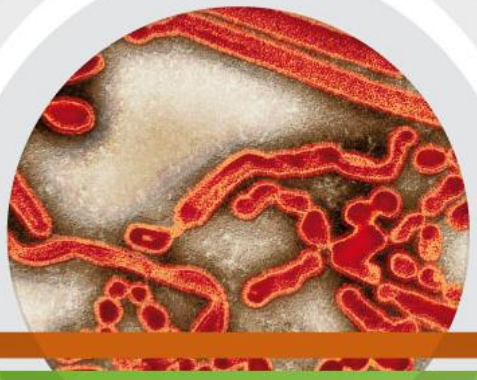

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, May 2014

Summary

During the 2013–14 season A(H1N1)pdm09, A(H3N2), B/Victoria- and B/Yamagata-lineage influenza viruses have continued to cocirculate in EU/EEA Member States. The relative prevalence has varied between countries. Viruses with collection dates after 1 January 2014, from 20 countries, have been received by the WHO Collaborating Centre in London.

- Type A and type B viruses have been received at a ratio of over 20:1.
- A(H3N2) and A(H1N1)pdm09 viruses have been received in similar numbers.
- Recently circulating A(H1N1)pdm09 viruses belonged to genetic subgroups 6B and 6C, with viruses in genetic subgroup 6B predominating greatly. Viruses in subgroups 6B and 6C 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.
- A small set of viruses in genetic subgroup 3C.3 were not recognised well by the panel of antisera and their HA gene sequences encode several amino acid substitutions compared to other viruses in genetic group 3C.3.
- 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.
- Few B/Victoria-lineage viruses have been received, and none were analysed in May. Over the season phylogenetic analysis revealed that all B/Victoria-lineage viruses received were in genetic clade 1A and antigenically similar to the prototype virus B/Brisbane/60/2008 and viruses genetically similar to this prototype virus. B/Brisbane/60/2008 has been recommended by WHO as a component in quadrivalent influenza vaccines for 2013–14 and 2014–15 influenza seasons.

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

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and Research on Influenza (WHO CC), from 20 countries in the EU/EEA region. The large majority (just over 96%) were type A viruses, with A(H3N2) viruses and A(H1N1)pdm09 viruses approximately equally represented (Table 1). Of the small number of type B viruses received (just under 4% of the specimens received), 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											
Belgium	4		3	in process	1	1					
Bulgaria	33		26	26	7	7					
Cyprus	13		9	7	4	4					
Finland	2		1	in process						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	in process				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	in process	11	in process					
Spain	52		38	29	13	11				1	1
Sweden	3		2	in process	1	in process					
United Kingdom	5		2	2	2	2				1	in process
FEBRUARY											
Belgium	6		3	in process	3	in process					
Bulgaria	28		22	22	6	5					
Cyprus	12	1	11	11							
Finland	6		3	3	3	in process					
Germany	11		4	4	3	3		2	2	2	2
Ireland	3		3	in process							
Italy	28		12	11	14	in process				2	2
Latvia	1		1	in process							
Norway	8				8	in process					
Poland	9		2	1	7	5					
Slovakia	5		3	3	2	in process					
Slovenia	20		6	in process	14	in process					
Sweden	6				4	in process				2	in process
United Kingdom	3				2	in process		1	1		
MARCH											
Belgium	7		4	in process	3	in process					
Bulgaria	1		1	1							
Finland	2		1	1	1	in process					
Ireland	3		3	in process							
Italy	3		2	2	1	1					
Latvia	11		7	in process	3	in process				1	in process
Norway	6				6	4					
Poland	26	2	2	0	22	8					
Slovakia	3		1	1	1	in process				1	1
Slovenia	3		2	in process	1	in process					
United Kingdom	8		4	4	2	in process		1	1	1	1
APRIL											
Belgium	10		2	in process	7	in process		1	in process		
Ireland	4		1	in process	3	in process					
Latvia	2				2	in process					
Poland	3		2	2	1	1					
Slovakia	3		1	in process	2	in process					
Slovenia	2		1	in process	1	in process					
	517	3	255	172	239	112	0	6	5	14	10
			49.3%		46.2%			1.2%		2.7%	
20 Countries			96.1%					3.9%			

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 received since the April 2014 report[1] are shown in Tables 2-1, 2-2 and 2-3. Antigenically, test viruses were similar to the vaccine virus as assessed by HI assay; all showed no more than twofold reduced HI titres with antiserum raised against the vaccine virus (A/California/7/2009), compared with the titre for the vaccine virus. Viruses for which gene sequences are included in the phylogenetic tree (Figure 1) are highlighted and, where known, the HA genetic group 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. Viruses collected after 31 December 2013 in the EU/EEA, and those characterised since the April 2014 report, fell into genetic subgroup 6B. Genetic subgroup 6B 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.

