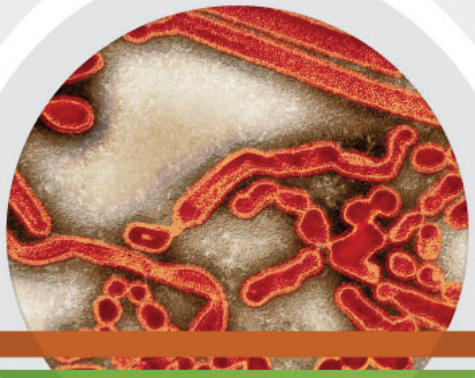

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2014

Summary

During the 2013–14 season A(H1N1)pdm09, A(H3N2) and B/Victoria- and B/Yamagata-lineage influenza viruses have been detected in ECDC-affiliated countries. The relative prevalence has varied between countries. Of the viruses received by the WHO Collaborating Centre in London:

- Type A and type B viruses have been received in the ratio 12:1.
- A(H3N2) and A(H1N1)pdm09 viruses have been received in similar numbers.
- Recently circulating H1N1pdm09 viruses belonged to genetic subgroups 6B and 6C, with viruses in genetic subgroup 6B predominating. 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. Antigenic analysis using antisera raised against cell-propagated H3N2 viruses indicates that the circulating viruses are antigenically similar to those in circulation in the 2012–13 influenza season.
- 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/2/2012 (the recommended vaccine component for the 2013–14 and 2014–15 influenza seasons). Viruses in each clade have been received in similar numbers.
- Few B/Victoria-lineage viruses have been received, and phylogenetic analysis revealed that all were in genetic clade 1A. Antigenically the viruses were 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 an additional 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 August 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 20 countries in the EU/EEA region. The large majority (92.5%) were type A viruses, with A(H3N2) viruses and A(H1N1)pdm09 viruses being approximately equally represented (Table 1). Of the small number of type B viruses received (~7.5% of the specimens), B/Yamagata lineage viruses predominated over those of the Victoria lineage by a ratio of 6:1. A number of the specimens have yet to be fully processed (in process: Table 1).

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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Table 1. Summary of clinical samples and isolates received from ECDC-affiliated countries, with collection dates after 31 August 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]
2013											
SEPTEMBER											
France	2				2	2					
Sweden	2				2	2					
United Kingdom	2		1	1	1	1					
OCTOBER											
Denmark	3		1	0	1	0				1	0
Finland	1		1	1							
France	4		1	1	1	1		1	1	1	1
Netherlands	3		1	1	2	2					
Norway	6				6	6					
Poland	1	1									
Portugal	1									1	1
Spain	2		2	2							
Sweden	2		2	2							
United Kingdom	2				1	1				1	1
NOVEMBER											
Belgium	1		1	1							
Denmark	2		1	0	1	1					
Finland	1		1	1							
France	9		3	3	3	3				3	3
Germany	4		1	1	2	2		1	1		
Ireland	3		1	0			1			1	1
Italy	2				2	2					
Norway	10		5	5	2	2		1	1	2	2
Poland	2	1			1	0					
Portugal	2				2	0					
Romania	1				1	in process					
Spain	7		3	3	4	4					
Sweden	5		3	3	2	2					
United Kingdom	2		2	2							
DECEMBER											
Belgium	8		2	0	5	5				1	0
Denmark	7		4	2	2	2				1	0
Finland	4		1	1	3	3					
France	33		17	17	14	14				2	2
Germany	3				3	3					
Iceland	2		1	1						1	1
Ireland	6		3	0	2	2				1	1
Italy	15		1	1	14	14					
Latvia	3		2	2	1	1					
Malta	1		1	in process							
Netherlands	1				1	1					
Norway	13		3	3	6	6				4	4
Portugal	9		6	5	3	2					
Romania	1		1	in process							
Slovenia	4				4	4					
Spain	28		16	13	12	10					
Sweden	6		1	1	4	4				1	1
United Kingdom	5		3	3	2	2					
2014											
JANUARY											
Belgium	3		2	2	1	1					
Germany	12		2	2	10	10					
Greece	35		32	in process	3	in process					
Iceland	4		4	4							
Ireland	3		1	1	2	2					
Italy	2				1	1				1	1
Latvia	1		1	1							
Malta	4		4	in process							
Portugal	9		6	6	3	3					
Romania	9		5	in process	4	4					
Slovenia	5				5	2					
Spain	23		19	19	4	4					
United Kingdom	4		2	2	2	2					
	345	2	170	113	147	133	1	3	3	22	19
			49.3%		42.6%			0.9%		6.4%	
20 Countries			92.5%					7.5%			

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

All H1N1 viruses collected after 31 August 2013 were antigenically similar to the vaccine virus as assessed by haemagglutination inhibition (HI) assay (Tables 2-1 to 2-4). Only two test viruses, A/Denmark/106/2013 and A/Lyon/2694/2013 (representing ~2% of the total tested) showed fourfold reductions, and none showed ≥eightfold reductions in HI titre compared with the titre of the vaccine virus (A/California/7/2009) with its homologous post-infection ferret antiserum (Tables 2-1 to 2-4). Viruses for which gene sequences are included in phylogenetic trees 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 August 2013 fell into genetic group 6 and clustered within two of the three subgroups of group 6, subgroups 6B and 6C (Figure 1). These two subgroups carry the substitutions **D97N**, **S185T, S203T** and **K283E** in **HA1** and **E47K, S124N and E172K** in **HA2** compared with A/California/7/2009. The subgroups 6B and 6C are defined by the following amino acid substitutions in **HA1** with none in **HA2**:

- Viruses in **subgroup 6B** carry substitutions **K163Q & A256T** in **HA1**, e.g. the reference virus A/South Africa/3626/2013
- Viruses in **subgroup 6C** carry the substitution **V234I** in **HA1**; some also carry the substitutions **V30A and A186T** in **HA1**, e.g. A/Paris/2496/2013.

Table 2-1. 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 4	A/HK 3934/11 F21/11 3	A/Astrak 1/11 F22/11 5	A/St. P 27/11 F23/11 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	
REFERENCE VIRUSES													
A/California/7/2009		2009-04-09	E1/E2	1280	640	1280	320	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	320	320	160	160	80	160	160	160	160	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	320	160	160	320	160	320	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	2560	1280	2560	5120	2560	2560	2560	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK4	1280	320	640	640	1280	1280	1280	5120	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	320	640	640	1280	1280	1280	2560	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	320	640	640	1280	1280	1280	1280	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	1280	1280	2560	2560	2560	2560	5120	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	320	160	640	640	640	1280	1280	
TEST VIRUSES													
A/England/621/2013	6C	2013-09-30	SIAT1/MDCK1	1280	640	1280	640	1280	1280	1280	2560	2560	
A/Asturias/1161/2013	6B	2013-10-01	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Stockholm/19/2013	6B	2013-10-03	MDCK0/MDCK1	1280	640	1280	1280	2560	1280	1280	2560	2560	
A/Netherlands/2248/2013	6B	2013-10-14	MDCK4/MDCK1	1280	320	1280	1280	1280	1280	1280	2560	2560	
A/Stockholm/23/2013	6B	2013-10-15	MDCK2/MDCK1	640	160	640	320	1280	640	640	1280	1280	
A/Valladolid/142/2013	6B	2013-10-22	SIAT1/MDCK1	1280	320	1280	640	1280	1280	1280	2560	2560	
A/Lyon/2694/2013	6B	2013-10-29	MDCK2/MDCK1	320	160	320	320	640	640	640	1280	1280	
A/Bayern/138/2013	6B	2013-11-01	C3/MDCK1	1280	320	1280	1280	2560	1280	1280	2560	2560	
A/Stockholm/21/2013	6B	2013-11-01	MDCK2/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	
A/England/624/2013		2013-11-04	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	1280	2560	2560	
A/Aragon/1368/2013	6B	2013-11-04	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Sweden/138/2013	6B	2013-11-08	MDCK0/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	
A/Lyon-CHU/46.08/2013	6B	2013-11-10	MDCK2/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	
A/Galicia/1485/2013	6B	2013-11-11	SIAT1/MDCK1	1280	320	1280	640	2560	1280	1280	2560	2560	
A/Norway/3073/2013	6B	2013-11-12	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Galicia/1484/2013	6B	2013-11-14	SIAT1/MDCK1	640	320	640	640	1280	1280	640	1280	1280	
A/England/640/2013	6B	2013-11-24	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Lyon/2868/2013		2013-11-25	MDCK2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Stockholm/33/2013	6B	2013-11-28	MDCK3/MDCK1	1280	640	640	320	640	640	320	640	640	N156N=D
A/Lyon/2899/2013	6B	2013-12-02	MDCK2/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	
A/Stockholm/35/2013	6B	2013-12-14	MDCK1/MDCK1	1280	320	640	640	1280	1280	1280	2560	2560	
Sequences in phylogenetic trees				Vaccine									

