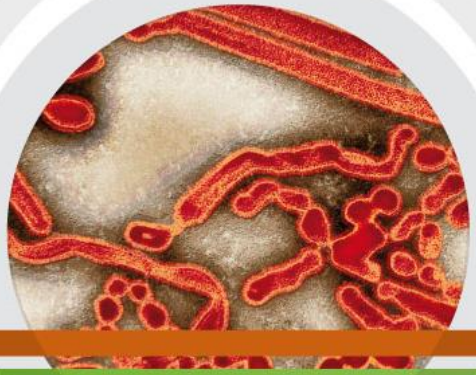

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2018

Summary

This is the third report of the 2017–18 influenza season. As of week 8/2018 over 151 000 influenza detections across the WHO European Region have been reported. Types A and B viruses have been detected in the proportions 40% and 60%, respectively, with A(H3N2) being slightly more prevalent than A(H1N1)pdm09 viruses (1.1:1) and B/Yamagata being significantly more prevalent than B/Victoria viruses (45.8:1).

Twenty-nine EU/EEA countries have shared influenza-positive specimens with the London WHO CC, Crick Worldwide Influenza Centre (WIC), since week 40/2017, with 871 specimens having collection dates after 31 August 2017.

The 101 A(H1N1)pdm09 test viruses characterised antigenically showed good reactivity with antiserum raised against the 2017–18 vaccine virus, A/Michigan/45/2015. The 102 test viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others from the European Region with collection dates after 31 August 2017 deposited in Global Initiative on Sharing All Influenza Data (GISAID), have all fallen in subclade 6B.1, defined by HA1 amino acid substitutions S162N and I216T, the great majority with additional substitutions of S74R, S164T and I295V.

Of 185 A(H3N2) viruses successfully recovered to date, only 30 (16%) had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir, of which 25 were tested since the last report. These viruses were poorly recognised by antisera raised against the currently used vaccine virus, egg-propagated A/Hong Kong/4801/2014, in HI assays. Of the 176 viruses with collection dates from week 40/2017 genetically characterised at the WIC, 120 were clade 3C.2a (with 98 3C.2a2; 18, 3C2a3 and four 3C2a4), 54 fell within 3C.2a1 (with two 3C2a1a and 51 3C2a1b), and two were 3C.3a.

The minority (30%) of B/Victoria-lineage viruses tested, were recognised well with post-infection ferret antisera raised against tissue culture-propagated surrogates of the currently used vaccine virus B/Brisbane/60/2008; by contrast, the majority (70%) reacted well with an antiserum raised against tissue culture-propagated B/Norway/2409/2017 that carries a deletion of two amino acids in HA1 (Δ162-163). Of the 28 viruses characterised genetically at the WIC with a collection date after week 40/2017, ten fell within clade 1A, and 18 fell within the subgroup carrying the HA1 double amino acid deletion.

A total of 163 B/Yamagata viruses were characterised antigenically, and 83% reacted well (within fourfold of the homologous titre) with post-infection ferret antiserum raised against egg-propagated B/Phuket/3073/2013, the recommended vaccine virus for use in quadrivalent vaccines for the northern hemisphere 2017–18 and 2018–2019 seasons and for trivalent vaccines in the southern hemisphere 2018 season. The 137 viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others recently circulating in the European Region and reported to GISAID, fall within clade 3.

This report was prepared by Rod Daniels, Vicki Gregory, Burcu Ermetal, Aine Rattigan and John McCauley (Crick Worldwide Influenza Centre (WIC)) for the European Centre for Disease Prevention and Control (ECDC) under an ECDC framework contract.

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Table 1 shows a summary of influenza virus detections in the WHO European Region reported to TESSy since the start of the 2017–18 season (weeks 40/2017-8/2018), with detections having exceeded the number for the entire 2016–17 season. Over 151 000 detections have been reported, an increase of approximately 114 000 compared with week 1/2018, with type B (60%) predominating over type A (40%) viruses. Of the type A viruses subtyped (n = 25 551) and the type B viruses ascribed to lineage (n = 10 757), A(H3N2) still prevailed over A(H1N1)pdm09, at a ratio of 1.1:1, and B/Yamagata prevailed over B/Victoria, at a ratio of 45.8:1; these ratios represent a decrease and an increase in relative prevalence, respectively, compared with week 1/2018 (as summarised in the December 2017 report[1]). Compared to the 2016–17 season, significant numbers of influenza type B viruses were detected early in the 2017–18 season and have predominated over type A throughout the season. The dominance of B/Yamagata over B/Victoria has increased from 2.7:1, seen in the 2016–2017 winter to 45.8:1 currently reported; overall, the ratio of type A to type B detections has decreased significantly compared to the 2016–17 season (~0.7:1 from 6.5:1); of the A subtyped viruses, a significant increase in the proportion of A(H1N1)pdm09 has been seen (47.4% in 2017–2018 compared with 1.1% in 2016–2017).

