	9	9	23	23
			38.3%		52.3%			2.3%		6.0%	
21 Countries		91.5%					8.5%				

1. Propagated to sufficient titre to perform HI assay (the totalled number does not include any from batches that are in process)
2. Propagated to sufficient titre to perform HI assay in presence of 20nM oseltamivir (the totalled number does not include any from batches that are in process)

Influenza A(H1N1)pdm09 virus analyses

The results of haemagglutination inhibition (HI) analyses of viruses performed since the July 2014 report[1] are shown in Tables 2-1 to 2-3. The test viruses were antigenically similar to the vaccine virus, A/California/7/2009; all test viruses analysed since the July 2014 report were recognised well by an antiserum raised against A/California/7/2009, with no virus showing more than a twofold decrease in titre compared to that obtained with the homologous virus. This indicates that no significant antigenic drift has occurred. For test viruses with known HA gene sequences, the genetic group to which the virus belongs is indicated.

Figure 1 shows a phylogenetic tree for the HA genes of representative A(H1N1)pdm09 viruses. Since 2009, the HA genes have evolved, and eight genetic groups have been designated, with A/California/7/2009 representing group 1. However, over the last season viruses in genetic group 6 have predominated, and all EU/EEA viruses characterised since the July 2014 report carried HA genes in genetic subgroup 6B. This subgroup carries the amino acid substitutions **D97N**, **K163Q, S185T, S203T, A256T** and **K283E** in **HA1** and **E47K, S124N and E172K** in **HA2** compared with A/California/7/2009.

Table 2-1. 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 F30/11	A/Bayern 69/09 F11/11	A/Lviv N6/09 C4/09/34	A/Chch 16/10 F30/10 4	A/HK 3934/11 F21/11 3	A/Astrak 1/11 F22/13 5	A/St. P 27/11 F23/11 6	A/St. P 100/11 F24/11 7	A/Sth Afr 3626/13 F3/14 6B	
REFERENCE VIRUSES													
A/California/7/2009		2009-04-09	E1/E2	640	640	640	160	160	160	160	320	160	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	320	640	160	40	40	80	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	320	160	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	2560	2560	5120	1280	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	640	320	640	320	1280	1280	1280	2560	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	1280	640	1280	640	1280	1280	1280	5120	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	640	1280	1280	1280	5120	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	1280	1280	1280	2560	2560	5120	1280	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	1280	1280	640	1280	1280	1280	2560	1280	
TEST VIRUSES													
A/Hungary/366/2014	6B	2014-01-02	MDCK2/E2/MDCK1	320	160	320	320	640	640	640	1280	1280	
A/Hungary/386/2014		2014-01-27	MDCK2/E2/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	
A/Hungary/399/2014	6B	2014-01-27	MDCK2/E2/MDCK1	640	640	640	640	1280	1280	1280	2560	1280	
A/Hungary/400/2014	6B	2014-02-04	MDCK2/E2/MDCK1	320	160	640	320	640	640	640	1280	640	
A/Hungary/403/2014		2014-02-06	MDCK2/E2/MDCK1	1280	320	640	640	1280	1280	1280	2560	1280	
A/Hungary/410/2014	6B	2014-02-06	MDCK2/E2/MDCK1	640	320	640	320	1280	640	1280	2560	1280	
A/Hungary/418/2014	6B	2014-02-10	MDCK2/E2/MDCK1	1280	640	640	640	1280	1280	1280	2560	1280	
A/Norway/681/2014		2014-02-11	MDCK3/MDCK2	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Norway/667/2014	6B	2014-02-17	MDCK2/MDCK2	2560	1280	2560	1280	1280	2560	5120	5120	2560	
A/Norway/778/2014	6B	2014-02-19	MDCK2/MDCK2	2560	1280	2560	2560	1280	2560	2560	5120	2560	
A/Norway/686/2014	6B	2014-02-24	MDCK3/MDCK2	1280	320	1280	640	640	1280	2560	2560	1280	
Sequences in phylogenetic trees				Vaccine									

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

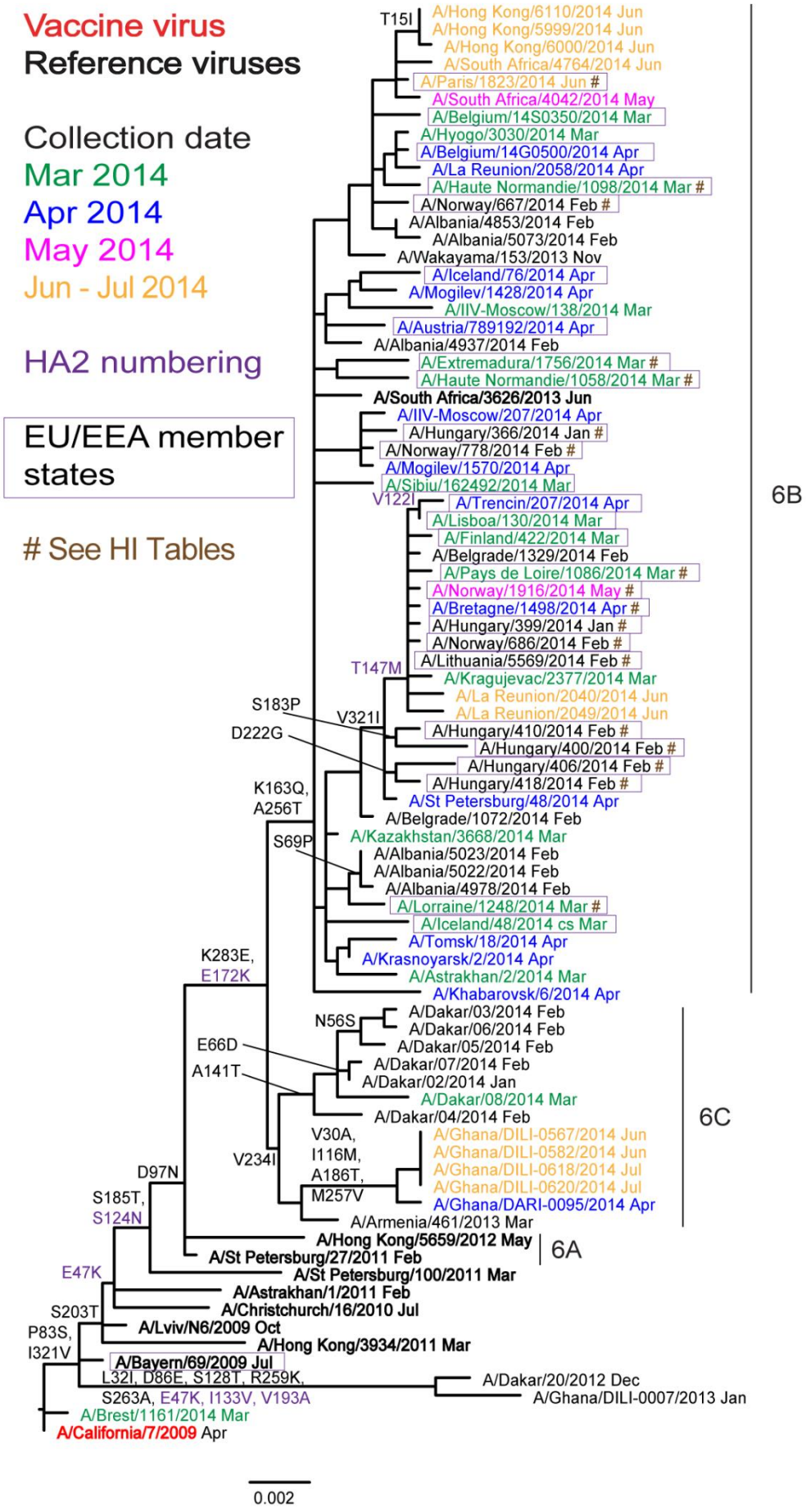
Table 2-2. Antigenic analysis of A(H1N1)pdm09 viruses by HI