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

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/HK 5659/12 F30/12 6A	A/SA 3626/13 F3/14 6B	G155E	G155E>G, D222G
REFERENCE VIRUSES															
A/California/7/2009		2009-04-09	E1/E2	1280	1280	1280	320	160	320	320	320	320	320		
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	160	160	40	80	80	80	80	80		
A/Lviv/N6/2009		2009-10-27	MDCK4/SI/MDCK3	640	1280	640	160	80	160	160	160	320	160		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	2560	5120	640	2560	1280	5120	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	640	320	640	1280	640	1280	2560	640		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	2560	1280	1280	2560	2560	5120	2560	1280		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	640	1280	1280	2560	2560	1280	5120	5120	1280		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	640	320	640	1280	640	2560	2560	640		
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	640	640	320	640	640	640	1280	1280	1280		
TEST VIRUSES															
A/Bulgaria/1042/2013	6B	2013-12-20	SIAT1/MDCK1	640	640	1280	640	1280	1280	1280	2560	2560	1280		
A/Bulgaria/009/2014		2014-01-05	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Bulgaria/015/2014		2014-01-07	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/017/2014		2014-01-07	SIAT2/MDCK1	640	320	1280	1280	1280	1280	1280	5120	2560	1280		
A/Bulgaria/039/2014		2014-01-08	SIAT2/MDCK1	640	320	1280	640	1280	1280	1280	5120	2560	1280		
A/Bulgaria/042/2014	6B	2014-01-08	SIAT2/MDCK1	1280	640	1280	1280	1280	1280	1280	2560	2560	1280		
A/Bulgaria/093/2014		2014-01-13	SIAT2/MDCK1	640	320	1280	640	1280	1280	1280	5120	2560	1280		
A/Bulgaria/121/2014	6B	2014-01-13	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	1280	5120	2560	2560		
A/Parma/9/2014		2014-01-15	MDCK1/MDCK1	1280	640	1280	640	1280	2560	2560	5120	5120	1280		
A/Bulgaria/171/2014		2014-01-16	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/177/2014		2014-01-16	SIAT2/MDCK1	640	640	640	640	1280	2560	1280	2560	2560	1280		
A/Bulgaria/211/2014		2014-01-16	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	5120	5120	5120	2560		
A/Bulgaria/217/2014	6B	2014-01-16	SIAT2/MDCK1	640	640	1280	640	1280	2560	1280	5120	2560	1280		
A/Bulgaria/218/2014		2014-01-16	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	5120	2560	1280		
A/Bulgaria/219/2014		2014-01-16	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Parma/7/2014		2014-01-20	MDCK2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Bulgaria/513/2014	6B	2014-01-22	SIAT2/MDCK1	640	320	1280	640	1280	2560	2560	5120	2560	1280		
A/Milano/24/2014		2014-01-22	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/348/2014		2014-01-23	SIAT2/MDCK1	640	320	640	640	640	1280	1280	2560	1280	1280		
A/Bulgaria/386/2014		2014-01-23	SIAT2/MDCK1	1280	640	1280	640	1280	2560	1280	5120	2560	1280		
A/Ukraine/28/2014	6B	2014-01-24	SIAT2/MDCK1	640	320	1280	640	2560	1280	1280	5120	2560	1280		
A/Bulgaria/408/2014		2014-01-27	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	1280		
A/Bulgaria/435/2014	6B	2014-01-28	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560		
A/Parma/15/2014		2014-01-28	MDCK1/MDCK1	1280	640	1280	640	5120	2560	2560	5120	5120	1280		
A/Bulgaria/447/2014		2014-01-29	SIAT1/MDCK1	1280	640	1280	2560	2560	2560	2560	5120	5120	2560		
A/Bulgaria/449/2014		2014-01-29	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	640		
A/Bulgaria/451/2014		2014-01-29	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	5120	2560	640		
A/Bulgaria/483/2014		2014-01-29	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Firenze/5/2014	6B	2014-01-30	SIAT1/MDCK1	640	320	640	320	1280	1280	1280	2560	2560	640		
A/Parma/23/2014		2014-01-31	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560		
A/Milano/69/2014	6B	2014-02-03	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	1280	5120	2560	1280		
A/Roma/9/2014	6B	2014-02-03	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	640		
A/Genova/04/2014		2014-02-07	SIAT1/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	1280		
A/Genova/6/2014	6B	2014-02-07	SIAT1/MDCK1	640	320	320	320	640	1280	640	1280	1280	640		
A/Roma/10/2014	6B	2014-02-09	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Genova/01/2014	6B	2014-02-10	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Parma/31/2014	6B	2014-02-11	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	1280	5120	2560	2560		

Vaccine

Sequence in phylogenetic tree

Table 2-2. 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 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	G155E	G155E>G, D222G
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		
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	320	160	320	160		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	1280	5120	1280	2560	1280	5120	2560	1280		
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	640	320	1280	1280	640	2560	1280	640		
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	640	320	640	640	640	1280	640	2560	1280	640		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	2560	1280	1280	2560	2560	5120	2560	1280		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	640	320	640	1280	640	2560	1280	640		
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	1280	640	1280	1280	1280	2560	1280	5120	2560	2560		
TEST VIRUSES															
A/Bulgaria/475/2014	6B	2014-01-30	SIAT1/MDCK1	1280	1280	2560	2560	2560	5120	2560	5120	5120	2560		
A/Bulgaria/478/2014		2014-01-30	SIAT1/MDCK1	640	640	1280	640	1280	1280	1280	2560	2560	1280		
A/Bulgaria/665/2014		2014-02-05	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Bulgaria/659/2014		2014-02-06	SIAT1/MDCK1	640	640	1280	1280	2560	1280	2560	2560	2560	1280		
A/Bulgaria/706/2014		2014-02-07	SIAT2/MDCK1	640	640	1280	1280	2560	2560	2560	2560	2560	1280		
A/Bulgaria/819/2014		2014-02-08	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	1280	1280	1280		
A/Bulgaria/821/2014		2014-02-08	SIAT2/MDCK1	640	320	640	640	1280	2560	2560	2560	2560	1280		
A/Bulgaria/823/2014		2014-02-08	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	2560	2560	1280		
A/Bulgaria/812/2014	6B	2014-02-09	SIAT2/MDCK1	640	640	1280	1280	1280	2560	1280	2560	2560	1280		
A/Bulgaria/775/2014	6B	2014-02-11	SIAT2/SIAT2	320	160	640	320	640	640	640	1280	1280	640		
A/Perugia/28/2014	6B	2014-02-14	MDCK1/MDCK1	1280	640	1280	1280	2560	1280	2560	5120	2560	1280		
A/Milano/117/2014		2014-02-17	SIAT1/MDCK1	1280	640	2560	2560	2560	2560	2560	5120	5120	2560		
A/Milano/112/2014	6C	2014-02-18	SIAT1/MDCK1	640	640	1280	640	1280	1280	2560	5120	2560	1280		
A/Poland/16K/2014	6C	2014-02-21	MDCK3	1280	640	1280	1280	1280	1280	1280	5120	2560	1280		
A/Perugia/38/2014	6B	2014-02-26	MDCK1/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	2560	2560		
A/Perugia/44/2014		2014-03-10	MDCK1/MDCK1	640	640	1280	1280	1280	2560	2560	2560	5120	1280		
A/Perugia/45/2014	6B	2014-03-14	MDCK2/MDCK1	640	320	640	640	1280	1280	640	1280	2560	1280		
A/Poland/1480/2014	6B		MDCK3	1280	640	2560	1280	2560	2560	2560	5120	5120	2560		
								Vaccine							

