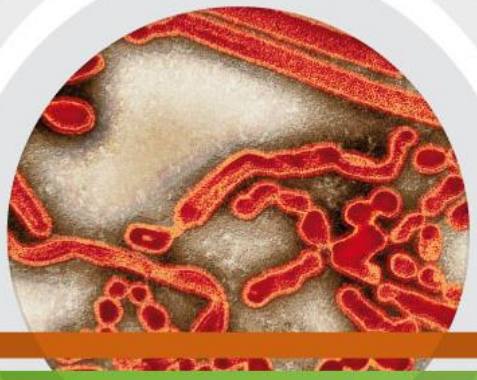

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2015

Summary

Over the course of the 2014–15 influenza season, influenza A(H3N2), A(H1N1)pdm09 and type B viruses have co-circulated in EU/EEA countries. To date, 21 EU/EEA countries have shared 545 influenza-positive specimens with the WHO Collaborating Centre in London for detailed characterisation. Since the December 2014 report[1], 236 viruses have been characterised.

The 71 A(H1N1)pdm09 viruses characterised, as those circulating worldwide, belonged to genetic subgroup 6B and were antigenically similar to the vaccine virus A/California/07/2009, based on HI analyses.

Many of the 101 A(H3N2) viruses characterised by HI assay were poorly recognised by antisera raised against the A/Texas/50/2012 vaccine virus but relatively well recognised by antisera raised against cell-propagated genetic subgroup 3C.3a viruses, although the small number of genetic subgroup 3C.2a viruses that could be analysed by HI assay showed somewhat lower HI titres.

The 85 viruses characterised genetically fell in genetic group/subgroups 3C.3 (17), 3C.3b (29), 3C.3a (15) and 3C.2a (24). Viruses in genetic group 3C.3 and subgroup 3C.3b were antigenically similar to A/Texas/50/2012, while those in subgroups 3C.2a and 3C.3a were antigenically distinct and the two subgroups were antigenically distinguishable despite antisera raised against representative viruses showing cross-reactivity. A subset of A(H3N2) viruses analysed by plaque reduction neutralisation assay (PRNA: n = 49, inclusive of many that could not be analysed by HI assay) also showed the cross-reactivity of antisera raised against genetic subgroup 3C.2a and 3C.3a viruses.

Only two B/Victoria-lineage viruses were received. Both were antigenically and genetically similar to B/Brisbane/60/2008.

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

This report was prepared by Rod Daniels, Burcu Ermetal, Aine Rattigan and John McCauley on behalf of the European Reference Laboratory Network for Human Influenza (ERLI-Net), under contract to the European Centre for Disease Prevention and Control (ECDC).

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The 62 B/Yamagata-lineage test viruses characterised fell in genetic clade 3 and showed good reactivity with antisera raised against B/Phuket/3073/2013 (the clade 3 virus recommended for the 2015 southern hemisphere season vaccine). Antisera raised against B/Massachusetts/02/2012 (the clade 2 virus recommended for the 2014–15 northern hemisphere season vaccine) did not recognise test viruses as well as antisera raised against B/Phuket/3073/2013. However, in terms of absolute titre, the titres observed for the test viruses were similar for antisera raised against both vaccine viruses.

These results formed part of the report prepared by the London WHO Collaborating Centre for consideration at the WHO Consultation on the Composition of Influenza Virus Vaccines for the northern hemisphere 2015–16; the meeting outcome was published on 26 February 2015[2].

Influenza-positive samples, 545 viruses or clinical specimens, with collection dates after 31 August 2014 have been received at the MRC National Institute for Medical Research, WHO Collaborating Centre for Reference and Research on Influenza (WHO CC), from 21 countries in the EU/EEA. Overall, the majority (~80%) were type A viruses and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 3:1 (Table 1). Of the 111 type B specimens received (~20 % of the specimens), 76 were of the B/Yamagata-lineage, 33 were not ascribed to a lineage, and only two were of the B/Victoria lineage. Some of these samples, mostly received as clinical specimens, are still in the process of being characterised. The antigenic and genetic properties of influenza virus isolates characterised since the December 2014 report[1] are presented and discussed in this report.

[2] Recommended composition of influenza virus vaccines for use in the 2015–2016 northern hemisphere influenza season. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/201502_recommendation.pdf

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

MONTH	TOTAL RECEIVED	A	H1N1pdm09		H3N2		B	B Victoria lineage		B Yamagata lineage	
Country			Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]
2014											
SEPTEMBER											
Belgium	1				1	1					
France	2				1	1				1	1
Spain	1				1	0 (1)					
Sweden	3				3	2 (1)					
OCTOBER											
Belgium	5				5	1 (4)					
Denmark	2				2	in process					
Finland	1				1	in process					
France	6				5	1 (4)				1	1
Germany	5		3	3	1	1		1	1		
Malta	4				4	3 (1)					
Netherlands	6				5	3 (2)				1	1
Norway	8		5	3	3	1					
Slovenia	3				1	1	1			1	0
Spain	10				7	5 (1)				3	3
Sweden	2				2	1 (1)					
United Kingdom	2				1	1				1	1
NOVEMBER											
Belgium	4		1	1	1	0 (1)				2	1
Denmark	1				1	in process					
Finland	2				2	in process					
France	6		1	1	3	0 (3)				2	2
Germany	8		2	2	5	3 (2)				1	1
Latvia	1		1	1							
Luxembourg	1		1	1							
Netherlands	3				3	0 (3)					
Norway	10				2	2				8	3
Portugal	2									2	2
Slovenia	1		1	in process							
Spain	11				9	6 (3)	1			1	1
Sweden	3				3	3					
United Kingdom	7				6	3 (2)				1	1
DECEMBER											
Austria	8				7	1 (6)				1	1
Belgium	5		3	3	1	1				1	1
Croatia	10		4	4	2	1	2			2	2
Czech Rep	7				7	in process					
Denmark	5		2	2	3	0					
Estonia	1				1	in process					
Finland	5		2	2	1	0 (1)				2	2
France	37		4	4	26	19 (7)				7	7
Germany	29		4	4	23	11 (12)		1	1	1	1
Greece	3				2	1 (1)				1	1
Italy	30		14	14	9	4 (5)				7	7
Latvia	8		1	1	5	3 (2)				2	2
Luxembourg	11		6	3	3	1 (2)	2				
Malta	4				4	in process					
Netherlands	1		1	1							
Norway	25		4	in process	14	in process				7	4
Portugal	10				3	1 (2)				7	7
Slovenia	19		17	in process	1	in process	1				
Spain	30				23	in process				7	7
United Kingdom	12		1	1	10	in process				1	1
2015											
JANUARY											
Croatia	1				1	0					
Denmark	2				2	2					
Estonia	24	4	1	in process	18	in process				1	in process
Germany	11				11	7 (4)					
Greece	58		11	in process	25	in process	22				
Italy	1		1	1							
Latvia	2				2	0 (2)					
Luxembourg	1						1				
Malta	5				5	in process					
Norway	4				4	1 (2)					
Portugal	6		2	1	2					2	1
Slovenia	15	2	7	7	2	0 (2)	3			1	1
Spain	7	1			5	4 (1)				1	1
United Kingdom	27		2	2	25	7 (8)					
	545	7	102	62	325	103 (86)	33	2	2	76	64
			18.7%		59.6%			0.4%		13.9%	
21 Countries			79.6%				20.4%				

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); numbers in parentheses show the number of viruses either not recovered (no neuraminidase activity detected by MUNANA-based assay) or with HA titres too low to allow HI assay

Influenza A(H1N1)pdm09 virus analyses

Haemagglutination inhibition (HI) analyses of viruses that have been performed since the December 2014 report are shown in Tables 2-1 to 2-3. All 71 of the recently circulating H1N1 viruses were antigenically similar to the vaccine virus, A/California/7/2009, showing no more than twofold reduction in HI titre compared to that for the homologous virus in all assays. All viruses were recognised by the extended panel of antisera at titres within fourfold of the titres for the homologous viruses, with the exception of the antiserum raised against A/Christchurch/16/2010. This antiserum recognised just over 50% (36/71) of the test viruses at a titre within fourfold of the titre for the homologous virus. It is also noteworthy that all antisera raised against viruses falling outside of genetic group 1, the A/California/7/2009 group, recognised the egg-propagated vaccine virus at titres ≥ fourfold reduced compared to the titres of the antisera with their homologous viruses.

Figure 1 shows a phylogenetic tree for the HA genes of representative, recently circulating A(H1N1)pdm09 viruses. Since 2009 the HA genes have evolved and eight genetic groups have been designated. Over the last two seasons viruses in genetic group 6, represented by A/St Petersburg/27/2011 and carrying amino acid substitutions of **D97N**, **S185T** and **S203T** in **HA1** and **E47K** and **S124N** in **HA2** compared with A/California/7/2009, have predominated worldwide with a number of subgroups emerging. All EU/EEA viruses characterised since the September 2014 report[3] carry HA genes in genetic subgroup 6B which is characterised by additional amino acid substitutions of **K163Q, A256T** and **K283E** in **HA1** and **E172K** in **HA2** compared with A/California/7/2009, e.g. A/South Africa/3626/2013.

These results contributed to the World Health Organisation recommendation[4] to retain the A/California/7/2009 vaccine virus for the northern hemisphere 2015–16 influenza season.

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

[4] Recommended composition of influenza virus vaccines for use in the 2015-2016 northern hemisphere influenza season. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/201502_recommendation.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 F14/13	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 F26/14 6	A/St. P 100/11 F24/11 7	A/HK 5659/12 F30/12 6A	A/Sth Afr 3626/13 F3/14 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E2	640	640	1280	160	160	160	160	320	160	160	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	320	40	40	40	40	80	40	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	320	1280	1280	160	80	80	80	160	160	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	1280	2560	5120	2560	2560	640	5120	2560	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	160	160	640	640	320	1280	640	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK4/MDCK1	640	640	640	320	1280	1280	640	2560	2560	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	640	1280	640	320	1280	1280	640	2560	1280	1280	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	640	640	640	320	1280	1280	640	2560	2560	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	160	640	640	320	1280	1280	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	320	640	640	320	640	640	640	2560	640	1280	
TEST VIRUSES														
A/Italy/FVG-27/2014	6B	unknown	Cx/MDCK1	640	320	320	640	1280	1280	1280	2560	1280	1280	
A/Italy/FVG-28/2014	6B	unknown	Cx/MDCK1	640	640	640	640	1280	1280	1280	2560	1280	1280	
A/Parma/84/2014	6B	unknown	MDCK2/MDCK2	1280	640	1280	640	2560	2560	2560	5120	2560	2560	
A/Rheinland-Pfalz/12/2014	6B	2014-10-24	C2/MDCK1	640	320	320	640	1280	1280	640	5120	2560	1280	
A/Hamburg/6/2014	6B	2014-10-27	C2/MDCK1	1280	640	640	1280	2560	2560	1280	5120	2560	2560	
A/Rheinland-Pfalz/14/2014	6B	2014-10-27	C3/MDCK1	320	320	320	320	640	640	640	1280	1280	640	
A/Norway/3023/2014	6B	2014-10-28	MDCK1	640	320	640	640	1280	1280	1280	5120	2560	1280	
A/Norway/3024/2014	6B	2014-10-31	MDCK1	640	640	640	640	1280	2560	1280	5120	2560	1280	
A/Mecklenburg-Vorpommern/5/2014	6B	2014-11-08	C2/MDCK1	640	320	640	640	640	1280	640	2560	2560	1280	
A/Belgium/G651/2014	6B	2014-11-24	MDCK1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Hamburg/7/2014	6B	2014-11-27	C3/MDCK1	640	640	640	640	1280	1280	1280	2560	2560	1280	
A/Belgium/G675/2014	6B	2014-12-03	MDCK1/MDCK1	320	160	160	160	1280	1280	1280	2560	1280	640	
A/Belgium/G683/2014	6B	2014-12-05	MDCK1/MDCK2	640	320	640	320	1280	1280	640	2560	1280	1280	
A/Rheinland-Pfalz/15/2014	6B	2014-12-15	C2/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	2560	2560	
A/Berlin/81/2014	6B	2014-12-26	C2/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	2560	2560	

