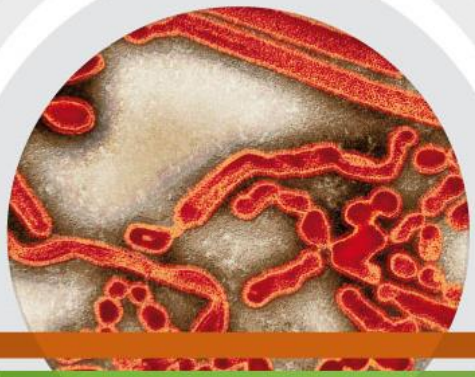


SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, June 2014

Summary

During the 2013–14 season, A(H1N1)pdm09, A(H3N2), B/Victoria- and B/Yamagata-lineage influenza viruses have continued to co-circulate in EU/EEA Member States. The relative prevalence has varied between countries. Viruses with collection dates after 31 December 2013, from 22 countries, have been received by the WHO Collaborating Centre in London.

- Type A and type B viruses have been received at a ratio of nearly 20:1.
- A(H3N2) and A(H1N1)pdm09 viruses have been received in similar numbers.
- Recently circulating A(H1N1)pdm09 viruses belonged to genetic subgroup 6B. Viruses in subgroup 6B 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, with viruses of genetic subgroup 3C.3 predominating. 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. Antisera raised against two reference viruses representative of viruses in genetic subgroup 3C.3 – with HA gene sequences encoding several amino acid substitutions compared to other viruses in genetic group 3C.3 – have been prepared. These antisera recognised the majority of test viruses well.
- Two genetic clades of B/Yamagata-lineage viruses continue to circulate: clade 3 represented by B/Wisconsin/1/2010 and clade 2 represented by B/Massachusetts/02/2012 (the recommended vaccine component for the 2013–14 and 2014-15 influenza seasons). Viruses in each clade have been received in similar numbers but with viruses in clade 3 predominating in those samples collected in 2014.
- Antigenic characterisation of two viruses of the B/Victoria lineage was performed in June. Neither virus was recognised well by the antiserum raised against the egg-propagated reference virus, A/Brisbane/60/2008, a virus previously recommended as a component of the trivalent influenza vaccine and recommended as a component of quadrivalent influenza vaccines for 2013–14 and 2014–15 influenza seasons. The test viruses were not recognised well by antisera raised against other reference viruses propagated in eggs. The test viruses were better recognised by some, but not all, antisera raised against reference viruses exclusively propagated in cells. Phylogenetic analysis revealed that all B/Victoria-lineage viruses received in 2014 were in genetic clade 1A, the B/Brisbane/60/2008 genetic clade.

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).

Suggested citation: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, June 2014. Stockholm: ECDC; 2014.

Influenza-positive samples, viruses or clinical specimens, with collection dates after 31 December 2013 (with week 40, the start of weekly monitoring of influenza activity for the 2013–14 influenza season, commencing on 30 September 2013) have been received at the MRC National Institute for Medical Research, WHO Collaborating Centre for Reference and Research on Influenza (WHO CC), from 22 countries in the EU/EEA region. The large majority (95%) were type A viruses, with A(H3N2) viruses and A(H1N1)pdm09 viruses equally represented (Table 1). Of the small number of type B viruses received (5% of the specimens), viruses of the B/Yamagata-lineage outnumbered those of the B/Victoria-lineages at a ratio of 2:1. Some samples have yet to be fully processed (in process: Table 1).

Table 1. Summary of clinical samples and virus isolates received from EU/EEA Member States, with collection dates after 31 December 2013

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]
2014											
JANUARY											
Austria	2				2	in process					
Belgium	4		3	3	1	1					
Bulgaria	33		26	26	7	7					
Cyprus	13		9	7	4	4					
Czech Republic	9		6	6	3	3					
Finland	2		1	1						1	1
Germany	22		4	4	17	17		1	1		
Greece	35		32	15	3	2					
Iceland	4		4	4							
Ireland	3		1	1	2	2					
Italy	20		6	6	12	11				2	2
Latvia	1		1	1							
Malta	4		4	4							
Norway	30				30	29					
Poland	4		1	0	3	3					
Portugal	11		8	6	3	3					
Romania	13		5	0	8	4					
Slovakia	1		1	1							
Slovenia	14		3	2	11	7					
Spain	52		38	29	13	11				1	1
Sweden	3		2	2	1	0					
United Kingdom	5		2	2	2	2				1	1
FEBRUARY											
Austria	3				3	in process					
Belgium	6		3	1	3	2					
Bulgaria	27		21	21	6	5					
Cyprus	12	1	11	11							
Finland	8		3	3	5	in process					
Germany	11		4	4	3	3		2	2	2	2
Iceland	6		3	in process	3	in process					
Ireland	4		4	4							
Italy	28		12	11	14	14				2	2
Latvia	1		1	1							
Norway	8				8	7					
Poland	9		2	1	7	5					
Portugal	6		4	in process	1	in process				1	in process
Slovakia	5		3	3	2	2					
Slovenia	20		6	6	14	11					
Sweden	7		1	1	4	4				2	2
United Kingdom	3				2	1		1	1		
MARCH											
Austria	10		2	in process	5	in process				3	in process
Belgium	7		4	2	3	1					
Bulgaria	1		1	1							
Finland	3		1	1	2	in process					
Iceland	7		5	in process				2	in process		
Ireland	2		2	2							
Italy	3		2	2	1	1					
Latvia	11		7	5	3	3				1	1
Norway	6				6	4					
Poland	26	1	2	0	23	9					
Portugal	2		1	in process	1	in process					
Romania	13		3	3	9	in process				1	1
Slovakia	3		1	1	1	1				1	1
Slovenia	3		2	2	1	1					
United Kingdom	8		4	4	2	2		1	1	1	1
APRIL											
Austria	3		1	in process	2	in process					
Belgium	10		2	1	7	in process		1	in process		
Finland	3				3	in process					
Iceland	3		2	in process				1	in process		
Ireland	6		1	1	5	5					
Latvia	2				2	2					
Poland	3		2	0	1	1					
Portugal	1				1	in process					
Slovakia	3		1	1	2	2					
Slovenia	2		1	1	1	1					
MAY											
Iceland	3				2	in process				1	in process
Portugal	1									1	in process
United Kingdom	1				1	in process					
JUNE											
Iceland	1				1	in process					
United Kingdom	1				1	in process					
	597	2	282	214	283	193	0	9	5	21	15
				47.2%		47.4%			1.5%		3.5%
22 Countries			95.0%					5.0%			

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 May 2014 report[1] are shown in Tables 2-1, 2-2 and 2-3. The test viruses were antigenically similar to the vaccine virus, A/California/7/2009; all but two of the 61 test viruses analysed since the May 2014 report were recognised by an antiserum raised against A/California/7/2009 at titres as good as, or better than, that obtained with the homologous virus. One of these two viruses showed significantly reduced HI titres with antisera raised against other reference viruses, and it contained an HA1 amino acid substitution of N156D. Amino acid substitutions in the 153–157 region of HA1 are known to cause altered antigenicity and are often selected for isolation in cell culture, notably on MDCK-SIAT1 cells which have been modified to over-express α2,6-linked sialic acid. For 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 H1N1 viruses. The HA genes cluster into eight designated genetic groups, of which seven are indicated, with A/California/7/2009 representing group 1. All viruses examined since the May2014 report carried HA genes in genetic subgroup 6B. This subgroup carries the 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