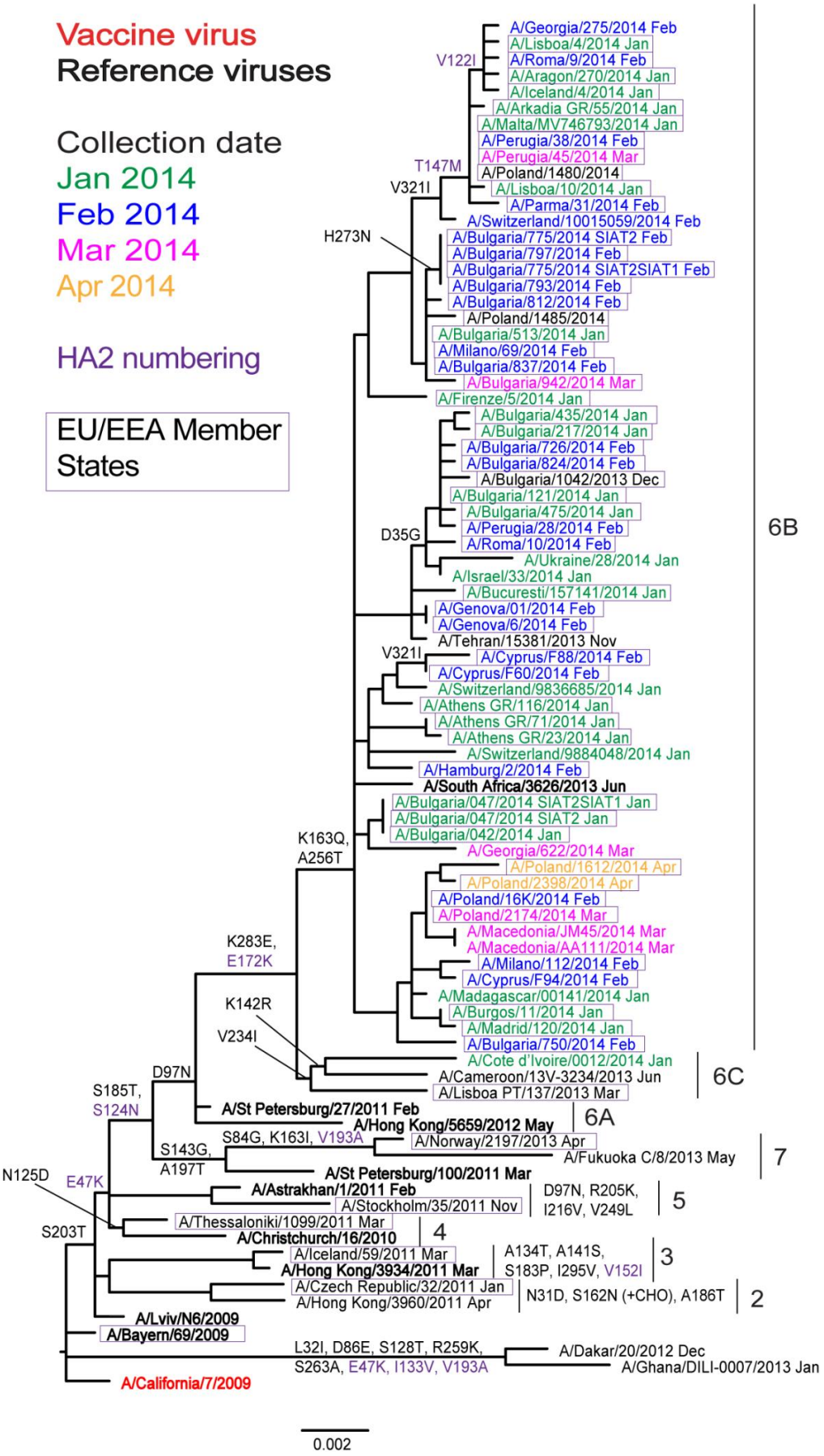
Sequence in phylogenetic tree

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

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera: A/Cal 7/09 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	G155E	G155E>G, D222G
REFERENCE VIRUSES															
A/California/7/2009		2009-04-09	E1/E2	1280	640	1280	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		
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	320	160	320	160		
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	2560	5120	2560	2560	2560	5120	2560	2560		
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	MDCK1/MDCK6	1280	640	1280	1280	2560	2560	2560	2560	2560	1280		
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	2560	1280	2560	1280	2560	2560	2560	5120	5120	2560		
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	640	320	1280	1280	640	1280	1280	1280		
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	320	640	640	1280	1280	640	1280	1280	1280		
TEST VIRUSES															
A/Bulgaria/047/2014	6B	2014-01-09	SIAT2/MDCK1	640	320	1280	1280	1280	1280	2560	2560	2560	1280		
A/Switzerland/10015059/2014	6B	2014-02-03	MDCK2	1280	640	1280	1280	2560	2560	2560	5120	5120	1280		
A/Bulgaria/700/2014		2014-02-10	SIAT2/MDCK1	1280	320	1280	1280	2560	1280	2560	2560	2560	2560		
A/Bulgaria/723/2014		2014-02-10	SIAT2/MDCK1	1280	640	2560	2560	2560	2560	2560	5120	2560	2560		
A/Bulgaria/750/2014	6C	2014-02-10	SIAT2/MDCK1	640	320	640	1280	1280	1280	1280	2560	2560	1280		
A/Bulgaria/726/2014	6B	2014-02-11	SIAT2/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/774/2014		2014-02-11	SIAT1/MDCK1	1280	640	2560	2560	2560	2560	2560	5120	5120	2560		
A/Bulgaria/747/2014		2014-02-12	SIAT2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560		
A/Bulgaria/824/2014	6B	2014-02-12	SIAT1/MDCK1	1280	640	2560	2560	2560	5120	2560	5120	5120	2560		
A/Bulgaria/793/2014	6B	2014-02-14	SIAT2/MDCK1	640	320	640	640	1280	2560	1280	2560	2560	2560		
A/Bulgaria/805/2014		2014-02-14	SIAT2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280		
A/Georgia/275/2014	6B	2014-02-14	MDCK2	640	640	1280	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/795/2014		2014-02-16	SIAT2/MDCK1	1280	320	1280	1280	2560	2560	2560	5120	5120	2560		
A/Bulgaria/797/2014	6B	2014-02-17	SIAT2/MDCK1	640	160	320	320	1280	1280	640	1280	1280	1280		
A/Bulgaria/837/2014	6B	2014-02-19	SIAT1/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	2560	2560		
A/Bulgaria/942/2014	6B	2014-03-03	SIAT2/MDCK1	1280	640	2560	1280	5120	2560	2560	5120	2560	2560		
A/Georgia/622/2014	6B	2014-03-18	MDCK2	1280	640	1280	2560	2560	2560	2560	5120	2560	2560		
				Vaccine											

Sequence in phylogenetic tree

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 one of the viruses examined since the April 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 and 3-3. Viruses for which gene sequences are included in the phylogenetic tree are highlighted and, where known, the HA genetic group is indicated.

All but seven of the 63 test viruses analysed since the April 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. 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 (>80%) of test viruses at titres within fourfold of the titres of the antisera with their corresponding homologous viruses.

Ferret antisera raised against reference viruses exclusively propagated in tissue culture cells, A/Stockholm/18/2011, A/Athens/112/2012, A/Samara/73/2013 and A/Victoria/361/2011 – recognised the test viruses more effectively. Each recognised ~95% of test viruses analysed since the April 2014 report at titres within fourfold of those for the antisera with their corresponding homologous viruses. Two viruses, A/Norway/466/2014 and one of two cultivars of A/Stockholm/6/2014, were recognised poorly by all four of the antisera raised against the cell-propagated reference viruses (Table 3-3).