Sequences in phylogenetic tree

Vaccine

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 F14/13	A/Chch 16/10 4	A/HK 3934/11 3	A/Astrak 1/11 5	A/St. P 27/11 6	A/St. P 100/11 7	A/HK 5659/12 6A	A/Sth Afr 3626/13 6B	
REFERENCE VIRUSES														
A/California/7/2009		2009-04-09	E1/E3	640	1280	1280	160	160	320	320	320	160	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	320	320	40	40	80	80	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	1280	1280	160	80	160	320	160	320	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	1280	2560	2560	5120	2560	2560	2560	5120	2560	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	160	320	320	640	1280	640	1280	1280	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	1280	640	640	640	1280	2560	1280	2560	2560	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	640	1280	2560	2560	5120	2560	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	1280	1280	1280	2560	2560	5120	5120	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	320	1280	1280	640	2560	1280	1280	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	640	640	320	640	1280	640	2560	1280	1280	
TEST VIRUSES														
A/Nice/2419/2014	6B	2014-11-22	MDCK2/MDCK1	640	320	640	320	1280	1280	1280	2560	1280	1280	
A/Marseille/ 2408/2014	6B	2014-12-02	MDCK2/MDCK1	640	640	640	640	1280	1280	1280	5120	2560	1280	
A/Belgium/G671/2014		2014-12-02	MDCK2	1280	320	320	640	1280	2560	1280	5120	2560	2560	
A/Luxembourg/14068163/2014	6B	2014-12-09	MDCK1/MDCK1	1280	1280	640	1280	2560	5120	2560	5120	5120	2560	
A/Latvia/12-020598/2014	6B	2014-12-09	C1/MDCK1	640	320	320	640	1280	1280	1280	2560	1280	1280	
A/Italy/FVG-30/2014	6B	2014-12-10	SIAT1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	2560	2560	
A/Lyon/2425/2014		2014-12-11	MDCK2/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	2560	2560	
A/Italy/FVG-32/2014		2014-12-11	SIAT1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Schleswig-Holstein/9/2014	6B	2014-12-11	C3/MDCK1	1280	640	1280	1280	2560	2560	2560	5120	5120	2560	
A/Netherlands/466/14	6B	2014-12-14	MDCK1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	2560	2560	
A/Poitiers/2483/2014	6B	2014-12-14	MDCKX/MDCK1/MDCK1	1280	640	1280	640	2560	2560	2560	5120	2560	1280	
A/Milano/166/2014		2014-12-15	SIAT1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Italy/FVG-33/2014	6B	2014-12-15	SIAT1/MDCK1	1280	1280	1280	1280	2560	5120	2560	5120	5120	2560	
A/Italy/FVG-34/2014		2014-12-15	SIAT1/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Lyon/2436/2014	6B	2014-12-16	MDCK2/MDCK1	1280	1280	1280	1280	2560	2560	2560	5120	2560	2560	
A/Milano/167/2014	6B	2014-12-16	SIAT1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	2560	2560	
A/Luxembourg/14069579/2014	6B	2014-12-17	MDCK1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	5120	2560	
A/Italy/FVG-38/2014		2014-12-17	SIAT1/MDCK1	2560	1280	1280	2560	2560	5120	5120	5120	5120	2560	
A/Luxembourg/14069580/2014	6B	2014-12-18	MDCK1/MDCK1	1280	640	640	640	1280	2560	2560	5120	2560	2560	
A/Italy/FVG-35/2014		2014-12-18	SIAT1/MDCK1	2560	1280	1280	2560	5120	5120	5120	5120	5120	2560	
A/Italy/FVG-37/2014	6B	2014-12-19	SIAT1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	2560	1280	
A/Italy/FVG-41/2014	6B	2014-12-24	SIAT1/MDCK1	2560	2560	1280	2560	5120	5120	5120	5120	5120	5120	
A/Italy/FVG-39/2014		2014-12-29	SIAT1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	2560	2560	
A/Italy/FVG-43/2014		2014-12-29	SIAT1/MDCK1	1280	640	640	1280	2560	2560	2560	5120	5120	2560	
A/Italy/FVG-42/2014	6B	2014-12-30	SIAT1/MDCK1	1280	640	640	640	1280	2560	2560	5120	5120	2560	
A/Italy/FVG-01/2015		2014-12-31	SIAT1/MDCK1	1280	1280	640	1280	2560	2560	2560	5120	2560	2560	
A/Berlin/87/2014	6B	2014-12-31	C2/MDCK1	1280	1280	1280	1280	2560	5120	2560	5120	5120	2560	
A/Lisboa/EVA60/2015	6B	2015-01-05	MDCK1	1280	640	640	1280	2560	2560	2560	5120	2560	2560	
A/Italy/FVG-02/2015	6B	2015-01-05	SIAT1/MDCK1	2560	1280	1280	2560	2560	5120	5120	5120	5120	5120	

Sequences in phylogenetic tree

Vaccine

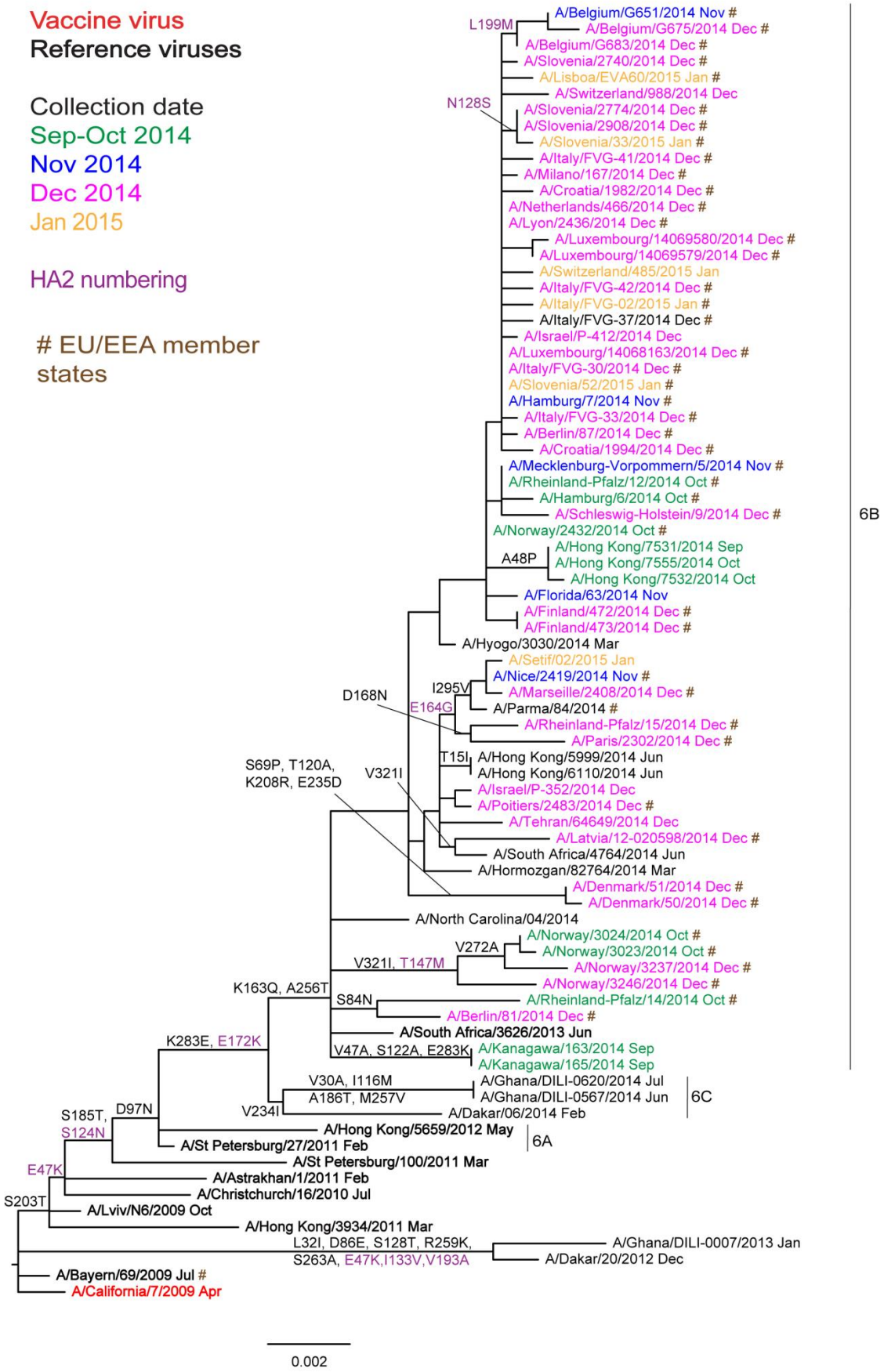
Table 2-3. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera											
				A/Cal 7/09 F1/15	A/Cal 7/09 F30/11	A/Bayern 69/09 F11/11	A/Lviv N6/09 F14/13	A/Chch 16/10 F15/14	A/HK 3934/11 F21/11	A/Astrak 1/11 F22/13	A/St. P 27/11 F23/11	A/St. P 100/11 F24/11	A/HK 5659/12 F30/12	A/Sth Afr 3626/13 F3/14	
								4	3	5	6	7	6A	6B	
REFERENCE VIRUSES															
A/California/7/2009		2009-04-09	EP1/E3	1280	640	1280	1280	320	160	320	320	320	320	320	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK2	160	160	640	640	160	40	80	160	80	80	80	G155E
A/Lviv/N6/2009		2009-10-27	MDCK4/S1/MDCK3	640	320	1280	1280	320	80	160	320	160	320	160	G155E>G, D222G
A/Christchurch/16/2010	4	2010-07-12	E1/E3	2560	2560	2560	5120	5120	2560	2560	2560	5120	5120	2560	
A/Hong Kong/3934/2011	3	2011-03-29	MDCK2/MDCK3	320	640	320	320	640	1280	1280	1280	2560	1280	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	320	640	320	320	640	640	1280	1280	2560	1280	640	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	2560	1280	1280	2560	2560	5120	2560	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E3	1280	1280	1280	1280	1280	2560	2560	2560	5120	5120	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	160	320	160	160	320	640	640	640	1280	1280	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E2	640	640	640	1280	640	1280	1280	1280	2560	1280	1280	
TEST VIRUSES															
A/Finland/472/2014	6B	2014-12-04	MDCK2/MDCK1		1280	640	1280	1280	1280	2560	2560	5120	2560	2560	
A/Finland/473/2014	6B	2014-12-04	MDCK2/MDCK1		640	160	320	320	640	1280	640	1280	1280	640	
A/Slovenia/2631/2014		2014-12-13	MDCK1/MDCK1		640	320	640	640	1280	1280	1280	5120	2560	1280	
A/Slovenia/2738/2014		2014-12-13	MDCK1/MDCK1		640	640	640	640	1280	1280	1280	5120	2560	1280	
A/Slovenia/2739/2014		2014-12-13	MDCK1/MDCK1		1280	640	640	640	1280	1280	1280	5120	2560	1280	
A/Slovenia/2740/2014	6B	2014-12-13	MDCKx/MDCK1		1280	640	640	640	1280	2560	1280	5120	2560	1280	
A/Norway/3237/2014	6B	2014-12-19	MDCK2		1280	640	640	1280	1280	1280	1280	5120	2560	1280	
A/Slovenia/2774/2014	6B	2014-12-19	MDCKx/MDCK1		1280	640	1280	1280	1280	2560	2560	5120	2560	2560	
A/Slovenia/2804/2014	6B	2014-12-19	MDCKx/MDCK1		320	320	320	320	640	1280	640	1280	1280	640	
A/Norway/3246/2014	6B	2014-12-20	MDCK1		1280	640	640	1280	1280	2560	2560	5120	2560	1280	
A/Slovenia/2805/2014		2014-12-22	MDCKx/MDCK1		1280	640	1280	1280	1280	2560	2560	5120	2560	1280	
A/England/579/2014	6B	2014-12-22	MDCK1/MDCK1		640	640	640	640	1280	1280	1280	2560	2560	1280	
A/Denmark/50/2014	6B	2014-12-25	MDCK3/MDCK1		640	320	320	640	640	1280	1280	2560	1280	1280	
A/Denmark/51/2014	6B	2014-12-25	MDCK3/MDCK1		640	320	320	640	1280	1280	1280	2560	1280	1280	
A/Croatia/1982/2014	6B	2014-12-28	MDCKx/MDCK1		640	640	640	640	1280	1280	1280	2560	2560	1280	
A/Croatia/1982/2014	6B	2014-12-28	E1/E1		1280	640	640	1280	2560	2560	2560	5120	2560	2560	
A/Croatia/1994/2014	6B	2014-12-29	MDCKx/MDCK1		640	640	640	640	1280	1280	1280	5120	2560	1280	
A/Slovenia/2908/2014	6B	2014-12-30	MDCKx/MDCK1		640	640	320	640	1280	1280	1280	2560	1280	1280	
A/Slovenia/9/2015		2015-01-02	MDCKx/MDCK1		640	320	320	640	1280	1280	1280	2560	1280	1280	
A/Slovenia/33/2015	6B	2015-01-02	MDCKx/MDCK1		1280	640	640	1280	2560	2560	2560	5120	2560	1280	
A/England/2/2015	6B	2015-01-05	MDCK1/MDCK1		1280	640	640	1280	2560	2560	2560	5120	2560	1280	
A/Slovenia/46/2015		2015-01-06	MDCKx/MDCK1		640	320	320	640	1280	1280	1280	2560	1280	640	
A/Slovenia/52/2015	6B	2015-01-06	MDCKx/MDCK1		640	320	320	640	1280	1280	1280	2560	1280	640	
A/England/6/2015	6B	2015-01-08	MDCK1/MDCK1		640	320	640	640	1280	1280	1280	2560	2560	1280	
A/Slovenia/119/2015	6B	2015-01-09	MDCKx/MDCK1		640	640	640	640	640	1280	1280	2560	1280	1280	
A/Slovenia/226/2015		2015-01-14	MDCKx/MDCK1		1280	640	640	1280	1280	2560	2560	5120	2560	1280	
A/Slovenia/233/2015		2015-01-14	MDCKx/MDCK1		1280	640	640	1280	1280	1280	2560	5120	2560	1280	

Sequences in phylogenetic tree

Vaccine

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



Influenza A(H3N2) virus analyses

As described in many previous reports[5], influenza A(H3N2) viruses continue to be difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells (RBCs) from guinea pigs, turkeys and humans or the loss of the ability of viruses to agglutinate any of the RBCs. This is a particular problem for most viruses that fall in genetic subgroup 3C.2a as was highlighted in the November 2014 report[6].

