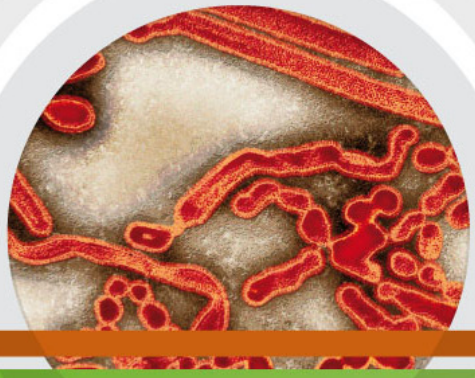

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, July 2012

Summary

Since 1 January 2012, influenza A(H1N1)pdm09, influenza A(H3N2) and influenza B/Victoria and B/Yamagata lineage viruses have been detected in ECDC-affiliated countries.

- Type A viruses have predominated over type B.
- A(H3N2) viruses have predominated over A(H1N1)pdm09 viruses.
- A(H1N1)pdm09 viruses continue to show genetic drift from the vaccine virus, A/California/07/2009, but the vast majority remain antigenically similar to it.
- During this time period, all European A(H3N2) viruses sequenced fell within five genetic groups. Test viruses isolated in mammalian cells show low titres with post-infection ferret antisera raised against egg-propagated viruses, including the new vaccine virus A/Victoria/361/2011. They react well with post-infection ferret antisera raised against A/Victoria/361/2011 and other current reference viruses propagated exclusively in tissue culture.
- Recent B/Victoria lineage viruses fell within the B/Brisbane/60/2008 genetic clade and were antigenically similar to reference cell-propagated viruses of the B/Brisbane/60/2008 genetic clade.
- Recent B/Yamagata-lineage viruses fell into two genetic clades, represented by B/Bangladesh/3333/2007 and B/Wisconsin/1/2010 (Clade 3) or B/Brisbane/3/2007 (Clade 2); viruses in these clades are antigenically distinguishable.
- Antigenic analysis of A(H3N2)v viruses, the cause of zoonotic infections in the USA, indicate that they are antigenically distinct from seasonal A(H3N2) viruses.

A summary of viruses received by the MRC National Institute for Medical Research WHO Collaborating Centre for Reference and Research on Influenza from EU and EEA countries since 1 January 2012 is shown in Table 1.

Viruses and/or clinical samples were received from 20 EU/EEA countries. The table is an update of the table shown in the previous report (June 2012). The majority (71%) of viruses received were influenza A(H3N2) viruses; among influenza B receipts, viruses of the B/Yamagata lineage have predominated over those of the B/Victoria lineage at a ratio of approximately 3:2; influenza A(H1N1)pdm09 viruses were received from only eight countries and in low numbers.

This report was prepared by Rod Daniels, Vicki Gregory and John McCauley on behalf of the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL), under contract to the European Centre for Disease Prevention and Control (ECDC).

Influenza A(H1N1)pdm09 virus analyses

No influenza A(H1N1)pdm09 influenza viruses have been analysed by HI assay since the previous report.

Phylogenetic analysis of the HA1 coding region of viruses collected throughout 2012 (Figure 1) show that the HA genes of the most recently detected H1N1 viruses from EU/EEA countries cluster into two of eight genetic groups that have been described previously. These viruses fall into genetic groups 6 and 7, which have the following amino acid substitutions in HA1:

- Group 6: **D97N & S185T**, e.g. A/St Petersburg/27/2011.
- Group 7: **S143G, S185T & A197T**, e.g. A/St Petersburg/100/2011.

Influenza A(H3N2) virus analyses

As described before, 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. Approximately 70% of viruses gave sufficient titre in HA assays to be analysed by HI assay using guinea pig red blood cells in the presence of 20nM oseltamivir, added to circumvent the NA-mediated binding of H3N2 viruses to the red blood cells (Lin et al. 2010).

The results of the HI assays carried out since the last report are shown in Table 2. HI assays using post-infection ferret antiserum raised against the virus recommended for the 2011/2012 northern hemisphere influenza vaccine, A/Perth/16/2009, showed that nearly 90% of the test viruses had a reduction in HI titre of ≥8-fold compared with the titre for the homologous virus.

Using post-infection ferret antiserum raised against the newly recommended, egg-propagated, vaccine virus for the northern hemisphere 2012/2013 influenza season, A/Victoria/361/2011, only one virus of the 24 tested gave an HI titre within 4-fold of that of the homologous virus. In contrast, with antiserum raised against the cell-culture propagated A/Victoria/361/2011 only two of 24 test viruses showed ≥8-fold reduced reactivity compared with the titre of the homologous cell-propagated virus (Tables 2). The test viruses also showed good reactivity with post-infection ferret antisera raised against other reference viruses propagated exclusively in cell culture: these post-infection ferret antisera were against cell-propagated A/Alabama/5/2010, A/Hong Kong/3969/2011, A/Stockholm/18/2011, A/Berlin/93/2011 and A/Athens/112/2012 but the results of HI analysis of the test viruses using antisera raised against other egg-propagated reference viruses, A/Victoria/208/2009 and A/Iowa/19/2010, showed low levels of reactivity compared with the reactivity of the homologous egg-propagated viruses. The low reactivity of test viruses with antisera raised against each of the egg-adapted viruses, importantly including the new vaccine virus A/Victoria/361/2011, suggests that egg adaptation of the H3N2 reference viruses influences the immune response of the ferret and the HI assay. In light of these observations, results of HI tests and other serological assays with currently circulating A(H3N2) viruses continue to warrant careful consideration.