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 HA genes of viruses characterised at NIMR from EU/EEA countries since the April 2014 report fell in genetic group 3. This group has three subdivisions: 3C.1, 3C.2 and 3C.3.

The vaccine virus A/Texas/50/2012 belongs to genetic subgroup 3C.1. Viruses characterised genetically since the April 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 HA genes of A/Norway/466/2014 and A/Stockholm/6/2014, viruses that reacted poorly with antisera raised against the cell-propagated reference viruses,fell within a discrete cluster in genetic subgroup 3C.3 (3C.3*). The HA genes encoded the amino acid substitutions A138S, F159S and N225D. 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	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1]											
				Post infection ferret antisera											
				A/Perth 16/09	A/Vic 361/11	A/Athens 112/12	A/Texas 50/12	A/Samara 73/13	A/Serbia NS-210/13	A/HK 146/13	NIB-85	A/SA 4655/13	A/Stock 1/13
				F35/11 T/C	F11/13	F16/12 Egg	F42/13	F24/13	F39/13	F40/13	F45/13	F10/14	F12/14
					3C.1	3B	3C.1	3C.3	3C.3	3C.2	3C.3	3C.3	3C.2
REFERENCE VIRUSES													
A/Perth/16/2009		2009-07-04	E3/E3	640	640	640	160	160	160	160	160	40	80
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT3	80	640	320	160	320	160	160	160	80	80
A/Athens/112/2012	3B	2012-02-01	SIAT5	80	640	640	160	320	320	320	320	80	160
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	5120	1280	1280	1280	2560	1280	640	160	320
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	1280	1280	320	1280	640	1280	640	160	320
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	2560	1280	1280	1280	1280	1280	1280	80	160
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	2560	1280	640	1280	640	2560	1280	160	320
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	320	5120	1280	1280	640	1280	2560	1280	160	160
A/South Africa/4655/2013	3C.3	2013-06-13	E7 clone 101-60	80	640	320	160	320	160	320	160	320	320
A/Stockholm/1/2013	3C.2	2013-01-13	E6 clone 36-18	80	640	320	160	320	160	320	160	320	320
TEST VIRUSES													
A/Norway/86/2014	3C.3	2014-01-08	MDCK2/SIAT1	<	320	160	80	320	160	160	160	80	80
A/Norway/160/2014		2014-01-08	MDCK1/SIAT1	<	640	640	160	320	320	320	320	80	160
A/Norway/184/2014	3C.3	2014-01-08	MDCK1/SIAT1	<	640	640	320	640	320	640	320	80	160
A/Norway/163/2014		2014-01-11	MDCK2/SIAT1	40	640	320	160	640	320	320	320	80	160
A/Norway/161/2014	3C.3	2014-01-12	MDCK2/SIAT1	40	640	320	160	640	320	320	320	80	160
A/Norway/228/2014		2014-01-12	MDCK2/SIAT1	80	640	320	160	640	320	320	320	80	160
A/Norway/162/2014		2014-01-13	MDCK1/SIAT1	<	640	320	160	320	320	320	320	80	160
A/Norway/120/2014	3C.3	2014-01-14	MDCK1/SIAT1	<	640	640	160	320	320	320	320	80	160
A/Norway/226/2014	3C.3	2014-01-14	MDCK1/SIAT1	<	320	320	80	320	160	160	160	80	80
A/Norway/208/2014		2014-01-16	MDCK1/SIAT1	<	320	320	160	320	320	320	320	80	160
A/Poland/1877/2014		2014-03-03	SIAT2	40	640	640	160	320	320	320	320	80	160
A/Norway/1003/2014	3C.3	2014-03-04	SIAT2	40	640	640	160	320	160	160	160	40	80
A/Norway/1020/2014	3C.3	2014-03-07	SIAT2	<	640	640	80	320	80	80	160	<	80
A/Norway/1130/2014		2014-03-11	SIAT2	<	640	320	160	640	160	320	160	80	160
A/Norway/1078/2014	3C.3	2014-03-16	SIAT2	<	320	320	80	320	160	160	160	40	160
A/Poland/3464/2014	3C.2	2014-03-19	SIAT2	<	640	320	160	320	160	320	320	80	160
							Vaccine						