Results of HI tests performed with guinea pig RBCs in the presence of 20nM oseltamivir, added to circumvent any NA-mediated binding of H3N2 viruses to the RBCs, since the December 2014 report are shown in Tables 3-1 to 3-3. The HA genetic group is indicated for those viruses that have been sequenced, and those included in the HA phylogenetic tree presented here (Figure 2) are highlighted. Of the successfully propagated viruses, only ~52% (n = 101) retained sufficient HA titre to be analysed by HI assay. The remainder were unable to agglutinate guinea pig RBCs at all (23% of the total) or were unable to agglutinate RBCs in the presence of 20nM oseltamivir (25% of the total). The vast majority (95%) of viruses in these last two categories belonged to genetic subgroup 3C.2a. Viruses in genetic subgroup 3C.2a have acquired a glycosylation motif at positions 158 to 160 in HA1; those viruses in genetic subgroup 3C.2a viruses that were able to bind guinea pig RBCs in the presence of oseltamivir (and so were analysed by HI assay) had either lost, or were polymorphic for, the glycosylaytion motif.

All test viruses that were propagated in MDCK-SIAT1 cells reacted poorly in HI assays (≥ eightfold decrease) with post-infection ferret antiserum raised against the egg-propagated vaccine virus, A/Texas/50/2012, compared to the titre of the antiserum with the homologous virus. Similarly, low levels of reactivity were seen with antisera raised against the egg-propagated reference virus A/Hong Kong/146/2013: only approximately 14% of test viruses reacted within fourfold of the titre with the homologous egg-propagated virus. Better reactivity was seen with test viruses when analysed with an antiserum raised against the exclusively egg-propagated A/Stockholm/6/2014 isolate 2, a virus belonging to genetic subgroup 3C.3a. This antiserum showed a low titre for the homologous virus but recognised over 75% of test viruses at titres within fourfold of the homologous titre. Antiserum raised against egg-propagated A/Switzerland/9715293/2013, the virus recommended for the southern hemisphere vaccine in 2015 and in genetic subgroup 3C.3a, had an homologous titre of 1280 and recognised only 2% of the test viruses at titres within fourfold of the homologous titre. Antiserum raised against egg-propagated A/Hong Kong/5738/2014 clone 121, a virus in genetic subgroup 3C.2a, had a homologous titre of 640 or 1280 and failed to recognise any of the test viruses at titres within fourfold of the homologous titre.

Ferret antisera raised against reference viruses propagated in tissue culture cells, A/Victoria/361/2011 and A/Samara/73/2013, recognised the test viruses somewhat more effectively. The antiserum raised against A/Victoria/361/2011 recognised ~73% of the test viruses at a titre within fourfold of the antiserum for the homologous virus, but the antiserum raised against A/Samara/73/2013 recognised only ~39% of test viruses at a titre within fourfold of the titre for the homologous virus. These reference viruses have HA genes from genetic groups 3C.1 and 3C.3, respectively. Antisera raised against reference viruses belonging to genetic subgroup 3C.3a that had been exclusively propagated in cell culture, A/Stockholm/6/2014 and A/Switzerland/9715293/2013, recognised 96% and 76%, respectively, of test viruses at titres within fourfold of those with the corresponding homologous viruses. An antiserum raised against a reference virus belonging to genetic subgroup 3C.2a that had been exclusively propagated in cell culture, A/Hong Kong/5738/2014, recognised 76% of test viruses at titres within fourfold of that for the homologous virus.

HI tests were complemented by using plaque reduction neutralisation assay (PRNA) to characterise a subset of viruses which included many for which analysis by HI was not possible. The results of PRNA performed with MDCK-SIAT1 cells are shown in Tables 4-1 and 4-2. A total of 49 test viruses recovered from recently collected specimens were analysed with a panel of antisera raised against both cell culture-propagated and egg-propagated viruses from genetic subgroups 3C.1, 3C.2a and 3C.3a. Where known, the genetic groups to which the HA genes of the reference viruses and the test viruses belong are shown; only three of the test viruses were not characterised genetically and, of the remaining 46, 44 were 3C.2a and two 3C.3. The titres given are to the nearest twofold dilution factor with the numbers in parentheses being interpolated directly from the results using image-processing software. Compared to their cell-propagated cultivars, the egg-propagated cultivar of the reference virus A/Switzerland/9715923/2013 (3C.3a) has the egg-adaptive amino acid substitutions I140R and G186V in HA1 and that of A/Hong Kong/5738/2014 (3C.2a) has HA1 substitutions of T160K (resulting in the loss of the potential glycosylation site motif at 158-160 in HA1), L194P and T203I. The cell culture-propagated cultivar of A/Hong Kong/5738/2014 is polymorphic at residue 160 leading to the partial loss of the potential glycosylation

[5] 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

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

site at residues 158–160; the cell culture-propagated cultivar of A/England/530/2014 has lost this motif, but it is retained in cell culture-propagated A/Hong Kong/7295/2014.

The two antisera raised against egg-propagated reference viruses have higher homologous titres than those raised against the cell-propagated viruses. Of the test viruses, 65% (32/49) were recognised at titres within fourfold of the titre for the homologous virus by the antiserum raised against the egg-propagated cultivar of A/Switzerland/9715293/2013 but the antiserum raised against the egg-propagated cultivar of A/Hong Kong/5738/2014 recognised only 2/23 (9%) of the test viruses at titres within fourfold of the titre for the homologous virus. Nevertheless, there was little difference in the absolute titres for the test viruses seen between the two antisera used in the same tests (Table 4-1).

The antiserum raised against cell culture-propagated A/Victoria/361/2011 recognised only 12% (6/49) of the test viruses at a titre within twofold of the titre for the homologous virus in the PRNA, but each of the other antisera raised against cell culture-propagated reference viruses in genetic subgroups 3C.3a (A/Switzerland/9715293/2013) or 3C.2a (A/England/530/2014, A/Hong Kong/5738/2014, A/Hong Kong/7295/2014) recognised between 77% and 100% of the test viruses at titres within twofold of their titres for the homologous viruses: these percentages were for the antiserum raised against A/England/530/2014, 77% (20/26); A/Switzerland/9715293/2013, 86% (42/49); A/Hong Kong/5738/2014, 96% (47/49); A/Hong Kong/7295/2014, 100% (39/39).

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 fell within genetic group 3C. This group has three subdivisions: 3C.1 (to which the recommended vaccine virus for the 2014–15 northern hemisphere season, A/Texas/50/2012, belongs), 3C.2 and 3C.3 containing viruses that have been antigenically similar. However in 2014 three new genetic subgroups emerged, one in subdivision 3C.2, 3C.2a, and two in 3C.3, 3C.3a and 3C.3b (Figure 2). While viruses in genetic subgroups 3C.2a and 3C.3a are antigenic drift variants, those in 3C.3b are antigenically similar to previously circulating viruses in the 3C.3 subdivision.

Viruses received from EU/EEA countries, with collection dates since 31 August 2014, that have been sequenced fall into subgroups 3C.2a (~50%), 3C.3b (~24%) and 3C.3a (~11%) with the remainder (~15%) being in subdivision 3C.3. Amino acid substitutions that define these subdivisions and subgroups compared with A/Texas/50/2012 are:

- (3C.2) **N145S** and **V186G*** in **HA1**, and **D160N** in **HA2**, e.g. A/Hong Kong/146/2013;
- (3C.2a) Those in 3C.2 plus **L3I**, **N144S** (resulting in the loss of a potential glycosylation site), **F159Y**, **K160T** (in the majority of viruses, resulting in the gain of a potential glycosylation site), **N225D** and **Q311H** in **HA1,** e.g. A/Hong Kong/5738/2014;
- (3C.3) **T128A** (resulting in the loss of a potential glycosylation site), **R142G**, **N145S** and **V186G*** in **HA1**, e.g. A/Samara/73/2013;
- (3C.3a) Those in 3C.3 plus **A138S**, **F159S** and **N225D** in **HA1**, many with **K326R**, e.g. A/Switzerland/9715293/2013;
- (3C.3b) Those in 3C.3 plus **E62K, K83R, N122D** (resulting in the loss of a potential glycosylation site), **T128A** (resulting in the loss of a potential glycosylation site), **R142G, N145S, L157S, V186G*** and **R261Q** in **HA1** with **M18K** in **HA2**, e.g. A/Newcastle/22/2014.

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

Based on results that show cross-reactivity of antisera raised against genetic subgroup 3C.3a and 3C.2a viruses but with issues of antigenic changes on egg-adaptation of genetic subgroup 3C.2a viruses, the World Health Organisation recommendation[2] was to use an A/Switzerland/9715293/2013-like virus as the H3N2 component of vaccines for the northern hemisphere 2015–16 influenza season.

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

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] Post infection ferret antisera										
				A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12 3C.1	A/Texas 50/12 Egg F42/13 3C.1	A/Samara 73/13 F24/13 3C.3	A/HK 146/13 F40/13 3C.2	A/Stock 6/14 T/C F14/14 3C.3a	A/Stock 6/14 Egg F20/14 3C.3a isolate 2	A/Switz 9715293/13 NIB F13/14 3C.3a	A/Switz 9715293/13 F25/14 3C.3a cl123	A/HK 5738/14 T/C F30/14 3C.2a	A/HK 5738/14 NIB F53/14 3C.2a cl 121
REFERENCE VIRUSES														
A/Perth/16/2009		2009-07-04	E3/E3	1280	160	160	160	320	40	160	40	160	<	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT5	160	320	160	640	320	320	160	160	160	160	40
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	640	160	640	80	640	160	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT3	320	640	320	1280	1280	320	640	160	640	640	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E3/E3	80	640	320	320	640	160	320	40	320	320	80
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	<	80	80	320	160	320	160	160	160	160	40
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1 isolate 2	80	320	160	160	320	160	320	80	640	320	40
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	<	40	40	160	160	320	160	160	160	80	<
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1 clone 123	40	320	160	160	640	320	320	160	1280	320	40
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	<	40	40	160	80	80	80	80	80	160	<
A/Hong Kong/5738/2014	3C.2a	2014-04-30	E5/E1 clone121	80	40	80	160	160	160	80	80	40	640	1280
TEST VIRUSES														
A/Stockholm/17/2014	3C.2a	2014-07-23	MDCK2/SIAT1	<	40	80	80	80	80	80	40	80	80	<
A/Stockholm/18/2014	3C.2a	2014-08-16	MDCK2/SIAT1	<	40	40	80	80	80	80	40	80	160	<
A/Stockholm/19/2014	3C.3b	2014-09-07	MDCK1/SIAT1	40	80	40	160	80	160	80	40	80	80	<
A/Stockholm/20/2014	3C.3a	2014-09-28	MDCK1/SIAT1	<	<	80	80	80	160	80	80	80	80	<
A/Belgium/H80/2014	3C.3b	2014-09-29	SIAT1/SIAT1	80	80	80	320	160	160	160	80	80	80	<
A/Netherlands/395/2014	3C.3	2014-10-02	SIAT3/SIAT1	80	160	80	320	160	160	160	80	80	160	40
A/La Rioja/2053/2014	3C.3b	2014-10-08	SIAT1/SIAT1	80	160	80	320	160	160	160	40	160	160	<
A/Stockholm/22/2014	3C.2a	2014-10-18	MDCK2/SIAT1	<	80	<	160	80	160	80	40	80	160	<
A/Pais Vasco/1979/2014	3C.3	2014-10-22	SIAT1/SIAT1	40	160	40	320	160	160	160	80	160	160	40
A/Belgium/G589/2014	3C.3b	2014-10-22	SIAT1/SIAT1	40	80	80	160	80	160	160	40	80	80	<
A/La Rioja/2052/2014	3C.3b	2014-10-22	MDCKx/SIAT2	40	80	80	160	80	160	80	40	80	40	<
A/La Rioja/2051/2014	3C.3b	2014-10-29	MDCKx/SIAT1	40	80	40	320	160	160	160	40	80	80	<
A/Sweden/76/2014	3C.3a	2014-11-02	MDCK1/SIAT1	<	40	40	160	80	320	160	80	160	80	<
A/Stockholm/26/2014	3C.3a	2014-11-03	MDCK1/SIAT1	<	<	<	80	40	80	40	<	80	<	<
A/Aragon/2031/2014	3C.3b	2014-11-07	SIAT1/SIAT1	40	80	40	160	160	160	160	40	80	80	<
A/Baden-Wurttemberg/85/2014	3C.2a	2014-11-10	C2/SIAT1	<	40	40	160	80	80	80	40	80	80	<
A/La Rioja/2050/2014	3C.3b	2014-11-15	SIAT1/SIAT1	80	80	80	320	160	160	160	40	80	80	<
A/Stockholm/29/2014	3C.2a	2014-11-18	MDCK1/SIAT1	<	<	<	40	<	40	<	<	<	40	<
A/Galicia/2055/2014	3C.3	2014-11-20	SIAT2/SIAT1	80	160	80	320	160	160	160	40	160	160	<
A/Galicia/2054/2014	3C.3	2014-11-24	SIAT1/SIAT1	40	160	80	320	160	160	160	40	80	80	<
A/Extremadura/2061/2014	3C.3a	2014-11-25	SIAT1/SIAT1	<	80	80	160	160	320	160	160	160	160	40
A/Aragon/2062/2014	3C.3b	2014-11-27	SIAT1/SIAT1	80	80	40	320	160	160	160	40	80	80	<
A/Norway/3082/2014		2014-11-28	SIAT1	40	80	80	160	80	160	160	40	80	40	<
A/Norway/3079/2014	3C.3b	2014-11-30	SIAT2	40	80	80	160	80	160	80	40	40	40	<
A/Norway/3107/2014		2014-12-02	SIAT1	<	40	40	160	80	160	80	40	80	80	<
A/Belgium/G678/2014	3C.3b	2014-12-04	SIAT1/SIAT2	80	160	80	160	80	160	80	80	80	80	<
A/Berlin/80/2014	3C.3b	2014-12-17	C2/SIAT1	40	80	80	160	80	320	80	40	80	80	<
A/Berlin/82/2014		2014-12-18	C3/SIAT1	<	40	40	160	80	80	80	<	80	80	<
A/Rheinland-Pfalz/16/2014	3C.3b	2014-12-21	C2/SIAT1	40	80	80	160	80	160	80	40	80	80	<
A/Nordrhein-Westfalen/18/2014	3C.3b	2014-12-22	C2/SIAT1	80	80	80	320	160	160	160	40	80	80	<
A/Baden-Wurttemberg/87/2014	3C.3b	2014-12-22	C2/SIAT1	40	80	80	160	80	160	80	40	80	40	<
A/Bayern/45/2014	3C.3b	2014-12-23	C1/SIAT1	40	80	40	160	80	160	80	40	80	40	<
A/Italy/FVG-29/2014	3C.2a	unknown	Cx/SIAT2	<	40	40	80	40	80	40	40	40	80	<
						Vaccine SH2014 NH 2014/15						Vaccine SH2015 NH 2015/16		