				Haemagglutination inhibition titre										
				Post infection ferret antisera										
Viruses		Collection date	Passage History	A/Cal 7/09 F30/11	A/Bayern 69/09 F11/11	A/Lviv N6/09 C4/09/34	A/Chch 16/10 F30/10	A/HK 3934/11 F21/11	A/Astrak 1/11 F22/13	A/St. P 27/11 F23/11	A/St. P 100/11 F24/11	A/HK 5659/12 F30/12	A/Sth Afr 3626/13 F3/14	
	Genetic group						4	3	5	6	7	6A	6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	EP1/E2	1280	1280	2560	320	320	640	640	640	640	640	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	320	640	320	80	40	80	160	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	320	160	320	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	5120	2560	5120	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	640	320	1280	640	1280	1280	1280	2560	2560	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	1280	640	2560	640	2560	2560	2560	5120	5120	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	2560	640	2560	2560	2560	5120	5120	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	2560	640	2560	2560	2560	5120	5120	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	640	320	1280	320	1280	1280	1280	5120	1280	1280	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	1280	1280	640	1280	1280	1280	2560	1280	2560	
TEST VIRUSES														
A/Hungary/367/2014		2014-01-08	MDCK1/E2/MDCK1	640	640	1280	640	1280	1280	2560	5120	1280	2560	
A/Hungary/406/2014	6B	2014-02-06	MDCK2/E2/MDCK1	640	640	1280	640	1280	1280	1280	2560	1280	1280	
A/Lithuania/5569/2014	6B	2014-02-24	MDCK1/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	5120	2560	
A/Paris/976/2014	6B	2014-03-06	MDCK1/MDCK1	1280	1280	2560	1280	5120	5120	5120	5120	5120	5120	
A/Paris/1050/2014	6B	2014-03-10	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	
A/Haute Normandie/1058/2014	6B	2014-03-11	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	
A/Paris/1045/2014	6B	2014-03-13	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	
A/Pays de Loire/1086/2014	6B	2014-03-14	MDCK1/MDCK1	2560	640	2560	2560	2560	2560	2560	5120	5120	5120	
A/Lorraine/1078/2014	6B	2014-03-17	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Haute Normandie/1098/2014	6B	2014-03-17	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	
A/Picardie/1221/2014	6B	2014-03-17	MDCK1/MDCK1	1280	1280	2560	1280	2560	2560	2560	5120	5120	2560	
A/Extremadura/1756/2014	6B	2014-03-17	SIAT1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Paris/1126/2014	6B	2014-03-21	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	
A/Lorraine/1248/2014	6B	2014-03-31	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Centre/1238/2014	6B	2014-04-01	MDCK1/MDCK1	1280	1280	2560	2560	2560	5120	5120	5120	5120	5120	
A/Bretagne/1498/2014	6B	2014-04-14	MDCK1/MDCK1	1280	1280	2560	2560	5120	5120	2560	5120	5120	5120	
A/Centre/1550/2014	6B	2014-04-22	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	2560	5120	5120	5120	
A/Norway/1916/2014	6B	2014-05-15	MDCK1/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	2560	
A/Paris/1823/2014	6B	2014-06-11	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	
Sequences in phylogenetic trees				Vaccine										