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

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre[1] 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 F22/11 5	A/St. P 27/11 F23/11 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	
REFERENCE VIRUSES													
A/California/7/2009		2009-04-09	E1/E2	1280	640	1280	320	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	320	320	160	40	40	80	40	40	40	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	160	160	320	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	2560	5120	1280	1280	2560	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK5	640	160	640	320	1280	640	640	1280	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK7	1280	640	1280	640	1280	1280	1280	2560	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	1280	640	1280	1280	1280	5120	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	640	1280	640	1280	1280	1280	5120	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	160	80	160	160	320	320	320	640	1280	
TEST VIRUSES													
A/Belguim/13G1251/2013	6B	2013-11-16	MDCK2	1280	1280	1280	1280	2560	2560	2560	5120	5120	
A/Paris/2401/2013	6C	2013-12-10	MDCK1/MDCK1	1280	640	1280	640	2560	2560	1280	5120	2560	
A/Latvia/12027346/2013	6B	2013-12-13	MDCK2/MDCK1	640	160	320	320	640	640	640	1280	1280	
A/Paris/2481/2013		2013-12-17	MDCK2/MDCK1	1280	320	640	640	1280	1280	1280	2560	2560	
A/Paris/2496/2013	6C	2013-12-17	MDCK1/MDCK1	1280	1280	1280	640	2560	2560	2560	5120	2560	
A/Denmark/106/2013	6B	2013-12-18	MDCK2/MDCK1	320	320	320	160	640	160	640	640	640	
A/Paris/2506/2013		2013-12-20	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	
A/Centre/2508/2013	6B	2013-12-23	MDCK1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	
A/Nord Pas de Calais/2519/2013	6B	2013-12-23	MDCK1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	
A/Latvia/12046984/2013	6C	2013-12-23	MDCK1/MDCK1	1280	320	640	640	1280	1280	1280	5120	2560	
A/Paris/2516/2013	6B	2013-12-24	MDCK1/MDCK1	1280	640	1280	1280	1280	1280	2560	5120	2560	
A/Denmark/101/2013	6B	2013-12-29	MDCK2	1280	1280	1280	1280	2560	1280	2560	5120	5120	
A/Belguim/14G0003/2014	6B	2014-01-02	MDCK2	1280	640	1280	1280	2560	2560	2560	5120	5120	
A/Belguim/14G0004/2014	6B	2014-01-03	MDCK2	1280	640	1280	1280	2560	1280	1280	5120	2560	
A/Latvia/01009567/2014	6B	2014-01-05	MDCK1/MDCK1	640	320	320	640	1280	1280	1280	2560	2560	
Sequences in phylogenetic trees				Vaccine									

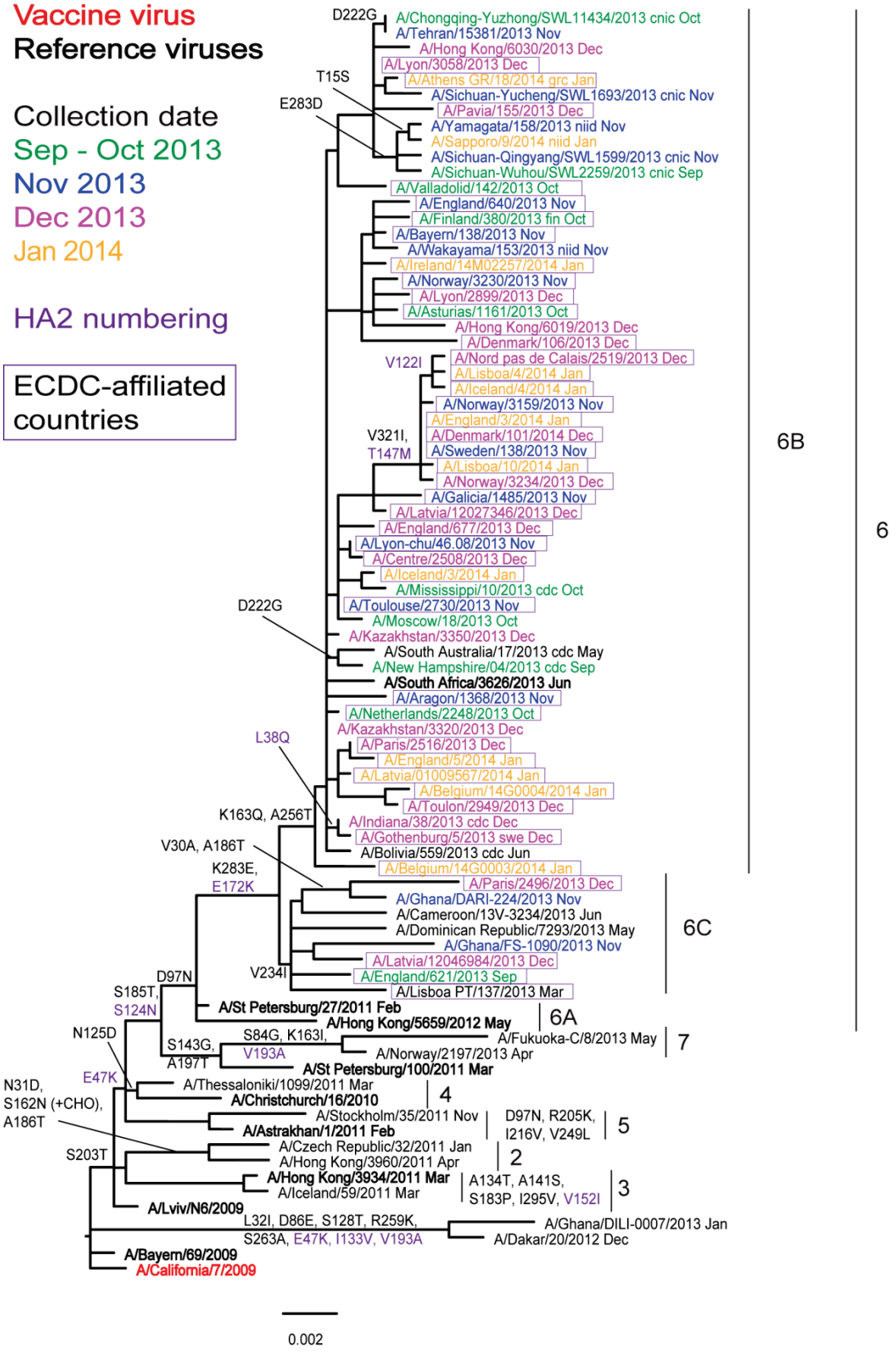
Table 2-3. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre[1] 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 F22/11 5	A/St. P 27/11 F23/11 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	
REFERENCE VIRUSES													
A/California/7/2009		2009-04-09	E1/E2	1280	640	1280	320	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	320	320	160	80	40	80	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	640	160	80	160	320	160	320	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	2560	2560	5120	5120	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK4	640	160	640	320	1280	640	640	1280	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK7	1280	640	1280	1280	2560	1280	2560	2560	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	640	1280	1280	2560	5120	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	320	640	640	1280	640	1280	2560	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	320	160	640	640	640	1280	1280	
TEST VIRUSES													
A/Finland/380/2013	6B	2013-10-14	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Toulouse/2730/13	6B	2013-11-02	MDCK3/MDCK1	1280	640	1280	1280	1280	1280	1280	2560	2560	
A/Norway/3159/2013	6B	2013-11-22	MDCK2/MDCK1	640	640	640	1280	1280	1280	1280	2560	5120	
A/Norway/3214/2013		2013-11-25	LLCMK2MDCK1/MDCK1	640	320	1280	1280	1280	1280	1280	2560	2560	
A/Norway/3175/2013		2013-11-27	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	
A/Norway/3230/2013	6B	2013-11-28	MDCK1/MDCK1	1280	640	1280	1280	2560	1280	1280	5120	5120	
A/Finland/383/2013	6B	2013-11-30	MDCK1/MDCK1	2560	1280	2560	1280	5120	2560	2560	5120	5120	
A/Toulon/2949/13	6B	2013-12-02	MDCK2/MDCK1	640	320	640	640	1280	1280	640	2560	1280	
A/Norway/3234/2013	6B	2013-12-04	MDCK1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Paris/2444/2013	6C	2013-12-06	MDCK2/MDCK2	1280	320	1280	640	1280	1280	2560	2560	2560	
A/Lyon/2954/13		2013-12-09	MDCK2/MDCK1	1280	640	1280	1280	2560	1280	1280	2560	2560	
A/Lyon/2963/13		2013-12-09	MDCK2/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Finland/384/2013	6B	2013-12-11	MDCK1/MDCK1	2560	1280	1280	1280	2560	2560	2560	5120	5120	
A/Lyon-CHU/ 51.200/13		2013-12-16	MDCK2/MDCK1	640	320	640	640	1280	1280	1280	2560	1280	
A/Lyon/3020/13		2013-12-17	MDCK2/MDCK1	640	160	640	640	640	640	640	2560	1280	
A/Lisboa/148/2013		2013-12-17	MDCK1/MDCK1	640	320	640	640	2560	1280	1280	2560	2560	
A/Lyon/3058/13	6B	2013-12-18	MDCK3/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Pavia/155/2013	6B	2013-12-20	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	
A/England/666/2013		2013-12-21	SIAT2/MDCK1	1280	320	640	1280	2560	1280	1280	2560	2560	
A/Lisboa/156/2013		2013-12-23	MDCK2/MDCK1	640	320	1280	640	2560	1280	1280	2560	2560	
A/Iceland/67/2013	6B	2013-12-24	MDCK1/MDCK1	1280	320	640	640	1280	1280	1280	2560	2560	
A/Lyon/3101/13		2013-12-26	MDCK4/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	
A/Desgenettes/3083/13		2013-12-27	MDCK2/MDCK1	640	320	640	1280	1280	1280	1280	2560	2560	
A/Lisboa/152/2013	6B	2013-12-27	MDCK2/MDCK1	1280	640	1280	1280	2560	1280	2560	5120	5120	
A/England/672/2013		2013-12-29	SIAT2/MDCK1	640	320	640	640	640	1280	640	2560	1280	
A/England/677/2013	6B	2013-12-30	MDCK1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	
A/Lisboa/157/2013		2013-12-30	SIAT1/MDCK1	1280	1280	2560	1280	5120	2560	2560	5120	5120	
A/Lisboa/153/2013		2013-12-31	SIAT1/MDCK1	1280	1280	1280	1280	5120	2560	2560	5120	5120	
A/Ireland/14M02257/2014	6B	2014-01-01	MDCK3	640	320	640	640	1280	1280	1280	2560	2560	
A/Lisboa/154/2013	6B	2014-01-01	MDCK1/MDCK1	1280	640	1280	1280	5120	2560	2560	5120	5120	
A/Lisboa/4/2014	6B	2014-01-04	SIAT1/MDCK1	640	320	640	640	2560	1280	1280	2560	2560	
A/Lisboa/6/2014		2014-01-04	SIAT1/MDCK1	1280	320	640	640	2560	1280	1280	2560	2560	
A/Lisboa/11/2014		2014-01-05	SIAT1/MDCK1	1280	640	640	640	5120	1280	2560	5120	5120	
A/England/5/2014	6B	2014-01-06	MDCK1/MDCK1	1280	640	1280	1280	2560	1280	2560	5120	2560	
A/Lisboa/10/2014	6B	2014-01-06	MDCK1/MDCK1	1280	640	1280	1280	2560	1280	1280	5120	2560	
A/Lisboa/12/2014		2014-01-06	SIAT1/MDCK1	2560	1280	2560	1280	5120	2560	2560	5120	5120	
A/England/3/2014	6B	2014-01-08	SIAT1/MDCK1	1280	640	640	1280	2560	1280	1280	5120	2560	
A/Iceland/1/2014		2014-01-10	MDCK1/MDCK1	1280	320	640	640	1280	1280	1280	2560	2560	
A/Iceland/2/2014	6B	2014-01-10	MDCK1/MDCK1	1280	640	640	1280	1280	1280	1280	2560	2560	
A/Iceland/3/2014	6B	2014-01-15	MDCK1/MDCK1	640	320	640	640	2560	1280	1280	2560	1280	
A/Iceland/4/2014	6B	2014-01-16	MDCK1/MDCK1	1280	640	1280	1280	5120	2560	2560	5120	2560	
Sequences in phylogenetic trees				Vaccine									