1. < = <40

Sequences in phylogenetic tree

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

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1]										
				Post infection ferret antisera										
				A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12	A/Texas 50/12 Egg F42/13	A/Samara 73/13 F24/13	A/HK 146/13 F40/13	A/Stock 6/14 T/C F14/14	A/Stock 6/14 Egg F20/14	A/Switz 9715293/13 NIB F13/14	A/Switz 9715293/13 F25/14	A/HK 5738/14 T/C F30/14	A/HK 5738/14 NIB F53/14
					3C.1	3C.1	3C.3	3C.2	3C.3a	3C.3a isolate 2	3C.3a	3C.3a cl123	3C.2a	3C.2a cl 121
REFERENCE VIRUSES														
A/Perth/16/2009		2009-07-04	E3/E3	640	160	160	160	320	40	160	<	80	<	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT5	80	160	160	320	160	320	160	80	160	160	40
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	640	640	160	640	80	640	160	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	160	320	320	640	640	320	320	160	320	320	40
A/Hong Kong/146/2013	3C.2	2013-01-11	E3/E3	320	640	640	640	1280	80	640	40	640	320	40
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	<	40	40	160	80	320	160	160	160	160	40
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1 isolate 2	80	160	160	80	160	160	320	80	640	160	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	<	40	40	160	80	320	160	160	160	80	<
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1 clone 123	40	160	160	160	320	320	320	80	1280	320	40
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	<	40	40	160	160	160	80	80	80	160	<
A/Hong Kong/5738/2014	3C.2a	2014-04-30	E5/E1 clone121	40	40	40	160	80	160	80	40	40	320	640
TEST VIRUSES														
A/Marseille/2180/2014	3C.2a	2014-09-11	MDCK3/SIAT1	<	<	<	80	40	80	40	<	40	80	<
A/Netherlands/398/2014	3C.3a	2014-10-27	SIAT3/SIAT1	<	40	40	160	80	320	160	160	160	80	<
A/Aragon/2102/2014	3C.3b	2014-12-05	SIAT2/SIAT1	<	80	40	80	80	160	80	40	40	40	<
A/Lyon/2397/2014		2014-12-08	MDCK2/SIAT1	<	<	40	80	80	320	80	40	80	80	<
A/Lyon/2398/2014		2014-12-08	MDCK2/SIAT1	80	160	80	320	160	320	80	40	80	80	<
A/Genova/1614/2014	3C.2a	2014-12-09	Cx/SIAT1	<	40	40	160	80	320	80	40	80	160	<
A/Lyon-CHU/21.99/2014	3C.3	2014-12-10	MDCK2/SIAT1	80	160	160	320	320	320	160	80	160	160	<
A/Milano/162/2014	3C.3	2014-12-10	SIAT1/SIAT1	40	80	80	160	80	160	80	40	80	80	<
A/Austria/830719/2014	3C.3b	2014-12-10	SIAT2/SIAT1	80	160	160	320	160	320	160	80	160	160	<
A/Latvia/12-030846/2014	3C.2a	2014-12-10	C2/SIAT1	<	<	<	80	40	160	40	<	40	80	<
A/Italy/FVG-31/2014	3C.3a	2014-12-12	SIAT1/SIAT1	<	80	80	320	160	640	160	160	160	160	40
A/Lyon/2429/2014	3C.3	2014-12-15	MDCK2/SIAT1	80	160	160	320	320	320	160	80	160	160	<
A/Lisboa/SU34/2014	3C.2a	2014-12-15	SIAT1/SIAT2	<	40	40	80	40	160	40	40	40	80	<
A/Baden-Wurttemberg/86/2014		2014-12-15	C2/SIAT1	80	80	80	320	160	320	160	40	80	80	<
A/Milano/169/2014	3C.2a	2014-12-16	SIAT1/SIAT2	<	80	40	160	80	320	80	80	40	160	<
A/Nimes/2454/2014	3C.3a	2014-12-18	MDCK2/SIAT1	<	<	40	160	80	320	80	80	80	80	<
A/Niedersachsen/12/2014		2014-12-18	C3/SIAT1	80	80	80	320	160	320	80	40	80	80	<
A/Latvia/12-051160/2014	3C.3b	2014-12-19	C2/SIAT1	80	160	160	320	160	320	160	80	160	160	<
A/Bayern/1/2015	3C.3	2014-12-20	C2/SIAT1	<	40	40	160	80	80	40	<	40	<	<
A/Madrid/15053/2014	3C.3	2014-12-22	SIAT2/SIAT1	80	80	80	160	160	160	80	40	80	80	<
A/Madrid/SO13031/2014		2014-12-22	SIAT2	80	80	80	160	160	320	80	40	80	80	<
A/Rheinland-Pfalz/17/2014	3C.3	2014-12-23	C2/SIAT1	40	40	40	160	80	80	40	<	40	<	<
A/Latvia/12-066660/2014	3C.2a	2014-12-28	C2/SIAT1	<	40	40	160	80	320	80	40	80	160	<
A/Baden-Wurttemberg/89/2014	3C.2a	2014-12-29	C2/SIAT1	<	<	<	80	80	160	40	<	40	80	<
A/Luxembourg/14070685/2014	3C.2a	2014-12-29	MDCK1/SIAT2	<	<	<	40	40	160	<	<	40	40	<
A/Castilla La Mancha/7/2015	3C.3	2015-01-02	SIAT2/SIAT1	80	80	80	320	160	80	80	40	80	80	<
A/Nordrhein-Westfalen/2/2015	3C.3b	2015-01-05	C2/SIAT1	<	40	40	80	40	80	40	<	40	<	<
A/Niedersachsen/1/2015		2015-01-05	C2/SIAT1	40	40	40	80	40	160	40	<	40	40	<
A/Saarland/1/2015	3C.3	2015-01-05	C2/SIAT1	<	40	40	160	80	80	40	<	40	<	<
A/Mecklenburg-Vorpommern/1/2	3C.3b	2015-01-05	C3/SIAT1	40	40	40	160	80	160	40	40	40	40	<
A/Berlin/1/2015	3C.2a	2015-01-06	C2/SIAT1	<	<	<	80	40	80	40	<	40	40	<
A/Niedersachsen/4/2015	3C.3	2015-01-07	C2/SIAT1	<	80	40	160	80	160	80	40	40	40	<
A/Niedersachsen/5/2015	3C.3b	2015-01-08	C2/SIAT1	<	40	40	80	40	160	40	<	40	<	<
						Vaccine SH2014 NH 2014/15						Vaccine SH2015 NH 2015/16		

1. < = <40

Sequences in phylogenetic tree

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

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] — Post infection ferret antisera										
				A/Perth 16/09 F18/11	A/Vic 361/11 T/C F09/12	A/Texas 50/12 Egg F42/13	A/Samara 73/13 F24/13	A/HK 146/13 F40/13	A/Stock 6/14 T/C F14/14	A/Stock 6/14 Egg F20/14	A/Switz 9715293/13 NIB F13/14	A/Switz 9715293/13 F25/14	A/HK 5738/14 T/C F30/14	A/HK 5738/14 NIB F53/14
					3C.1	3C.1	3C.3	3C.2	3C.3a	3C.3a isolate 2	3C.3a	3C.3a cl123	3C.2a	3C.2a cl 121
REFERENCE VIRUSES														
A/Perth/16/2009		2009-07-04	E3/E2	640	80	160	160	160	40	80	<	80	<	40
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT5	160	320	320	640	640	640	320	160	320	160	80
A/Texas/50/2012	3C.1	2012-04-15	E5/E2	640	1280	1280	1280	1280	320	640	80	640	160	80
A/Samara/73/2013	3C.3	2013-03-12	C1/SIAT4	320	320	320	1280	1280	640	640	160	640	640	80
A/Hong Kong/146/2013	3C.2	2013-01-11	E3/E3	640	640	640	1280	2560	160	640	80	1280	640	80
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	<	80	80	320	160	640	160	320	160	160	80
A/Stockholm/6/2014	3C.3a	2014-02-06	E4/E1 isolate 2	80	320	160	160	320	320	320	160	640	160	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	<	40	40	320	160	640	160	160	160	160	40
A/Switzerland/9715293/2013	3C.3a	2013-12-06	E4/E1 clone 123	40	160	160	320	640	320	640	160	1280	320	40
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	40	80	80	320	160	320	160	160	160	320	80
A/Hong Kong/5738/2014	3C.2a	2014-04-30	E5/E1 clone121	40	40	80	320	160	320	160	80	40	640	1280
TEST VIRUSES														
A/Paris/2337/2014		2014-12-04	MDCK2/SIAT1	<	160	80	320	320	640	640	640	640	320	80
A/Rouen/2273/2014	3C.3a	2014-12-05	MDCK1/SIAT1	<	40	40	160	80	320	80	80	80	80	<
A/Paris/2304/2014		2014-12-06	MDCK2/SIAT1	40	40	40	160	80	320	160	160	80	80	40
A/Malta/MX001759/2014	3C.3a	2014-12-09	SIAT1	40	80	40	160	80	160	80	40	40	40	<
A/Rouen/2291/2014	3C.2a	2014-12-09	MDCK1/SIAT1	<	80	80	160	80	160	80	40	80	80	<
A/Picardie/2297/2014	3C.3a	2014-12-13	MDCK2/SIAT1	40	<	<	80	40	80	<	<	40	80	<
A/Paris/2306/2014	3C.3a	2014-12-13	MDCK2/SIAT1	<	40	40	80	80	160	80	40	80	80	<
A/Caen/2354/2014	3C.3a	2014-12-14	MDCK2/SIAT1	40	80	80	320	80	160	80	40	80	80	<
A/Asturias/15059/2014		2014-12-15	SIAT2/SIAT3	40	80	40	320	80	160	80	40	80	80	<
A/Bourgogne/2295/2014	3C.3b	2014-12-15	MDCK2/SIAT1	40	80	80	160	80	160	160	40	80	40	<
A/Nord Pas de Calais/2317/2014		2014-12-15	MDCK2/SIAT1	<	40	40	80	40	160	40	<	40	<	<
A/Croatia/1923/2014	3C.2a	2014-12-16	MDCKx/SIAT1	40	160	80	320	160	320	160	40	80	80	<
A/Nord Pas de Calais/2301/2014	3C.3	2014-12-16	MDCK1/SIAT1	160	160	160	640	160	320	160	80	160	80	<
A/Caen/2343/2014	3C.2a	2014-12-16	MDCK2/SIAT1	<	80	40	160	80	320	160	80	80	80	40
A/Nord Pas de Calais/2318/2014	3C.2a	2014-12-17	MDCK1/SIAT1	40	80	80	160	80	320	80	40	80	40	<
A/Burgos/262/2014	3C.3b	2014-12-19	SIAT1	160	320	160	320	160	640	320	80	320	160	<
A/England/561/2014	3C.3	2014-12-21	MDCK1/SIAT1	40	80	40	160	80	160	80	40	80	40	<
A/Paris/2332/2014	3C.3a	2014-12-22	MDCK1/SIAT1	<	80	40	160	80	640	160	160	160	80	40
A/Lorraine/2355/2014	3C.2a	2014-12-22	MDCK2/SIAT1	<	<	<	80	40	160	40	<	40	40	<
A/England/607/2014	3C.2a	2014-12-27	MDCK2/SIAT1	<	40	<	80	80	160	40	<	40	40	<
A/Greece/1/2014	3C.2a	2014-12-28	SIAT1	<	<	<	40	40	160	<	<	<	40	<
A/Norway/3224/2014	3C.3a	2014-12-28	SIAT1	40	80	80	160	80	160	80	40	80	40	<
A/Norway/3226/2014		2014-12-28	SIAT1	40	80	80	160	80	160	80	40	80	40	<
A/Norway/3229/2014	3C.3b	2014-12-28	SIAT1	<	40	<	80	<	80	<	<	<	<	<
A/Norway/3293/2014	3C.3b	2014-12-30	SIAT1	40	80	80	160	80	160	80	40	80	40	<
A/Norway/3298/2014		2014-12-30	SIAT1	40	80	80	160	80	160	80	40	40	40	<
A/Denmark/02/2015	3C.2a	2015-01-02	SIAT3/SIAT1	<	80	40	80	40	320	80	40	40	80	<
A/England/15/2015	3C.3	2015-01-02	SIAT1/SIAT1	40	80	40	160	40	80	40	<	40	<	<
A/Norway/0144/2015	3C.3b	2015-01-03	SIAT1	<	80	40	160	80	160	80	<	80	40	<
A/Malta/MX502071/2015	3C.3b	2015-01-05	SIAT1	<	80	40	160	80	160	80	<	40	40	<
A/Denmark/01/2015	3C.2a	2015-01-05	SIAT3/SIAT1	<	40	<	80	40	320	80	40	40	80	<
A/England/13/2015	3C.3	2015-01-05	MDCK1/SIAT1	<	80	80	320	160	640	320	160	160	160	40
A/England/18/2015		2015-01-07	SIAT1/SIAT1	40	80	40	160	80	160	40	<	40	40	<
A/Castilla La Mancha/76/2015	3C.3a	2015-01-08	SIAT1	<	80	40	160	80	640	160	160	160	160	<
A/England/32/2015	3C.3b	2015-01-09	SIAT2/SIAT1	40	80	80	160	80	160	80	40	80	40	<
						Vaccine SH2014 NH 2014/15						Vaccine SH2015 NH 2015/16		