Phylogenetic analysis of the HA gene sequences of representative viruses has been carried out (Figure 2). Viruses from the EU/EEA collected since January have HA genes that fall into HA genetic groups 3A, 3B, 3C, 5 and 6.

The amino acid substitutions that are associated with each of these groups are:

- Group 3A: **N144D** (resulting in the loss of a glycosylation site), **N145S & V223I**, e.g. A/Stockholm/18/2011;
- Group 3B: **N145S, A198S, V223I & N312S**, e.g. A/Athens/GR112/2012;
- Group 3C: **S45N, T48I, A198S, V223I & N312S**, e.g. A/Hong Kong/3969/2011 and the prototype vaccine virus A/Victoria/361/2011, with some viruses also carrying the substitutions **D53N**, or **Q33R & N278K**;
- Group 5: **D53N, Y94H, I230V & E280A**, e.g. A/Alabama/5/2010;
- Group 6: **D53N, Y94H, S199A, I230V & E280A**, e.g. A/Iowa/19/2010.

Influenza B virus analyses

B/Victoria lineage viruses

B/Victoria lineage viruses have now been received from 13 EU/EEA Member States. The results of HI analyses of influenza B viruses of the B/Victoria lineage done since the last report are shown in Table 3. All four of the test viruses showed reduced reactivity (≥8-fold reduction in titre compared with the homologous titre) with post-infection ferret antiserum raised against the egg-propagated vaccine virus recommended for the northern hemisphere 2011/2012 season, B/Brisbane/60/2008. In contrast, they reacted well with antisera raised against viruses genetically closely related to the vaccine virus but propagated in cells. These antisera are raised against B/Paris/1762/2008, B/Hong Kong/514/2009 and B/Odessa/3886/2010, which are surrogate cell-propagated antigens for the egg-propagated vaccine virus. The reactivity of test viruses with antiserum raised against B/Malta/MV636714/2011, another egg isolate, was low and similar to their reactivities with antiserum raised against B/Brisbane/60/2008.

Phylogenetic analysis of the HA1 coding region of the HA gene of representative B/Victoria lineage viruses is shown in Figure 3. The HA genes of all recently collected viruses received from EU and EEA laboratories fell into Clade 1, the B/Brisbane/60 clade.

B/Yamagata lineage viruses

Influenza B viruses of the B/Yamagata lineage have now been received from 14 EU/EEA Member States. Table 4 shows the results of HI assays of the propagated viruses examined since the last report. Ten of the twelve test viruses reacted within a 4-fold titre of that of the homologous virus with the post-infection ferret antiserum raised against the recommended egg-propagated vaccine virus for the northern hemisphere 2012/2013 influenza season, B/Wisconsin/1/2010. These 10 viruses reacted poorly (>4-fold reduction compared to the homologous titre) with post-infection ferret antiserum raised against B/Estonia/55669/2011, while B/Roma/01/2012 and B/Stockholm/9/2012 displayed the opposite pattern of reactivity. This indicates the co-circulation of two antigenically distinguishable clades within the B/Yamagata lineage.

Figure 4 shows a phylogenetic analysis of the HA1 coding region of B/Yamagata lineage viruses. The HA genes of these viruses fall into two genetic clades, one defined as Clade 3, represented by B/Bangladesh/3333/2007 (and includes B/Wisconsin/1/2010 and B/Stockholm/12/2011), and the other defined as Clade 2 represented by the reference viruses B/Brisbane/3/2007 and B/Estonia/55669/2011. Viruses falling within these two clades are antigenically distinguishable.

The two clades are differentiated by substitutions at HA residues 48, 108, 150, 165, 181 and 229. The HA gene of viruses of Clade 2 encodes **K48**, **A108**, **S150**, **N165**, **A181** and **G229**; the HA gene of viruses in Clade 3 encodes **R48**, **P108**, **I150**, **Y165**, **T181** and **D229**.

Clade 2 appears to be genetically homogenous but Clade 3 can be sub-divided into four genetic groups:

- a group defined by the amino acid substitution **N202S** similar to B/Wisconsin/1/2010;
- a group defined by the substitution **T181K** (e.g. B/Ireland/M1522/2012);
- a group defined by the substitution **M251V** with the substitutions **T181A** and **K253R** (e.g. B/Serbia/1894/2011);
- a group defined by the substitution **M251V** with the substitutions **V29A** and **L172Q** (e.g. B/Stockholm/12/2011).

Influenza A(H3N2)v virus

On 3 August, the United States CDC issued a Health Advisory describing an increase in the number of influenza A(H3N2)v infections in three States, and CDC prepared further background information and an update. Antigenic and genetic characterisation of H3N2v viruses has been described by Lindstrom et al., 2012 The virus was characterised as being antigenically distinct from human seasonal influenza viruses currently circulating and to be a reassortant virus with seven genes from swine influenza 'triple reassortant' H3N2 viruses and the M-gene from an influenza A(H1N1)pdm09 virus.