Table 2-4. 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 F22/11 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/S. Africa 3626/13 F3/14 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E2	1280	640	640	320	320	320	320	320	320	160	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	320	320	160	80	40	80	80	80	80	40	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	2560	2560	2560	5120	2560	2560	2560	5120	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK4	640	160	640	640	1280	1280	1280	1280	2560	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	640	320	640	320	1280	640	1280	2560	2560	640	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	1280	2560	2560	2560	5120	5120	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	640	640	1280	1280	1280	2560	2560	640	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	320	320	640	640	640	1280	1280	320	
A/South Africa/3626/2013	6B	2013-06-06	MDCK2/MDCK2	1280	640	1280	1280	2560	2560	2560	5120	5120	1280	
TEST VIRUSES														
A/Andalucia/1584/2013		2013-12-11	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Navarra/1564/2013		2013-12-12	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Andalucia/1586/2013		2013-12-12	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Pais Vasco/1569/2013		2013-12-13	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Andalucia/1585/2013		2013-12-14	SIAT1/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	1280	
A/Norway/3322/2013	6B	2013-12-16	MDCK1/MDCK2	1280	320	640	640	1280	1280	1280	2560	2560	1280	
A/Norway/3293/2013	6B	2013-12-17	MDCK1/MDCK2	640	320	640	640	1280	1280	1280	2560	2560	640	
A/Castilla La Mancha/131557/2013		2013-12-17	SIAT1/MDCK1	1280	640	1280	1280	2560	1280	1280	2560	2560	1280	
A/Andalucia/14175/2013	6B	2013-12-17	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Madrid/SO11395/2013	6B	2013-12-21	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Aragon/14040/2013	6B	2013-12-26	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Aragon/14041/2013		2013-12-26	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Aragon/14042/2013		2013-12-26	SIAT1/MDCK1	640	160	640	640	640	640	1280	2560	1280	640	
A/Aragon/14276/2013	6B	2013-12-26	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Andalucia/14173/2013		2013-12-29	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Madrid/31/2014		2014-01-03	SIAT1/MDCK1	1280	320	1280	1280	2560	2560	1280	5120	2560	1280	
A/Navarra/220/2014		2014-01-03	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	1280	
A/Madrid/SO11443/2014		2014-01-04	SIAT1/MDCK1	1280	640	1280	1280	2560	1280	1280	5120	2560	1280	
A/Castilla La Mancha/147/2014		2014-01-05	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	1280	2560	2560	1280	
A/Castilla La Mancha/148/2014	6B	2014-01-07	SIAT1/MDCK1	1280	320	1280	1280	1280	1280	1280	2560	2560	1280	
A/Castilla La Mancha/145/2014		2014-01-08	SIAT1/MDCK1	640	320	640	640	1280	640	1280	2560	2560	1280	
A/Castilla La Mancha/106/2014		2014-01-09	SIAT1/MDCK1	640	640	1280	640	1280	1280	1280	2560	2560	1280	
A/Castilla La Mancha/104/2014		2014-01-09	SIAT1/MDCK1	1280	320	1280	1280	1280	1280	2560	2560	2560	1280	
A/Aragon/267/2014	6B	2014-01-09	SIAT1/MDCK1	2560	1280	2560	2560	5120	2560	5120	5120	5120	2560	
A/Aragon/268/2014		2014-01-09	SIAT1/MDCK1	1280	640	1280	1280	2560	1280	2560	5120	2560	1280	
A/Aragon/269/2014		2014-01-10	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	1280	5120	2560	1280	
A/Brandenburg/1/2014	6B	2014-01-10	C2/MDCK1	1280	1280	2560	1280	2560	2560	2560	5120	2560	2560	
A/Madrid/107/2014		2014-01-13	SIAT1/MDCK1	1280	320	1280	1280	2560	1280	1280	5120	2560	1280	
A/Castilla La Mancha/119/2014	6B	2014-01-13	SIAT1/MDCK1	1280	320	1280	1280	2560	2560	1280	5120	2560	2560	
A/Madrid/125/2014		2014-01-13	SIAT1/MDCK1	1280	640	1280	1280	2560	1280	1280	2560	2560	1280	
A/Madrid/127/2014		2014-01-13	SIAT1/MDCK1	640	160	1280	640	1280	1280	1280	2560	2560	640	
A/Aragon/270/2014	6B	2014-01-13	SIAT1/MDCK1	1280	640	1280	1280	2560	1280	1280	5120	2560	1280	
A/Madrid/120/2014	6B	2014-01-14	SIAT1/MDCK1	640	320	640	640	1280	1280	1280	2560	2560	1280	
A/Andalucia/174/2014		2014-01-14	SIAT1/MDCK1	1280	640	2560	1280	2560	2560	2560	5120	5120	2560	
A/Schleswig-Holstein/1/2014	6B	2014-01-15	C2/MDCK1	640	320	1280	640	1280	1280	1280	2560	2560	1280	
A/Andalucia/171/2014	6B	2014-01-16	SIAT1/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
				Vaccine										

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



Influenza A(H3N2) virus analyses

As described in previous reports, e.g. http://www.ecdc.europa.eu/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf, influenza A(H3N2) viruses have continued to be difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells from guinea pigs, turkeys and humans. All viruses received/isolated this season 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 3-5. Viruses for which gene sequences are included in phylogenetic trees are highlighted and, where known, the HA genetic group is indicated.

Over 70% of test viruses 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. Test viruses examined with antisera raised against three other egg-propagated reference viruses, A/Serbia/NS-210/2013, A/Hong Kong/146/2013 and A/Almaty/2958/2013, showed variable results. Compared with the corresponding homologous titres, approximately 55%, 20% and 36% of test viruses reacted within fourfold of the titre against the homologous egg-propagated virus for antisera raised against A/Serbia/NS-210/2013, A/Hong Kong/146/2013 and A/Almaty/2958/2013 (using NIB85 as the antigen) respectively. Much better reactivity of the test viruses was seen with antiserum raised against egg-propagated A/New York/39/2012 that had an homologous titre of 640; all test viruses were recognised by this antiserum at a titre within fourfold of the titre with the homologous virus (Table 3-5).

Ferret antisera raised against reference viruses propagated in tissue culture cells, notably those raised against A/Stockholm/18/2011, A/Athens/112/2012, A/Samara/73/2013 and A/Victoria/361/2011, recognised the test viruses more effectively. Notably, between 93% and 96% of test viruses propagated in MDCK-SIAT1 cells were recognised at titres within fourfold of those for the antisera with their corresponding homologous viruses for antisera raised against cell-propagated A/Victoria/361/2011, A/Athens/112/2012 and A/Samara/73/2013, reference viruses with HA genes falling in genetic subgroups 3B and 3C.