Since week 40/2017, 47 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC) from 29 EU/EEA countries. These packages contained 871 specimens, a mix of clinical samples and virus isolates, with specimen collection dates after August 2017 (Table 2). The majority (52%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 1.1:1. Of the 416 type B specimens received (48% of the specimens), 43 were B/Victoria-lineage and 326 were B/Yamagata-lineage. The antigenic and genetic properties of influenza viruses, characterised since the December 2017 report, are presented and discussed in this surveillance report. Since the majority of shipments were received after week 3/2018, a significant proportion of the specimens have not yet been characterised (in process: Table 2).

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2017–18 season (weeks 40/2017–8/2018)

	Cumulative number of detections			Totals*		Totals for 2016-17 season*		
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Number	%	Ratios
Influenza A	**6 221**	**54 054**	**60 275**	**39.8**	**0.7:1**	**126 614**	**86.6**	**6.5:1**
A(H1N1)pdm09	3 403	8 716	12 119	47.4		591	1.1	
A(H3N2)	1 836	11 596	13 432	52.6	1.1:1	53 101	98.9	89.8:1
A not subtyped	982	33 742	34 724			**72 922**		
Influenza B	**12 389**	**78 630**	**91 019**	**60.2**		**19 570**	**13.4**	
Victoria lineage	169	61	230	2.1		749	27.1	
Yamagata lineage	5 271	5 256	10 527	97.9	45.8:1	2 016	72.9	2.7:1
Lineage not ascribed	6 949	73 313	80 262			16 805		
Total detections (total tested)	**18 610 (45 320)**	**132 684 (485 278)**	**151 294 (530 598)**			**146 184 (686 477)**		

*** Percentages are shown for total detections (types A & B [in bold type], and for viruses ascribed to influenza A subtype and influenza B lineage). Ratios are given for type A:B [in bold type], A(H3N2):A(H1N1)pdm09 and Yamagata:Victoria lineages.**

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, December 2017. Stockholm: ECDC; 2017. Available from: https://ecdc.europa.eu/sites/portal/files/documents/ERLI-Net-report-Dec-2017.pdf

Table 2. Summary of clinical samples and virus isolates, contained in packages received from EU/EEA Member States since week 40/2017