1. < = <40

Sequence in phylogenetic tree

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/Stock 18/11 F12/13 3A	A/Iowa 19/10 F18/13 6	A/Vic 361/11 T/C F11/13 3C.1	A/Athens 112/12 F16/12 3B	A/Texas 50/12 Egg F42/13 3C.1	A/Samara 73/13 F24/13 3C.3	A/Serbia NS-210/13 F39/13 3C.3	A/HK 146/13 F40/13 3C.2	NIB-85 F45/13 3C.3
REFERENCE VIRUSES													
A/Perth/16/2009		2009-07-04	E3/E3	640	320	160	640	640	320	160	160	160	160
A/Stockholm/18/2011	3A	2011-03-28	SIAT5	80	640	160	640	640	160	640	320	160	320
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	1280	1280	2560	2560	1280	1280	1280	640	640
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT3	80	320	160	320	320	160	320	160	160	160
A/Athens/112/2012	3B	2012-02-01	SIAT5	160	640	320	640	640	160	320	320	320	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	1280	640	2560	1280	1280	640	1280	640	1280
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	1280	320	1280	640	320	1280	640	640	640
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	2560	640	2560	1280	1280	1280	1280	1280	1280
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	2560	640	2560	1280	640	1280	640	2560	640
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	2560	1280	2560	2560	1280	1280	1280	2560	1280
TEST VIRUSES													
A/Bulgaria/040/2014	3C.3	2014-01-08	SIAT2/SIAT1	40	640	320	1280	640	160	640	320	320	320
A/Bulgaria/127/2014	3C.3	2014-01-14	SIAT2/SIAT1	40	640	320	640	640	320	640	320	320	320
A/Bulgaria/200/2014		2014-01-15	SIAT2/SIAT1	40	640	320	1280	640	160	640	320	320	320
A/Norway/309/2014		2014-01-17	MDCK1/SIAT1	<	320	80	640	640	160	640	320	160	160
A/Norway/211/2014	3C.3	2014-01-18	LLC/MDCK2/MDCK1/SIAT1	40	320	160	640	640	160	640	320	160	320
A/Norway/293/2014		2014-01-20	LLC/MDCK2/MDCK1/SIAT1	40	320	160	640	640	160	640	320	160	320
A/Norway/272/2014	3C.3	2014-01-23	MDCK1/SIAT1	40	640	320	1280	640	320	1280	640	640	640
A/Norway/313/2014	3C.3	2014-01-23	MDCK1/SIAT1	40	640	160	640	640	160	640	320	320	320
A/Norway/371/2014		2014-01-23	MDCK1/SIAT1	160	1280	640	1280	640	320	1280	640	640	640
A/Norway/277/2014	3C.3	2014-01-26	MDCK1/SIAT1	40	640	160	640	640	160	640	320	320	320
A/Norway/369/2014		2014-01-29	MDCK2/SIAT1	40	320	160	640	640	320	640	320	320	320
A/Poland/896/2014	3C.3	2014-01-29	SIAT2	40	320	160	640	320	160	640	320	320	320
A/Norway/409/2014	3C.3	2014-01-30	LLC/MDCK2/MDCK1/SIAT1	40	640	160	640	640	320	640	640	320	320
A/Poland/1861/2014		2014-02-24	SIAT2	<	320	160	640	320	80	320	160	160	160
A/Poland/39/2014	3C.3	2014-02-26	SIAT2	<	320	160	640	320	80	160	160	160	160
A/Poland/40/2014	3C.3	2014-02-26	SIAT2	<	320	160	640	320	160	320	160	160	160
A/Poland/1955/2014	3C.3	2014-02-26	SIAT2	<	320	160	640	320	160	640	320	320	160
A/Poland/758/2014		2014-02-28	SIAT2	<	640	640	1280	640	640	640	640	640	640
A/Poland/2175/2014		2014-03-04	SIAT2	<	320	160	640	640	160	640	320	320	160
A/Poland/1899/2014	3C.3	2014-03-12	SIAT2	<	640	160	640	640	160	640	320	320	160
A/Poland/1905/2014	3C.3	2014-03-21	SIAT2	80	1280	320	1280	1280	160	1280	320	320	320
A/Poland/3487/2014	3C.3	2014-03-26	SIAT2	80	640	320	320	640	160	1280	320	640	320
A/Poland/120/2014	3C.3		SIAT2	<	320	160	320	320	160	320	160	160	160
A/Poland/148/2014	3C.3		SIAT2	40	320	80	320	320	80	320	160	160	80
A/Poland/154/2014	3C.3		SIAT2	<	320	160	320	320	160	640	320	320	160
A/Poland/160/2014	3C.3		SIAT2	40	320	160	640	640	80	640	320	320	160
A/Poland/179/2014	3C.3		SIAT2	40	640	160	640	2560	160	640	320	320	320