One test virus, A/Stockholm/18/2013, showed evidence of altered antigenic characteristics in the HI assay (Table 3-2). This virus belongs to the minority 3C.2 genetic subgroup and carries a number of additional substitutions in HA1, including a polymorphism at position 221 (P221L>P). The antigenic characteristics of A/Stockholm/18/2013 require further examination. Another virus, A/England/651/2013, also showed low reactivity in HI assay: it was isolated from an immunocompromised patient that had shed virus over a long period and its HA belonged to genetic subgroup 3C.3 but carried additional substitutions in HA1 and HA2 (Table 3-3).

Previously, seven genetic groups based on the HA gene have been defined for H3N2 viruses, two derived from A/Perth/16/2009 and five from A/Victoria/208/2009. Phylogenetic analysis of the HA genes of representative recently circulating H3N2 viruses is shown in Figure 2. The HA genes of viruses received at NIMR from EU/EEA countries fell within the A/Victoria/208 genetic clade and predominantly in genetic subgroup 3C of group 3. This subgroup has three subdivisions: 3C.1, 3C.2 and 3C.3.

The vaccine virus A/Texas/50/2012 belongs to genetic subgroup 3C.1. Most of the viruses received since 31 August 2013 fall into subgroups 3C.2 and 3C.3. 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.

While viruses in the 3C.2 and 3C.3 subgroups remain antigenically similar to the vaccine virus, A/Texas/50/2012, for both subgroups there are small clusters of viruses carrying additional HA amino acid substitutions, a significant number of which fall in HA2, and some intra-clade reassortment has taken place involving HA-3C.3 and NA-3A, e.g. A/Netherlands/2244/2013 (Figure 2).

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/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	F28/11	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	1280	320	320	320	640	320	320	320	320	160
A/Stockholm/18/2011	3A	2011-03-28	SIAT4	160	640	320	640	640	320	1280	320	320	320
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	640	2560	1280	1280	1280	1280	640	640	640
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT6	80	320	320	320	640	320	640	320	320	320
A/Athens/112/2012	3B	2012-02-01	SIAT4	80	320	320	320	1280	320	1280	320	320	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	2560	2560	1280	2560	2560	1280
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	320	320	640	640	640	1280	640	640	640
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	640	1280	640	1280	1280	1280	1280	640	1280
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	640	1280	1280	1280	1280	640	1280	640	2560	1280
NIB-85 (A/Almaty/2958/2013)	3C.3		E5/E1	640	1280	1280	1280	1280	1280	1280	1280	1280	1280
TEST VIRUSES													
A/Bordeaux/2456/2013	3C.2	2013-08-27	MDCK2/SIAT1	<	80	80	160	320	80	320	80	160	160
A/Toulouse/2460/2013		2013-08-29	MDCK2/SIAT1	160	320	320	640	640	320	1280	640	640	320
A/Lyon/37.477/2013	3C.3	2013-09-13	MDCK2/SIAT1	40	320	160	320	640	320	640	320	320	320
A/Norway/2916/2013	3C.3	2013-10-01	MDCK2/SIAT1	40	80	160	160	640	160	640	320	320	320
A/Norway/2920/2013	3C.2	2013-10-01	MDCK1/SIAT1	40	160	160	160	640	160	320	160	160	320
A/Norway/2940/2013	3C.3	2013-10-03	MDCK2/SIAT1	40	160	160	320	640	320	640	640	320	320
A/Norway/2938/2013	3C.3	2013-10-04	MDCK2/SIAT1	80	320	160	320	640	320	1280	640	320	320
A/Norway/2965/2013	3C.3	2013-10-08	MDCK2/SIAT1	80	320	160	320	640	160	640	320	320	320
A/Norway/2967/2013	3C.3	2013-10-10	MDCK2/SIAT1	40	160	160	320	640	160	640	320	320	320
A/England/620/2013	3C.3	2013-10-16	SIAT1/SIAT1	40	160	160	320	640	160	640	320	320	320
A/Nimes/2658/2013	3C.3	2013-10-24	MDCK2/SIAT1	<	160	80	160	320	160	320	160	160	160
A/Clermont Ferrand/2731/2013		2013-11-02	MDCK2/SIAT1	40	160	160	320	320	160	640	320	320	320
A/Norway/3060/2013	3C.3	2013-11-06	MDCK1/SIAT1	40	160	80	320	640	320	640	320	320	320
A/Pais Vasco/1403/2013	3C.3	2013-11-08	SIAT1/SIAT1	80	320	160	320	1280	320	640	320	640	320
A/Baleares/1441/2013	3C.3	2013-11-19	SIAT1/SIAT1	80	320	160	320	640	320	640	320	320	320
A/Aix-en-Provence/2846/2013	3C.2	2013-11-22	MDCK2/SIAT1	40	320	160	320	640	320	640	640	320	320
A/Thuringen/123/2013	3C.3	2013-11-25	C2/SIAT1	<	160	80	160	320	160	320	80	160	80
A/Bayern/139/2013	3C.3	2013-11-26	C2/SIAT1	80	320	320	320	640	320	640	320	320	320
A/Navarra/1503/2013	3C.3	2013-11-27	SIAT1/SIAT1	80	320	160	640	640	320	640	320	320	320
A/Toulouse/2892/2013	3C.3	2013-11-28	MDCK2/SIAT1	<	80	80	160	320	80	320	80	160	80
A/Baleares/1498/2013	3C.3	2013-11-29	SIAT1/SIAT1	80	640	320	640	1280	320	1280	640	640	640
A/Soria/143/2013	3C.3	2013-12-03	SIAT1/SIAT1	<	320	320	320	640	320	320	320	320	320
A/Lyon/2909/2013		2013-12-05	MDCK2/SIAT1	40	160	160	320	640	160	640	320	320	320
A/Lyon/2923/2013		2013-12-05	MDCK2/SIAT1	80	160	320	320	640	320	640	320	320	320
A/Baleares/1521/2013	3C.3	2013-12-07	SIAT1/SIAT1	80	320	160	320	640	160	640	320	320	320
A/Baleares/1520/2013	3C.3	2013-12-08	SIAT1/SIAT1	40	320	160	320	640	160	640	320	320	320
A/Navarra/1528/2013	3C.3	2013-12-10	SIAT1/SIAT1	80	320	160	640	1280	320	640	320	320	320

< = <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	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	F28/11	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	160	160	160	320	160	160	160	160	160	
A/Stockholm/18/2011	3A	2011-03-28	SIAT5	40	320	160	320	640	160	640	320	160	160	
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	640	1280	1280	1280	1280	1280	640	640	640	
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT6	80	320	160	640	640	320	640	320	320	320	
A/Athens/112/2012	3B	2012-02-01	SIAT4	80	320	160	640	1280	320	640	320	320	320	
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	320	640	640	1280	1280	1280	1280	1280	640	1280	
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	640	320	640	1280	640	1280	640	640	640	
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	640	640	640	1280	1280	1280	1280	640	1280	
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	1280	1280	1280	1280	640	1280	640	1280	640	
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	1280	1280	1280	1280	1280	1280	1280	1280	1280	
TEST VIRUSES														
A/Stockholm/17/2013	3C.2	2013-09-03	MDCK2/SIAT1	<	80	40	80	320	160	320	160	160	160	
A/Stockholm/18/2013	3C.2	2013-09-04	MDCK2/SIAT1	<	<	<	<	80	40	80	40	40	40	*
A/England/617/2013	3C.3	2013-09-15	SIAT2/SIAT2	<	80	40	160	320	80	320	160	160	160	
A/Paris/2031/2013	3C.3	2013-09-30	MDCK2/SIAT1	80	320	320	640	640	160	1280	320	320	320	
A/Netherlands/2244/2013	3C.3	2013-10-19	MDCK3/SIAT1	<	80	40	80	320	80	320	160	80	160	
A/Netherlands/2247/2013	3C.3	2013-10-23	MDCK3/SIAT1	40	160	80	160	320	160	320	160	160	160	
A/Denmark/96/2013	3C.3	2013-11-03	SIAT4/SIAT1	40	160	40	320	640	80	640	160	320	320	
A/Stockholm/22/2013	3C.3	2013-11-09	MDCK1/SIAT1	<	80	80	160	320	160	320	160	160	160	
A/Stockholm/30/2013	3C.2	2013-11-26	MDCK1/SIAT1	<	80	40	80	320	80	320	160	160	160	
A/Stockholm/34/2013	3C.3	2013-12-04	MDCK3/SIAT1	<	160	80	160	640	160	320	320	160	320	
A/Netherlands/2249/13	3C.3	2013-12-05	MDCK2/SIAT1	<	160	80	160	320	80	320	160	160	160	
A/Stockholm/31/2013	3C.2	2013-12-08	MDCK1/SIAT1	40	160	80	160	640	160	640	320	320	320	
A/Berlin/215/2013	3C.3	2013-12-10	C2/SIAT1	<	160	80	160	640	160	320	160	160	320	
A/Latvia/12019591/2013	3C.3	2013-12-10	MDCK2/SIAT1	40	160	160	320	640	160	1280	320	320	320	
A/Stockholm/29/2013	3C.3	2013-12-11	MDCK1/SIAT1	320	640	320	640	2560	640	1280	640	640	640	
A/Stockholm/36/2013	3C.3	2013-12-15	MDCK1/SIAT1	80	320	160	320	1280	320	640	640	320	640	
A/Centre/2484/2013	3C.3	2013-12-17	MDCK2/SIAT1	80	320	320	640	1280	320	1280	640	640	320	
A/Lorraine/2485/2013	3C.2	2013-12-17	MDCK1/SIAT1	40	160	160	320	640	160	640	320	320	160	
A/Provence-Alpes-Côte d'Azur	3C.2	2013-12-18	MDCK2/SIAT1	80	320	160	320	640	160	640	320	320	320	
A/Denmark/104/2013	3C.2	2013-12-23	SIAT2/SIAT1	80	320	320	320	320	160	640	320	320	320	
A/Denmark/103/2013	3C.3	2013-12-30	SIAT2/SIAT1	40	160	160	320	640	160	640	320	320	320	
A/Lorraine/004/2014	3C.2	2013-12-30	MDCK1/SIAT1	40	320	160	320	640	160	640	320	320	320	
A/Bretagne/014/2014	3C.3	2013-12-30	MDCK1/SIAT1	80	320	160	320	640	160	640	320	320	160	