MONTH		A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[1]
2017														
SEPTEMBER														
Finland	2					2	0	2						
France	4			2	2						1	1	1	1
Germany	1												1	1
Netherlands	1					1	0	0						
Norway	2			1	1								1	1
Spain	1			1	1									
Sweden	1					1	0	1						
United Kingdom	2					1	0	1			1	1		
OCTOBER														
Belgium	1			1	in process									
Croatia	2					2	0	2						
Denmark	2					2	1	1						
Finland	1					1	0	1						
France	12			4	4	7	7	0					1	1
Ireland	4			2	in process	1	0	1					1	1
Netherlands	3					1	0	1					2	in process
Norway	21			3	2	15	0	15					3	2
Slovakia	1					1	0	1						
Slovenia	1					1	1	0						
Spain	7			1	1	5	0	5					1	1
Sweden	3					3	2	1						
United Kingdom	7			2	2	3	0	3			1	1	1	1
NOVEMBER														
Austria	3	1	0			2	0	2						
Belgium	1												1	in process
Croatia	4												4	4
Denmark	2					1	0	1					1	in process
Estonia	1					1	in process							
Finland	7					3	0	3			1	0	3	3
France	23			7	7	10	1	9			1	1	5	5
Germany	6			2	2	2	0	2					2	2
Greece	2												2	in process
Hungary	1												1	1
Ireland	5			1	in process	2	0	2					2	in process
Italy	1												1	in process
Latvia	2			1	1	1	1	0						
Netherlands	3			1	1	2	0	1						
Norway	24			3	3	10	1	9			2	in process	9	in process
Portugal	4					1	0	1			1	1	2	2
Slovakia	1			1	1									
Slovenia	1												1	1
Spain	31			1	1	9	1	7	3	0	5	4	13	11
Sweden	7					5	1	4					2	2
United Kingdom	5					3	0	3			1	1	1	1
DECEMBER														
Austria	37			18	18	7	0	7					12	12
Belgium	19			7	in process	1	0	1					11	in process
Bulgaria	3			2	in process								1	in process
Croatia	6			3	3	3	1	2						
Cyprus	3	2	In process			1	in process							
Czech Republic	1												1	1
Denmark	17					9	in process						8	in process
Estonia	5	2	In process			2	in process						1	in process
Finland	1					1	0	1						
France	36			12	12	11	2	9			1	1	12	12
Germany	17			5	5	5	0	5					7	7
Greece	2			1	in process	1	0	1						
Hungary	6			1	1								5	5
Iceland	15			1	1	8	3	5					6	6
Ireland	13			1	in process	5	in process						7	in process
Italy	25			12	in process	2	0	2	2	in process			9	in process
Latvia	2			2	2									
Lithuania	9			3	in process						1	1	5	in process
Malta	1			1	in process									
Netherlands	16			1	0	1	0	1					14	in process
Norway	35			5	in process	15	in process				2	in process	13	in process
Poland	9	1	0	2	2				4	in process	2	2		
Portugal	30			2	2	3	0	3			6	6	19	19
Romania	9			4	in process	2	in process						3	in process
Slovakia	5												5	in process
Slovenia	12			4	4	3	1	2			3	2	2	2
Spain	52			18	in process	8	0	6	3	0	6	6	17	in process
United Kingdom	6												6	6
2018														
JANUARY														
Belgium	25			12	in process	5	in process						8	in process
Bulgaria	10			3	2	1	0	0					6	in process
Cyprus	8	2	in process	2	in process				2	in process			2	in process
Czech Republic	1			1	1									
Denmark	4												4	in process
Estonia	14	2	in process	3	2	3	in process		1	in process			5	in process
France	4			2	2	1	0	1					1	1
Germany	23			6	6	5	0	5			5	5	7	7
Greece	21			8	in process	2	in process						11	in process
Hungary	7			3	3								4	4
Iceland	6					2	2	0					4	4
Ireland	13			1	in process	4	1	2	8	in process				
Italy	12			4	in process	2	0	2	4	in process			2	2
Lithuania	16					3	in process		2	in process	2	1	9	in process
Malta	39			3	in process	13	in process		11	in process			12	in process
Netherlands	7			1	1								6	in process
Norway	15			5	in process	6	in process						4	in process
Poland	1										1	1		
Portugal	6												6	6
Romania	9			3	in process				4	in process			2	in process
Slovakia	1			1	1									
Slovenia	19			7	in process	2	0	2	3	0			7	in process
Spain	5			3	3	2	0	2						
	871	10	0	207	100	238	26	138	47	0	43	35	326	135
					23.8%		27.3%					4.9%		37.4%
29 Countries					52.2%							47.8%		

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 the presence of 20nM oseltamivir (the totalled number does not include any from batches that are in process)

Numbers in red indicate viruses recovered but with insufficient HA titre to permit HI assay

* As of 2018-02-28

Influenza A(H1N1)pdm09 virus analyses

Results of haemagglutination inhibition (HI) analyses of viruses performed since the December 2017 report are shown in Tables 3-1 to 3-6. All 101 A(H1N1)pdm09 test viruses antigenically characterised were similar to the vaccine virus for the present northern hemisphere 2017–18 influenza season, A/Michigan/45/2015 [1], with all viruses being recognised at titres within fourfold of the titre of the antiserum for the homologous virus and 99 (98%) within twofold. Of the other 12 antisera used, in at least one HI assay, 11 recognised all test viruses at titres within fourfold of their respective homologous titres, with recognition within twofold being in the range of 86% to 100% for individual antisera. The antiserum raised against A/Lviv/N6/2009 was the only antiserum that yielded eightfold or greater reduced recognition of test viruses compared with homologous titres: 48 (48%) within twofold, 45 (45%) within fourfold, and eight (8%) at eightfold or greater.