The prevalence of antibodies in human sera cross-reactive with H3N2v virus has been examined in Norway; the authors concluded that there was a high level of immunity in young adults but less so in other groups. Active surveillance of swine influenza has shown that influenza A(H3N2)v viruses have not circulated in pigs in Europe. Antigenic analysis of two H3N2v viruses, three viruses from humans infected with triple reassortant swine influenza viruses (TRV) and two human seasonal H3N2 viruses, performed at the WHO CC in London (Table 5), support the conclusion that both triple reassortant H3N2 and H3N2v influenza viruses are antigenically distinct from recent human seasonal influenza viruses.

Risk assessments for these A(H3N2)v viruses as a risk to public health are underway.

A description of results generated by the WHO Collaborating Centre for Reference and Research on Influenza, based at the MRC National Institute for Medical Research in London, and evaluated at the WHO Vaccine Composition Meeting held at WHO Geneva on 20-22 February 2012 can be found at: http://www.nimr.mrc.ac.uk/documents/about/interim-report-feb-2012.pdf

Note on the figures

The phylogenetic trees were constructed using RAxML and drawn using FigTree. The bars indicate the proportion of nucleotide changes in the sequence. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the date of sample collection. Isolates from WHO NICs in ECDC countries are highlighted within boxes. Sequences for some of the viruses from non-EU/EEA countries were recovered from GISAID, and we acknowledge all laboratories who submitted sequences directly to the London WHO CC.

Table 1. Summary of clinical samples and isolates received from ECDC-affiliated countries, collection dates since 2012-01-01

MONTH	TOTAL RECEIVED	A	H1N1pdm09		H3N2		B	B Yamagata lineage		B Victoria lineage	
		Not subtyped					Lineage unknown				
Country			Number received	Number propagated	Number received	Number propagated[1]		Number received	Number propagated	Number received	Number propagated
JANUARY											
Austria	6				4	4		1	1	1	1
Bulgaria	4				4	3					
Denmark	2				2	1					
Estonia	1				1	0					
Finland	3				3	2					
France	4				4	4					
Germany	15				14	13				1	1
Greece	18				8	7	5	1	1	4	4
Iceland	9				9	7					
Ireland	9				7	2		1	1	1	1
Italy	14				13	12				1	1
Latvia	7				6	5		1	1		
Netherlands	2				2	2					
Norway	16		5	2	11	11					
Portugal	7				7	4					
Romania	3				3	3					
Slovenia	3				3	3					
Spain	21		1	0	18	10		2	2		
Sweden	11		2	2	8	7		1	1		
United Kingdom	4				3	3		1	1		
FEBRUARY											
Bulgaria	8				8	8					
Denmark	11				6	4		3	3	2	2
Estonia	18				18	2					
Finland	5				4	2				1	1
France	5		2	in progress	3	in progress					
Greece	24				14	13	4	4	4	2	2
Iceland	11				11	11					
Ireland	3		1	1	1	1				1	1
Italy	12				6	5		5	5	1	1
Norway	28		10	6	14	14		3	3	1	1
Portugal	3				1	1		2	1		
Slovenia	12		1	1	9	7		1	0	1	0
Sweden	5		3	3				1	1	1	1
United Kingdom	7				5	4		1	1	1	1
MARCH											
Denmark	13		3	0	8	7		1	0	1	0
Estonia	11				11	7					
Finland	1				1	1					
France	23		2	in progress	13	in progress		3	in progress	5	in progress
Iceland	3				3	2					
Ireland	4				4	4					
Italy	11				4	1		6	6	1	0
Norway	1									1	0
Portugal	10				6	4		3	2	1	1
Slovenia	16		1	0	9	7		2	0	4	1
Sweden	2				1	1		1	1		
United Kingdom	10		1	1	7	4		1	1	1	1
APRIL											
Denmark	6				4	3		1	0	1	1
Estonia	8				7	3		1	1		
France	6							3	in progress	3	in progress
Iceland	1				1	1					
Ireland	10				10	2					
Slovenia	2				1	1	1				
Sweden	5		1	1	3	2		1	1		
United Kingdom	10				7	6		1	1	2	2
MAY											
Finland	1									1	1
	465	0	33	17	330	231	10	52	39	40	25
				7.1%		71.0%	2.1%		11.2%		8.6%

1. Propagated to sufficient titre to perform HI assay in presence of 20nm oseltamivir

Figure 1. Phylogenetic comparison of influenza A(H1N1)pdm HA genes (HA1 coding region)