1. < = <40

Vaccine

Sequence in phylogenetic tree

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

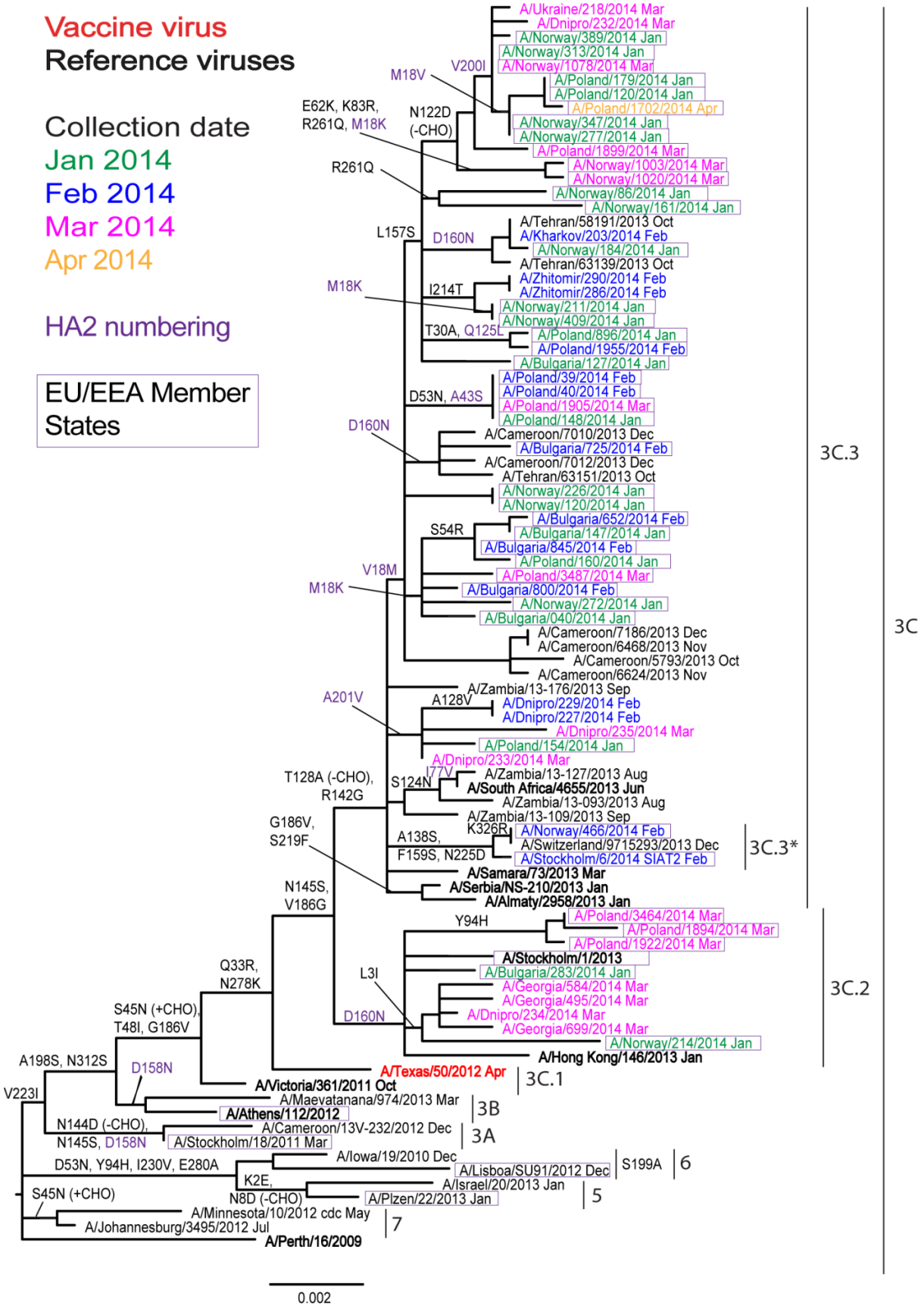
Viruses	Collection Date	Passage History	Haemagglutination inhibition titre[1]											
			Post infection ferret antisera											
			A/Perth 16/09	A/Stock 18/11	A/Iowa 19/10	A/Vic 361/11	A/Athens 112/12	A/Texas 50/12	A/Samara 73/13	A/Serbia NS-210/13	A/HK 146/13	NIB-85		
			F35/11	F12/13	F15/11	T/C F11/13	F16/12	Egg F42/13	F24/13	F39/13	F40/13	F45/13		
Genetic group				3A	6	3C.1	3B	3C.1	3C.3	3C.3	3C.2	3C.3		
REFERENCE VIRUSES														
A/Perth/16/2009	2009-07-04	E3/E3	640	320	320	320	640	160	160	160	160	160		
A/Stockholm/18/2011 3A	2011-03-28	SIAT5	40	640	160	320	320	160	320	160	160	160		
A/Iowa/19/2010 6	2010-12-30	E3/E1	640	2560	5120	2560	2560	2560	1280	1280	1280	1280		
A/Victoria/361/2011 3C.1	2011-10-24	MDCK2/SIAT3	80	320	160	320	320	160	320	160	160	160		
A/Athens/112/2012 3B	2012-02-01	SIAT4	80	640	160	320	640	320	320	320	320	320		
A/Texas/50/2012 3C.1	2012-04-15	E5/E2	320	1280	1280	1280	1280	1280	320	1280	1280	320		
A/Samara/73/2013 3C.3	2013-03-12	C1/SIAT2	80	640	320	640	1280	640	640	320	1280	640		
A/Serbia/NS-210/2013 3C.3	2013-01-18	E5/E1	320	1280	1280	1280	1280	1280	640	1280	1280	1280		
A/Hong Kong/146/2013 3C.2	2013-01-11	E5/E1	320	1280	1280	640	1280	1280	320	320	1280	1280		
NIB-85 (A/Almaty/2958/2013) 3C.3	2013-01-27	E5/E1	320	1280	1280	1280	1280	1280	640	1280	2560	1280		
TEST VIRUSES														
A/Bulgaria/147/2014 3C.3	2014-01-14	SIAT1/SIAT2	<	160	80	320	160	40	160	80	80	160	A138S, F159S, N225D, K326R	
A/Bulgaria/283/2014 3C.2	2014-01-21	SIAT2/SIAT1	<	320	80	160	320	160	160	160	160	160	A138S, 159F=S, N225D	
A/Bulgaria/507/2014	2014-01-22	SIAT2/SIAT1	40	320	80	160	640	160	320	160	160	160	A138S, F159S, N225D	
A/Norway/347/2014 3C.3	2014-01-24	MDCK2/SIAT2	<	320	160	640	320	80	320	160	160	320		
A/Norway/328/2014	2014-01-25	MDCK2/SIAT2	<	320	160	320	320	80	320	160	160	160		
A/Norway/358/2014	2014-01-27	MDCK1/SIAT2	<	160	80	320	160	40	320	160	80	160		
A/Norway/389/2014 3C.3	2014-01-29	MDCK1/SIAT2	<	160	80	320	160	40	320	80	80	160		
A/Bulgaria/477/2014	2014-01-30	SIAT2/SIAT1	40	320	80	160	640	160	320	160	320	160		
A/Norway/466/2014[2] 3C.3	2014-02-03	SIAT2	<	40	<	40	80	<	80	80	80	80		
A/Stockholm/6/2014[2] 3C.3	2014-02-06	MDCK1/SIAT1	<	80	40	80	160	80	160	80	80	80		
A/Stockholm/6/2014[2] 3C.3	2014-02-06	SIAT2	<	40	<	<	80	<	80	80	80	80		
A/Bulgaria/652/2014 3C.3	2014-02-06	SIAT1/SIAT1	<	320	80	160	640	80	320	80	160	80		
A/Bulgaria/725/2014 3C.3	2014-02-11	SIAT2/SIAT1	<	320	80	160	320	160	320	160	160	160		
A/Bulgaria/806/2014	2014-02-13	SIAT2/SIAT1	<	320	80	160	320	160	320	160	160	160		
A/Bulgaria/800/2014 3C.3	2014-02-14	SIAT2/SIAT1	<	160	80	160	160	80	320	160	160	160		
A/Bulgaria/845/2014 3C.3	2014-02-19	SIAT2/SIAT1	<	320	80	320	320	160	320	160	160	160		
A/Poland/1111/2014	2014-03-10	SIAT3	<	640	320	640	640	160	640	320	320	160		
A/Poland/1900/2014	2014-03-12	SIAT3	<	160	160	640	320	80	320	160	160	160		
A/Poland/1256/2014	2014-03-18	SIAT3	<	640	160	640	320	160	640	160	160	320		
A/Poland/1702/2014 3C.3	2014-04-08	SIAT3	<	320	160	640	640	160	640	160	160	320		
								Vaccine						