				Haemagglutination inhibition titre										
				Post infection ferret antisera										
Viruses	Genetic group	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 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/HK 5659/12 F30/12 6A	A/SA 3626/13 F3/14 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E2	640	640	640	320	160	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	160	80	40	80	80	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	1280	320	160	160	320	160	640	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	2560	2560	2560	5120	1280	5120	2560	5120	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	320	320	640	1280	640	1280	1280	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	1280	640	640	640	1280	2560	1280	1280	2560	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	1280	640	1280	2560	1280	2560	2560	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	640	1280	1280	2560	2560	1280	2560	2560	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	640	320	640	640	1280	2560	1280	2560	5120	1280	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	640	640	640	1280	640	1280	1280	1280	1280	
TEST VIRUSES														
A/Finland/402/2014		2014-01-20	MDCK1/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	1280	
A/Poprad/104/2014		2014-01-30	MDCK1/MDCK1	1280	640	2560	1280	2560	5120	2560	5120	5120	2560	
A/Prievidza/109/2014	6B	2014-02-06	MDCK1/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	5120	2560	
A/Finland/416/2014		2014-02-11	MDCK1/MDCK1	640	640	640	640	2560	1280	1280	2560	2560	1280	
A/Finland/417/2014		2014-02-12	MDCK1/MDCK1	640	640	640	640	1280	1280	1280	2560	2560	1280	
A/Lubica/131/2014		2014-02-20	MDCK1/MDCK1	640	640	1280	640	2560	2560	1280	2560	2560	1280	
A/Kosice/132/2014	6B	2014-02-20	MDCK1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Latvia/02-053060/2014	6B	2014-02-24	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	
A/Finland/420/2014	6B	2014-02-26	MDCK1/MDCK1	2560	1280	2560	2560	5120	5120	2560	5120	5120	2560	
A/Latvia/03-020560/2014	6B	2014-03-10	MDCK1/MDCK1	1280	640	2560	1280	2560	1280	1280	2560	2560	1280	
A/Finland/422/2014	6B	2014-03-10	MDCK1/MDCK1	1280	640	2560	1280	2560	2560	5120	5120	5120	2560	
A/England/348/2014		2014-03-11	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Latvia/03-023857/2014		2014-03-11	MDCK1/MDCK1	640	640	1280	1280	5120	2560	2560	5120	5120	5120	
A/Latvia/03-028999/2014		2014-03-12	MDCK1/MDCK1	640	640	640	640	2560	1280	1280	2560	2560	2560	
A/England/378/2014	6B	2014-03-17	SIAT1/MDCK1	2560	2560	2560	2560	5120	5120	2560	5120	5120	2560	
A/Latvia/03-043266/2014	6B	2014-03-19	MDCK2/MDCK1	1280	320	640	320	1280	1280	640	1280	1280	1280	
A/Latvia/03-050084/2014	6B	2014-03-20	MDCK1/MDCK1	1280	1280	2560	1280	2560	2560	2560	5120	5120	2560	
A/England/395/2014		2014-03-25	SIAT1/MDCK1	640	640	1280	1280	2560	1280	2560	2560	2560	1280	
A/England/403/2014	6B	2014-03-26	SIAT1/MDCK1	640	640	1280	1280	2560	2560	2560	2560	2560	1280	
A/Nove Zamky/202/2014	6B	2014-03-26	MDCK1/MDCK1	1280	1280	2560	2560	2560	5120	2560	5120	5120	2560	
A/Trencin/207/2014	6B	2014-04-02	MDCK2/MDCK1	1280	640	1280	1280	2560	2560	1280	5120	5120	2560	
				Vaccine										