Genetic analyses of many test viruses are in process but the 74 antigenically characterised viruses for which gene sequencing is complete all carried haemagglutinins (HAs) belonging to genetic subclade 6B.1 (Tables 3-1 to 3-4), as was observed for all EU/EEA A(H1N1)pdm09 viruses characterised throughout the 2016–17 season. This trend is continuing with all A(H1N1)pdm09 viruses from European countries, as defined in GISAID, with collection dates after 31 August 2017 falling in subclade 6B.1, with the majority of HA genes of recently circulating viruses from EU/EAA countries clustering in a genetic subgroup defined by HA1 amino acid substitutions of S74R, S164T and I295V (Figure 1).

Table 3-1. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera										
					A/Mich 45/15 Egg NIB F42/16[*1]	A/Cal 7/09 Egg F06/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F14/13[*1]	A/Astrak 1/11 MDCK F22/13[*1]	A/St. P 27/11 Egg F26/14[*1]	A/St. P 100/11 Egg F24/11[*1]	A/HK 5659/12 MDCK F30/12[*1]	A/Sth Afr 3626/13 Egg F03/14[*1]	A/Slov 2903/2015 Egg F02/16[*2]	A/Israel Q-504/15 MDCK F08/16[*2]
		Genetic group			6B.1				5	6	7	6A	6B	6B.1	6B.2
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	320	320	1280	320	2560	1280	640	2560	1280
A/California/7/2009	clone38-32		2009-04-09	E3/E3	640	640	320	320	1280	320	2560	640	640	1280	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	< 40	320	320	40	40	80	80	40	80	40	
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	40	80	640	640	80	80	160	160	80	320	80
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	640	640	640	320	1280	640	2560	1280	640	1280	1280
A/St. Petersburg/27/2011		6	2011-02-14	E1/E4	640	640	640	640	1280	640	2560	1280	640	2560	1280
A/St. Petersburg/100/2011		7	2011-03-14	E1/E4	320	320	320	320	640	320	1280	640	640	1280	640
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	160	160	80	80	320	80	640	320	320	640	160
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	320	320	640	640	640	1280	640	640	1280	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	640	320	320	1280	640	2560	1280	640	2560	1280
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	320	1280	320	2560	1280	640	2560	1280
TEST VIRUSES															
A/Sachsen-Anhalt/101/2017		6B.1	2017-11-06	C1/MDCK1	640	320	320	160	640	160	1280	640	640	1280	640
A/Norway/3433/2017		6B.1	2017-11-10	MDCK1	640	640	640	320	1280	640	2560	1280	1280	2560	1280
A/Norway/3499/2017		6B.1	2017-11-11	MDCK1	1280	1280	640	320	1280	640	5120	1280	1280	2560	1280
A/Baden-Wurttemberg/252/2017		6B.1	2017-11-20	C1/MDCK1	640	640	320	320	640	320	2560	1280	1280	2560	1280
A/Bayern/95/2017		6B.1	2017-12-04	C1/MDCK1	640	640	640	320	1280	640	2560	1280	1280	2560	1280
A/Norway/3787/2017		6B.1	2017-12-07	MDCK1	640	640	320	160	640	320	2560	640	640	1280	640
A/Rheinland-Pfalz/52/2017		6B.1	2017-12-11	C1/MDCK1	640	640	320	320	640	320	1280	640	640	2560	640
A/Thuringen/170/2017		6B.1	2017-12-11	C2/MDCK1	640	640	640	320	1280	320	2560	1280	640	2560	1280
A/Slovenia/2642/2017		6B.1	2017-12-12	SIATx/MDCK1	1280	1280	640	320	1280	640	5120	1280	1280	2560	1280
A/Slovenia/2639/2017		6B.1	2017-12-12	SIATx/MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280
A/Navarra/2488/2017		6B.1	2017-12-13	MDCK1	640	640	320	160	640	320	2560	640	640	1280	640
A/Slovenia/2686/2017		6B.1	2017-12-18	SIATx/MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280
A/Bayern/96/2017		6B.1	2017-12-18	C2/MDCK1	1280	640	640	640	1280	320	2560	1280	1280	2560	1280
A/Galicia/2443/2017		6B.1	2017-12-20	MDCK1	640	640	320	320	1280	320	2560	1280	640	2560	1280
A/Austria/1030576/2017		6B.1	2017-12-20	SIAT2/MDCK1	1280	640	640	640	1280	640	2560	1280	1280	2560	1280
A/Saarland/25/2017		6B.1	2017-12-21	C2/MDCK1	320	320	320	320	640	320	1280	640	640	1280	640
A/Austria/1031030/2017		6B.1	2017-12-21	SIAT1/MDCK1	320	320	320	320	640	160	1280	640	640	1280	640
A/Austria/1031031/2017		6B.1	2017-12-21	SIAT1/MDCK1	1280	640	640	640	1280	640	2560	1280	1280	2560	1280
A/Austria/1031040/2017		6B.1	2017-12-21	SIAT1/MDCK1	640	640	320	320	640	320	2560	640	640	1280	1280
A/Austria/1030864/2017			2017-12-21	SIAT1	1280	1280	640	640	1280	640	2560	1280	1280	5120	2560
A/Austria/1031039/2017		6B.1	2017-12-22	SIAT1/MDCK1	320	320	320	160	640	160	1280	640	640	1280	640
A/Austria/1031050/2017		6B.1	2017-12-24	SIAT1/MDCK1	640	640	640	320	1280	320	2560	1280	640	2560	640
A/Slovenia/2794/2017		6B.1	2017-12-29	SIATx/MDCK1	1280	1280	640	320	1280	640	5120	1280	1280	5120	2560
A/Slovenia/37/2018		6B.1	2018-01-05	SIATx/SIAT1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280
					Vaccine										