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

				Haemagglutination inhibition titre[1]										
				Post infection ferret antisera										
Viruses		Collection date	Passage History	A/Cal 7/09 F30/11	A/Bayern 69/09 F11/11	A/Lviv N6/09 F14/13	A/Chch 16/10 F30/10	A/HK 3934/11 F21/11	A/Astrak 1/11 F22/13	A/St. P 27/11 F23/11	A/St. P 100/11 F24/11	A/HK 5659/12 F30/12	A/Sth Afr 3626/13 F3/14	X-243 NIBSC F48/14	
	Genetic group						4	3	5	6	7	6A	6B	6B	
REFERENCE VIRUSES															
A/California/7/2009		2009-04-09	EP1/E2	1280	1280	1280	320	320	320	640	1280	320	640	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	320	640	640	80	80	80	160	160	80	160	40	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	2560	160	80	160	320	160	320	160	80	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	2560	2560	5120	2560	2560	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	640	320	640	640	1280	1280	1280	2560	1280	1280	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	2560	1280	1280	1280	2560	2560	2560	5120	5120	2560	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	1280	1280	2560	2560	5120	2560	2560	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	1280	1280	1280	2560	2560	5120	2560	1280	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	640	320	640	640	1280	2560	2560	5120	2560	1280	1280	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	1280	1280	1280	640	1280	1280	1280	5120	1280	2560	2560	
X-243 (A/South Africa/3626/2013)	6B	2013-06-06	EX/E1	2560	1280	2560	2560	5120	5120	5120	5120	5120	2560	5120	
TEST VIRUSES															
A/Estonia/84627/2014		2014-02-10	MDCK2/MDCK1	2560	640	1280	2560	2560	2560	5120	5120	5120	5120	2560	
A/Estonia/84639/2014	6B	2014-02-10	MDCK2/MDCK1	1280	320	640	640	1280	2560	2560	5120	2560	2560	2560	
A/Estonia/84981/2014		2014-02-20	MDCK2/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/85066/2014		2014-02-21	MDCK2/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	5120	
A/Estonia/85108/2014		2014-02-25	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/84490/2014		2014-02-06	MDCK2/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	5120	
A/Estonia/85212/2014		2014-02-27	MDCK2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/85246/2014		2014-02-28	MDCK1/MDCK1	2560	640	1280	2560	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/85353/2014		2014-03-04	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	5120	
A/Estonia/85408/2014		2014-03-05	MDCK2/MDCK1	2560	1280	2560	2560	2560	5120	5120	5120	5120	2560	5120	
A/Estonia/85422/2014		2014-03-06	MDCK2/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	5120	
A/Estonia/85519/2014	6B	2014-03-10	MDCK1/MDCK1	1280	640	1280	1280	1280	2560	2560	5120	2560	2560	1280	
A/Estonia/85629/2014		2014-03-13	MDCK2/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	2560	
A/Estonia/85660/2014		2014-03-13	MDCK2/MDCK1	1280	1280	1280	1280	2560	5120	5120	5120	5120	5120	2560	
A/Estonia/85729/2014		2014-03-17	MDCK1/MDCK1	2560	1280	2560	1280	2560	2560	5120	5120	5120	5120	2560	
A/Estonia/85739/2014	6B	2014-03-18	MDCK2/MDCK1	1280	640	640	640	1280	1280	2560	5120	2560	2560	1280	
A/Estonia/85759/2014		2014-03-18	MDCK2/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/85792/2014		2014-03-19	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	2560	
A/Estonia/85847/2014		2014-03-20	MDCK2/MDCK1	1280	1280	1280	1280	2560	5120	2560	5120	5120	2560	2560	
A/Estonia/85829/2014	6B	2014-03-21	MDCK2/MDCK1	640	640	640	640	1280	1280	1280	2560	2560	1280	1280	
A/Estonia/85899/2014		2014-03-25	MDCK2/MDCK1	2560	1280	2560	1280	2560	2560	2560	5120	5120	2560	2560	
A/Estonia/86382/2014	6B	2014-04-16	MDCK2/MDCK1	2560	1280	2560	2560	5120	5120	5120	5120	5120	5120	5120	
				Vaccine											

Figure 1. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes



Influenza A(H3N2) virus analyses

As described in many previous reports[2], influenza A(H3N2) viruses continue to be difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells from guinea pigs, turkeys and humans. All but two of the viruses examined since the July 2014 report had sufficient HA titre in assays conducted using guinea pig red blood cells in the presence of 20nM oseltamivir (added to circumvent any NA-mediated binding of H3N2 viruses to red blood cells) to be analysed by HI assay.

HI results are shown in Tables 3-1 to 3-3. The genetic group of the HA gene is indicated for viruses for which gene sequences have been determined.

All but five of the 47 test viruses analysed since the July 2014 report 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. Similar results were seen with antisera raised against the egg-propagated reference viruses A/Hong Kong/146/2013 and A/South Africa/4655/2013 with only seven and 11 test viruses, respectively, being recognised at titres within fourfold of the titres of the antisera with their homologous viruses. Somewhat better reactivity was observed with antiserum raised against egg-propagated A/Stockholm/1/2013, with 26 (79%) of 33 test viruses reacting within fourfold of the titre of the antiserum with the homologous virus (Tables 3-2 and 3-3).

Ferret antisera raised against reference viruses exclusively propagated in tissue culture cells – A/Samara/73/2013, A/Stockholm/6/2014, A/Norway/466/2014, A/Switzerland/9715293/2013 (Table 3-1), and the exclusively cell-propagated cultivar of A/Victoria/361/2011 – recognised the test viruses more effectively. The reference viruses A/Stockholm/6/2014, A/Norway/466/2014 and A/Switzerland/9715293/2013 are representative of an emerging genetic cluster of viruses, 3C.3a. Viruses with HA genes falling into the 3C.3a genetic cluster were recognised less well by antisera raised against the cell-propagated cultivar of A/Victoria/361/2011 and A/Samara/73/2013 than those with HA genes in genetic subgroup 3C (see July 2014 report). Antisera raised against cell-propagated reference viruses A/Stockholm/6/2014, A/Norway/466/2014 and A/Switzerland/9715293/2013 recognised the majority of viruses from each genetic grouping at titres within twofold of the titres of the antisera with their homologous viruses.

Since 2009, seven genetic groups based on the HA gene have been defined for H3N2 viruses. Phylogenetic analysis of the HA genes of representative, recently circulating H3N2 viruses is shown in Figure 2. The vaccine virus A/Texas/50/2012 belongs to genetic subgroup 3C.1. Viruses characterised genetically since the July 2014 report fall into subgroups 3C.2, 3C.3 and 3C.3a, with viruses in 3C.3 predominating (Figure 2). Amino acid substitutions that define subgroups 3C.2, 3C.3 and 3C.3a are:

- 3C.2 N145S in **HA1**, and **D160N** in **HA2**, e.g. A/Hong Kong/146/2013;
- 3C.3 **T128A** (resulting in the loss of a potential glycosylation site), **R142G,** and **N145S** in **HA1**, e.g. A/Samara/73/2013; and
- 3C.3a Those in 3C.3 plus **A138S**, **F159S** and **N225D** in **HA1**, many with **K326R**, e.g. A/Switzerland/9715293/2013.

Another emerging genetic cluster of viruses based on the HA gene, designated 3C.2a, has been observed. Viruses in this cluster carry the amino acid substitutions **L3I, N144S, F159Y, K160T, N225D** and **Q311H** in **HA1**. The substitutions at residues 144 and 160 result in the loss and the gain, respectively, of potential N-linked glycosylation sites at residues 144 and 158 of **HA1**.

In light of the emergence of antigenically distinct groups of influenza A(H3N2) viruses the WHO recommended composition of influenza vaccines for use in the 2015 southern hemisphere influenza season differed from that recommended for use in the 2014–15 northern hemisphere influenza season. The recommendation made on 25 September 2014 was that the vaccine should contain an A/Switzerland/9715293/2013 (H3N2)-like virus, and advised that A/Norway/466/2014, A/Stockholm/6/2014 and A/South Australia/55/2014 are A/Switzerland/9715293/2013 (H3N2)-like viruses [7]. Egg-propagated cultivars of these four viruses are available for development for use in vaccines. Each egg-propagated virus has acquired HA amino acid substitutions during propagation. As in previous years, the antigenic properties of the vaccine virus are influenced by adaptation to propagation in eggs and post-infection ferret antisera raised against many of the potential, egg-propagated, candidate vaccine viruses show poor recognition of currently circulating viruses propagated in cell culture.