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

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

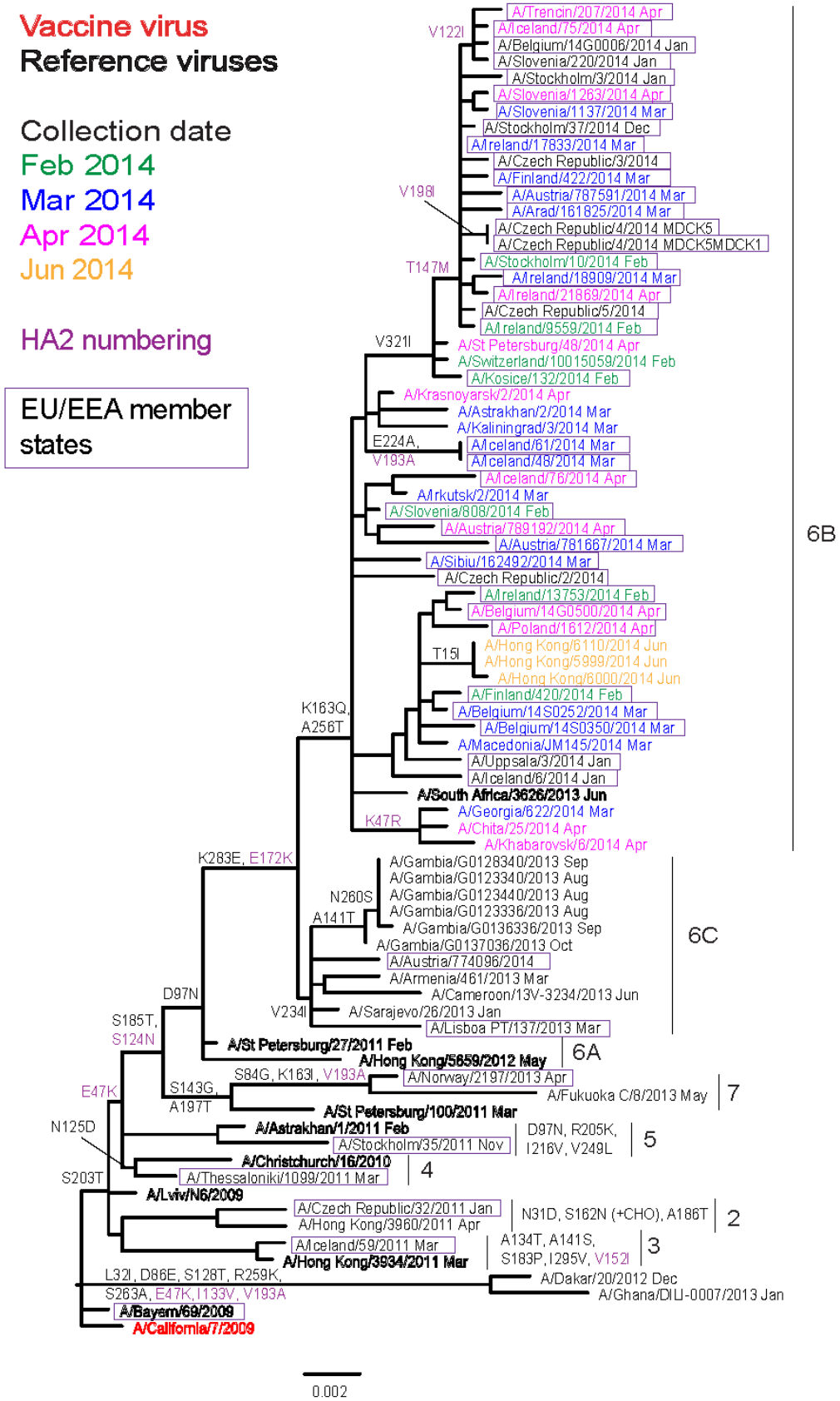
				Haemagglutination inhibition titre										
				Post infection ferret antisera										
Viruses	Genetic group	Collection date	Passage History	A/Cal 7/09 F30/11	A/Bayern 69/09 F11/11	A/Lviv N6/09 C4/09/34	A/Chch 16/10 F30/10 4	A/HK 3934/11 F21/11 3	A/Astrak 1/11 F22/13 5	A/St. P 27/11 F23/11 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	A/SA 3626/13 F3/14 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E2	640	640	640	160	160	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	160	40	40	40	40	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	320	1280	640	160	80	80	160	320	640	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	5120	640	1280	2560	2560	5120	1280	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	640	320	640	640	640	1280	1280	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	640	320	320	320	640	640	640	1280	2560	640	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	640	640	640	640	640	1280	1280	2560	2560	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	1280	640	640	1280	1280	1280	2560	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	640	640	640	1280	1280	2560	5120	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	320	640	640	640	640	640	1280	1280	1280	
TEST VIRUSES														
A/Stockholm/37/2013	6B	2013-12-23	MDCK0/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Stockholm/3/2014	6B	2014-01-06	MDCK2/MDCK1	640	640	1280	320	640	1280	640	1280	1280	1280	
A/Serbia/NS-601/2014	6B	2014-01-08	MDCK1	1280	640	1280	1280	1280	2560	2560	5120	5120	2560	
A/Uppsala/3/2014	6B	2014-01-20	MDCK2/MDCK1	1280	640	1280	640	1280	2560	2560	5120	2560	1280	
A/Slovenia/215/2014		2014-01-22	MDCKx/MDCK1	1280	640	1280	640	2560	2560	2560	5120	2560	2560	
A/Slovenia/220/2014	6B	2014-01-22	MDCK1/MDCK1	640	320	640	320	1280	1280	1280	2560	2560	1280	
A/Slovenia/401/2014		2014-02-04	MDCK1/MDCK1	1280	640	1280	640	2560	1280	1280	5120	2560	2560	
A/Slovenia/423/2014		2014-02-05	MDCKx/MDCK1	1280	640	1280	640	2560	2560	2560	5120	5120	2560	
A/Slovenia/461/2014		2014-02-07	MDCK1/MDCK1	640	320	640	320	1280	1280	640	2560	1280	1280	
A/Ireland9559/2014	6B	2014-02-09	MDCK1/MDCK1	640	640	1280	640	1280	2560	2560	5120	2560	2560	
A/Slovenia/608/2014		2014-02-13	MDCKx/MDCK1	1280	640	1280	640	2560	2560	1280	5120	2560	1280	
A/Stockholm/10/2014	6B	2014-02-18	MDCK0/MDCK1	640	640	640	640	1280	1280	1280	2560	2560	1280	
A/Ireland/11861/2014	6B	2014-02-19	MDCK1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280	
A/Slovenia/748/2014		2014-02-21	MDCKx/MDCK1	1280	640	1280	640	2560	2560	1280	5120	2560	1280	
A/Ireland/13388/2014		2014-02-21	MDCK1/MDCK1	1280	640	1280	640	1280	2560	1280	2560	2560	2560	
A/Ireland/13753/2014	6B	2014-02-24	MDCK1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280	
A/Slovenia/808/2014	6B	2014-02-25	MDCKx/MDCK1	1280	640	1280	640	2560	2560	2560	5120	2560	2560	
A/Serbia/NS-703/2014	6B	2014-02-28	MDCK2	1280	640	1280	640	2560	2560	2560	5120	2560	2560	
A/Slovenia/896/2014		2014-03-04	MDCKx/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	1280	
A/Belgium/14S0252/2014	6B	2014-03-04	MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	
A/Serbia/NS-735/2014	6B	2014-03-06	MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280	
A/Ireland/17883/2014	6B	2014-03-14	MDCK3/MDCK1	1280	640	1280	640	1280	2560	2560	2560	2560	2560	
A/Serbia/NS-772/2014	6B	2014-03-18	MDCK1	1280	640	1280	640	1280	2560	2560	5120	2560	2560	
A/Ireland/18909/2014	6B	2014-03-22	MDCK1/MDCK1	1280	640	1280	1280	1280	2560	2560	5120	2560	2560	
A/Slovenia/1137/2014	6B	2014-03-24	MDCK1/MDCK1	1280	640	1280	640	1280	2560	1280	2560	2560	1280	
A/Ireland/21869/2014	6B	2014-04-06	MDCK1/MDCK1	640	640	1280	640	1280	2560	1280	5120	2560	1280	
A/Slovenia/1263/2014	6B	2014-04-10	MDCK1/MDCK1	1280	640	1280	1280	1280	2560	2560	5120	2560	2560	
A/Belgium/14G0500/2014	6B	2014-04-10	MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	
				Vaccine										

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

				Haemagglutination inhibition titre[1]										
				Post infection ferret antisera										
Viruses	Genetic group	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 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/HK 5659/12 F30/12 6A	A/SA 3626/13 F3/14 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E2	640	640	640	160	160	160	160	160	160	160	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	160	40	40	40	80	40	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	320	1280	640	160	80	160	160	160	320	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	2560	1280	1280	1280	2560	2560	1280	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	320	320	640	640	640	1280	1280	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	640	320	320	320	1280	1280	640	1280	1280	640	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	640	640	640	320	640	640	640	1280	1280	640	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	1280	640	1280	1280	1280	2560	2560	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	320	320	640	640	640	1280	1280	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	320	320	1280	320	320	640	320	640	640	640	
TEST VIRUSES														
A/Czech Republic/3/2014	6B	unknown	MDCK4/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	1280	
A/Czech Republic/4/2014	6B	unknown	MDCK5/MDCK1	640	320	640	320	1280	1280	1280	2560	1280	1280	
A/Czech Republic/5/2014	6B	unknown	MDCK5/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	2560	
A/Czech Republic/2/2014	6B	unknown	MDCK7/MDCK2	320	160	80	40	<	40	80	40	40	80	N156D
A/Czech Republic/4/2014	6B	unknown	C2/E3/MDCK1	1280	640	1280	640	2560	1280	1280	5120	2560	1280	
A/Czech Republic/5/2014	6B	unknown	C2/E2/MDCK1	640	320	320	320	640	640	1280	2560	1280	640	
A/Belgium/14G0006/2014	6B	2014-01-04	MDCK1	1280	640	1280	2560	2560	2560	2560	5120	2560	2560	
A/Belgium/14H0004/2014		2014-02-04	MDCK1	1280	640	1280	1280	2560	2560	1280	5120	2560	2560	
A/Arad/161825/2014	6B	2014-03-07	MDCK1/MDCK1	320	160	320	320	640	640	640	1280	1280	1280	
A/Belgium/14S0350/2014	6B	2014-03-13	MDCK2	1280	640	1280	1280	5120	2560	1280	2560	2560	1280	
A/Arges/161972/2014		2014-03-13	MDCK1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	2560	
A/Sibiu/162492/2014	6B	2014-03-19	MDCK1/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	2560	
				Vaccine										

1. < = <40

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 three of the viruses examined since the May 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, 3-2, 3-3 and 3-4. The genetic group of the HA gene is indicated for viruses for which gene sequences have been determined.

All but eight of the 84 test viruses analysed since the May 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 with the titre of the antiserum with the homologous virus. Similar results were seen with an antiserum raised against the egg-propagated reference virus A/Hong Kong/146/2013. The test viruses were recognised better when examined with antisera raised against four other egg-propagated reference viruses – A/Serbia/NS-210/2013, A/Almaty/2958/2013 (represented by the high-growth reassortant NIB-85), A/South Africa/4655/2013 and A/Stockholm/1/2013. Notably antisera raised against A/South Africa/4655/2013 and A/Stockholm/1/2013 recognised the majority (~70% and >90%) of test viruses at titres within fourfold of the titres of the antisera for their corresponding homologous viruses.