1. < = <40

Vaccine

Sequences in phylogenetic trees

* HA substitutions N144S (-CHO), K160T (+CHO), P221L>P, N225D, Q311H

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 F35/11	A/Stock 18/11 F28/11 3A	A/Iowa 19/10 F15/11 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	160	160	160	320	160	160	80	160	160
A/Stockholm/18/2011	3A	2011-03-28	SIAT4	80	640	160	320	640	160	1280	320	320	320
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	1280	1280	1280	1280	640	1280	640	640	640
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT6	160	320	320	640	1280	320	1280	320	320	640
A/Athens/112/2012	3B	2012-02-01	SIAT4	80	320	160	640	1280	160	640	320	320	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	2560	1280	1280	1280	1280	1280
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	80	320	160	640	640	320	1280	320	640	640
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	1280	1280	1280	2560	1280	2560	1280	1280	1280
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	1280	1280	1280	1280	640	2560	640	2560	1280
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	2560	2560	2560	2560	2560	2560	2560	2560	2560
TEST VIRUSES													
A/Norway/3105/2013	3C.2	2013-11-11	MDCK2/SIAT1	<	80	40	80	320	40	160	40	80	80
A/Norway/3265/2013		2013-12-04	MDCK2/SIAT1	40	160	80	320	640	160	640	160	320	320
A/Norway/3266/2013	3C.3	2013-12-05	MDCK1/SIAT1	<	80	40	160	320	160	320	160	160	320
A/Lyon/2959/2013	3C.2	2013-12-07	MDCK2/SIAT1	<	80	40	160	320	80	320	80	160	160
A/England/650/2013		2013-12-09	MDCK2/SIAT1	40	160	80	320	640	160	640	320	320	320
A/Finland/385/2013		2013-12-11	SIAT1/SIAT1	<	160	80	160	320	160	640	160	160	160
A/Ireland/14M00263/2013		2013-12-13	SIAT3	<	80	80	160	320	80	320	160	160	160
A/Slovenia/2527/2013		2013-12-13	SIATx/SIAT1	<	160	80	320	640	160	640	320	160	160
A/Slovenia/2528/2013	3C.3	2013-12-14	MDCKx/SIAT1	<	80	40	160	320	80	640	160	160	160
A/Lisboa/147/2013	3C.3	2013-12-15	SIAT3/SIAT1	<	160	80	160	320	160	320	160	160	160
A/Finland/386/2013		2013-12-16	MDCK2/SIAT1	<	160	80	320	640	160	640	320	160	320
A/Finland/386/2013		2013-12-16	MDCK1/SIAT1/SIAT1	<	160	80	320	640	160	640	320	320	320
A/Toulon/3038/2013	3C.2	2013-12-16	MDCK3/SIAT1	<	160	80	320	640	160	640	160	320	320
A/Lyon/2990/2013		2013-12-16	MDCK2/SIAT1	<	80	80	160	320	80	320	160	160	160
A/Lyon/3014/2013		2013-12-16	MDCK2/SIAT1	<	160	160	160	640	80	320	160	160	160
A/Milano/59/2013	3C.3	2013-12-17	SIAT1/SIAT1	<	160	80	160	640	160	640	160	160	160
A/Milano/60/2013		2013-12-17	SIAT1/SIAT1	<	80	40	160	320	80	320	160	160	160
A/Lyon/3018/2013		2013-12-17	MDCK2/SIAT1	40	160	160	320	640	160	1280	320	320	320
A/Norway/3290/2013	3C.2	2013-12-17	MDCK1/SIAT1	<	80	40	160	160	80	160	40	80	80
A/Norway/3303/2013	3C.2	2013-12-17	MDCK1/SIAT1	<	80	40	80	160	80	160	80	80	80
A/Norway/3325/2013		2013-12-17	MDCK1/SIAT1	<	80	40	160	320	80	320	160	160	160
A/Pavia/154/2013	3C.3	2013-12-18	MDCK1/SIAT1	<	160	80	320	640	160	640	160	160	160
A/England/651/2013	3C.3	2013-12-18	SIAT1/SIAT1	<	40	<	80	80	40	160	40	80	40
A/Lyon-chu/ 51.726/2013		2013-12-20	MDCK2/SIAT1	<	160	160	320	640	160	640	160	320	320
A/Norway/3314/2013	3C.3	2013-12-24	MDCK1/SIAT1	<	80	40	160	320	80	320	160	160	160
A/Slovenia/2576/2013	3C.2	2013-12-25	SIATx/SIAT1	40	160	80	320	640	160	640	160	320	160
A/Belgium/13G1346/2013	3C.3	2013-12-27	SIAT3	<	160	80	320	640	80	640	160	160	160
A/Parma/1/2014		2013-12-30	MDCK2/SIAT1	40	320	160	640	1280	320	1280	320	320	320
A/Parma/2/2014		2013-12-30	MDCK2/SIAT1	<	80	40	160	320	80	320	160	80	160
A/Limoges/3105/2013	3C.3	2013-12-30	Cx/MDCK1	<	80	80	160	320	80	640	160	160	160
A/Lisboa/149/2013		2013-12-30	SIAT1/SIAT1	<	160	80	320	640	160	320	320	320	320
A/Ireland/14M02879/2014	3C.3	2014-01-02	SIAT3	<	80	80	160	320	80	160	80	80	80
A/England/2/2014	3C.3	2014-01-03	SIAT1/SIAT1	<	80	40	160	320	80	320	160	160	160
A/England/1/2014	3C.3	2014-01-03	SIAT1/SIAT1	<	160	80	160	320	80	640	160	160	160
A/Parma/3/2014	3C.3	2014-01-04	MDCK2/SIAT1	<	160	80	320	640	160	640	320	160	320
A/Lisboa/1/2014	3C.3	2014-01-04	SIAT1/SIAT1	<	160	80	320	640	160	320	160	160	320
A/Ireland/14M03520/2014	3C.3	2014-01-06	SIAT3	40	160	80	320	640	160	320	160	160	160
A/Lisboa/2/2014	3C.3	2014-01-06	SIAT1/SIAT1	<	80	80	160	320	80	320	160	160	160
A/Lisboa/3/2014		2014-01-06	SIAT1/SIAT1	<	160	80	320	320	80	160	160	160	160
A/Romania/157360/2014	3C.2	2014-01-07	MDCK2/SIAT1	<	80	40	160	160	40	160	80	160	160
A/Mures/157328/2014	3C.3	2014-01-07	MDCK2/SIAT1	<	160	80	160	320	160	640	320	160	320
A/Maramures/157552/2014	3C.3	2014-01-07	MDCK1/SIAT1	<	80	40	160	320	80	320	80	80	80
A/Iasi/157785/2014	3C.3	2014-01-13	MDCK1/SIAT1	<	160	80	320	320	80	640	160	160	160
A/Slovenia/108/2014	3C.2	2014-01-14	SIATx/SIAT1	40	160	80	320	640	160	640	160	320	160