[2] 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

Table 3-1. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Genetic group	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 3C.1	A/Texas 50/12 Egg F42/13 3C.1	A/Samara 73/13 F24/13 3C.3	A/HK 146/13 F40/13 3C.2	A/Sth Afr 4655/13 F10/14 3C.3 cl 101-60	A/Stock 6/14 F14/14 3C.3a	A/Nor 466/14 F13/14 3C.3a	A/Switz 9715293/13 NIBSC 13/4 3C.3a
REFERENCE VIRUSES												
A/Perth/16/2009		2009-07-04	E3/E3	640	80	160	160	160	40	80	40	<
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	160	320	320	640	320	160	640	320	160
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	640	80	320	80	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	320	320	320	1280	640	160	640	320	160
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	640	640	640	1280	2560	160	160	80	80
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	80	160	320	320	320	160	80	40
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT1	<	80	80	320	160	80	640	320	160
A/Norway/466/2014	3C.3a	2014-02-03	SIAT2/SIAT2	<	<	40	160	80	40	640	320	160
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	<	40	80	320	160	80	640	320	160
TEST VIRUSES												
A/Hungary/480/2014		2014-02-24	MDCK3/E2/SIAT2	40	80	80	160	80	40	320	160	40
A/Haute Normandie/1087/2014	3C.2	2014-03-17	MDCK1/SIAT3	40	160	80	320	160	80	320	160	40
A/Paris/1124/2014	3C.3	2014-03-21	MDCK1/SIAT2	40	160	80	320	160	40	320	160	80
A/Pays de Loire/1260/2014	3C.3	2014-03-26	MDCK1/SIAT2	80	160	160	640	320	80	640	320	80
A/Pays de Loire/1262/2014	3C.3	2014-03-29	MDCK1/SIAT2	80	160	160	640	320	80	640	320	80
A/Bretagne/1267/2014	3C.3	2014-04-02	MDCK1/SIAT2	80	160	160	640	320	80	640	320	80
A/Paris/1268/2014	3C.3	2014-04-07	MDCK1/SIAT2	40	160	80	320	160	40	320	160	40
A/Centre/1329/2014	3C.3	2014-04-08	MDCK2/SIAT2	40	80	80	160	160	40	320	160	40
A/Centre/1497/2014	3C.2	2014-04-14	MDCK1/SIAT2	80	160	160	320	320	80	320	160	80
A/Norway/2006/2014	3C.3a	2014-06-17	SIAT1	40	160	80	320	160	80	640	160	80
A/Norway/2034/2014	3C.3a	2014-06-23	SIAT1	40	80	80	320	160	40	320	160	40
A/Lithuania/9947/2014		2014-04-02	SIAT2	40	80	80	160	160	<	160	80	160
A/Norway/1648/2014		2014-04-25	SIAT3	80	80	160	320	160	<	320	80	160
A/Paris/1846/2014	3C.3a	2014-08-17	MDCK1/SIAT1	<	40	40	160	80	40	640	320	80

1. < = <40

Vaccine

Sequences in phylogenetic trees

Table 3-2. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] Post infection ferret antisera A/Perth 16/09 F35/11	A/Vic 361/11 T/C F09/12 3C.1	A/Texas 50/12 Egg F36/12 3C.1	A/Samara 73/13 F24/13 3C.3	A/HK 146/13 F40/13 3C.2	A/Sth Afr 4655/13 F10/14 3C.3 cl 101-60	A/Stock 1/13 F12/14 3C.2 cl 36-18	A/Stock 6/14 F14/14 3C.3a	A/Nor 466/14 F13/14 3C.3a
REFERENCE VIRUSES												
A/Perth/16/2009		2009-07-04	E3/E3	1280	160	320	160	160	40	80	80	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	160	320	1280	1280	640	160	160	640	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	1280	5120	640	640	80	160	160	40
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	320	1280	1280	1280	160	320	640	320
A/Hong Kong/146/2013	3C.2	2013-01-11	E6	320	320	2560	640	1280	80	320	80	80
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	40	160	320	320	320	320	160	80
A/Stockholm/1/2013	3C.2	2013-01-13	E7 clone 36-18	40	40	160	160	160	320	320	80	40
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT1	<	80	80	160	160	40	80	640	160
A/Norway/466/2014	3C.3a	2014-02-03	SIAT2/SIAT2	<	40	40	80	40	<	80	320	160
TEST VIRUSES												
A/Lithuania/5009/2014	3C.3	2014-02-17	MDCK2/SIAT1	<	40	320	160	40	<	40	160	80
A/Lithuania/5879/2014	3C.3	2014-02-25	MDCK2/SIAT1	<	40	160	160	40	<	40	160	80
A/Lithuania/7266/2014		2014-03-10	MDCK2/SIAT1	40	320	640	640	320	40	80	160	160
A/Lithuania/7452/2014	3C.3	2014-03-12	MDCK2/SIAT1	<	80	320	160	80	<	40	160	80
A/Lithuania/7489/2014		2014-03-13	MDCK2/SIAT1	80	160	640	640	320	40	160	320	160
A/Lithuania/7802/2014	3C.3	2014-03-17	MDCK2/SIAT1	<	160	640	320	160	160	160	320	160
A/Lithuania/8237/2014	3C.3	2014-03-19	MDCK3/SIAT1	160	320	1280	640	640	80	80	320	320
A/Lithuania/8397/2014		2014-03-19	MDCK4/SIAT1	<	160	320	320	160	160	80	320	160
A/Lithuania/9144/2014		2014-03-22	MDCK2/SIAT1	<	80	160	160	80	<	40	160	160
A/Lithuania/9133/2014	3C.3	2014-03-27	MDCK2/SIAT1	<	80	640	320	160	40	80	320	160
A/Lithuania/9404/2014		2014-03-28	MDCK2/SIAT1	40	160	640	320	320	40	80	320	320
A/Lithuania/9430/2014	3C.3	2014-03-30	MDCK2/SIAT1	<	40	160	160	80	<	40	160	80
A/Lithuania/10213/2014		2014-04-07	MDCK2/SIAT1	40	80	320	320	160	40	80	160	160
A/Lithuania/10373/2014	3C.3	2014-04-07	MDCK2/SIAT1	<	80	160	160	80	<	80	160	80
A/Lithuania/10543/2014	3C.3	2014-04-08	MDCK2/SIAT1	40	160	640	320	160	40	80	320	160
A/Lithuania/10716/2014	3C.3	2014-04-11	MDCK2/SIAT1	40	160	640	320	320	40	80	320	160
A/Lithuania/11727/2014		2014-04-11	MDCK2/SIAT1	40	160	1280	320	160	40	80	320	160
A/Lithuania/11496/2014	3C.3	2014-04-18	MDCK2/SIAT1	40	160	320	320	160	40	80	320	160
A/Lithuania/11607/2014		2014-04-18	MDCK2/SIAT1	<	80	160	160	80	<	40	160	80
A/Lithuania/13347/2014	3C.3	2014-05-08	MDCK2/SIAT1	40	80	320	320	160	<	80	320	160
A/Norway/1903/2014	3C.2	2014-05-20	MDCK1/SIAT1	<	80	160	160	80	<	40	160	80