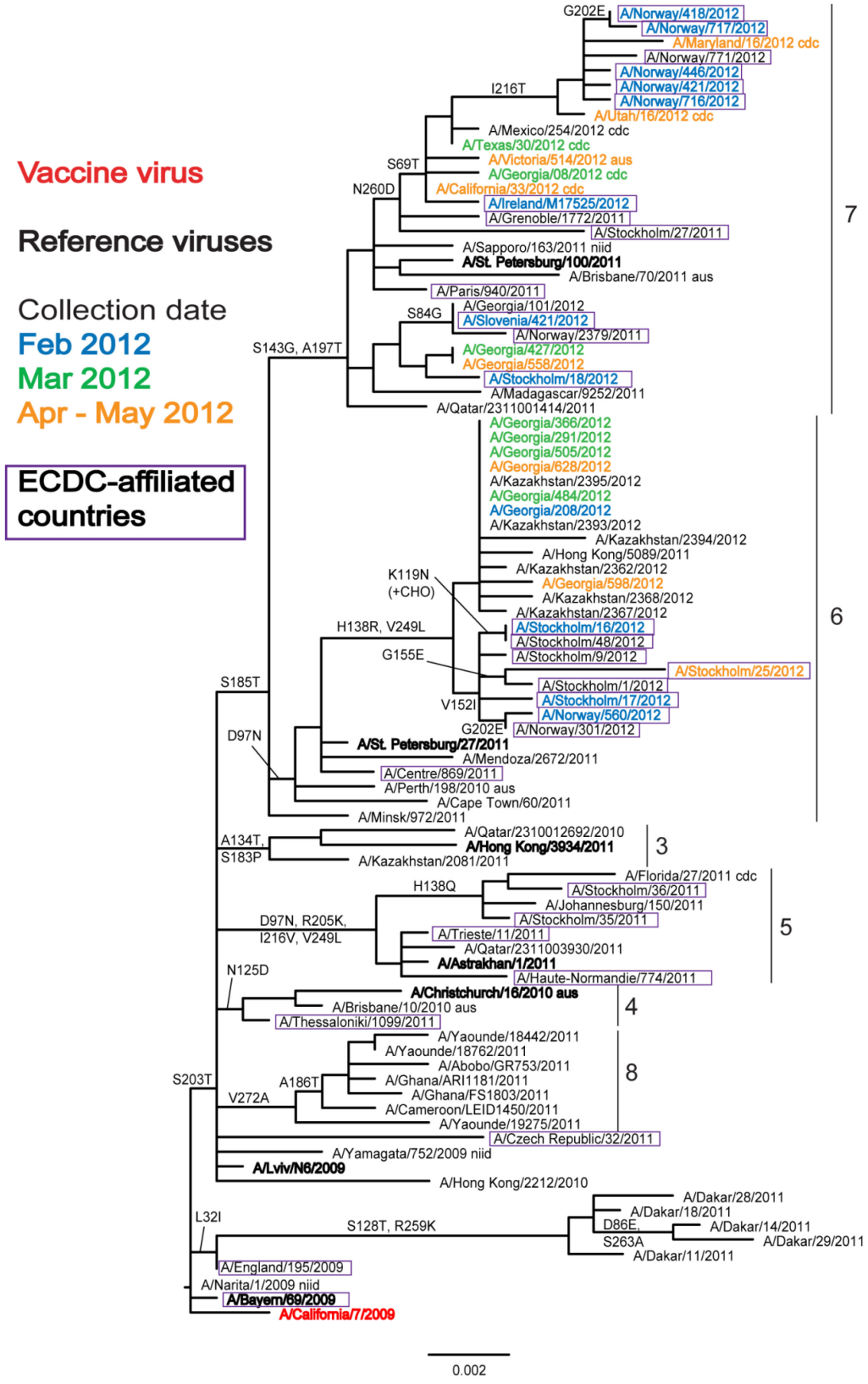

Table 2. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBCs with 20nM oseltamivir)