1. < = <40

2. HA1 amino acid substitutions and polymorphisms relative to the HAs of other 3C.3 viruses

Sequence in phylogenetic tree

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/Yamagata-lineage from EU/EEA countries, analysed since the March 2014 report[3], are shown in Table 4. The clades into which the HAs fall are shown. Post-infection ferret antiserum raised against the current, egg-propagated, vaccine virus B/Massachusetts/02/2012 recognised all three test viruses at titres fourfold or eightfold reduced compared to the titre with the homologous virus. A ferret antiserum raised against a cell-propagated cultivar of B/Massachusetts/02/2012 recognised two of the three test viruses at titres within twofold of its titre with the homologous virus. One of the test viruses, B/Sassari/10/2014, was recognised by ferret antisera raised against two other viruses with HA genes belonging to the B/Massachusetts/02/2012 clade (Clade 2), B/Estonia/55669/2011 and B/Hong Kong/3577/2012, at titres equal to or within twofold of the titres of the antisera with their homologous viruses. All three test viruses were recognised well by an antiserum raised against the previous vaccine virus B/Wisconsin/1/2010, and all three were recognised at titres within fourfold of the homologous titre by antiserum raised against cell-propagated B/Novosibirsk/1/2012, a virus belonging to the B/Wisconsin/1/2010 clade, Clade 3.