1. < = <40

Vaccine

Sequences in phylogenetic trees

Table 3-3. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

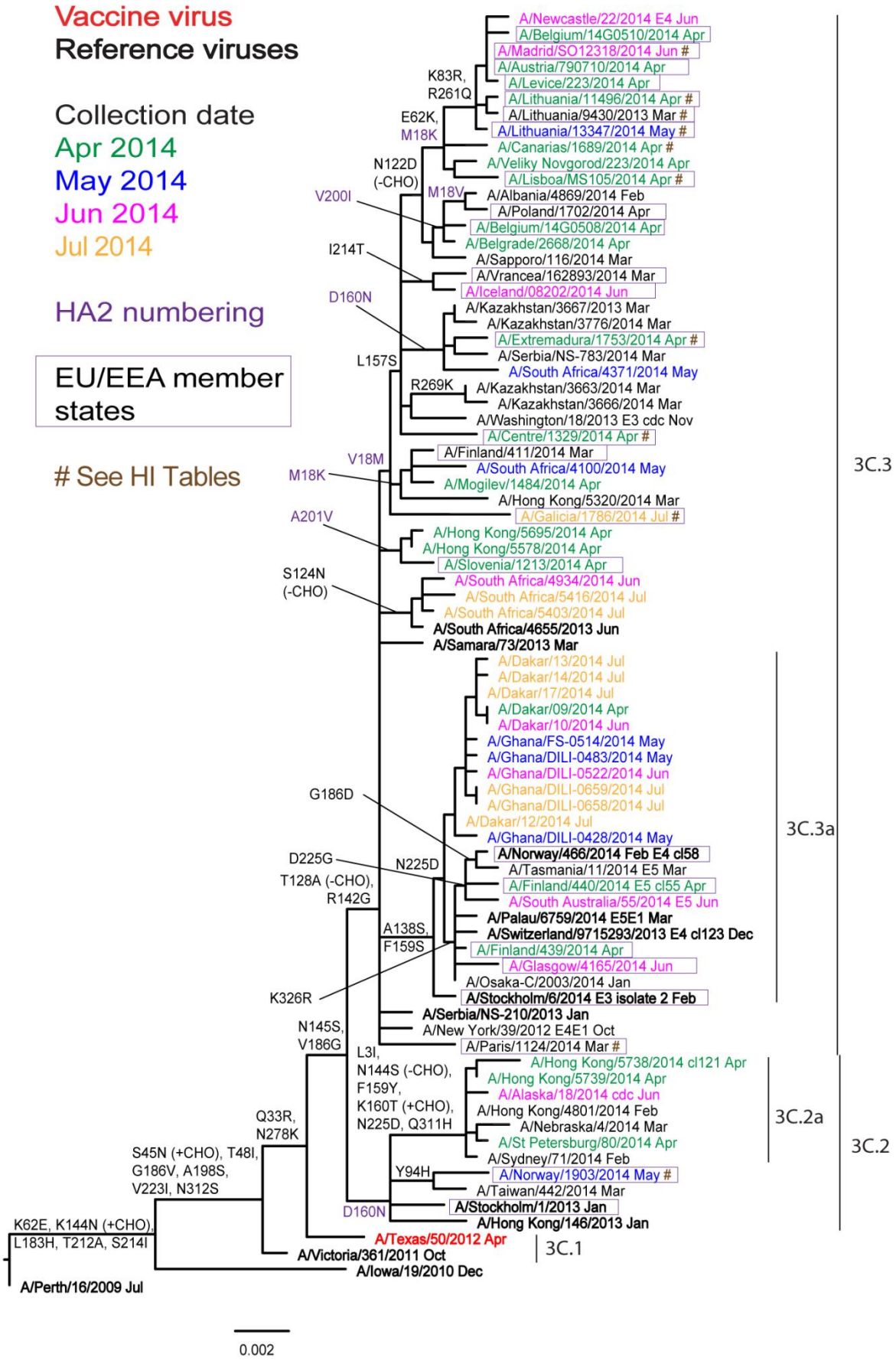
Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] Post infection ferret antisera								
				A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12	A/Texas 50/12 Egg F42/13	A/Samara 73/13 F24/13	A/HK 146/13 F40/13	A/Sth Afr 4655/13 F10/14	A/Stock 1/13 F12/14	A/Stock 6/14 F14/14	A/Nor 466/14 F13/14
					3C.1	3C.1	3C.3	3C.2	3C.3 cl 101-60	3C.2 cl 36-18	3C.3a	3C.3a
REFERENCE VIRUSES												
A/Perth/16/2009		2009-07-04	E3/E3	1280	160	320	160	320	40	160	80	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	320	320	320	1280	640	160	320	640	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	1280	160	320	320	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	320	320	320	1280	640	160	320	1280	320
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	640	640	640	1280	2560	160	320	160	160
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	160	320	640	640	640	640	320	160
A/Stockholm/1/2013	3C.2	2013-01-13	E7 clone 36-18	80	80	160	320	320	320	320	160	80
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT2	<	80	80	320	160	80	160	640	320
A/Norway/466/2014	3C.3a	2014-02-03	SIAT2/SIAT2	<	40	40	160	80	40	80	640	320
TEST VIRUSES												
A/Lisboa/SU540/2014	3C.2	2014-02-26	SIAT2	80	80	80	320	160	40	80	80	160
A/Lisboa/MS102/2014	3C.3	2014-03-19	SIAT2	<	80	80	320	160	40	80	320	160
A/Lisboa/MS105/2014	3C.3	2014-04-02	SIAT1	80	160	160	320	160	80	160	320	320
A/Extremadura/1753/2014	3C.3	2014-04-07	SIAT1/SIAT1	80	160	160	640	160	40	80	160	160
A/Canarias/1686/2014		2014-04-08	SIAT1/SIAT1	160	160	320	640	320	80	160	640	320
A/Canarias/1687/2014	3C.3	2014-04-08	SIAT1/SIAT1	80	160	160	320	160	40	80	320	320
A/Canarias/1688/2014		2014-04-08	SIAT1/SIAT1	80	160	160	640	160	40	80	320	320
A/Canarias/1689/2014	3C.3	2014-04-08	SIAT1/SIAT1	80	160	160	320	160	40	80	320	320
A/Extremadura/1752/2014		2014-04-10	SIAT1/SIAT1	640	640	640	1280	640	160	320	1280	640
A/Extremadura/1749/2014	3C.3	2014-04-23	SIAT1/SIAT1	160	320	320	640	640	160	320	1280	640
A/Madrid/SO12318/2014	3C.3	2014-06-12	SIAT1/SIAT1	80	160	160	320	160	40	80	320	320
A/Galicia/1786/2014	3C.3	2014-07-03	SIAT1	40	80	80	320	80	40	80	320	160