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)

1 < = <40; 2 < = <80

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre												
				Post-infection ferret antisera												NEW
				A/Mich 45/15 Egg NIB F42/16[-1]	A/Cal 7/09 Egg F06/16[-1]	A/Bayern 69/09 MDCK F09/15[-1]	A/Lviv N6/09 MDCK F14/13[-1]	A/Astrak 1/11 MDCK F22/13[-1]	A/St. P 27/11 Egg F26/14[-1]	A/St. P 100/11 Egg F24/11[-1]	A/HK 5659/12 MDCK F30/12[-1]	A/Sth Afr 3626/13 Egg F03/14[-1]	A/Slov 2903/2015 Egg F02/16[-2]	A/Israel Q-504/15 MDCK F08/16[-2]	A/Paris 1447/17 MDCK F03/18[-2]
Passage history																
Ferret number								5	6	7	6A	6B	6B.1	6B.2	6B.1
Genetic group				6B.1												
REFERENCE VIRUSES																
A/Michigan/45/2015		2015-09-07	E3/E3	1280	1280	640	320	1280	320	2560	1280	640	2560	1280	2560	
A/California/7/2009	clone38-32	2009-04-09	E3/E3	1280	640	640	640	1280	320	2560	1280	640	2560	640	2560	
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	<	80	640	320	80	40	80	80	80	80	40	320	
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK3	80	160	1280	1280	160	80	160	160	80	320	80	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	640	640	640	320	640	320	2560	1280	640	1280	640	1280	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	1280	640	1280	640	2560	1280	1280	2560	1280	2560	
A/St. Petersburg/100/2011	7	2011-03-14	E1/E4	320	320	640	320	320	320	1280	320	320	640	320	640	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	160	320	160	80	320	160	640	320	320	640	320	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	1280	1280	1280	1280	1280	640	2560	1280	1280	2560	1280	2560	
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	640	640	320	320	640	320	1280	640	640	1280	640	1280	
A/Israel/Q-504/2015	6B.2	2015-12-15	C1/MDCK2	1280	1280	640	320	1280	320	2560	1280	640	2560	1280	2560	
A/Paris/1447/2017	6B.1	2017-10-20	MDCK1/MDCK2	1280	640	640	320	640	320	2560	640	640	2560	640	2560	
TEST VIRUSES																
A/Partizanske/44/2017	6B.1	2017-11-30	MDCK1/MDCK1	640	640	320	320	640	320	2560	1280	640	2560	1280	>5120	
A/Croatia/3609/2017	6B.1	2017-12-12	MDCKx/MDCK1	1280	1280	640	640	1280	640	5120	1280	1280	2560	1280	>5120	
A/Poland/3986/2017	6B.1	2017-12-19	SIAT1	2560	2560	640	640	2560	640	5120	1280	1280	5120	2560	>5120	
A/Croatia/3774/2017	6B.1	2017-12-19	MDCKx/MDCK1	2560	2560	1280	640	2560	640	5120	2560	2560	2560	2560	>5120	
A/Poland/4005/2017	6B.1	2017-12-21	SIAT1	640	1280	640	320	1280	320	2560	1280	1280	2560	1280	>5120	
A/Portugal/SU114/2017	6B.1	2017-12-27	MDCK2/MDCK1	640	640	640	320	1280	320	2560	1280	640	2560	1280	>5120	
A/Bretagne/1964/2017	6B.1	2017-12-27	MDCK1/MDCK1	320	320	320	160	640	160	1280	640	640	2560	640	2560	
A/Iceland/145/2017	6B.1	2017-12-31	MDCK1/MDCK1	640	640	640	640	640	320	1280	640	640	2560	1280	>5120	
A/Bretagne/002/2018	6B.1	2018-01-02	MDCK2/MDCK1	1280	640	640	320	1280	320	2560	1280	1280	2560	1280	>5120	
A/Centre/043/2018	6B.1	2018-01-02	MDCK1/MDCK1	640	640	320	320	640	320	1280	1280	640	2560	1280	>5120	
A/Komarno/75/2018	6B.1	2018-01-04	MDCKx/MDCK1	1280	1280	640	640	1280	640	2560	1280	1280	2560	1280	>5120	
A/Slovenia/59/2018	6B.1	2018-01-05	SIAT1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280	>5120	
A/Bulgaria/053/2018	6B.1	2018-01-08	MDCK1	1280	640	640	320	1280	320	2560	1280	640	2560	1280	>5120	
A/Bulgaria/049/2018	6B.1	2018-01-08	MDCK1	1280	1280	640	320	1280	640	2560	1280	1280	2560	1280	>5120	
A/Hungary/4/2018	6B.1	2018-01-09	MDCK1/MDCK1	1280	1280	640	640	1280	640	2560	1280	1280	2560	1280	>5120	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80
Sequences in phylogenetic trees