Figure 3 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. The HA genes of viruses collected since 01 January 2014 fell 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 majority. Four viruses from outside the EU/EAA were reassortant viruses between the two influenza B lineages, with HA genes from the B/Yamagata lineage and NA genes from the B/Victoria lineage.

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

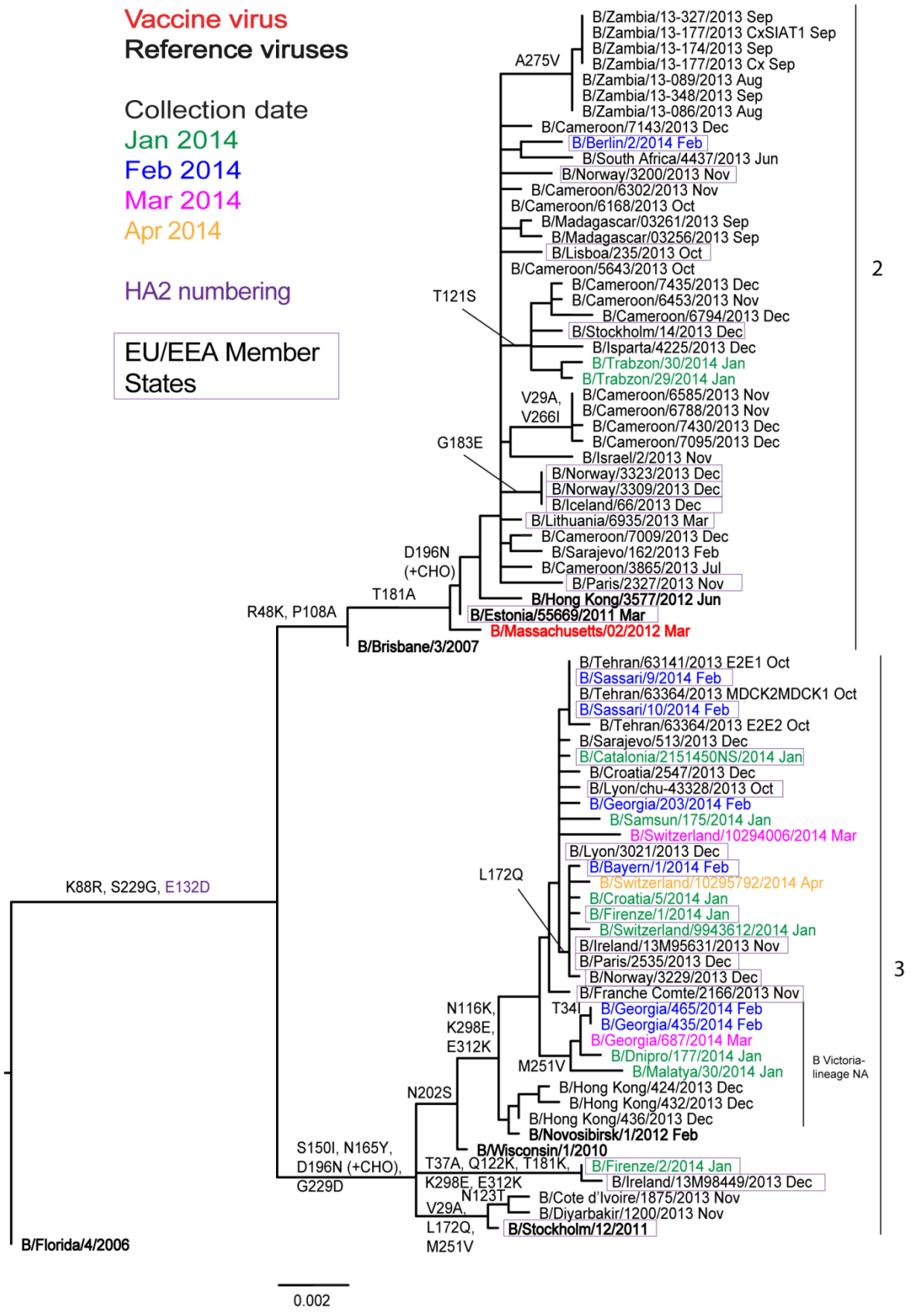
Table 4. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglution Inhibition Titre[1]													
				Post infection ferret sera													
				B/Fl[2] 4/06 SH479 1	B/Fl 4/06 F1/10 1	B/Bris 3/07 F21/12 2	B/Wis 1/10 F10/13 3	B/Stock 12/11 F12/12 3	B/Estonia 55669/11 F26/11 2	B/Novo 1/12 F31/12 3	B/HK 3577/12 F33/12 2	B/Mass 02/12 Egg F2/13 2	B/Mass 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	2560	640	640	80	320	80	20	160	640	160				
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	640	160	320	320	40	640	320	640				
TEST VIRUSES																	
B/Firenze/2/2014	3	2014-01-14	MDCK2/MDCK1	640	40	40	40	40	20	40	80	80	80				
B/Sassari/9/2014	3	2014-02-13	Cx/MDCK1	1280	80	80	160	160	80	160	160	80	320				
B/Sassari/10/2014	3	2014-02-25	Cx/SIAT1	2560	160	160	320	320	320	320	640	160	320				
														Vaccine			

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

Sequence in phylogenetic tree

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



Influenza A(H7N9) virus

On 1 April 2013, the WHO Global Alert and Response [1] reported that the China Health and Family Planning Commission notified the World Health Organization (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 May 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 28 February 2014 [5]. The most recent update of the epidemiological situation published by WHO was posted on 15 May 2014. The numbers of cases of human infection and their geographic location has been summaried by WHO on 08 April 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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