1. < = <40

Vaccine

Sequences in phylogenetic trees

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



Influenza B virus analyses

The results of HI analyses for propagated viruses of the B/Victoria- and B/Yamagata-lineages from EU/EEA countries, performed since the July 2014 report[1], are shown in Tables 4 and 5, respectively. The genetic clades into which the HA genes fall are shown.

Influenza B – Victoria lineage

Two viruses of the B/Victoria lineage from Germany and Norway were characterised. Post-infection ferret antiserum raised against B/Brisbane/60/2008, an exclusively egg-propagated virus previously recommended as a component of the trivalent influenza vaccine and currently recommended as a component of the quadrivalent influenza vaccine, recognised both test viruses at titres eightfold reduced compared to the titre with the homologous virus (Table 4). Antisera raised against other viruses exclusively propagated in eggs, B/Malaysia/2506/2004, B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012, recognised the cell-propagated test viruses poorly. Ferret antiserum raised against viruses propagated exclusively in cells, B/Paris/1762/2009, B/Hong Kong/514/2009, B/Odessa/3886/2010 and B/Formosa/V2367/2012, showed varying recognition of the test viruses. Although the titres of the antisera for the homologous cell-propagated viruses were low, ranging from 80 to 320, the antisera recognised both test viruses at titres within fourfold of the titres with the respective homologous viruses.

Figure 3 shows a phylogenetic analysis of the HA genes of representative B/Victoria-lineage viruses. The HA genes of viruses collected since 1 January 2014 fall into the B/Brisbane/60/2008 genetic clade (Clade 1A).

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

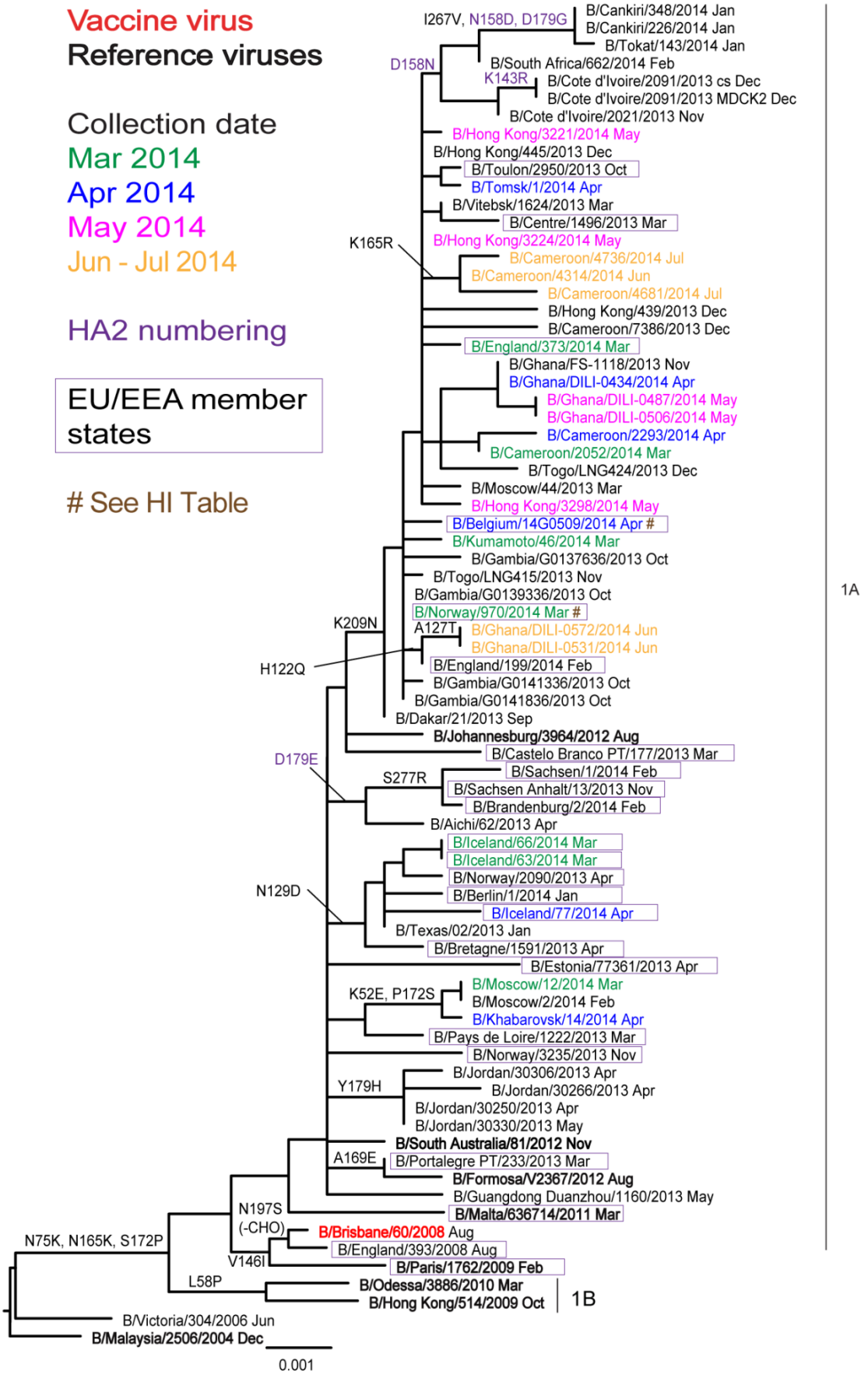
				Haemagglutination inhibition titre									
				Post infection ferret sera									
Viruses		Collection date	Passage History	B/Bris[1,3] 60/08 Sh 522	B/Mal[2] 2506/04 F37/11	B/Bris[2] 60/08 F22/12	B/Paris[2] 1762/09 F07/11	B/HK[2] 514/09 F9/13	B/Odessa[2] 3886/10 F19/11	B/Malta[2] 636714/11 F29/13	B/Jhb[2] 3964/12 F01/13	B/For[2] V2367/12 F04/13	B/Sth Aus[2] 81/12 F41/13
	Genetic group			1A		1A	1A	1B	1B	1A	1A	1A	1A
REFERENCE VIRUSES													
B/Malaysia/2506/2004		2004-12-06	E3/E6	2560	1280	80	20	20	<	80	320	80	160
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	2560	160	320	80	80	40	640	320	320	1280
B/Paris/1762/2008	1A	2009-02-09	C2/MDCK2	2560	10	40	160	80	80	20	40	40	80
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	10	40	160	80	160	80	80	80	160
B/Odessa/3886/2010	1B	2010-03-19	MDCK2/MDCK4	5120	10	40	160	80	160	40	40	80	80
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	160	320	80	80	80	640	320	320	1280
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	640	1280	320	320	160	1280	1280	1280	1280
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	2560	80	320	80	80	40	160	320	320	640
B/South Australia/81/2012	1A	2012-11-28	E4/E1	2560	160	320	80	80	40	320	640	320	1280
TEST VIRUSES													
B/Norway/970/2014	1A	2014-03-07	MDCK1	5120	10	40	80	80	160	40	40	80	160
B/Belgium/14G0509/2014	1A	2014-04-16	MDCK1	2560	20	40	160	80	40	80	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 trees