1. < = <40

Sequences in phylogenetic tree

Table 4-1. Antigenic analysis of A(H3N2) viruses by plaque reduction neutralisation (MDCK-SIAT)

Viruses		Collection Date	Passage History	Neutralisation titre[1]					
				Post infection ferret sera					
				A/Vic/ 361/11 T/C F09/12	A/Switz/ 9715923/13 cl123 Egg F25/14	A/Switz/ 9715923/13 T/C NIB F13/14	A/HK/ 5738/14 cl121 Egg NIB F53/14	A/HK/ 5738/14 T/C F30/14	A/HK 7295/14 T/C F02/15
Amino acid sequence at the HA1 158-160 glycosylation site				NFK	NSK	NSK	NYK	N/KYT	NYT
Genetic group				3C.1	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a
REFERENCE VIRUSES									
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	320 (255)	320 (200)	80 (100)	ND	40 (26)	40(47)
A/Switzerland/9715293/2013 cl123	3C.3a	2013-12-06	E5	80 (62)	640 (534)	80 (65)	ND	80 (90)	80(95)
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	40 (45)	80 (79)	160 (138)	ND	40 (33)	40 (48)
A/Hong Kong/5738/2014 cl121	3C.2a	2014-04-30	E6	40 (48)	40 (36)	80 (62)	2560 (2237)	320 (422)	160-320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2	40 (45)	80 (75)	80 (60)	80 (59)	320 (304)	320
A/Hong Kong/7295/2014	3C.2a	2014-08-07	MDCK3	80 (71)	160 (130)	80 (80)	80 (87)	320 (247)	320
TEST VIRUSES									
A/Paris/1971/2014	3C.2a	2014-10-02	MDCK2/SIAT1	160 (145)	160 (224)	320 (349)	320 (302)	320 (315)	ND
A/Stockholm/25/2014	3C.2a	2014-10-21	MDCK3/SIAT1	80 (79)	80 (75)	80 (69)	80 (78)	160 (217)	ND
A/Belgium/H82/2014	3C.2a	2014-10-23	SIAT1/SIAT1	80 (73)	320 (300)	320 (346)	160 (189)	1280 (1579)	ND
A/Belgium/G604/2014	3C.2a	2014-10-29	SIAT1/SIAT1	160 (155)	320 (450)	160 (137)	320 (272)	1280 (1034)	ND
A/England/527/2014	3C.3	2014-11-18	SIAT1/SIAT1	320 (364)	320 (338)	320 (381)	40 (37)	80 (70)	ND
A/Galicia/2056/2014	3C.2a	2014-11-19	MDCKx/SIAT1	80 (74)	160 (190)	80 (118)	320 (288)	1280 (1046)	ND
A/England/528/2014	3C.2a	2014-11-20	SIAT2/SIAT1	40 (28)	160 (132)	80 (60)	160 (179)	1280 (1227)	ND
A/England/530/2014	3C.2a	2014-11-26	MDCK1/SIAT1	40 (56)	160 (192)	80 (91)	80 (109)	160 (194)	ND
A/Finland/485/2014	3C.2a	2014-12-01	SIAT1/SIAT1	80 (69)	160 (133)	160 (149)	160 (143)	640 (624)	320-640
A/Galicia/2084/2014	3C.3	2014-12-02	MDCKx/SIAT1	320 (325)	320 (274)	160 (190)	160 (159)	320 (427)	ND
A/Andalucia/2098/2014	3C.2a	2014-12-04	SIAT2/SIAT1	160 (123)	160 (158)	160 (187)	160 (145)	640 (502)	160-320
A/Andalucia/2095/2014	3C.2a	2014-12-08	SIAT2/SIAT1	160 (179)	320 (256)	160 (225)	320 (314)	320 (426)	320
A/Andalucia/2096/2014	3C.2a	2014-12-10	SIAT2/SIAT1	80 (106)	320 (425)	1280 (1002)	640 (553)	1280 (1638)	320-640
A/Castilla La Mancha/2121/2014	3C.2a	2014-12-16	SIAT2/SIAT1	80 (77)	320 (440)	320 (283)	320 (359)	1280 (1388)	320-640
A/Latvia/12-060164/2014	3C.2a	2014-12-22	C2/SIAT1	40 (43)	40 (59)	40 (38)	40 (47)	80 (86)	160-320
A/Sachsen-Anhalt/25/2014	3C.2a	2014-12-22	C2/SIAT1	80 (70)	160 (150)	160 (153)	160 (116)	320 (279)	320
A/Bayern/47/2015		2014-12-22	C3/SIAT1	40 (41)	80 (87)	80 (84)	80 (90)	320 (286)	320
A/Roma/14/2014		2014-12-27	SIAT1/SIAT1	80 (64)	160 (136)	80 (107)	160 (123)	640 (598)	320
A/Slovenia/44/2015	3C.2a	2015-01-06	MDCKx/SIAT1	80 (83)	320 (307)	640 (787)	1280 (1071)	1280 (1388)	320
A/Nordrhein-Westfalen/1/2015	3C.2a	2015-01-06	C2/SIAT1	40 (55)	80 (92)	80 (97)	80 (78)	160 (215)	160
A/Bayern/2/2015	3C.2a	2015-01-07	C2/SIAT1	80 (69)	160 (148)	160 (135)	160 (120)	640 (533)	320
A/Slovenia/141/2015	3C.2a	2015-01-12	MDCKx/SIAT1	80 (67)	320 (310)	640 (942)	160 (164)	1280 (1297)	320-640
A/Italy/FVG-29/2014	3C.2a	Unknown	Cx/SIAT2	80 (84)	80 (102)	40 (56)	80 (106)	320 (259)	ND
					Vaccine				

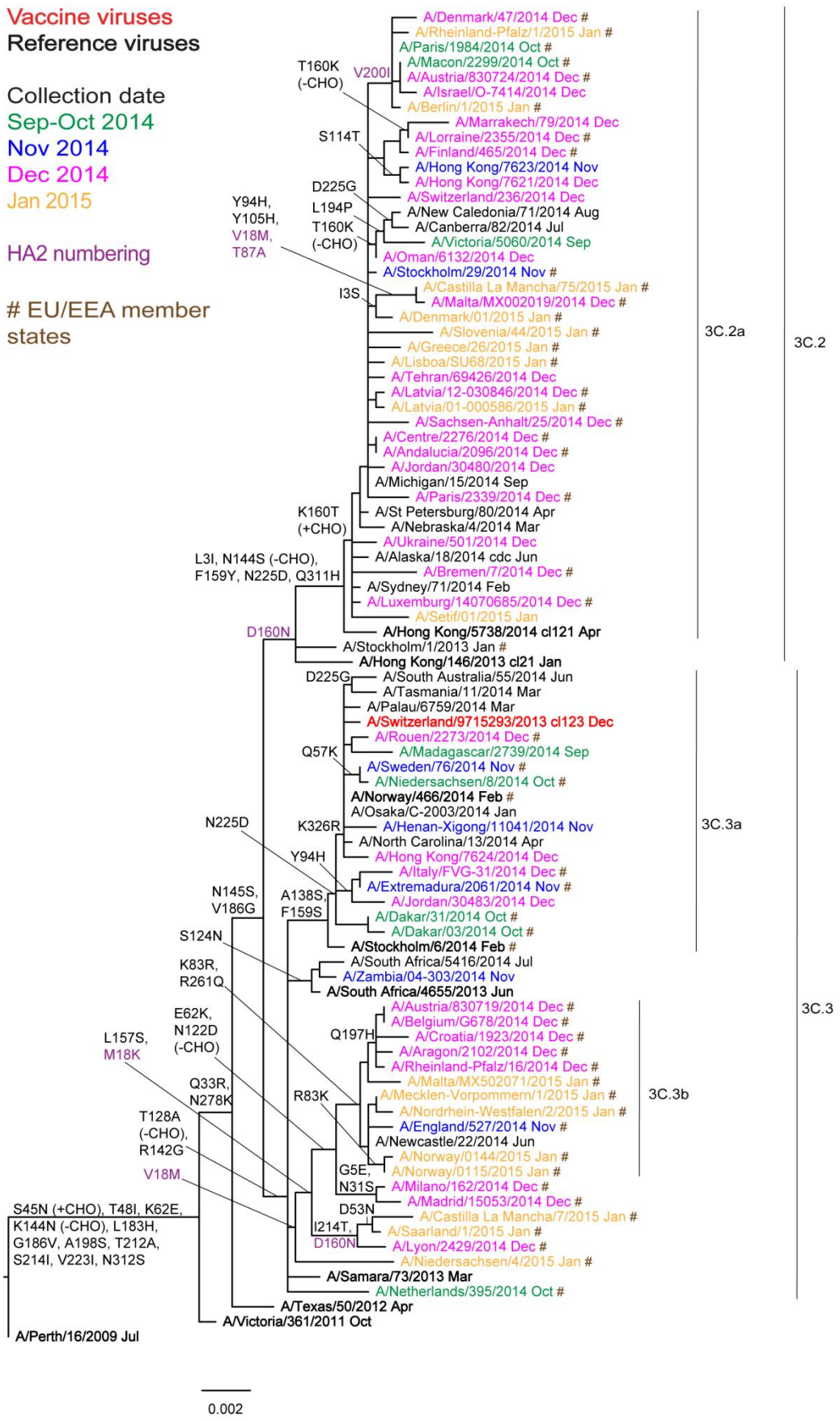
1. The titres associated with a 50% reduction in plaque formation are shown based on doubling dilution of antisera closest to the automated reading value (shown in parentheses)
ND = Not Done

Table 4-2. Antigenic analysis of A(H3N2) viruses by plaque reduction neutralisation (MDCK-SIAT)