Viruses	Genetic group	Collection Date	Passage History	Haemagglutination inhibition titre[1] Post infection ferret sera									
				A/Perth 16/09 F35/11	A/Vic 208/09 F7/10	A/Ala 5/10 F27/10	A/HK 3969/11 F27/11	A/Stock 18/11 F28/11	A/Iowa 19/10 F15/11	A/Vic 361/11 Egg F05/12	A/Berlin 93/11 T/C F11/12	A/Vic 361/11 T/C F15/12	A/Athens 112/12 F16/12
						group 5	group 3C	group 3A	group 6	group 3C	group 3C	group 3C	group 3B
REFERENCE VIRUSES													
A/Perth/16/2009		2009-07-04	E3/E2	1280	80	320	640	320	320	160	640	640	640
A/Victoria/208/2009		2009-06-02	E3/E1	1280	5120	2560	5120	2560	5120	5120	5120	5120	5120
A/Alabama/5/2010		2010-07-13	MK1/C2/SIAT2	<	<	80	320	80	80	40	160	160	320
A/Hong Kong/3969/2011		2011-05-19	MDCK2/SIAT4	80	80	160	640	320	320	320	1280	640	640
A/Stockholm/18/2011		2011-03-28	MDCK2/SIAT4	<	40	80	320	320	80	160	640	160	640
A/Iowa/19/2010		2010-12-30	E3/E1	320	1280	640	1280	1280	1280	1280	2560	1280	1280
A/Victoria/361/2011		2011-10-24	E3/E2	320	1280	320	1280	160	1280	5120	1280	320	320
A/Berlin/93/2011		2011-12-07	NVD3/SIAT2	160	320	320	1280	640	640	640	1280	1280	1280
A/Victoria/361/2011		2011-10-24	MDCK2/SIAT2	160	320	320	1280	640	640	640	1280	1280	1280
A/Athens/112/2012		2012-02-01	SIAT4	160	320	320	640	320	320	320	1280	640	1280
TEST VIRUSES													
A/Torino/01/2011		2011-11-22	SIAT1/SIAT2	80	160	320	1280	640	320	320	1280	640	1280
A/Torino/03/2012		2012-01-06	SIAT1/SIAT1	80	160	320	640	320	320	160	640	640	640
A/Torino/05/2012		2012-01-10	SIAT1/SIAT1	40	80	160	320	160	160	80	640	320	320
A/Genova/04/2012		2012-01-11	MDCK2/SIAT1	640	80	160	640	160	320	160	320	320	640
A/Parma/09/2012		2012-01-12	MDCK1/SIAT1	<	40	80	160	80	80	40	160	160	320
A/Milano/20/2012		2012-01-12	SIAT1/SIAT1	80	160	320	640	320	640	320	640	640	1280
A/Genova/05/2012		2012-01-17	MDCK2/SIAT1	640	640	1280	2560	1280	1280	1280	2560	1280	2560
A/Milano/44/2012		2012-01-18	SIAT1/SIAT1	80	160	320	640	320	320	160	640	640	640
A/Pavia/14/2012		2012-01-18	MDCK2/SIAT1	40	80	80	640	320	160	160	640	320	640
A/Milano/57/2012		2012-01-23	SIAT1/SIAT2	40	160	320	640	320	320	160	320	640	320
A/Iceland/08/2012		2012-01-25	MDCK3/SIAT3	160	320	320	640	320	320	320	1280	640	1280
A/Finland/217/2012		2012-01-25	SIAT4/SIAT1	<	80	40	320	160	40	80	320	160	320
A/Pavia/42/2012		2012-01-27	MDCK2/SIAT1	40	320	80	320	320	320	160	640	320	640
A/Parma/87/2012		2012-01-30	MDCK2/SIAT1	40	160	160	320	640	160	160	640	320	640
A/Milano/136/2012	3A	2012-02-06	SIAT1/SIAT1	40	160	160	320	320	160	160	640	320	640
A/Finland/227/2012		2012-02-06	SIAT2/SIAT1	40	80	160	320	160	320	160	320	320	320
A/Finland/252/2012		2012-02-16	SIAT2/SIAT1	160	320	320	1280	640	640	320	1280	1280	1280
A/Pavia/128/2012		2012-02-17	MDCK2/SIAT1	80	160	320	640	320	160	160	640	640	640
A/Parma/139/2012	6	2012-02-20	MDCK2/SIAT1	160	320	640	1280	640	640	320	1280	640	1280
A/Perugia/21/2012		2012-02-22	MDCK2/SIAT1	40	160	320	640	320	320	160	640	640	640
A/Pavia/158/2012		2012-02-27	MDCK2/SIAT1	80	160	160	640	640	320	320	640	320	640
A/Perugia/44/2012		2012-03-05	MDCK2/SIAT2	40	80	80	320	320	80	160	320	320	320
A/Finland/263/2012		2012-03-07	SIAT2/SIAT1	40	80	80	320	320	160	160	320	160	640
A/Stockholm/21/2012		2012-04-21	C2/SIAT1	160	160	320	1280	320	640	320	1280	640	1280
			Vaccine	2011-12						Vaccine		Vaccine	