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



Influenza B – Yamagata lineage

Post-infection ferret antiserum raised against the current, egg-propagated vaccine virus B/Massachusetts/02/2012 recognised eight of 11 test viruses at titres twofold or fourfold reduced compared to the titre with the homologous virus. A ferret antiserum raised against a cell-propagated cultivar of B/Massachusetts/02/2012 recognised seven of the test viruses at titres within fourfold of its titre with the homologous virus. The antisera raised against cell-cultivars of B/Estonia/55669/2011 and B/Hong Kong/3577/2012, viruses belonging to the B/Massachusetts/02/2012 clade (clade 2), recognised three and 10 of the test viruses, respectively, at titres within fourfold of the titres of the antisera with their homologous viruses. In all instances the poorly recognised viruses had HA genes falling in clade 3. The test viruses were recognised better with antisera raised against clade 3 viruses; that raised against cell-propagated B/Novosibirsk/1/2012 recognised five viruses at titres within fourfold reduced compared to that with the homologous virus, while those raised against egg-propagated viruses B/Wisconsin/1/2010 (the previous vaccine virus) and B/Stockholm 12/2011 recognised nine and 11 (all) test viruses, respectively, at titres within fourfold reduced compared to titres with their corresponding homologous viruses.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. The HA genes of viruses collected since 1 January 2014 fall into the B/Massachusetts/02/2012 clade (clade 2) and the B/Wisconsin/1/2010 and B/Phuket/3073/2014 clade (clade 3), with those in clade 3 being in the majority in recent months. A small number of viruses were identified with HA genes of clade 3 of the B/Yamagata lineage combined with NA genes of the B/Victoria lineage. Similar reassortant viruses have been detected in many parts of the world.

As a result of the prevalence of influenza B viruses of the B/Yamagata lineage, with the majority having HA genes falling in clade 3, WHO recommended that the influenza vaccine for use in the 2015 southern hemisphere influenza season should contain a virus from that clade and recommended that the vaccine contain a virus antigenically similar to B/Phuket/3073/2013.