Vaccine

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
				A/Mich 45/15	A/Cal 7/09	A/Bayern 69/09	A/Lviv N6/09	A/Astrak 1/11	A/St. P 27/11	A/HK 5659/12	A/Sth Afr 3626/13	A/Slov 2903/2015	A/Israel Q-504/15	A/Paris 1447/17
			Passage history	Egg	Egg	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK
			Ferret number	NIB F42/16^{-1}	F06/16^{-1}	F09/15^{-1}	F14/13^{-1}	F22/13^{-1}	F26/14^{-1}	F30/12^{-1}	F03/14^{-1}	F02/16^{-2}	F08/16^{-2}	F03/18^{-2}
			Genetic group	6B.1				5	6	6A	6B	6B.1	6B.2	6B.1
REFERENCE VIRUSES														
A/California/7/2009	clone38-32	2015-09-07	E3/E3	640	1280	320	320	1280	320	1280	640	1280	1280	2560
A/Bayern/69/2009	G155E	2009-04-09	E3/E3	640	640	640	320	640	320	640	640	1280	640	2560
A/Lviv/N6/2009	G155E, D222G	2009-07-01	MDCK5/MDCK1	<	40	640	320	40	<	40	40	80	40	160
A/Astrakhan/1/2011		2009-10-27	MDCK4/SIAT1/MDCK3	40	160	1280	640	80	80	160	80	160	80	640
A/St. Petersburg/27/2011	5	2011-02-28	MDCK1/MDCK4	640	1280	1280	640	1280	640	1280	640	1280	640	2560
A/Hong Kong/5659/2012	6	2011-02-14	E1/E4	640	640	640	640	640	320	640	640	2560	640	2560
A/South Africa/3626/2013	6A	2012-05-21	MDCK4/MDCK2	160	160	160	80	320	80	320	160	320	160	640
A/Slovenia/2903/2015	6B	2013-06-06	E1/E3	640	640	640	640	640	320	640	640	1280	640	2560
A/Israel/Q-504/2015	clone 37	2015-10-26	E4/E1	640	1280	640	320	1280	640	1280	640	1280	1280	2560
A/Paris/1447/2017	6B.2	2015-12-15	C1/MDCK2	640	640	320	160	640	320	640	320	1280	640	2560
	6B.1	2017-10-20	MDCK1/MDCK2	640	640	320	160	640	160	640	640	1280	640	2560
TEST VIRUSES														
A/Poitiers/2380/2017	6B.1	2017-12-05	MDCK2/MDCK1	320	640	320	160	640	160	640	320	1280	640	2560
A/Toulon/2336/2017	6B.1	2017-12-11	MDCK2/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Lyon/2376/2017	6B.1	2017-12-12	MDCK2/MDCK1	640	1280	320	320	640	320	1280	640	2560	1280	2560
A/Croatia/3750/2017	6B.1	2017-12-18	MDCKx/MDCK1	1280	2560	1280	640	1280	640	1280	1280	2560	2560	>5120
A/Bucuresti/221745/2017	6B.1	2017-12-20	MDCK1/MDCK1	640	640	320	320	640	320	640	320	1280	640	2560
A/Bucuresti/221744/2017	6B.1	2017-12-20	MDCK1/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560
A/Bucuresti/221746/2017	6B.1	2017-12-20	MDCK1/MDCK1	640	1280	640	320	1280	320	1280	1280	2560	1280	>5120
A/Belgium/G0003/2018	6B.1	2017-12-22	SIAT1/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560
A/Portugal/SU117/2017	6B.1	2017-12-27	MDCK2/MDCK1	640	640	320	160	640	160	640	640	1280	640	2560