1. < = <40

Vaccine

Sequences in phylogenetic trees

* HA substitutions A138S, N144K (-CHO), S145N, F193Y, R307I, S312N, L98F

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/Stock 18/11 F28/11 3A	A/Iowa 19/10 F15/11 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	A/NY 39/12 Egg F1/14 3C.3	A/NY 39/12 T/C F2/14 3C.3
REFERENCE VIRUSES															
A/Perth/16/2009		2009-07-04	E3/E3	640	160	160	160	320	160	160	80	160	160	80	80
A/Stockholm/18/2011	3A	2011-03-28	SIAT4	80	1280	160	320	640	160	1280	320	320	320	320	320
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	1280	2560	1280	1280	640	1280	640	640	640	1280	640
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT6	160	320	320	640	1280	320	1280	320	320	640	320	160
A/Athens/112/2012	3B	2012-02-01	SIAT4	80	320	160	640	640	160	640	320	320	320	320	160
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	2560	1280	1280	1280	640	1280	1280	640
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	80	320	160	640	640	320	1280	320	640	640	320	320
A/Serbia/NS-210/2013	3C.3	2013-01-18	E5/E1	320	1280	1280	1280	2560	1280	2560	1280	1280	1280	1280	640
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	320	1280	1280	1280	1280	640	2560	640	2560	1280	1280	640
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	2560	2560	2560	2560	2560	2560	2560	2560	2560	1280	640
A/New York/39/2012	3C.3	2012-10-20	E4/E1	320	320	640	640	1280	320	1280	320	640	320	640	320
A/New York/39/2012	3C.3	2012-10-20	C2/SIAT3	40	160	80	320	320	160	640	320	320	320	320	160
TEST VIRUSES															
A/Trieste/37/2013	3C.3	2013-11-26	MDCK3/SIAT1	80	320	160	640	1280	320	1280	640	640	320	320	320
A/Pavia/145/2013	3C.3	2013-11-28	MDCK2/SIAT1	40	320	160	320	640	160	640	320	320	320	320	160
A/Pavia/146/2013		2013-12-02	MDCK2/SIAT1	40	320	160	640	1280	320	1280	640	320	320	320	160
A/Pavia/147/2013		2013-12-03	Cx/SIAT1	80	320	320	640	1280	320	1280	640	640	320	320	320
A/Pavia/148/2013		2013-12-05	MDCK1/SIAT1	80	320	320	640	1280	320	1280	640	640	640	320	320
A/Pavia/149/2013		2013-12-06	MDCK1/SIAT1	80	320	320	320	1280	320	1280	640	640	320	320	320
A/Trieste/38/2013		2013-12-06	Cx/SIAT1	<	160	160	320	640	160	640	320	320	320	160	160
A/Trieste/39/2013		2013-12-09	Cx/SIAT1	40	160	160	320	1280	160	640	320	320	320	320	160
A/Ireland/14M00149/2013	3C.3	2013-12-10	SIAT4	<	160	80	160	320	160	640	160	160	320	160	80
A/Trieste/40/2013		2013-12-10	Cx/SIAT1	40	320	320	640	1280	320	1280	320	320	320	320	160
A/Navarra/1565/2013	3C.3	2013-12-10	SIAT1/SIAT1	<	160	160	320	640	160	640	320	320	320	160	160
A/Belgium/13G1308/2013	3C.2	2013-12-10	SIAT4	80	320	160	320	640	160	640	320	320	320	320	160
A/Aragon/1548/2013		2013-12-11	SIAT1/SIAT1	40	320	320	640	1280	320	1280	640	640	640	320	320
A/Baleares/1582/2013		2013-12-11	SIAT1/SIAT1	<	320	160	320	640	160	640	320	320	320	160	160
A/Navarra/1552/2013		2013-12-12	SIAT1/SIAT1	40	320	160	640	1280	320	1280	640	640	640	320	320
A/Milano/58/2013		2013-12-13	SIAT1/SIAT1	<	160	160	320	1280	320	640	320	320	320	320	160
A/Slovenia/2529/2013	3C.3	2013-12-15	MDCKx/SIAT2	80	320	160	320	640	160	640	320	320	640	320	160
A/Trieste/41/2013	3C.3	2013-12-16	Cx/SIAT1	<	160	80	160	640	160	640	160	160	160	160	80
A/Baleares/14038/2013		2013-12-27	SIAT1/SIAT1	80	320	320	640	1280	320	1280	640	640	320	320	160
A/Baleares/14037/2013	3C.3	2013-12-29	SIAT1/SIAT1	40	320	320	640	1280	320	1280	320	320	320	320	160
A/Slovenia/17/2014	3C.2	2014-01-03	MDCKx/SIAT2	80	320	160	320	640	320	640	640	640	640	320	320
A/Aragon/271/2014		2014-01-08	SIAT1/SIAT1	40	320	160	640	1280	320	1280	640	640	320	320	320
A/Navarra/218/2014	3C.3	2014-01-09	SIAT1/SIAT1	<	160	80	320	640	160	640	160	160	320	160	80
A/Aragon/266/2014	3C.3	2014-01-09	SIAT1/SIAT1	<	320	160	320	640	160	640	320	320	320	320	160
A/Castilla La Mancha/155/2014	3C.2	2014-01-10	SIAT1/SIAT1	80	320	160	320	640	160	640	320	640	320	320	320

1. < = <40

Vaccine

Table 3-5. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBC with 20nM oseltamivir)

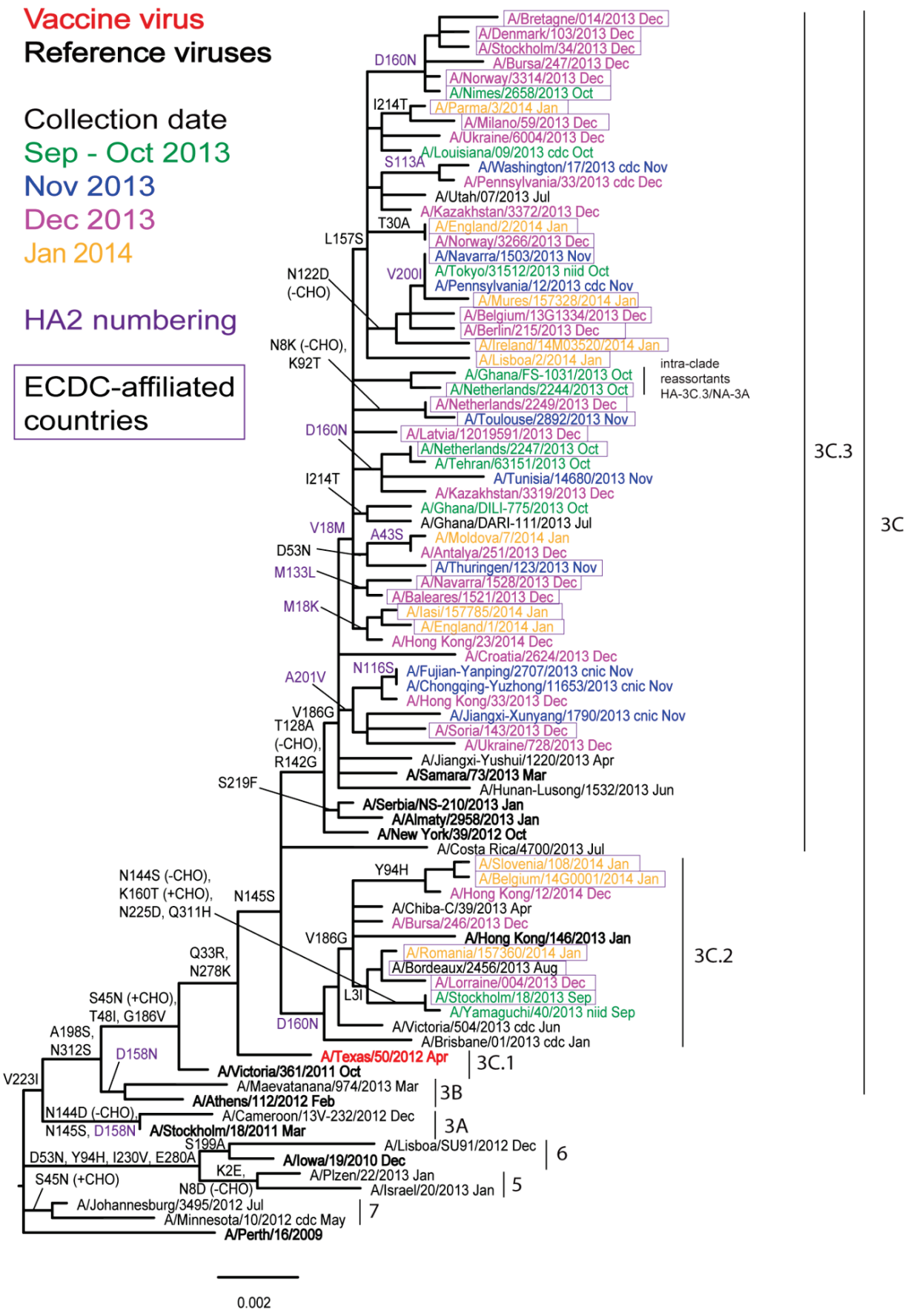
Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] Post infection ferret antisera									
				A/Perth 16/09	A/Stock 18/11	A/Iowa 19/10	A/Vic 361/11	A/Athens 112/12	A/Texas 50/12	A/Samara 73/13	A/Serbia NS-210/13	A/HK 146/13	NIB-85
				F35/11	F28/11	F15/11	T/C 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	160	160	160	320	160	160	80	160	160
A/Stockholm/18/2011	3A	2011-03-28	SIAT4	80	320	160	320	640	160	640	160	320	160
A/Iowa/19/2010	6	2010-12-30	E3/E2	320	1280	2560	1280	2560	1280	1280	640	640	1280
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT6	160	320	320	640	1280	320	1280	320	320	320
A/Athens/112/2012	3B	2012-02-01	SIAT4	80	320	320	640	1280	320	640	320	320	320
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	2560	1280	1280	1280	1280	1280
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT2	160	320	320	640	1280	320	1280	640	1280	640
A/Serbia/NS210/2013	3C.3	2013-01-18	E5/E1	320	640	1280	1280	1280	1280	1280	1280	1280	1280
A/Hong Kong/146/2013	3C.2	2013-01-11	E5/E1	640	2560	2560	1280	2560	320	2560	640	2560	1280
NIB-85 (A/Almaty/2958/2013)	3C.3	2013-01-27	E5/E1	640	1280	1280	1280	2560	1280	1280	1280	1280	1280
TEST VIRUSES													
A/Belguim/13G1319/2013	3C.3	2013-12-12	SIAT2	<	160	160	320	640	160	640	320	320	320
A/Belguim/13G1334/2013	3C.3	2013-12-16	SIAT2	<	80	40	320	640	80	640	320	160	320
A/Niedersachsen/113/2013		2013-12-19	C4/SIAT1	40	160	160	320	640	160	640	320	320	320
A/Belguim/13G1326/2013	3C.2	2013-12-19	SIAT2	40	160	80	320	320	80	640	160	320	160
A/Berlin/216/2013		2013-12-28	C2/SIAT1	<	80	80	160	320	80	320	160	160	160
A/Belguim/14G0001/2014	3C.2	2014-01-03	SIAT2	40	160	160	320	640	80	640	160	320	320
A/Rheinland-Pfalz/1/2014	3C.3	2014-01-07	C3/SIAT1	<	160	80	320	640	160	320	160	160	160
A/Berlin/2/2014		2014-01-09	C2/SIAT1	40	160	160	640	320	80	320	320	320	160
A/Niedersachsen/1/2014	3C.3	2014-01-10	C2/SIAT1	<	160	80	320	640	160	320	320	160	320
A/Berlin/1/2014		2014-01-13	C2/SIAT1	<	160	80	160	320	160	320	160	160	160
A/Mecklenburg-Vorpommern/1/2014	3C.3	2014-01-13	C2/SIAT1	<	160	80	320	640	160	640	160	160	320
A/Baden-Württemberg/1/2014	3C.3	2014-01-13	C2/SIAT1	40	160	160	640	640	320	320	320	320	320
A/Rheinland-Pfalz/2/2014		2014-01-14	C2/SIAT1	<	160	80	320	640	160	640	320	320	320
A/Berlin/3/2014		2014-01-16	C2/SIAT1	<	80	80	320	320	160	320	160	160	160
A/Berlin/4/2014	3C.3	2014-01-20	C2/SIAT1	<	160	160	320	640	160	320	320	160	160
A/Bayern/1/2014	3C.3	2014-01-20	C2/SIAT1	<	160	80	320	640	160	320	160	160	160