Ferret antisera raised against reference viruses exclusively propagated in tissue culture cells – A/Samara/73/2013, A/Stockholm/6/2014 and Norway466/2014, and the exclusively cell-propagated cultivar of A/Victoria/361/2011 – recognised the test viruses more effectively. Each recognised >95% of test viruses analysed since the May 2014 report at titres within fourfold of those for the antisera with their corresponding homologous viruses. The reference viruses A/Stockholm/6/2014 and A/Norway/466/2014 are representative of an emerging group of viruses, 3C.3a, described in the May report as 3C.3*. An additional cluster of six viruses from Ireland and Slovakia, with HA genes encoding amino acid substitutions **E62K**, **K83R** and **R261Q** in **HA1,** and **M18K** in **HA2**, are marked (*) in Table 3-3. These six viruses are recognised well generally by antisera raised against cell-propagated reference viruses but three of the four viruses from Ireland having HA genes that fall into this group were poorly recognised (eightfold decrease) by the antiserum raised against A/Samara/73/2013.

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 May 2014 report fall into subgroups 3C.2 and 3C.3, with viruses in 3C.3 predominating (Figure 2). Amino acid substitutions that define subgroups 3C.2 and 3C.3 are:

- 3C.2 **N145S** in **HA1**, and **D160N** in **HA2**, e.g. A/Hong Kong/146/2013; and
- 3C.3 **T128A** (resulting in the loss of a potential glycosylation site), **R142G,** and **N145S** in **HA1**, e.g. A/Samara/73/2013.

The new cluster of viruses within subgroup 3C.3, 3C.3a, is highlighted. The HA genes of 3C.3a viruses encode the substitutions **A138S**, **F159S** and **N225D** in **HA1**. Viruses in this new cluster have been reported at an increasing frequency by WHO CCs in North America and Asia.

[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	Collection Date	Genetic group	Passage History	Haemagglutination inhibition titre[1]											
				Post infection ferret antisera											
				A/Perth 16/09 F35/11	A/Vic 361/11 T/C F09/12	A/Texas 50/12 Egg F42/13	A/Sam 73/13 F24/13	A/Serbia NS-210/13 F39/13	A/HK 146/13 F40/13	NIB-85 F45/13	A/SA 4655/13 F10/14	A/Stock 1/13 F12/14	A/Stock 6/14 F14/14
				3C.1	3C.1	3C.1	3C.3	3C.3	3C.2	3C.3	3C.3 cl 101-60	3C.2 cl 36-18	3C.3a
REFERENCE VIRUSES													
A/Perth/16/2009	2009-07-04		E3/E3	640	160	160	160	160	160	160	40	80	40
A/Victoria/361/2011	2011-10-24	3C.1	MDCK2/SIAT3	80	320	320	640	320	320	320	80	160	320
A/Texas/50/2012	2012-04-15	3C.1	E5/E2	320	1280	1280	1280	1280	640	1280	80	160	320
A/Samara/73/2013	2013-03-12	3C.3	C1/SIAT2	80	320	320	640	640	640	640	80	160	640
A/Serbia/NS-210/2013	2013-01-18	3C.3	E5/E1	320	1280	1280	1280	1280	1280	1280	80	160	320
A/Hong Kong/146/2013	2013-01-11	3C.2	E5/E1	320	640	640	1280	640	2560	640	80	160	160
NIB-85 (A/Almaty/2958/2013)	2013-01-27	3C.3	E5/E1	640	1280	1280	1280	1280	2560	1280	160	320	320
A/South Africa/4655/2013	2013-06-25	3C.3	E7 clone 101-60	80	80	160	320	160	320	160	320	160	80
A/Stockholm/1/2013	2013-01-13	3C.2	E7 clone 36-18	40	80	160	320	160	320	160	320	320	160
A/Stockholm/6/2014	2014-02-06	3C.3a	SIAT2/SIAT1	<	40	40	320	160	160	160	40	80	640
TEST VIRUSES													
A/Norway/53/2014	2013-12-20		MDCK2/SIAT1	<	160	160	320	160	160	160	80	80	320
A/Norway/3331/2013	2013-12-25		MDCK1/SIAT1	<	160	160	320	160	160	160	80	80	320
A/Norway/104/2014	2013-12-25		MDCK1/SIAT1	<	320	160	640	320	320	320	80	160	640
A/Norway/18/2014	2013-12-31	3C.2	MDCK2/SIAT1	<	80	80	160	40	160	160	<	40	80
A/Norway/58/2014	2014-01-02	3C.3	MDCK2/SIAT1	<	160	160	320	320	160	160	40	80	320
A/Norway/70/2014	2014-01-02		MDCK2/SIAT1	80	320	160	640	320	320	320	160	160	640
A/Norway/115/2014	2014-01-06		MDCK1/SIAT1	<	320	160	640	320	320	320	80	160	320
A/Norway/133/2014	2014-01-06		LLC/MDCK2/ MDCK1/SIAT1	40	320	320	640	320	320	320	80	160	640
A/Norway/67/2014	2014-01-07		MDCK2/SIAT1	80	320	160	640	320	320	640	80	160	640
A/Roma/2/2014	2014-01-13		SIAT1/SIAT1	<	160	160	640	320	320	320	80	160	640
A/Sassari/1/2014	2014-01-14		SIAT2/SIAT1	<	160	160	640	320	160	320	80	80	320
A/Parma/8/2014	2014-01-17		MDCK1/SIAT1	80	320	320	1280	640	640	640	160	160	640
A/Roma/3/2014	2014-01-17		SIAT1/SIAT1	<	160	160	640	320	160	160	80	80	320
A/Trieste/10/2014	2014-01-23	3C.3	SIAT1/SIAT1	<	160	160	320	160	160	160	40	80	320
A/Milano/31/2014	2014-01-23		SIAT1/SIAT1	<	160	160	320	160	320	160	40	80	320
A/Roma/5/2014	2014-01-23		SIAT1/SIAT1	40	320	160	640	320	320	320	80	160	640
A/Roma/7/2014	2014-01-24		SIAT1/SIAT1	<	160	160	640	320	160	320	80	160	320
A/Milano/58/2014	2014-01-28	3C.3	SIAT1/SIAT1	<	160	80	320	160	160	160	40	80	320
A/Firenze/6/2014	2014-02-03		MDCK2/SIAT1	40	160	160	640	320	320	320	80	160	320
A/Sassari/10/2014	2014-02-03		SIAT1/SIAT1	<	160	160	320	160	160	160	80	80	320
A/Parma/28/2014	2014-02-03		MDCK2/SIAT1	40	160	160	320	160	320	320	80	160	320
A/Parma/33/2014	2014-02-03		MDCK2/SIAT1	40	320	320	1280	320	320	320	80	160	640
A/Milano/84/2014	2014-02-03		SIAT1/SIAT1	<	320	160	640	320	320	320	80	160	640
A/Roma/11/2014	2014-02-04	3C.3	SIAT1/SIAT1	40	320	160	640	320	320	320	80	160	640
A/Firenze/9/2014	2014-02-05	3C.3	MDCK2/SIAT1	<	80	80	320	160	80	80	40	80	160
A/Sassari/12/2014	2014-02-06	3C.2	SIAT2/SIAT1	40	160	160	320	160	320	160	80	80	320
A/Milano/72/2014	2014-02-06	3C.3	SIAT1/SIAT1	<	80	80	160	160	160	160	40	40	160
A/Sassari/15/2014	2014-02-07		Cx/SIAT1	<	160	160	320	320	320	320	80	80	320
A/Ukraine/67/2014	2014-02-07		SIAT2/SIAT4	<	160	160	640	160	160	160	80	80	320
A/Milano/101/2014	2014-02-10		SIAT1/SIAT1	40	320	320	640	320	320	320	80	160	640
A/Parma/40/2014	2014-02-13	3C.3	SIAT1/SIAT1	<	160	160	320	160	160	160	40	80	320
A/Milano/113/2014	2014-02-18	3C.2	SIAT1/SIAT1	<	160	160	320	160	320	160	80	80	320
A/Genova/09/2014	2014-02-25	3C.3	SIAT1/SIAT1	<	160	160	320	320	320	160	80	80	640
A/Sassari/17/2014	2014-03-05	3C.3	Cx/SIAT1	<	160	160	320	160	160	160	40	80	320