Viruses		Collection Date	Passage History	Neutralisation titre[1]					
				Post infection ferret sera					
				A/Vic/ 361/11 T/C F09/12	A/Switz/ 9715923/13 cl123 Egg F25/14	A/Switz/ 9715923/13 T/C NIB F13/14	A/HK/ 5738/14 T/C F30/14	A/HK/ 7295/14 T/C F02/15	A/Eng/ 530/2014 T/C F04/15
Amino acid sequence at the HA1 158-160 glycosylation site				NFK	NSK	NSK	N/KYT	NYT	NYK
Genetic group				3C.1	3C.3a	3C.3a	3C.2a	3C.2a	3C.2a
REFERENCE VIRUSES									
A/Victoria/361/2011	3C.1	2011-10-24	MDCK2/SIAT4	320 (255)	320 (200)	80 (100)	40 (26)	40 (47)	<
A/Switzerland/9715293/2013 cl123	3C.3a	2013-12-06	E5	80 (62)	640 (534)	80 (65)	80 (90)	80 (95)	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT2	40 (45)	80 (79)	160 (138)	40 (33)	40 (48)	40
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2	40 (45)	80 (75)	80 (60)	320 (304)	320 (308)	80
A/Hong Kong/7295/2014	3C.2a	2014-08-07	MDCK3	80 (71)	160 (130)	80 (80)	320 (247)	320 (315)	80-160
A/England/530/2014	3C.2a	2014-11-26	MDCKx/SIAT2	40 (30)	80 (79)	40 (38)	80 (78)	80 (117)	160
TEST VIRUSES									
A/Stockholm/24/2014	3C.2a	2014-09-26	MDCK2/SIAT2	80 (89)	160 (129)	80 (90)	320 (343)	320 (377)	80-160
A/Norway/3086/2014	3C.2a	2014-12-02	SIAT1	80 (65)	160 (180)	80 (109)	640 (860)	640 (730)	160
A/Austria/830096/2014	3C.2a	2014-12-04	SIAT4/SIAT1	40 (26)	40 (35)	40 (33)	160 (118)	160 (123)	<
A/Austria/830857/2014	3C.2a	2014-12-08	SIAT1/SIAT1	40 (40)	160 (140)	80 (90)	320 (252)	320 (269)	40
A/Austria/830724/2014	3C.2a	2014-12-09	SIAT2/SIAT1	80 (61)	160 (126)	160 (188)	320 (475)	640 (512)	40
A/Austria/830722/2014	3C.2a	2014-12-10	SIAT1/SIAT1	40 (44)	80 (83)	80 (73)	320 (266)	320 (317)	40
A/Austria/831131/2014	3C.2a	2014-12-12	SIAT2/SIAT1	80 (60)	160 (122)	80 (102)	320 (306)	320 (310)	80
A/Lisboa/SU34/2014	3C.2a	2014-12-15	SIAT1/SIAT1	40 (48)	80 (95)	80 (67)	640 (507)	640 (480)	80-160
A/Roma/13/2014	3C.2a	2014-12-16	SIAT1/SIAT1	40 (37)	160 (197)	160 (200)	1280 (1081)	640 (764)	40-80
A/Milano/169/2014	3C.2a	2014-12-16	SIAT1/SIAT1	40 (59)	80 (118)	80 (68)	640 (499)	640 (516)	40
A/Milano/168/2014	3C.2a	2014-12-17	SIAT1/SIAT1	40 (49)	160 (222)	320 (353)	1280 (1103)	640 (827)	80-160
A/Castilla La Mancha/2131/2014	3C.2a	2014-12-18	SIAT2/SIAT1	80 (83)	160 (154)	160 (148)	1280 (1077)	640 (760)	80-160
A/Italy/FVG-36/2014		2014-12-19	SIAT1/SIAT1	40 (30)	80 (66)	40 (53)	320 (386)	320 (451)	80
A/Bremen/7/2014	3C.2a	2014-12-22	C3/SIAT1	40 (26)	40 (49)	40 (46)	160 (157)	160 (175)	40
A/Italy/FVG-40/2014	3C.2a	2014-12-23	SIAT1/SIAT1	80 (81)	160 (137)	160 (120)	640 (629)	640 (643)	80
A/Madrid/15051/2014	3C.2a	2014-12-26	SIAT2/SIAT1	80 (94)	160 (135)	80 (116)	640 (709)	640 (592)	80
A/Madrid/15050/2014	3C.2a	2014-12-26	SIAT2/SIAT1	80 (94)	160 (224)	160 (135)	1280 (1018)	640 (630)	80-160
A/Berlin/90/2014	3C.2a	2014-12-26	C3/SIAT1	40 (31)	40 (55)	40 (40)	160 (146)	160 (178)	80
A/Latvia/12-066494/2014	3C.2a	2014-12-28	C2/SIAT1	40 (46)	80 (90)	80 (94)	320 (216)	320 (243)	40-80
A/Luxembourg/14070685/2014	3C.2a	2014-12-29	MDCK1/SIAT1	80 (82)	320 (336)	160 (152)	640 (705)	640 (583)	160
A/Lisboa/SU63/2014	3C.2a	2014-12-29	SIAT1/SIAT1	80 (70)	160 (141)	160 (173)	640 (515)	640 (532)	80-160
A/Schleswig-Holstein/10/2014	3C.2a	2014-12-29	C3/SIAT1	40 (47)	80 (77)	80 (78)	320 (334)	320 (216)	160
A/Latvia/01-000487/2015	3C.2a	2015-01-01	C2/SIAT1	40 (38)	80 (65)	40 (40)	160 (150)	160 (209)	40-80
A/Latvia/01-000586/2015	3C.2a	2015-01-01	C1/SIAT1	40 (36)	80 (70)	80 (57)	160 (142)	160 (138)	80
A/Lisboa/SU61/2015	3C.2a	2015-01-04	SIAT1/SIAT1	80 (74)	160 (144)	160 (148)	640 (579)	640 (556)	160
A/Brandenburg/1/2015	3C.2a	2015-01-05	C2/SIAT1	80 (59)	80 (87)	80 (81)	320 (300)	160 (152)	80-160
					Vaccine				

1. The titres associated with a 50% reduction in plaque formation are shown based on doubling dilution of antisera closest to the automated reading value (shown in parentheses); < = <40

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



Influenza B virus analyses

Influenza B viruses represented just over 20% of samples received from EU/EEA countries with collection dates after 31 August 2014 (Table 1). Of the 78 viruses pre-ascribed to a lineage, B/Yamagata viruses predominated over those of B/Victoria at a ratio of 38:1.

Influenza B – Victoria lineage

The two test viruses of the B/Victoria lineage were received from Germany and HI results are shown in Table 5. Both viruses carried HA genes of genetic group 1A.

B/Baden-Wurttemberg/3/2014 showed ≥ eightfold reductions in HI titres compared with the titre for the homologous virus with post-infection ferret antisera raised against the recommended vaccine virus for quadrivalent live and inactivated vaccines, B/Brisbane/60/2008. Similarly, it was poorly recognised by post-infection ferret antisera raised against the egg-propagated reference viruses B/Malta/636714/2011 and B/Johannesburg/3964/2012, and showed fourfold reduction compared to the homologous titre with that raised against the egg-propagated reference virus B/South Australia/81/2012. In contrast, B/Baden-Wurttemberg/3/2014 showed reactivity within fourfold of the titres for the corresponding homologous viruses with antisera raised against viruses genetically closely related to B/Brisbane/60/2008 but propagated in cell culture; these antisera were raised against B/Paris/1762/2009, B/Hong Kong/514/2009 and B/Odessa/3886/2010, viruses that are considered to be surrogate cell-propagated antigens representing the egg-propagated prototype strain. The other testvirus, B/Rheinland-Pfalz/1/2014, showed a reactivity profile with the panel of antisera similar to that of the vaccine virus, B/Brisbane/60/2008.

Phylogenetic analysis of the HA gene of representative recently collected B/Victoria lineage viruses is shown in Figure 3. Worldwide the vast majority of recent viruses have HA genes that fall into the B/Brisbane/60/2008 genetic clade (clade 1A) and remain antigenically similar to the recommended vaccine virus, B/Brisbane/60/2008, for use in quadrivalent vaccines. B/Rheinland-Pfalz/1/2014, which clusters closely with B/Brisbane/60/2008 in the phylogenetic tree, was isolated from a child recently vaccinated with a live attenuated influenza vaccine.

Influenza B – Yamagata lineage

HI results for the 62 B/Yamagata-lineage test viruses analysed since the December 2014 report[1] are shown in Tables 6-1 to 6-4. All 51 test viruses for which HA gene sequencing was performed fell in genetic clade 3 and viruses for which gene sequences are included in the phylogenetic tree are highlighted.

Post-infection ferret antiserum raised against the egg-propagated vaccine virus B/Massachusetts/02/2012, recommended for use in the 2014–15 northern hemisphere influenza season, recognised approximately 23% (14/62) of test 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 53% (33/62) of test viruses at titres within fourfold of its titre with the homologous virus. Another antiserum, used in all HI assays, raised against cell-propagated B/Estonia/55669/2011 and belonging to the B/Massachusetts/02/2012 clade (clade 2) recognised only 21% (13/62) of the test viruses at a titre within fourfold of the titre of the antiserum with the homologous virus.

An antiserum raised against a previously recommended vaccine virus B/Wisconsin/1/2010 (clade 3) recognised all 62 test viruses at titres within fourfold of the titre of the antiserum with the homologous virus. Approximately 97% (60/62) of the test viruses were recognised similarly by antiserum raised against egg-propagated B/Stockholm/12/2011, a virus also belonging to clade 3 represented by B/Wisconsin/1/2010 and B/Phuket/3073/2013. All test viruses were recognised at titres within fourfold of the titre for the homologous virus, with 76% (47/62) of titres being within twofold, by an antiserum raised against the egg-propagated vaccine virus B/Phuket/3073/2013, recommended as a vaccine virus for the southern hemisphere 2015 influenza season. Antiserum raised against a cell-propagated cultivar of B/Phuket/3073/2013 recognised only 63% (39/62) of the test viruses at titres within fourfold of the titre for the homologous virus. However, an antiserum raised against another exclusively egg-propagated virus, B/Hong Kong/3417/2014, recognised all 45 test viruses it was tested against at titres within twofold of the titre for the homologous virus (Tables 6-2 to 6-4).

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses. The HA genes of recently collected viruses were in the B/Wisconsin/1/2010 - B/Phuket/3073/2013 clade (clade 3). A small proportion of viruses, detected in many parts of the world, have HA genes of clade 3 of the B/Yamagata lineage combined with NA genes of the B/Victoria lineage. A small group of viruses that are antigenically distinguishable from the great majority of clade 3 viruses, designated as clade 3a, have emerged in Australia.

These results contributed to the World Health Organisation recommendation2 for B/Phuket/3073/2013 to be included in vaccines for the northern hemisphere 2015–16 influenza season.

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

Viruses	Genetic group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera										
				B/Bris[1,3] 60/08 Sh 522	B/Mal[2] 2506/04 F37/11	B/Bris[2] 60/08 F22/12	B/Paris[2] 1762/09 F07/11	B/HK[2] 514/09 F19/13	B/Odessa[2] 3886/10 F19/11	B/Malta[2] 636714/11 F33/11	B/Jhb[4] 3964/12 F01/13	B/For[2] V2367/12 F04/13	B/Sth Aus[2] 81/12 F41/13	
				1A		1A	1A	1B	1B	1A	1A	1A	1A	
REFERENCE VIRUSES														
B/Malaysia/2506/2004		2004-12-06	E3/E4	2560	1280	80	10	10	<	80	160	40	160	
B/Brisbane/60/2008	1A	2008-08-04	E4/E3	2560	80	320	80	80	80	320	320	160	640	
B/Paris/1762/2008	1A	2009-02-09	C2/MDCK2	5120	10	40	160	160	160	40	40	80	160	
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	5120	20	80	160	160	320	80	160	160	320	
B/Odessa/3886/2010	1B	2010-03-19	MDCK2/MDCK4	5120	10	40	160	320	160	40	80	160	160	
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	80	320	80	80	80	640	320	320	640	
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	1280	1280	320	640	320	1280	1280	1280	1280	
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	80	320	80	80	80	160	160	320	640	
B/South Australia/81/2012	1A	2012-11-28	E4/E1	2560	80	320	40	80	80	320	320	320	640	
TEST VIRUSES														
B/Baden-Wurttemberg/3/2014	1A	2014-10-24	C2/MDCK1	1280	<	<	160	80	80	40	<	40	160	
B/Rheinland-Pfalz/1/2014	1A	2014-12-16	C2/MDCK1	2560	80	320	40	80	40	320	320	320	1280	197/199 DET