1. < = <40

Vaccine

Sequences in phylogenetic trees

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



Influenza B virus analyses

B/Victoria-lineage viruses

Only three viruses of the B/Victoria-lineage were received at the WHO CC. HI results for the propagated viruses are shown in Table 3. All cell-propagated test viruses reacted with post-infection ferret antisera raised against the recommended vaccine virus for quadrivalent vaccines, B/Brisbane/60/2008, at titres within fourfold of the titre with the homologous virus. The test viruses were poorly recognised by post-infection ferret antisera raised against other egg-propagated reference viruses, B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012. In contrast, all viruses showed reactivity within fourfold of the titre of the homologous virus with antisera raised against viruses genetically closely related to B/Brisbane/60/2008 but propagated in cells. As shown in Tables 3, these antisera were raised against B/Paris/1762/2008, B/Hong Kong/514/2009, B/Odessa/3886/2010 and B/Formosa/V2367/2012. These viruses are considered as surrogate cell-propagated antigens representing the egg-propagated prototype B/Brisbane/60/2008.

Phylogenetic analysis of the HA genes of representative B/Victoria-lineage viruses is shown in Figure 3. The HA genes of the majority of recently collected viruses from EU/EEA countries sent to NIMR fell into the B/Brisbane/60/2008 genetic clade in subgroup 1A.

Table 3. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

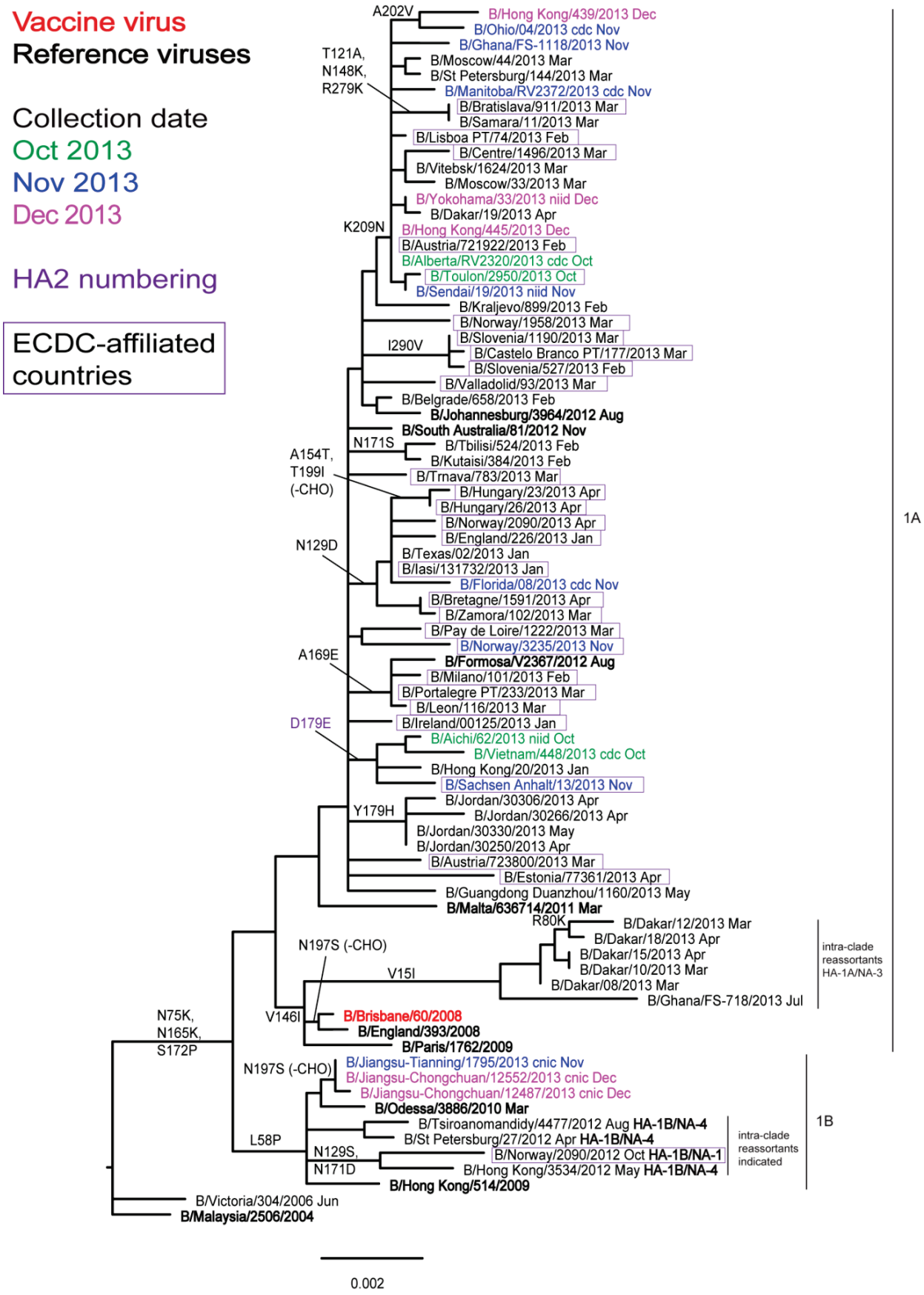
Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret sera[1]									
				B/Bris[2] 60/08 Sh 522	B/Mal 2506/05 F37/11	B/Bris 60/08 F26/13	B/Paris 1762/08 F7/11	B/HK 514/09 F9/13	B/Odessa 3886/10 F19/11	B/Malta 636714/11 F29/13	B/Jhb 3964/12 F1/13	B/For V2367/12 F4/13	B/Sth Aus 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	640	20	<	<	<	80	160	80	160
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	2560	80	320	40	80	80	320	320	320	1280
B/Paris/1762/2008	1A	2009-02-09	C2/MDCK2	2560	10	40	40	40	80	<	40	80	80
B/Hong Kong/514/2009	1B	2009-10-11	MDCK4	2560	10	40	80	80	160	<	40	80	160
B/Odessa/3886/2010	1B	2010-03-19	C2/MDCK2	2560	40	80	40	80	160	80	160	160	640
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	80	320	40	80	80	320	320	320	640
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	640	1280	80	160	160	640	1280	1280	1280
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK2	1280	20	160	40	40	80	80	80	160	640
B/South Australia/81/2012	1A	2012-11-28	E4/E1	5120	80	1280	40	80	80	320	320	320	1280
TEST VIRUSES													
B/Toulon/2950/2013	1A	2013-10-23	MDCK2/MDCK1	5120	10	160	40	80	80	40	40	80	160
B/Sachsen Anhalt/13/2013	1A	2013-11-29	MDCK1	2560	40	80	40	40	80	20	<	40	80
B/Norway/3235/2013	1A	2013-11-30	MDCK1	2560	10	80	40	40	80	40	20	40	80
						Vaccine*							

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

Sequence in phylogenetic trees

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

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



B/Yamagata-lineage viruses

The results of HI analyses for propagated viruses of the B/Yamagata-lineage are shown in Table 4. The clade into which the HA falls is shown where known. Post infection ferret antiserum raised against the current, egg-propagated, vaccine virus B/Massachusetts/02/2012 recognised approximately 25% only of viruses at titres within fourfold of the titre with the homologous virus. A ferret antiserum raised against a cell-propagated cultivar of B/Massachusetts/02/2012 recognised 80% of the examined viruses at titres within fourfold of its titre with the homologous virus. Approximately 60% of the test viruses were 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 within fourfold of the titres of the antisera with their homologous viruses. Approximately 90% of test viruses were recognised by an antiserum raised against the previous vaccine virus B/Wisconsin/1/2010 at titres within fourfold of the titre of the antiserum with the homologous virus, and ~50% were similarly recognised by antiserum raised against cell-propagated B/Novosibirsk/01/2012, a virus belonging to the B/Wisconsin/1/2010 clade, Clade 3.