Vaccine

1. < = <40

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	A/Vic 361/11	A/Texas 50/12	A/Sam 73/13	A/Serbia NS-210/13	A/HK 146/13	NIB-85	A/SA 4655/13	A/Stock 1/13	A/Stock 6/14
				F35/11	T/C F09/12	Egg F42/13	F24/13	F39/13	F40/13	F45/13	F10/14	F12/14	F14/14
	Genetic group				3C.1	3C.1	3C.3	3C.3	3C.2	3C.3	3C.3 cl 101-60	3C.2 cl 36-18	3C.3a
REFERENCE VIRUSES													
A/Perth/16/2009		2009-07-04	E3/E3	640	160	160	160	160	160	160	40	80	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT3	80	320	320	640	320	320	320	80	160	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	1280	1280	1280	1280	1280	1280	80	160	320
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	80	320	320	640	640	640	640	80	160	640
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	1280	1280	1280	1280	1280	1280	80	160	320
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	640	640	1280	640	2560	640	80	160	160
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	1280	1280	1280	1280	2560	1280	160	320	320
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	80	160	320	160	320	160	320	160	80
A/Stockholm/1/2013	3C.2	2013-01-13	E7 clone 36-18	40	80	160	320	160	320	160	320	320	160
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT1	<	40	40	160	160	80	80	40	80	320
TEST VIRUSES													
A/Trieste/01/2014		2013-12-28	SIAT1/SIAT1	<	160	160	320	160	160	160	80	80	320
A/Milano/13/2014		2014-01-12	SIAT1/SIAT1	<	160	160	320	320	160	320	80	80	320
A/Norway/513/2014		2014-01-29	SIAT1	40	320	320	640	320	640	640	160	160	640
A/Norway/504/2014		2014-02-01	SIAT1	<	320	160	640	320	320	320	80	160	640
A/Norway/507/2014	3C.3	2014-02-03	SIAT1	<	160	80	320	160	160	160	40	80	160
A/Norway/627/2014		2014-02-04	SIAT1	40	320	160	640	160	320	320	80	80	640
A/Norway/467/2014		2014-02-06	SIAT1	<	320	160	640	320	320	320	80	80	320
A/Norway/580/2014	3C.3	2014-02-11	SIAT2	<	160	160	640	320	160	320	80	80	320
A/Belgium/14H0010/2014	3C.3	2014-02-13	SIAT1	<	160	80	320	160	160	160	80	80	320
A/Belgium/14S0070/2014	3C.2	2014-02-16	SIAT1	40	160	160	640	160	160	320	80	80	320
A/Belgium/14S0265/2014	3C.3	2014-03-07	SIAT1	<	160	80	320	320	160	160	80	80	320

1. < = <40

Vaccine

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	A/Vic 361/11	A/Texas 50/12	A/Sam 73/13	A/Serbia NS-210/13	A/HK 146/13	NIB-85	A/SA 4655/13	A/Stock 1/13	A/Stock 6/14	A/Norway 466/14	
				F35/11	T/C F09/12	Egg F42/13	F24/13	F39/13	F40/13	F45/13	F10/14	F12/14	F14/14	F13/14	
					3C.1	3C.1	3C.3	3C.3	3C.2	3C.3	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	640	160	160	160	160	160	160	40	80	40	40	
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	80	320	320	640	160	320	160	160	160			
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	1280	1280	640	1280	640	1280	80	160	160	40	
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	640	320	1280	640	640	640	160	160	640	320	
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	1280	2560	1280	2560	1280	2560	80	160	160	160	
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	640	1280	1280	1280	2560	1280	160	320	160	160	
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	2560	2560	1280	2560	2560	2560	160	320	320	160	
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	80	160	320	160	320	160	320	160	160	80	
A/Stockholm/1/2013	3C.2	2013-01-13	E6 clone 36-18	80	80	160	320	160	320	160	320	320	160	80	
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT2	<	80	80	320	160	160	160	40	160	320	320	
A/Norway/466/2014	3C.3a	2014-02-03	SIAT2/SIAT1	<	40	40	80	40	80	80	<	80	320	160	
TEST VIRUSES															
A/Bratislava/111/2014	3C.3	2014-02-06	MDCK1/SIAT1	<	160	160	640	320	320	320	80	80	320	160	
A/Sastin/137/2014	3C.3	2014-02-24	MDCK1/SIAT1	<	160	80	320	160	160	160	<	80	320	160	*
A/England/256/2014	3C.3	2014-02-27	SIAT1/SIAT1	<	320	160	320	320	320	320	80	160	320	160	
A/Norway/850/2014	3C.3	2014-02-27	SIAT3	40	320	160	640	320	320	320	80	160	640	320	
A/Latvia/03-013033/2014	3C.2	2014-03-06	MDCK1/SIAT1	<	40	40	160	40	80	80	40	40	80	80	
A/Latvia/03-018148/2014		2014-03-08	MDCK1/SIAT1	40	320	320	640	320	640	320	160	320	640	320	
A/Latvia/03-026603/2014	3C.3	2014-03-12	MDCK1/SIAT1	40	320	320	640	320	320	640	160	160	640	320	
A/Prievidza/182/2014	3C.3	2014-03-18	MDCK1/SIAT1	<	160	160	320	320	320	320	80	160	320	320	
A/England/400/2014	3C.2	2014-03-21	SIAT1/SIAT1	40	320	160	640	160	320	320	80	160	320	320	
A/Ireland/21550/2014	3C.3	2014-04-04	MDCK2/SIAT1	<	80	80	160	80	80	80	<	40	160	80	*
A/Ireland/22350/2014	3C.3	2014-04-07	MDCK2/SIAT1	<	160	80	160	160	80	160	40	80	160	160	*
A/Ireland/22359/2014	3C.3	2014-04-07	MDCK2/SIAT1	<	320	160	640	320	320	320	80	160	320	160	
A/Ireland/22041/2014	3C.3	2014-04-08	MDCK1/SIAT1	<	80	80	160	160	160	160	<	80	160	160	*
A/Ireland/22878/2014	3C.3	2014-04-09	MDCK1/SIAT1	40	160	160	320	160	160	160	40	80	320	160	*
A/Levice/221/2014	3C.3	2014-04-11	MDCK1/SIAT1	<	160	160	320	160	160	160	40	80	320	160	
A/Levice/223/2014	3C.3	2014-04-15	MDCK1/SIAT1	40	160	160	320	320	160	160	40	80	320	160	*
						Vaccine									