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

Vaccine*

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

Sequences in phylogenetic tree

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

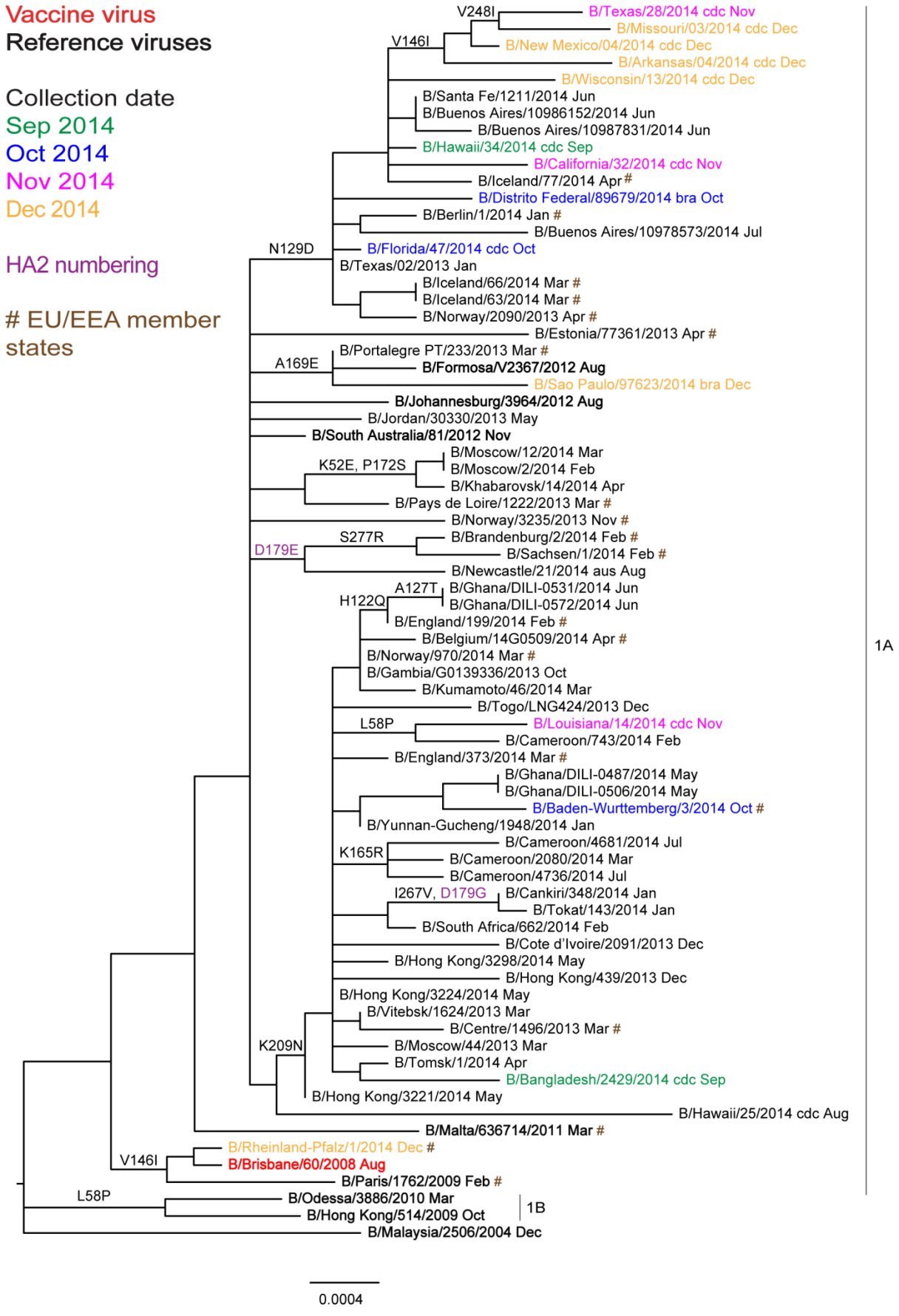


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera										
				B/Fl[1,3] 4/06 SH479	B/Fl[1] 4/06 F1/10	B/Bris[2] 3/07 F21/12	B/Wis[2] 1/10 F10/13	B/Stock[2] 12/11 F12/12	B/Estonia[2] 55669/11 F26/11	B/HK[2] 3577/12 F33/12	B/Mass[2] 02/12 Egg	B/Mass[2] 02/12 F28/13	B/Mass[2] 02/12 T/C	B/Phuket[2] 3073/13 F15/13	B/Phuket[2] 3073/13 Egg F33-34/14	B/Phuket[2] 3073/13 T/C F35/14
				1	1	2	3	3	2	2	2	2	2	3	3
REFERENCE VIRUSES															
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	640	640	160	640	160	320	640	320	320	320	10
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	1280	640	320	640	160	320	1280	320	320	320	10
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	320	80	160	320	<	20	320	40	160	160	10
B/Stockholm/12/2011	3	2011-03-28	E4/E1	2560	160	80	80	320	<	20	320	40	80	80	10
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	2560	80	40	20	80	640	640	160	640	40	40	40
B/Hong Kong/3577/2012	2	2012-06-13	MDCK4	2560	80	40	40	80	640	640	160	640	40	40	40
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	640	640	160	640	160	320	1280	320	320	320	10
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	320	160	320	640	640	320	640	160	160	20
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	320	80	160	320	10	40	160	40	160	160	20
B/Phuket/3073/2013	3	2013-11-21	M2/M2	1280	160	80	160	320	80	320	160	320	160	160	320
TEST VIRUSES															
B/Paris/2058/2014	3	2014-09-25	MDCK1	640	80	40	160	160	40	80	80	80	80	80	40
B/Asturias/1952/2014	3	2014-10-10	SIAT1/MDCK2	640	80	40	160	160	80	160	40	160	80	80	80
B/Pais Vasco/1978/2014	3	2014-10-21	SIAT1/MDCK2	640	80	20	80	160	40	80	40	160	80	80	160
B/Castilla La Mancha/1986/2014	3	2014-10-25	MDCK1	5120	320	160	320	640	320	640	320	640	320	320	80
B/Paris/2052/2014	3	2014-10-27	MDCK1	640	80	20	80	80	20	80	40	80	80	80	80
B/Thuringen/3/2014	3	2014-11-08	C2/MDCK1	640	80	20	80	80	20	40	40	40	40	40	160
B/Belgium/G634/2014	3	2014-11-17	MDCK1/MDCK1	640	80	20	80	160	20	80	40	80	40	40	40
B/Bretagne/2216/2014	3	2014-11-24	MDCK1/MDCK1	1280	160	40	160	160	80	80	80	160	80	80	40
B/Norway/3085/2014	3	2014-11-24	MDCK1	320	80	20	40	80	20	40	20	40	40	40	40
B/Centre/2213/2014	3	2014-11-25	MDCK1/MDCK1	640	80	20	80	80	20	80	40	80	40	40	40
B/Norway/3108/2014	3	2014-11-29	MDCK1	640	80	40	160	160	80	160	80	160	80	80	1280
B/Baden-Wurttemberg/2/2014	3	2014-12-01	C2/MDCK1	640	160	40	80	160	20	80	40	80	40	40	80
B/Paris/2232/2014	3	2014-12-02	MDCK1/MDCK1	320	80	20	80	80	20	40	40	80	40	40	320
B/Belgium/G668/2014	3	2014-12-02	MDCK1/MDCK1	640	80	20	80	160	20	40	40	40	40	40	80
B/Madrid/SO12928/2014	3	2014-12-05	MDCK1	320	80	20	80	80	10	40	40	40	40	40	40
B/Castilla La Mancha/2082/2014	3	2014-12-09	MDCK1	320	40	20	40	40	10	40	20	40	40	40	40
B/Castilla La Mancha/2083/2014	3	2014-12-11	MDCK1	320	40	20	40	40	10	40	20	40	40	40	40
											Vaccine NH2013/14 SH 2014 NH 2014/15			Vaccine SH2015 NH 2015/16	

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

Sequences in phylogenetic tree

Table 6-2. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera										
				B/Fl[1,3] 4/06 SH479	B/Fl[1] 4/06 F1/10	B/Bris[2] 3/07 F21/12	B/Wis[2] 1/10 F10/13	B/Stock[2] 12/11 F12/12	B/Estonia[2] 55669/11 F26/11	B/Mass[2] 02/12 Egg	B/Mass[2] 02/12 F28/13	B/Mass[2] 02/12 T/C	B/Phuket[2] 3073/13 F15/13	B/Phuket[2] 3073/13 Egg F33-34/14	B/Phuket[2] 3073/13 T/C F35/14	B/HK[2,4] 3417/14 St Judes F715/14
	1			1	1	2	3	3	2		2		2	3	3	3
REFERENCE VIRUSES																
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	1280	640	160	640	160		1280		320	320	<	320
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	1280	640	320	640	160		1280		320	320	<	320
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	320	160	160	320	<		320		80	320	20	320
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	160	80	80	320	<		160		40	80	<	160
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	1280	80	40	20	80	640		80		640	80	40	160
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	1280	640	160	640	160		1280		320	320	<	320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	640	320	160	320	320		320		640	160	40	320
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	320	160	160	320	<		160		80	160	20	320
B/Phuket/3073/2013	3	2013-11-21	M2/M2	1280	160	80	160	320	80		80		320	160	320	160
B/Hong Kong/3417/2014	3	2014-06-04	E5	160	80	40	80	80	<		40		40	20	<	160
TEST VIRUSES																
B/Netherlands/382/2014	3	2014-10-16	MDCK1/SIAT1	1280	160	40	160	160	80		80		160	80	640	320
B/Norway/3078/2014		2014-11-24	MDCK3	640	80	40	80	160	20		40		80	40	80	160
B/Extremadura/2067/2014	3	2014-11-27	MDCKx/MDCK2	640	160	40	160	320	40		80		320	160	80	160
B/Lyon-CHU/23.76/2014		2014-12-14	MDCK2/SIAT1	640	160	40	160	160	40		80		80	80	80	160
B/Lyon/2423/2014	3	2014-12-15	MDCK2/SIAT1	640	80	20	80	80	10		40		40	40	40	160
B/Lyon/2433/2014		2014-12-15	MDCK2/SIAT1	2560	160	80	160	160	640		160		640	80	80	160
B/Lyon-CHU/23.84/2014	3	2014-12-15	MDCK2/SIAT1	640	160	40	160	160	40		80		80	80	80	160
B/Lyon/2455/2014	3	2014-12-16	MDCK2/SIAT1	640	80	20	80	80	20		40		80	40	80	160
B/Clermont-Ferrand/2467/2014	3	2014-12-17	MDCK2/SIAT1	640	80	20	80	80	20		40		80	40	40	160
											Vaccine NH2013/14 SH 2014 NH 2014/15			Vaccine SH2015 NH 2015/16		

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

Sequences in phylogenetic tree

Table 6-3. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre: Post infection ferret antisera											
				B/Fl[1,3] 4/06 SH479	B/Fl[1] 4/06 F1/10	B/Bris[2] 3/07 F21/12	B/Wis[2] 1/10 F10/13	B/Stock[2] 12/11 F12/12	B/Estonia[2] 55669/11 F26/11	B/Mass[2] 02/12 Egg	B/Mass[2] 02/12 F28/13	B/Mass[2] 02/12 T/C	B/Phuket[2] 3073/13 F15/13	B/Phuket[2] 3073/13 Egg F36/14	B/Phuket[2] 3073/13 T/C F35/14	B/HK[2,4] 3417/14 St Judes F715/14
				1	1	2	3	3	2	2	2	2	3	3	3
REFERENCE VIRUSES															
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	640	1280	320	640	160	1280	320	160	<	320	
B/Brisbane/3/2007	2	2007-09-03	E2/E2	5120	1280	1280	640	640	320	1280	320	320	<	640	
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	320	320	640	320	<	160	80	160	20	320	
B/Stockholm/12/2011	3	2011-03-28	E4/E1	2560	160	160	160	320	<	160	80	80	<	160	
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	1280	160	160	80	80	1280	40	640	80	40	320	
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	640	1280	320	320	160	1280	160	160	<	320	
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	640	640	320	640	640	640	320	40	640	
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	320	320	640	640	80	320	80	160	20	320	
B/Phuket/3073/2013	3	2013-11-21	M2/M2	2560	320	320	640	640	160	160	320	320	640	320	
B/Hong Kong/3417/2014	3	2014-06-04	E5	320	80	80	160	80	<	40	40	40	<	320	
TEST VIRUSES															
B/Lisboa/5/2014		2014-11-17	SIAT1/MDCK1	1280	160	160	320	320	40	80	160	320	80	320	
B/Lisboa/6/2014	3	2014-11-20	SIAT1/MDCK1	1280	320	320	640	640	80	160	320	640	40	640	
B/Lisboa/7/2014		2014-12-01	SIAT1/MDCK1	1280	160	160	320	160	80	40	160	320	80	320	
B/Andalucía/2092/2014	3	2014-12-02	SIAT2/MDCK1	1280	160	320	320	320	160	160	320	320	320	320	
B/Latvia/12-016677/2014	3	2014-12-06	C2/MDCK1	640	160	160	160	160	40	40	80	160	320	320	
B/Milano/1/2014	3	2014-12-09	SIAT1/MDCK1	1280	160	160	320	160	80	80	160	160	320	640	
B/Austria/830502/2014	3	2014-12-09	SIAT1/MDCK1	5120	320	320	640	640	320	320	640	640	320	320	
B/Madrid/15046/2014	3	2014-12-15	SIAT2/MDCK1	1280	160	320	320	320	160	160	320	320	320	640	
B/Italy/FVG-01/2014	3	2014-12-15	SIAT1/MDCK1	640	80	160	160	80	20	40	80	80	80	320	
B/Latvia/12-043751/2014	3	2014-12-16	C1/MDCK1	640	80	160	160	80	20	40	80	80	640	640	
B/Lisboa/9/2014		2014-12-17	SIAT2/MDCK2	1280	160	160	320	160	160	160	160	320	40	320	
B/Lisboa/10/2014	3	2014-12-18	SIAT1/MDCK1	1280	160	160	320	160	80	80	160	320	80	320	
B/Roma/3/2014	3	2014-12-20	SIAT1/MDCK1	5120	320	320	640	640	320	320	640	640	160	320	
B/Lisboa/12/2014		2014-12-22	SIAT2/MDCK1	1280	160	160	320	160	80	80	160	320	80	640	
B/Roma/1/2014	3	2014-12-22	SIAT1/MDCK1	640	80	160	160	80	20	40	80	80	80	320	
B/Roma/2/2014		2014-12-22	SIAT1/MDCK1	640	80	160	160	160	40	40	160	160	320	640	
B/Lisboa/18/2014		2014-12-29	SIAT1/MDCK1	2560	160	160	640	320	160	160	320	640	80	320	
B/Navarra/15036/2014	3	2014-12-29	SIAT2/MDCK1	1280	160	160	320	320	160	80	320	320	640	320	
B/Italy/FVG-02/2014	3	2014-12-29	SIAT1/MDCK1	640	80	160	160	160	40	40	160	160	80	320	
B/Lisboa/14/2014		2014-12-30	SIAT1/MDCK1	1280	160	160	640	320	80	160	320	640	40	320	
B/Lisboa/17/2014	3	2014-12-30	SIAT1/MDCK1	1280	160	160	320	160	40	80	160	160	160	320	
B/Greece/8/2014	3	2014-12-30	MDCK1	640	80	160	320	80	20	40	80	160	1280	640	
B/Madrid/052/2015	3	2014-12-30	SIAT2/MDCK1	5120	320	320	640	640	320	320	640	1280	40	320	
B/Roma/4/2014	3	2014-12-30	SIAT1/MDCK1	2560	320	320	320	320	160	160	640	640	1280	640	
B/Lisboa/1/2015	3	2015-01-04	SIAT1/MDCK1	640	80	160	320	80	40	40	80	160	80	640	
										Vaccine NH2013/14 SH 2014 NH 2014/15			Vaccine SH2015 NH 2015/16		