1. < = <40

Sequence in phylogenetic tree

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

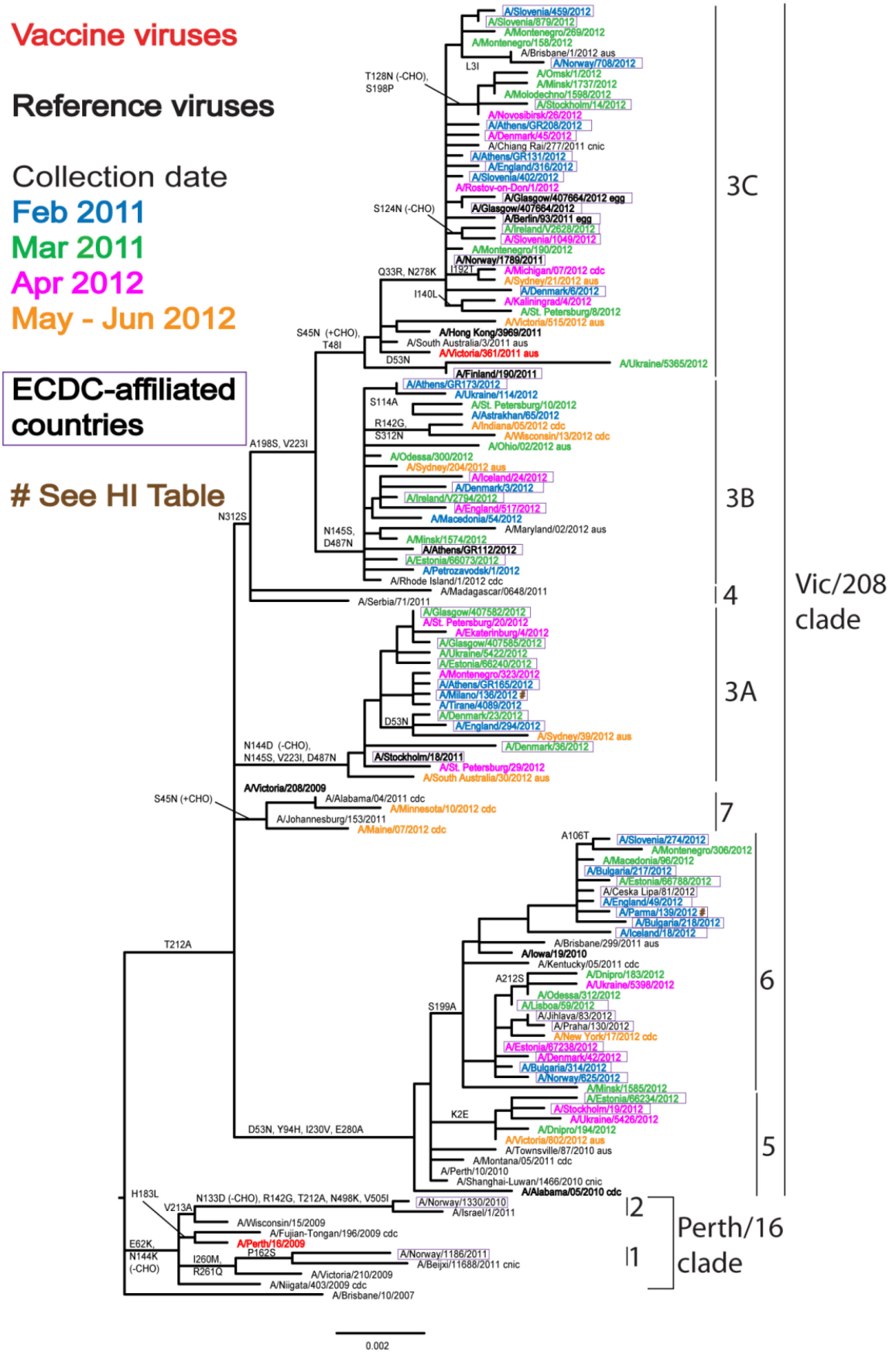

Table 3. Antigenic analysis of influenza B/Victoria-lineage viruses by HI (turkey RBCs)

Viruses	Collection date	Passage History	Haemagglutination inhibition titre[1]							
			Post infection ferret sera							
			B/Bris[2] 60/08 Sh 523	B/Mal 2506/04 F28/05	B/England 393/08 F05/11	B/Bris 60/08 F06/11	B/Paris 1762/08 F07/11	B/HK 514/09 F13/10	B/Odessa 3886/10 F19/11	B/Malta 636714/11 F33/11
REFERENCE VIRUSES										
B/Malaysia/2506/2004	2004-12-06	E3/E5	1280	640	40	160	10	<	<	80
B/England/393/2008	2008-08-29	E1/E6	2560	160	320	640	80	80	40	320
B/Brisbane/60/2008	2008-08-04	E4/E3	2560	160	160	640	80	80	80	320
B/Paris/1762/2008	2009-02-09	C2/MDCK4	5120	40	40	80	160	160	80	40
B/Hong Kong/514/2009	2009-10-11	MDCK1/MDCK3	5120	40	40	80	160	160	160	40
B/Odessa/3886/2010	2010-03-19	C2/MDCK4	5120	20	40	80	160	80	160	40
B/Malta/636714/2011	2011-03-07	E4/E1	1280	160	320	640	80	80	80	320
TEST VIRUSES										
B/Roma/02/2012	2012-01-19	MDCK3/MDCK1	2560	20	40	80	160	80	80	40
B/Finland/235/2012	2012-02-01	MDCK1/MDCK1	2560	40	40	80	160	160	160	40
B/Milano/03/2012	2012-02-16	MDCK2/MDCK1	2560	20	20	80	160	80	80	40
B/Finland/292/2012	2012-05-14	MDCK1/MDCK1	2560	40	40	80	160	160	160	40

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

Vaccine 2011-12

Sequence in phylogenetic tree

Table 4. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI (turkey RBCs)

Viruses	Collection date	Passage History	B/Fl[2] 4/06 SH479	Haemagglutination inhibition titre									
				Post infection ferret sera									
				B/Eg[1] 144/05 F3/07	B/Fl[1] 4/06 F21/07	B/Bris[1] 3/07 F24/07	B/Eng[1] 145/08 F9/08	B/Bang[1] 3333/07 F21/08	B/Wis[1] 1/10 F7/12	B/Stock[1] 12/11 F12/12	B/Estonia[1] 55669/11 F26/11	B/Serbia[1] 1894/11 F25/11	B/Stock[1] 12/11 T/C F8/12
REFERENCE VIRUSES													
B/Egypt/144/2005	2005-05-01	E3/E5	5120	640	640	1280	320	640	320	640	320	40	640
B/Florida/4/2006	2006-12-15	E3/E4	5120	320	1280	1280	80	160	640	640	160	10	160
B/Brisbane/3/2007	2007-09-03	E2/E1	2560	160	640	640	40	80	160	320	160	<	160
B/England/145/2008		Ex/E1	320	<	40	20	160	20	20	80	<	<	20
B/Bangladesh/3333/2007	2007-08-07	E4/E1	1280	40	80	160	20	320	40	320	<	10	80
B/Wisconsin/1/2010	2007-08-07	E4/E1	1280	80	160	160	80	160	160	640	10	40	160
B/Stockholm/12/2011	2007-08-07	E4/E1	2560	80	160	160	80	320	80	640	<	40	160
B/Estonia/55669/2011	2011-03-14	MDCK2/MDCK2	2560	40	80	80	20	40	20	80	1280	80	<
B/Serbia/1894/2011	2011-03-08	MDCK1/MDCK4	2560	40	160	80	80	160	160	320	160	320	160
B/Stockholm/12/2011	2011-03-28	Cx/MDCK1	2560	80	160	80	80	160	160	320	160	320	160
TEST VIRUSES													
B/Milano/05/2012	2012-02-21	MDCK3/MDCK1	2560	10	40	40	80	80	160	160	80	160	80
B/Milano/08/2012	2012-02-27	MDCK2/MDCK1	1280	10	20	40	80	80	160	160	80	160	80
B/Roma/01/2012	2012-02-27	MDCK3/MDCK1	1280	<	<	40	40	40	20	40	640	40	<
B/Milano/10/2012	2012-02-29	MDCK2/MDCK1	1280	10	20	20	80	80	160	320	40	80	80
B/Milano/11/2012	2012-02-29	MDCK2/MDCK1	1280	10	20	40	80	160	160	160	80	80	80
B/Milano/12/2012	2012-03-01	MDCK2/MDCK1	1280	<	10	20	80	80	160	160	40	80	40
B/Milano/13/2012	2012-03-01	MDCK2/MDCK1	2560	10	20	40	80	160	160	160	160	320	80
B/Milano/19/2012	2012-03-05	MDCK2/MDCK1	1280	<	<	20	40	40	80	160	40	40	40
B/Milano/15/2012	2012-03-06	MDCK2/MDCK1	1280	10	20	40	80	80	160	160	80	80	80
B/Milano/16/2012	2012-03-07	MDCK2/MDCK1	2560	<	10	40	80	80	160	160	80	80	80
B/Perugia/02/2012	2012-03-30	MDCK2/MDCK1	1280	10	20	40	40	40	80	160	20	40	20
B/Stockholm/9/2012	2012-04-17	C1/MDCK1	1280	10	20	40	20	20	20	40	640	40	<