1. < = <40

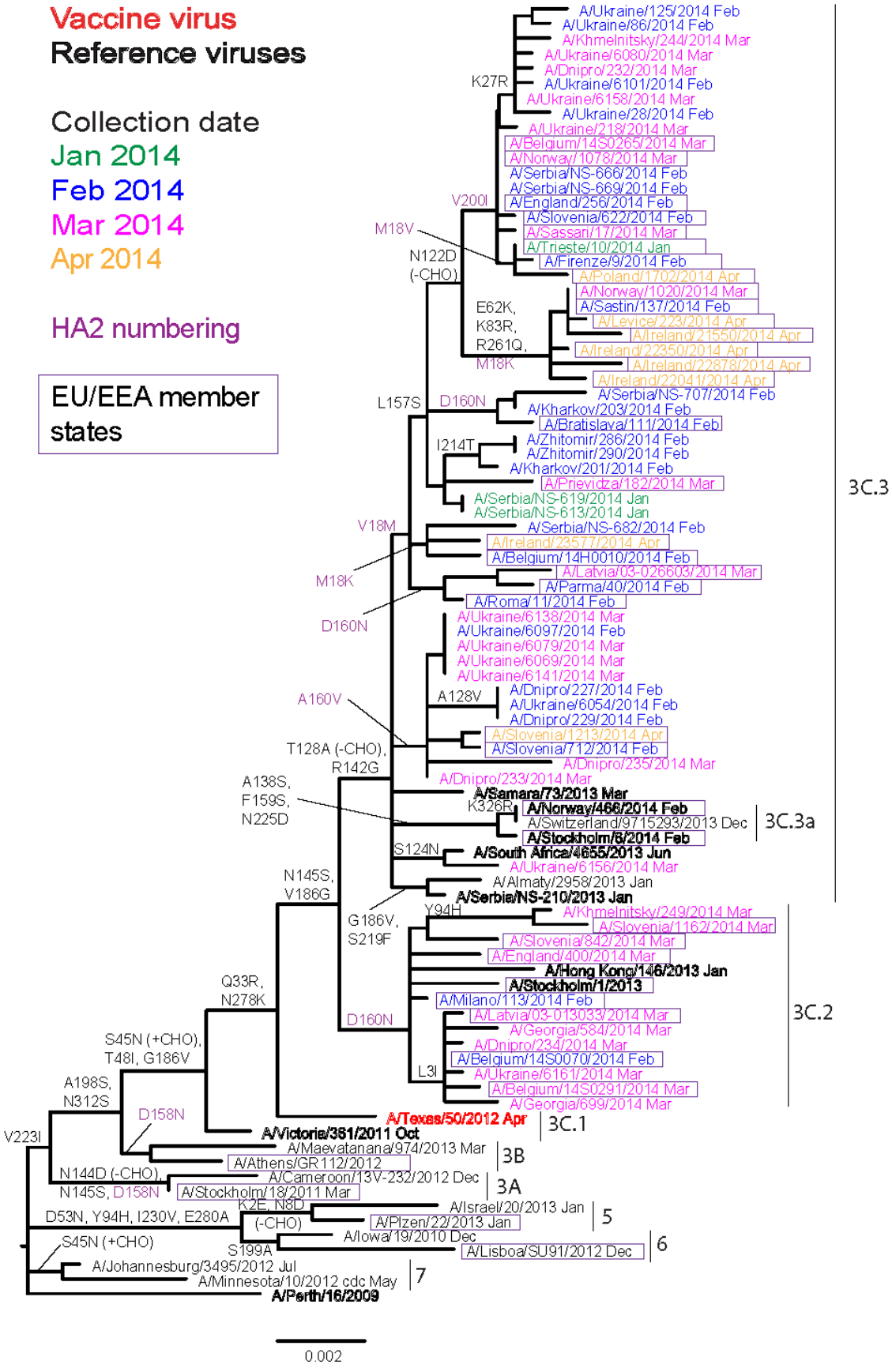
* See Figure 2 = genetic subgroup defined by E62K, K83R, R261Q, M18K (HA2)

Table 3-4. 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 F42/13 3C.1	A/Sam 73/13 F24/13 3C.3	A/Serbia NS-210/13 F39/13 3C.3	A/HK 146/13 F40/13 3C.2	A/SA 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/Norway 466/14 F13/14 3C.3a
REFERENCE VIRUSES													
A/Perth/16/2009		2009-07-04	E3/E3	320	80	80	160	80	160	<	40	<	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	80	320	160	640	320	320	80	160	320	160
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	1280	1280	1280	1280	1280	80	160	160	40
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	320	320	1280	640	640	160	160	640	320
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	1280	1280	1280	1280	640	80	160	160	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	160	320	320	1280	640	1280	80	160	80	80
A/South Africa/4655/2013	3C.3	2013-06-25	E7 clone 101-60	80	80	160	320	160	320	320	320	80	80
A/Stockholm/1/2013	3C.2	2013-01-13	E7 clone 36-18	80	80	160	320	160	320	320	320	80	80
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT2/SIAT2	<	40	40	160	160	80	40	80	320	160
A/Norway/466/2014	3C.3a	2014-02-03	SIAT2/SIAT1	<	40	<	80	40	80	<	80	320	160
TEST VIRUSES													
A/Czech Republic/1/2014	3C.3	unknown	MDCK3/SIAT1	80	160	160	320	320	320	80	80	320	160
A/Czech Republic/6/2014	3C.3	unknown	MDCK3/SIAT1	40	80	80	160	160	80	40	40	160	80
A/Slovenia/142/2014		2014-01-16	MDCK0/SIAT1	80	160	160	320	320	320	80	160	320	160
A/Slovenia/254/2014		2014-01-24	MDCK0/SIAT1	<	160	80	320	160	160	40	80	320	160
A/Slovenia/286/2014		2014-01-28	MDCK1/SIAT1	40	320	160	640	320	320	80	160	320	320
A/Slovenia/321/2014		2014-01-29	SIAT1/SIAT1	<	160	160	320	160	160	40	80	320	160
A/Slovenia/417/2014		2014-02-05	MDCK0/SIAT1	<	160	80	320	160	160	40	80	320	160
A/Slovenia/609/2014		2014-02-13	MDCK1/SIAT1	40	160	160	640	160	320	80	160	320	160
A/Slovenia/622/2014	3C.3	2014-02-14	MDCK1/SIAT1	<	80	80	160	160	80	40	80	160	160
A/Slovenia/694/2014		2014-02-18	SIAT0/SIAT1	<	160	160	640	320	320	80	160	320	160
A/Slovenia/697/2014		2014-02-18	SIAT0/SIAT1	<	160	160	320	160	320	80	160	320	160
A/Slovenia/706/2014		2014-02-19	MDCK0/SIAT1	80	640	320	1280	640	640	160	320	640	320
A/Slovenia/712/2014	3C.3	2014-02-19	SIAT0/SIAT1	<	160	80	320	160	320	40	160	320	160
A/Slovenia/752/2014		2014-02-21	MDCK1/SIAT1	40	320	160	640	320	320	80	160	640	320
A/Slovenia/823/2014		2014-02-26	MDCK0/SIAT1	<	160	160	320	160	160	80	80	320	160
A/Slovenia/842/2014	3C.2	2014-02-28	MDCK1/SIAT1	<	160	80	320	160	160	40	80	320	160
A/Slovenia/853/2014		2014-02-28	MDCK1/SIAT1	<	160	160	320	320	320	80	80	320	160
A/England/399/2014		2014-03-10	SIAT1/SIAT3	80	160	160	320	320	320	80	80	320	160
A/Slovenia/1162/2014	3C.2	2014-03-27	SIAT1/SIAT1	40	320	160	640	320	320	80	160	320	160
A/Slovenia/1213/2014	3C.3	2014-04-02	MDCK1/SIAT2	<	160	160	320	160	160	80	80	160	160
A/Latvia/04-003950/2014		2014-04-02	MDCK2/SIAT1	80	320	320	640	320	320	80	160	320	320
A/Latvia/04-011765/2014		2014-04-04	MDCK1/SIAT1	160	320	320	640	320	320	80	160	320	160
A/Ireland/23577/2014	3C.3	2014-04-12	MDCK1/SIAT2	<	160	80	320	160	160	40	80	320	160
						Vaccine							

1. < = <40

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 May 2014 report[1], are shown in Tables 4 and 5. The clades into which the HA genes fall are shown.