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

Sequences in phylogenetic tree

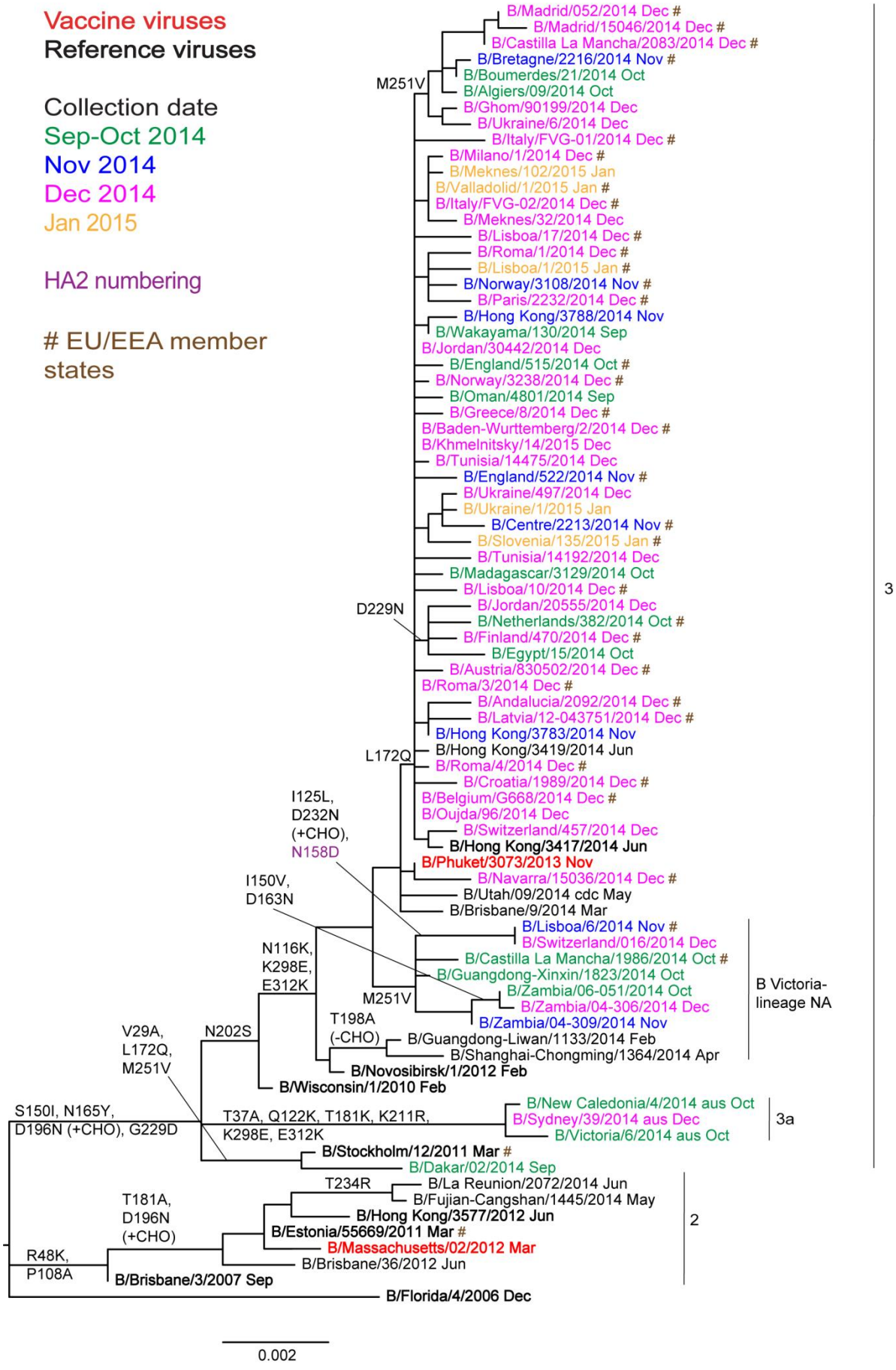
Table 6-4. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Genetic Group	Collection date	Passage History	Haemagglutination inhibition titre										
				Post infection ferret sera										
				B/Fl[1,3]	B/Fl[1]	B/Bris[2]	B/Wis[2]	B/Stock[2]	B/Estonia[2]	B/Mass[2]	B/Mass[2]	B/Phuket[2]	B/Phuket[2]	B/HK[2,4]
				4/06	4/06	3/07	1/10	12/11	55669/11	02/12	02/12	3073/13	3073/13	3417/14
				SH479	F1/10	F21/12	F10/13	F12/12	F32/12	Egg F2/13	T/C F15/13	Egg F36/14	T/C F35/14	Egg St Judes F715/14
	Genetic Group			1	1	2	3	3	2	2	2	3	3	
REFERENCE VIRUSES														
B/Florida/4/2006	1	2006-12-15	E7/E1	5120	640	1280	160	640	80	1280	160	160	<	320
B/Brisbane/3/2007	2	2007-09-03	E2/E3	2560	320	640	80	320	80	640	160	160	<	160
B/Wisconsin/1/2010	3	2010-02-20	E3/E3	1280	320	320	160	320	20	320	40	160	<	320
B/Stockholm/12/2011	3	2011-03-28	E4/E1	2560	160	160	80	320	10	320	40	80	<	160
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	1280	80	160	80	80	320	160	640	80	80	320
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	5120	640	640	80	320	80	640	160	160	<	320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	5120	640	640	160	320	160	640	640	160	<	320
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	160	160	320	20	320	40	160	<	320
B/Phuket/3073/2013	3	2013-11-21	M2/M2	2560	160	160	320	320	320	320	640	320	320	320
B/Hong Kong/3417/2014	3	2014-06-04	E5	160	80	80	80	80	<	160	20	40	<	160
TEST VIRUSES														
B/Norway/3136/2014	3	2014-12-07	MDCK1	640	80	80	160	160	40	160	40	80	80	320
B/Norway/3147/2014		2014-12-10	MDCK1	640	80	80	80	80	40	160	80	80	80	160
B/Finland/470/2014	3	2014-12-10	MDCK1/MDCK1	1280	80	80	160	80	80	80	160	160	80	160
B/Norway/3322/2014	3	2014-12-15	MDCK1	640	40	80	80	80	40	160	40	40	160	160
B/Finland/471/2014	3	2014-12-15	MDCK1/MDCK1	1280	80	80	160	160	80	160	160	160	160	320
B/Norway/3238/2014	3	2014-12-19	MDCK1	1280	160	160	160	160	80	160	160	160	160	320
B/Croatia/1988/2014	3	2014-12-29	MDCKx/MDCK1	1280	160	160	320	160	80	160	80	160	160	320
B/Croatia/1989/2014	3	2014-12-29	MDCKx/MDCK1	1280	160	160	320	320	80	320	160	320	160	640
B/England/598/2014	3	2014-12-31	SIAT1/MDCK1	1280	80	80	160	160	80	160	80	160	320	640
B/Valladolid/1/2015	3	2015-01-08	MDCK1	640	80	160	320	160	80	160	160	160	160	320
B/Slovenia/135/2015	3	2015-01-09	MDCKx/MDCK1	1280	160	160	320	320	80	160	160	160	160	640
										Vaccine NH2013/14 SH 2014 NH 2014/15		Vaccine SH2015 NH 2015/16		

1. < = <40; 2. < = <10; 3. hyperimmune sheep serum; 4. RDE-treated antiserum pre-absorbed with TRBC; ND = Not Done

Sequences in phylogenetic tree

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



Summary of genetic data submitted to TESSy

As of 1 March 2015, the majority of influenza viruses identified genetically since week 40/2014 were A(H3N2) viruses (69%), with lower numbers of influenza B viruses (20%) and A(H1N1)pdm09 viruses (11%) being reported. This compares to proportions of 80%, 16% and 4%, respectively, as of 8 January 2015 (see December 2014 report[1]).

All influenza A(H1N1)pdm09 viruses fell into genetic clade 6B, represented by A/South Africa/3626/2013. Influenza B viruses of the B/Yamagata lineage outnumbered those of the B/Victoria lineage by 70 to 1. The majority of influenza A(H3N2) viruses belonged to genetic subgroup 3C.2a (63%), represented by A/Hong Kong/5738/2014; smaller proportions were in genetic subgroup 3C.3 (27%), represented by A/Samara/73/2013, genetic subgroup 3C.3a (9%), represented by A/Switzerland/9715293/2013, and genetic subgroup 3C.1 (1%), represented by A/Texas/50/2012, the vaccine virus for the 2014–15 northern hemisphere influenza season.

Antiviral susceptibility

Between weeks 40/2014 – 09/2015, based on reports to TESSy, 1164 influenza viruses (946 A(H3N2), 137 A(H1N1)pdm09 and 81 type B) were subjected to phenotypic or genotypic testing for neuraminidase inhibitor (NAI) susceptibility. None showed evidence of reduced susceptibility to either oseltamivir or zanamivir. Thirteen A(H1N1)pdm09 viruses and 101 A(H3N2) viruses were assessed for M2 ion channel blocker (adamantane) susceptibility; all were resistant due to the S31N amino acid substitution in the M2 protein.

A total of 402 viruses from EU/EEA countries, with collection dates after 31 August 2014, have been assessed phenotypically for NAI susceptibility at the London WHO CC: 84 influenza B, 80 A(H1N1)pdm09 and 238 A(H3N2) inclusive of many 3C.2a genetic subgroup viruses that could not be analysed by HI assay. All 402 viruses were susceptible to oseltamivir and zanamivir.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [1] reported that the China Health and Family Planning Commission notified the WHO of three cases of human infection with influenza A(H7N9). The cases were confirmed by laboratory testing on 29 March 2013 by the Chinese CDC. A description of the characteristics of H7N9 viruses can be found on the WHO website [2]. Increased numbers of cases were reported over the course of the 2013–14 and 2013–14 seasons. A revised Rapid Risk Assessment [3] for these A(H7N9) viruses was carried out by ECDC and posted on 2 February 2015. WHO posted a summary of human infection on 31 January 2014 [4] and conducted a new risk assessment on 23 February 2015 [5]. In light of the assessment WHO advised that countries continue to strengthen influenza surveillance. WHO last summarised the numbers of cases of human infection related to their geographic location on 14 July 2014 [6].

Influenza A(H5N1) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 26 January 2015 [7]. The assessment included a description of 24 new laboratory-confirmed human cases of avian influenza A(H5N1) virus infection, including 11 fatal cases, as reported by Egypt. ECDC published a new rapid risk assessment on the situation in Egypt in December 2014 [8].

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

http://www.nimr.mrc.ac.uk/documents/about/NIMR-VCM-report-Sep-14-web.pdf

http://www.nimr.mrc.ac.uk/documents/about/NIMR-report-Feb2015-web.pdf

Note on the figures

The phylogenetic trees were constructed using RAxML, drawn using FigTree and annotated using Adobe Illustrator. The bars indicate the proportion of nucleotide changes between sequences. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the month of sample

collection. Isolates from WHO NICs in EU/EEA countries are marked (#). 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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