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

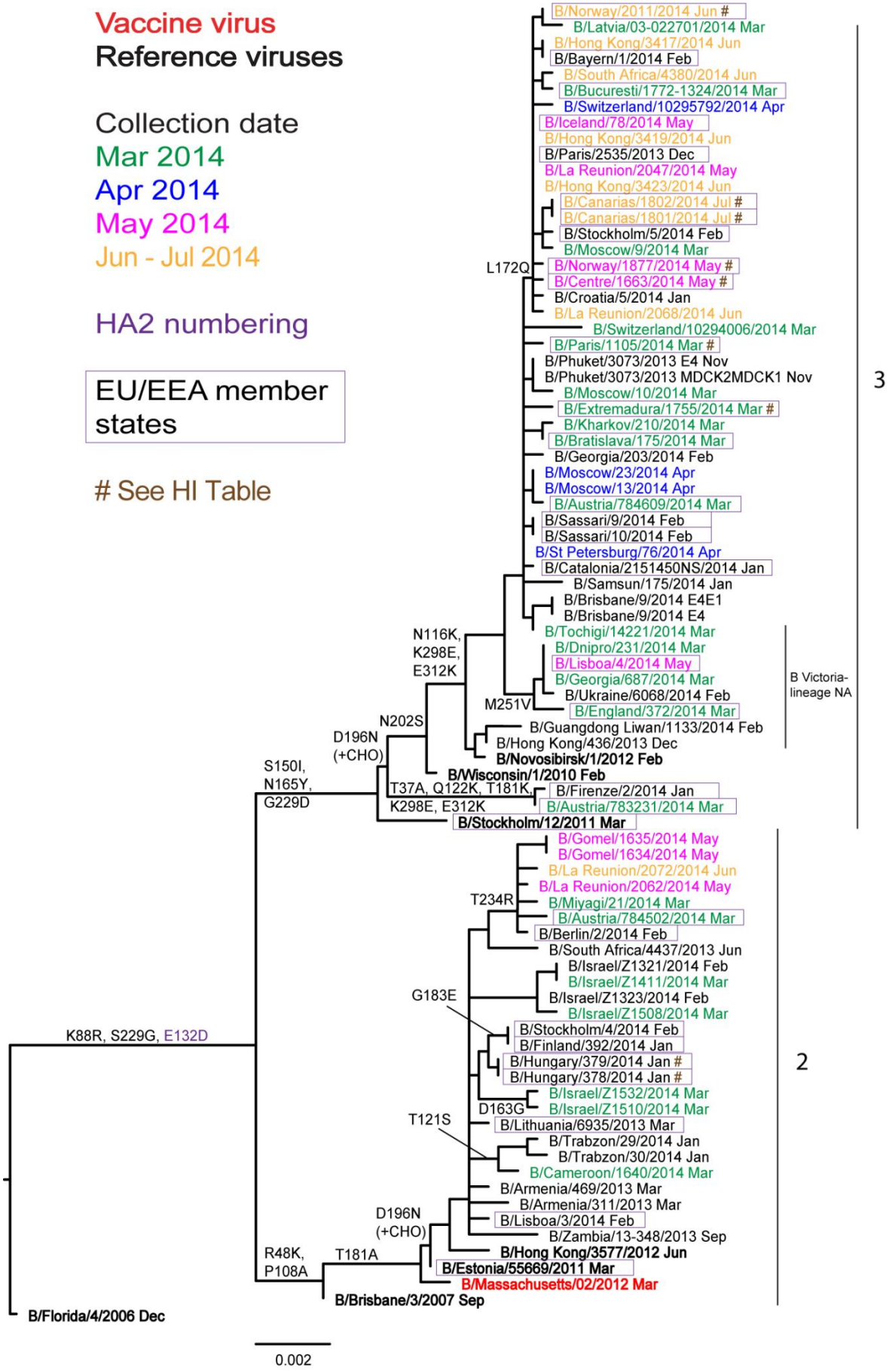
				Haemagglution Inhibition Titre									
				Post infection ferret sera									
Viruses		Collection date	Passage History	B/Fl[1,3] 4/06 SH479	B/Fl[1] 4/06 F1/10	B/Bris[2] 3/07 F21/12	B/Wis[2] 1/10 F10/13	B/Stock[2] 12/11 F12/12	B/Estonia[2] 55669/11 F26/11	B/Novo[2] 1/12 F31/12	B/HK[2] 3577/12 F33/12	B/Mass[2] 02/12 Egg F2/13	B/Mass[2] 02/12 T/C F15/13
	Genetic Group			1	1	2	3	3	2	3	2	2	2
REFERENCE VIRUSES													
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	1280	640	320	640	160	80	320	1280	320
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	1280	1280	320	640	160	20	640	1280	320
B/Wisconsin/1/2010	3	2007-08-07	E3/E2	1280	320	160	320	640	<	20	40	320	40
B/Stockholm/12/2011	3	2007-08-07	E4/E1	2560	320	160	80	320	<	20	40	320	40
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	2560	160	80	80	160	1280	80	640	160	640
B/Novosibirsk/1/2012	3	2012-02-14	C2/MDCK3	5120	320	160	320	640	320	640	640	320	640
B/Hong Kong/3577/2012	2	2012-06-13	MDCK4	2560	160	80	80	160	640	80	640	320	640
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	1280	640	160	640	160	20	320	1280	160
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	320	320	320	640	80	640	640	640
TEST VIRUSES													
B/Hungary/379/2014	2	2014-01-17	MDCK2/E2/MDCK1	2560	320	320	160	160	320	20	320	640	320
B/Hungary/378/2014	2	2014-01-20	MDCK2/E2/MDCK1	2560	320	160	160	320	640	40	640	320	320
B/Extremadura/1755/2014	3	2014-03-17	SIAT1/MDCK1	5120	320	320	320	640	320	640	640	320	640
B/Paris/1105/2014	3	2014-03-20	MDCK1/MDCK1	1280	320	160	320	640	40	160	320	320	160
B/Estonia/86059/2014	3	2014-04-01	MDCK1/MDCK1	1280	160	80	320	320	40	160	160	320	160
B/Centre/1663/2014	3	2014-05-12	MDCK1/MDCK1	1280	160	80	320	320	40	160	320	320	80
B/Norway/1877/2014	3	2014-05-21	MDCK1	1280	160	80	20	320	80	80	160	320	160
B/Norway/2045/2014	3	2014-05-28	MDCK2	1280	160	80	160	320	80	80	160	160	160
B/Norway/2011/2014	3	2014-06-19	MDCK1	640	160	80	20	320	40	80	160	320	80
B/Canarias/1801/2014	3	2014-07-02	Cx/MDCK1	640	80	80	160	160	40	160	80	160	80
B/Canarias/1802/2014	3	2014-07-02	Cx/MDCK1	1280	80	80	160	160	40	80	160	160	80

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

Vaccine

Sequences in phylogenetic trees

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



Antiviral susceptibility

All 356 viruses recovered at WHO CC London, with collection dates after 31 January 2014, have been subjected to phenotypic testing against oseltamivir and zanamivir: 157 A(H1N1)pdm09, 171 A(H3N2) and 28 influenza B viruses. All viruses showed normal inhibition (NI) by zanamivir. A single (0.6%) A(H1N1)pdm09 virus showed highly reduced inhibition (HRI) by oseltamivir due to NA H275Y amino acid substitution, and three (1.8%) A(H3N2) viruses showed reduced inhibition by oseltamivir (RI; 10- to 26-fold increase in IC_{50}), with the three viruses having NA S331R amino acid substitution in common. All influenza B viruses showed NI by oseltamivir.

M-gene sequencing of A(H1N1)pdm09 and A(H3N2) viruses showed all to carry a S31N amino acid substitution in the M2-ion channel which has been associated with resistance to adamantanes.

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 have been reported over the course of the 2013–14 season, continuing into August 2014. A revised Rapid Risk Assessment [3] for these A(H7N9) viruses was carried out by ECDC and posted on 27 January 2014, and an updated summary of human infection was posted by WHO on 31 January 2014 [4], followed by an updated risk assessment on 27 June 2014 [5]. The most recent update of the epidemiological situation published by WHO was posted on 4 September 2014. WHO summarised the numbers of cases of human infection and their geographic location on 14 July 2014 [6].

WHO CC reports

A description of results generated by the WHO Collaborating Centre for Reference and Research on Influenza at the MRC National Institute for Medical Research in London, and evaluated at the WHO Vaccine Composition Meetings held at WHO Geneva on 17–19 February 2014 and 22–24 September 2014, can be found at:

http://www.nimr.mrc.ac.uk/documents/about/NIMR-report-Feb2014-web.pdf

http://www.nimr.mrc.ac.uk/documents/about/NIMR-VCM-report-Sep-14-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 ECDC countries are highlighted within boxes. Sequences for many 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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