Influenza B – Victoria lineage

Two viruses of the B/Victoria lineage were received from the National Influenza Centre in England. 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 the test viruses at titres fourfold or eightfold reduced compared to the titre with the homologous virus (Table 4). Antisera raised against other viruses exclusively propagated in eggs, B/Malaysia/2506/2006, B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012 similarly 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 two test viruses. Although the titres of the antisera for the homologous cell-propagated viruses were low, ranging from as low as a titre of 40 to 160, only two of the antisera recognised the two test viruses at titres within fourfold of the titres for the 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).

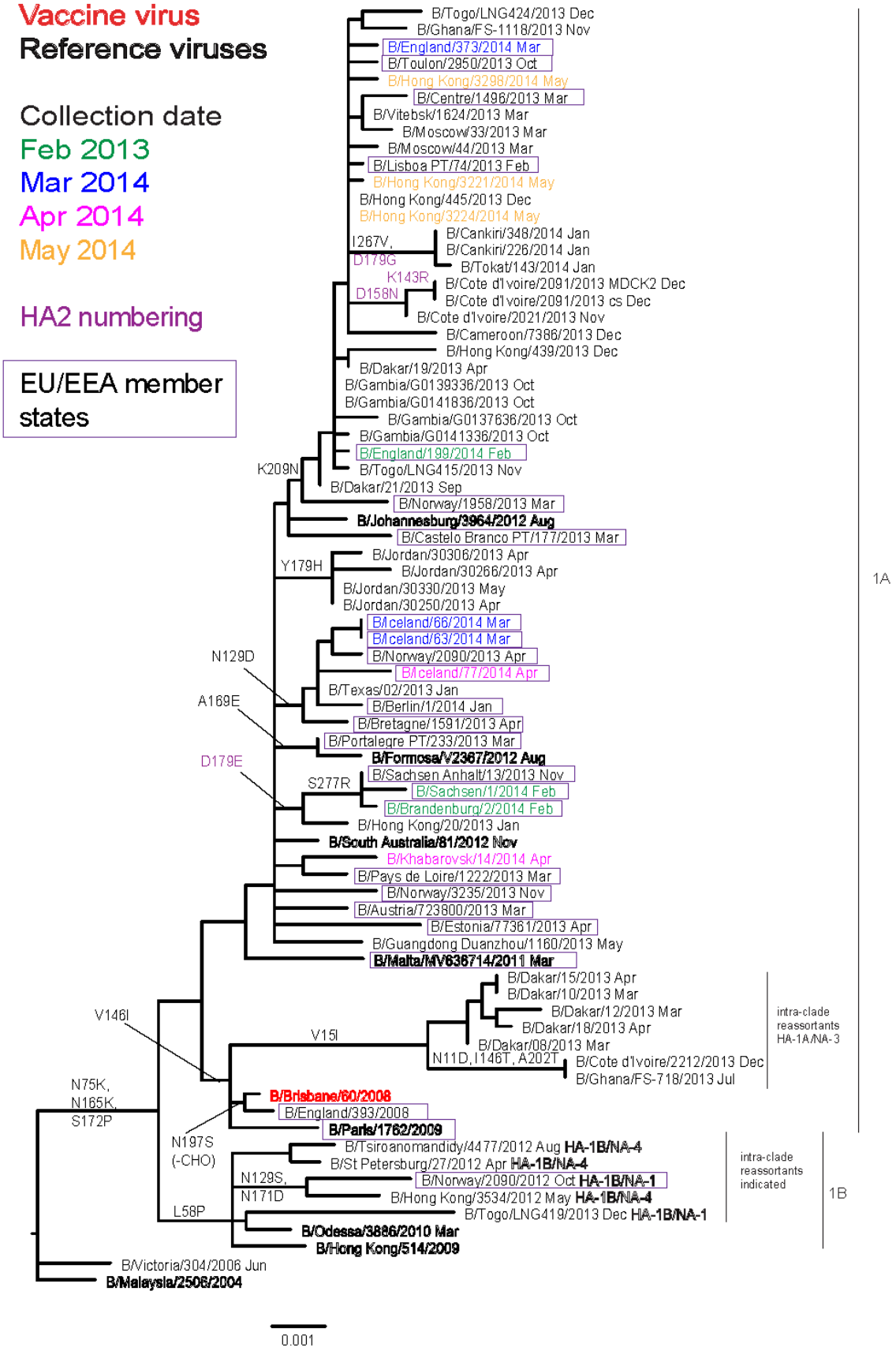
Table 4. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

				Haemagglutination inhibition titre										
				Post infection ferret antisera										
Viruses	Genetic group	Collection date	Passage History	B/Bris[1,3] 60/08 Sh 522 1A	B/Mal[2] 2506/04 F37/11	B/Bris[2] 60/08 F26/13 1A	B/Paris[2] 1762/09 F07/11 1A	B/HK[2] 514/09 F9/13 1B	B/Odessa[2] 3886/10 F19/11 1B	B/Malta[4] 636714/11 F29/13 1A	B/Jhb[1] 3964/12 F01/13 1A	B/For[2] V2367/12 F04/13 1A	B/Sth Aus[2] 81/12 F41/13 1A
REFERENCE VIRUSES														
B/Malaysia/2506/2004		2004-12-06	E3/E6	1280	320	80	<	10	<	80	160	80	320
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	1280	80	320	40	40	40	320	320	160	1280
B/Paris/1762/2008	1A	2009-02-09	C2/MDCK1	2560	10	80	40	80	80	40	20	40	80
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	20	160	80	160	160	160	80	80	320
B/Odessa/3886/2010	1B	2010-03-19	C2/MDCK2	2560	40	320	40	80	80	160	160	160	640
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	80	320	40	40	40	320	160	160	640
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	320	1280	20	160	80	640	1280	640	1280
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK2	2560	20	160	80	80	40	160	80	160	640
B/South Australia/81/2012	1A	2012-11-28	E4/E1	5120	160	1280	80	160	<	320	640	320	1280
TEST VIRUSES														
B/England/199/2014	1A	2014-02-14	MDCK1/MDCK1	2560	20	80	80	80	<	<	<	<	80
B/England/373/2014	1A	2014-03-12	SIAT1/MDCK1	2560	20	40	40	80	<	<	<	<	40
						Vaccine*								

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

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

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 three of the eight 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 six of the test viruses at titres within fourfold of its titre with the homologous virus. Four of the eight viruses were recognised by 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), at titres within fourfold of the titres of the antisera with their homologous viruses. All eight test viruses were recognised well by an antiserum raised against the previous vaccine virus B/Wisconsin/1/2010 and all viruses were recognised well by antiserum raised against B/Stockholm/12/2011, another virus in the B/Wisconsin/1/2010 clade (clade 3). Seven of the eight viruses were recognised at titres within fourfold of the homologous titre by antiserum raised against cell-propagated B/Novosibirsk/1/2012, another virus belonging to clade 3.