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

Vaccine

Sequence in phylogenetic tree

Figure 3. Phylogenetic comparison of influenza B/Victoria-lineage HA genes (HA1 coding region)

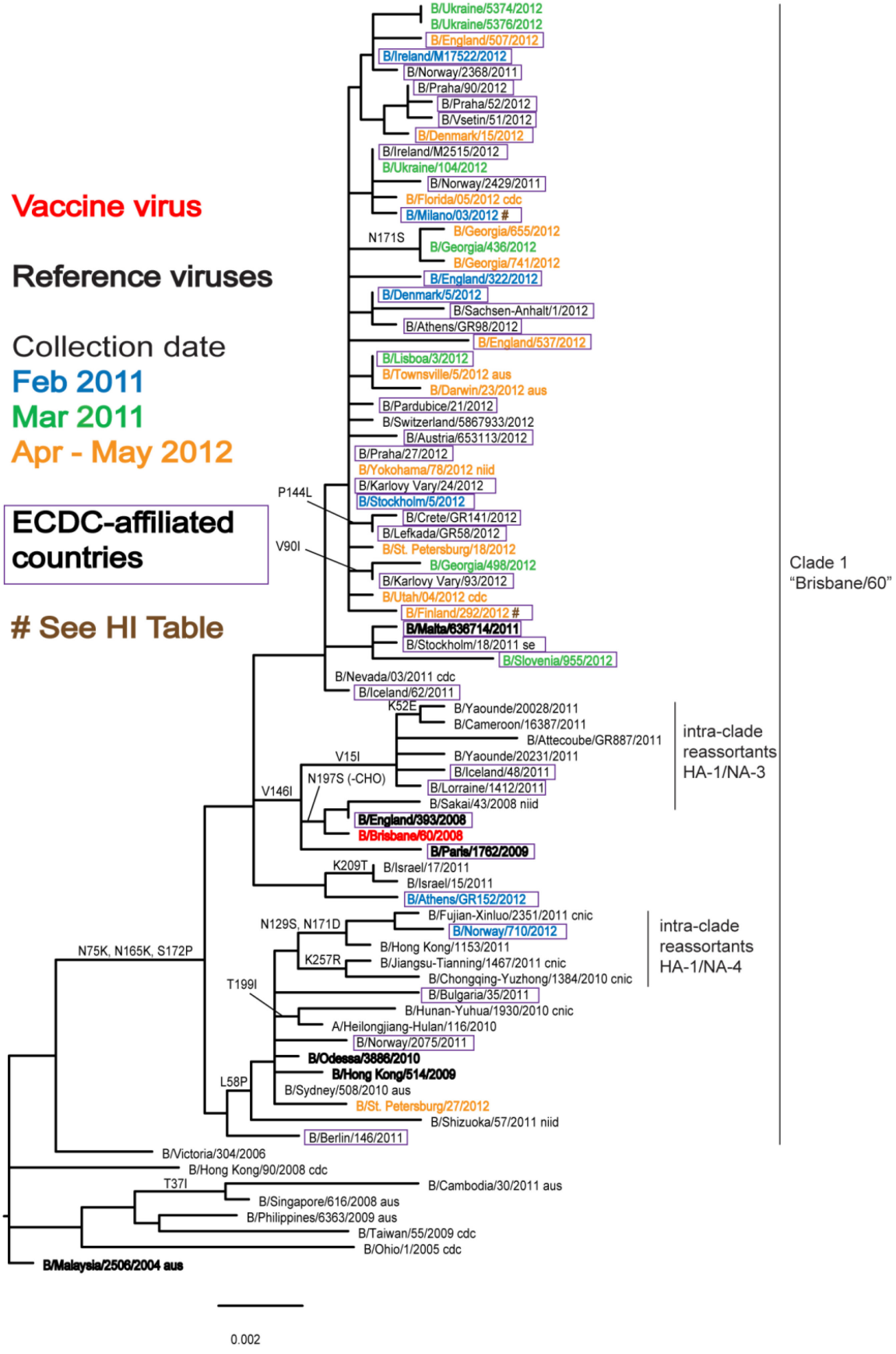

Figure 4. Phylogenetic comparison of influenza B/Yamagata-lineage HA genes (HA1 coding region)