Many, but not all, viruses carrying Clade 2 HA genes could be differentiated antigenically from those with HA genes falling within Clade 3. However, not all antisera were able to antigenically differentiate between viruses falling in the alternate clades.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. The HA genes of recently collected viruses fell into the B/Massachusetts/02/2012 clade (Clade 2) and the B/Wisconsin/1/2010 clade (Clade 3) in approximately equal proportions. A subset of Clade 3 viruses from mainland China and Hong Kong SAR were reassortants containing NA genes derived from B/Victoria-lineage viruses – such viruses were not found in B/Yamagata-lineage specimens submitted to WHO CC, London, by EU/EEA countries.

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

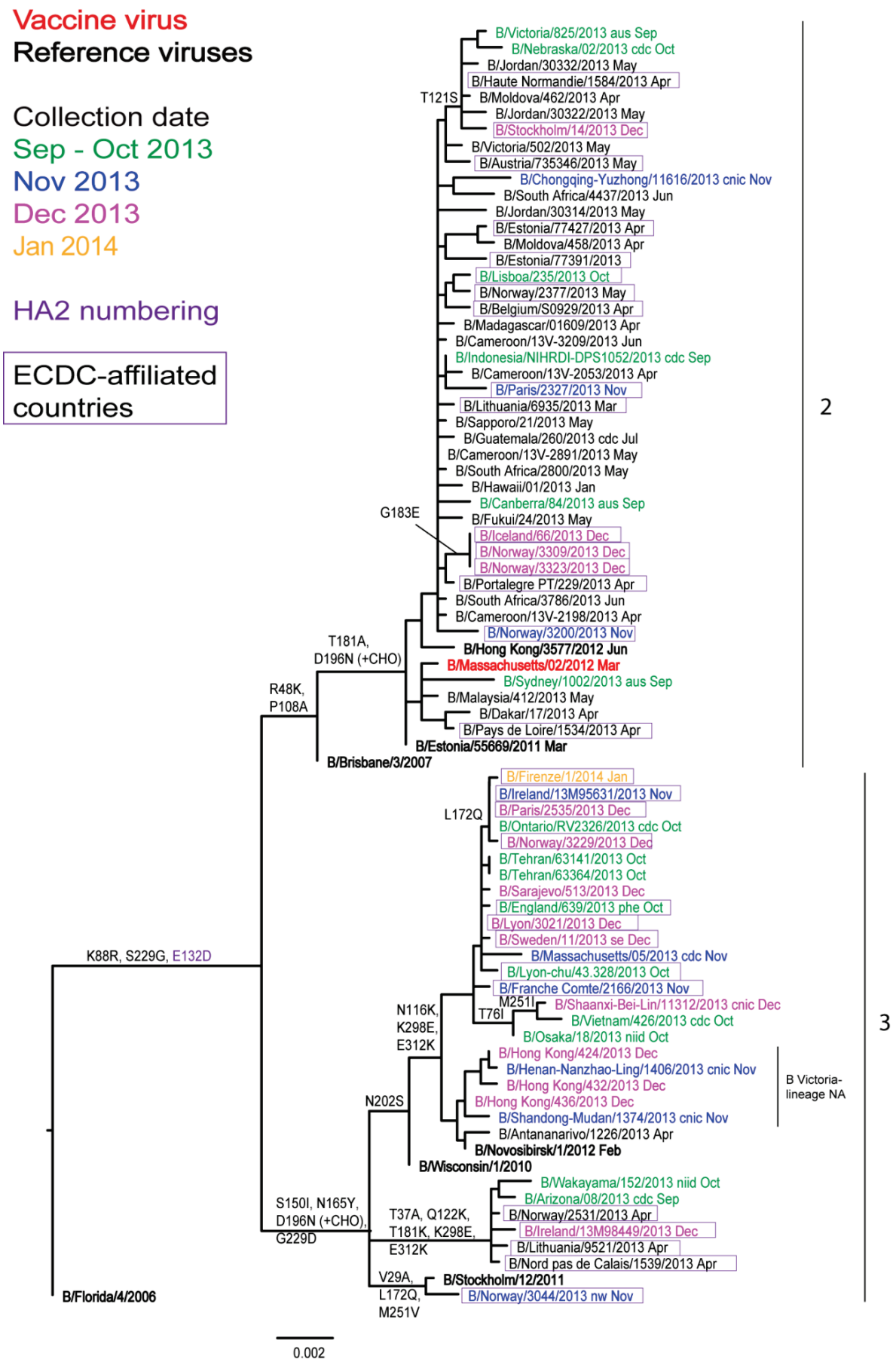
Viruses	Genetic Group	Collection date	Passage History	Haemagglution Inhibition Titre: Post infection ferret sera									
				B/Fl[3] 4/06 SH479 1	B/Fl[1] 4/06 F1/10 1	B/Bris[2] 3/07 F24/07 2	B/Wis[2] 1/10 F24/12 3	B/Stock[2] 12/11 F12/12 3	B/Estonia[2] 55669/11 F26/11 2	B/Novo[2] 1/12 F31/12 3	B/HK[2] 3577/12 F33/12 2	B/Mass[2] 2/12 Egg F2/13 2	B/Mass[2] 2/12 T/C F3/13 2
REFERENCE VIRUSES													
B/Florida/4/2006	1	2006-12-15	E7	5120	1280	1280	320	640	160	80	320	1280	160
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	640	640	320	640	160	80	320	640	160
B/Wisconsin/1/2010	3	2007-08-07	E3/E2	640	160	160	160	320	<	40	40	320	40
B/Stockholm/12/2011	3	2007-08-07	E4/E1	2560	160	80	80	160	10	40	40	160	20
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	1280	160	80	80	80	640	80	640	160	640
B/Novosibirsk/1/2012	3	2012-02-14	C2/MDCK3	2560	160	160	160	160	160	320	320	160	640
B/Hong Kong/3577/2012	2	2012-06-13	MDCK4	1280	80	80	80	80	640	80	640	160	320
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	640	1280	320	640	160	40	320	1280	160
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	320	320	160	320	320	80	320	640	320
TEST VIRUSES													
B/Lyon-chu/43.328/2013	3	2013-10-23	MDCK2/MDCK1	2560	320	160	160	320	160	160	160	320	320
B/England/639/2013	3	2013-10-24	SIAT1/MDCK1	1280	160	160	160	320	40	80	80	320	160
B/Lisboa_PT/235/2013	2	2013-10-29	SIAT2/MDCK1	2560	160	160	160	320	640	160	640	320	640
B/Norway/3044/2013	3	2013-11-03	MDCK1/MDCK1	640	80	40	80	160	40	80	80	320	80
B/Franche Comte/2166/2013	3	2013-11-04	MDCK1/MDCK1	1280	160	80	160	160	160	320	160	160	640
B/Ireland/13M95631/2013	3	2013-11-21	Cx/MDCK1	1280	160	80	80	160	80	160	160	160	320
B/Norway/3200/2013	2	2013-11-22	MDCK1/MDCK1	640	80	80	40	80	320	20	320	160	160
B/Paris/2327/2013	2	2013-11-25	MDCK1/MDCK1	640	80	40	20	20	160	20	160	80	160
B/Paris/2375/2013	3	2013-11-26	MDCK1/MDCK1	640	80	40	40	80	20	40	40	80	40
B/Stockholm/14/2013	2	2013-12-02	MDCK2/MDCK4	1280	80	40	40	40	640	80	320	160	320
B/Norway/3229/2013	3	2013-12-04	MDCK2/MDCK1	5120	160	160	160	320	320	320	640	160	1280
B/Ireland/13M98449/2013	3	2013-12-04	Cx/MDCK1	640	80	40	80	80	40	40	40	160	80
B/Lyon/3021/2013	3	2013-12-16	MDCK2/MDCK1	640	80	40	80	80	20	80	40	160	40
B/Norway/3323/2013	2	2013-12-19	MDCK1/MDCK1	2560	160	80	80	80	320	40	320	160	160
B/Norway/3324/2013		2013-12-19	MDCK1/MDCK2	1280	80	80	20	80	320	20	640	80	320
B/Iceland/66/2013	2	2013-12-23	MDCK1/MDCK1	1280	160	160	80	160	320	40	320	320	320
B/Norway/3309/2013	2	2013-12-24	MDCK1	1280	80	80	40	80	160	40	320	160	160
B/Paris/2535/2013	3	2013-12-28	MDCK1/MDCK1	320	80	40	40	80	20	40	40	80	40
B/Firenze/1/2014	3	2014-01-07	MDCK2	640	80	80	80	160	10	80	80	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



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 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 in recent months. 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].

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 and drawn using FigTree. 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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