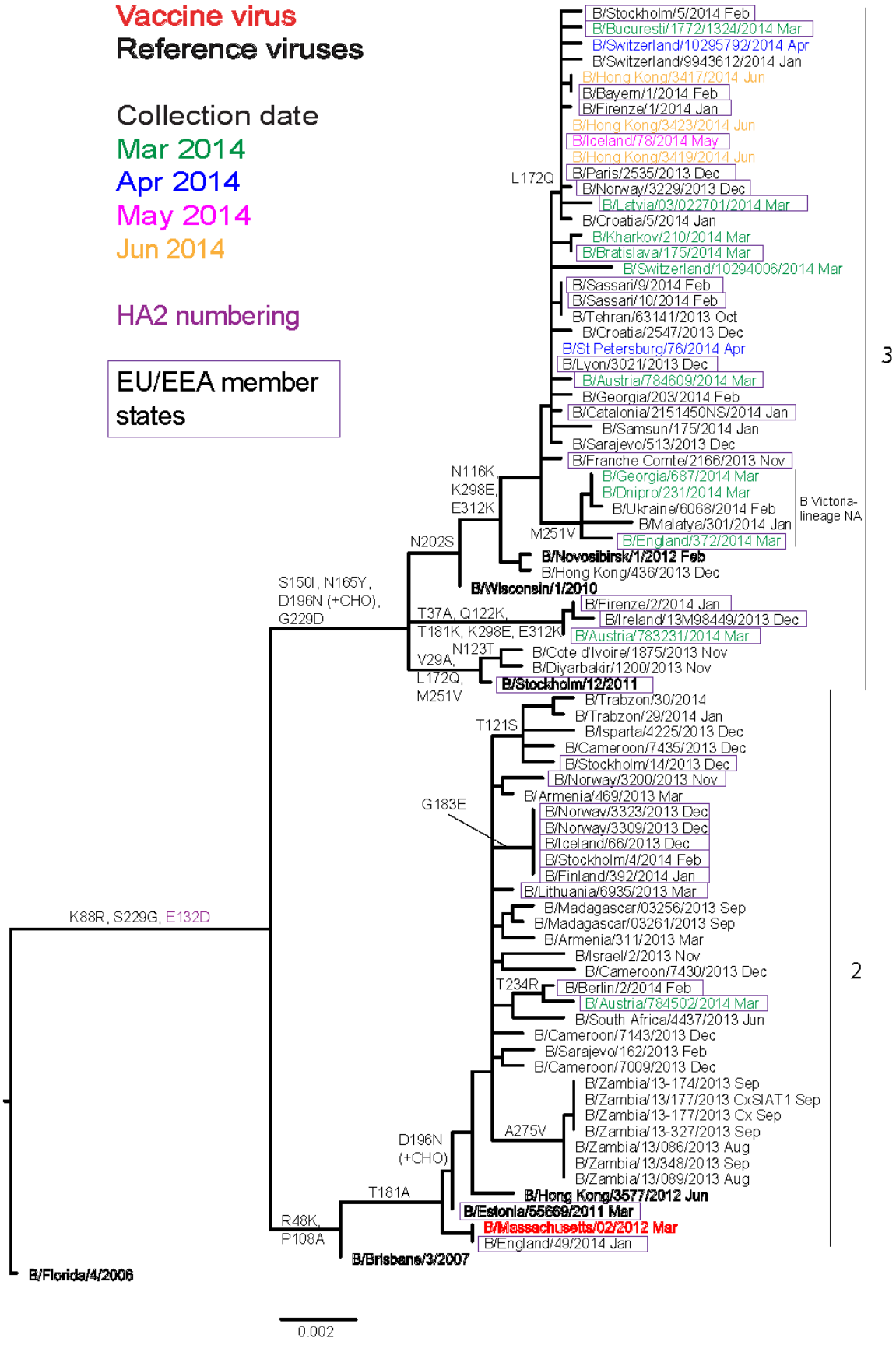
Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. The HA genes of viruses collected since 1 January 2014 fall into the B/Massachusetts/02/2012 clade (clade 2) and the B/Wisconsin/1/2010 clade (clade 3), with those in clade 3 being in the clear majority. Several viruses display reassortment between the two influenza B lineages, with HA genes from the B/Yamagata lineage and NA genes from the B/Victoria lineage, one of which was detected in the EU, B/England/372/2014. The HA sequence of B/England/49/2014 was identical to the vaccine virus B/Massachusetts/02/2012, as was the NA gene sequence. B/England/49/2014 was isolated from a three-year old. It is likely that the B/England/49/2014 was the live-attenuated vaccine virus in use in the United Kingdom.

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

				Haemagglution Inhibition Titre										
				Post infection ferret sera										
Viruses	Genetic Group	Collection date	Passage History	B/Fl[1,3] 4/06 SH479 1	B/Fl[1] 4/06 F1/10 1	B/Bris[2] 3/07 F21/12 2	B/Wis[2] 1/10 F10/13 3	B/Stock[2] 12/11 F12/12 3	B/Est[2] 55669/11 F26/11 2	B/Novo[2] 1/12 F31/12 3	B/HK[2] 3577/12 F33/12 2	B/Mass[2] 02/12 Egg F2/13 2	B/Mass[2] 02/12 T/C F15/13 2	
REFERENCE VIRUSES														
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	640	640	160	320	160	20	160	1280	320	
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	640	640	160	320	160	20	320	1280	320	
B/Wisconsin/1/2010	3	2007-08-07	E3/E2	640	160	160	80	160	<	20	40	160	40	
B/Stockholm/12/2011	3	2007-08-07	E4/E1	1280	80	80	40	160	<	20	40	160	20	
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	640	80	40	20	20	640	40	640	80	320	
B/Novosibirsk/1/2012	3	2012-02-14	C2/MDCK3	640	80	80	160	160	80	160	160	80	320	
B/Hong Kong/3577/2012	2	2012-06-13	MDCK4	2560	80	80	80	160	320	80	640	160	320	
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	640	640	160	320	160	20	160	1280	320	
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	640	160	320	320	40	640	320	640	
TEST VIRUSES														
B/England/49/2014	2	2014-01-21	SIAT1/MDCK1	2560	640	640	160	640	160	80	320	640	320	
B/Finland/392/2014	2	2014-01-26	MDCK1/MDCK1	1280	160	160	80	80	320	20	160	320	640	
B/Stockholm/4/2014	2	2014-02-17	MDCK1MDCK1	1280	160	80	40	80	640	40	640	160	320	
B/Stockholm/5/2014	3	2014-02-21	MDCK0/MDCK1	640	80	40	80	160	40	80	80	80	80	
A/Latvia/03-022701/2014	3	2014-03-11	MDCK 1/MDCK1	640	80	80	160	160	40	80	40	160	160	
B/England/372/2014	3	2014-03-13	SIAT1/MDCK1	1280	80	80	160	160	40	80	40	160	160	B/Vic NA
B/Bratislava/175/2014	3	2014-03-13	MDCK1/MDCK1	640	80	80	160	160	20	80	40	160	80	
B/Bucuresti/1772-1324/2014	3	2014-03-20	MDCK1/MDCK1	2560	160	160	320	320	320	320	640	320	640	
												Vaccine		

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

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



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 June 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 27 June 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 23–25 September 2013 and 17–19 February 2014, can be found at:

http://www.nimr.mrc.ac.uk/documents/about/NIMR-report-Sep2013final.pdf

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