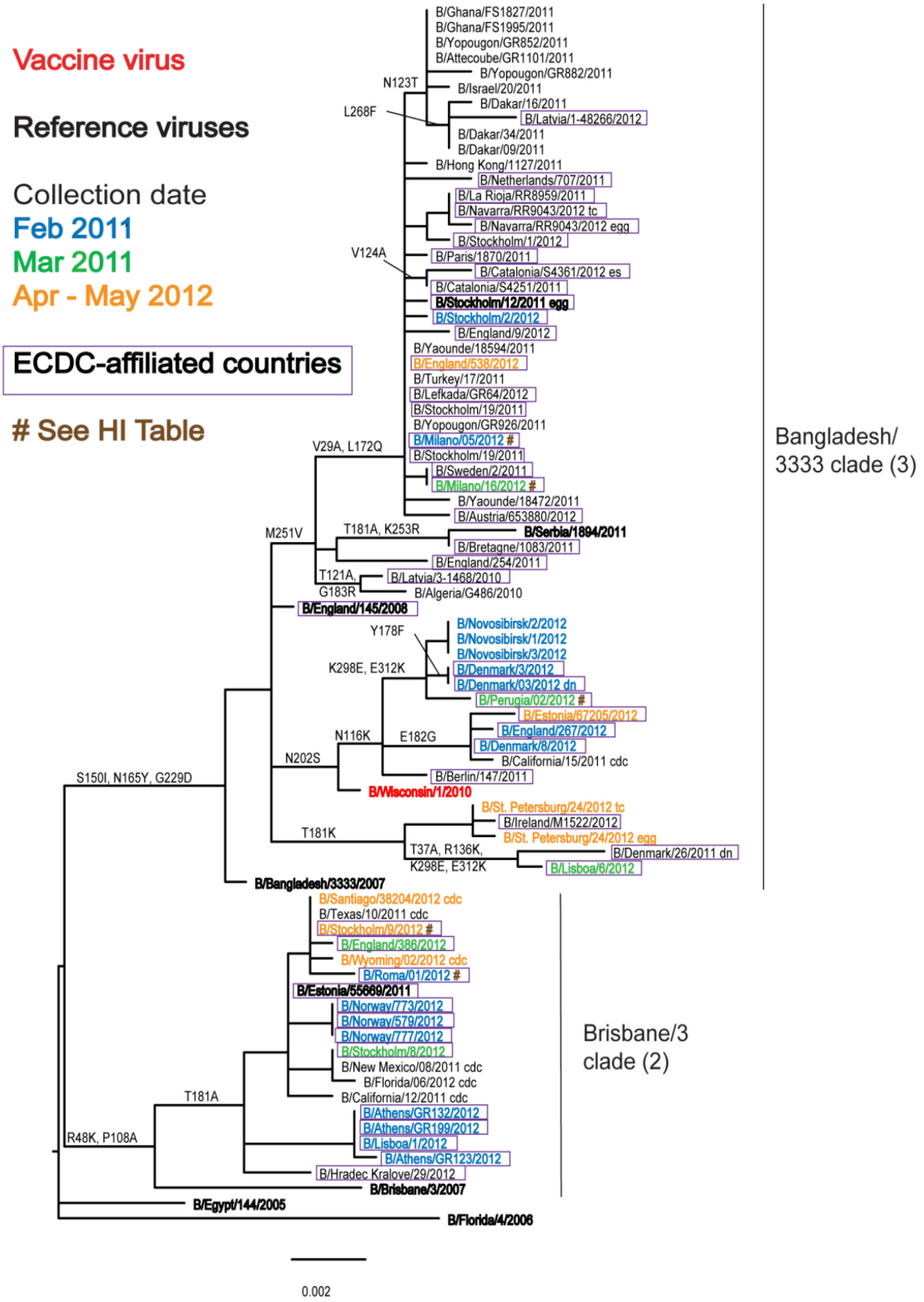

Table 5. Antigenic analysis of triple reassortant (TRV) influenza A(H3N2)v and human H3N2 viruses by HI (turkey RBCs)

Viruses		Passage History	Haemagglutination inhibition titre[1] Post infection ferret sera A/Pan 2007/99 F03/06	A/Perth 16/09 F35/11	A/Wis 12/10 F36/11	A/Pen 14/10 F39/11	A/Ind 8/11 F38/11
VIRUSES							
A/Panama/2007/99	Seasonal	Ex/1	2560	<	<	<	<
A/Perth16/2009	Seasonal	E3/E1	<	1280	<	<	<
A/Wisconsin/12/2010	TRV	M1/C1/MDCK2	<	<	640	40	<
A/Minnesota/11/2010	TRV	E2/E1	<	<	320	160	80
A/Pennsylvania/14/2010	TRV	E2/E2	<	<	1280	1280	1280
A/Indiana/8/2011	H3N2v	C2/MDCK2	<	<	1280	640	640
A/Indiana/10/2011	H3N2v	E2/E1	<	<	640	160	320

1. < = <40