A/Lithuania/36856/2017	6B.1	2017-12-27	MDCK2/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560
A/Hungary/2/2018	6B.1	2017-12-28	MDCK1/MDCK1	320	80	320	320	320	80	320	320	1280	640	1280
A/Belgium/G0008/2018	6B.1	2017-12-28	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Belgium/G0014/2018	6B.1	2018-01-02	SIAT1/MDCK1	640	1280	320	320	640	320	640	1280	2560	1280	2560
A/Padova/3/2018	6B.1	2018-01-02	MDCK2/MDCK1	640	640	320	320	640	320	640	640	2560	1280	2560
A/Pavia/2/2018	6B.1	2018-01-03	MDCK2/MDCK1	640	1280	640	320	1280	320	1280	640	2560	1280	>5120
A/Padova/11/2018	6B.1	2018-01-04	MDCK2/MDCK1	640	640	320	160	640	160	640	640	1280	640	2560
A/Athens.GR/39/2018	6B.1	2018-01-05	MDCK1	640	1280	640	320	1280	320	1280	640	2560	1280	>5120
A/Hungary/5/2018	6B.1	2018-01-05	MDCK1/MDCK1	640	640	640	320	640	320	640	640	1280	1280	>5120
A/Estonia/111272/2018	6B.1	2018-01-05	MDCK1/MDCK1	640	1280	320	320	640	320	640	640	1280	1280	2560
A/Netherlands/10010/2018	6B.1	2018-01-05	(MDCK/SIAT)1/MDCK2	640	640	320	320	640	320	640	640	1280	640	>5120
A/Estonia/111324/2018	6B.1	2018-01-08	MDCK1/MDCK1	640	640	320	160	640	160	640	640	1280	640	2560
A/Czech Republic/85/2018	6B.1	2018-01-09	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	1280	2560

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) Vaccine

1 < = <40; 2 < = <80

Sequences in phylogenetic trees

Table 3-4. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera											
					A/Mich 45/15	A/Cal 7/09	A/Bayern 69/09	A/Lviv N6/09	A/Astrak 1/11	A/St. P 27/11	A/HK 5659/12	A/Sth Afr 3626/13	A/Slov 2903/2015	A/Israel Q-504/15	A/Paris 1447/17	A/Mich 272/17
		Passage history			Egg	Egg	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	Egg
		Ferret number			NIB F42/16*1	F06/16*1	F09/15*1	F14/13*1	F22/13*1	F26/14*1	F30/12*1	F03/14*1	F02/16*2	F08/16*2	F03/18*2	CDC F032/18*2
		Genetic group			6B.1				5	6	6A	6B	6B.1	6B.2	6B.1	6B.1
REFERENCE VIRUSES																
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	1280	1280	640	320	640	640	640	640	1280	1280	2560	640
A/California/7/2009	clone38-32		2009-04-09	E3/E3	640	1280	640	640	1280	640	640	640	2560	1280	2560	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	80	640	320	80	40	40	80	80	40	320	40
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	160	1280	1280	160	80	160	160	320	160	1280	320
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK6	640	640	640	320	1280	320	640	640	1280	640	2560	640
A/St. Petersburg/27/2011		6	2011-02-14	E1/E4	1280	1280	1280	1280	1280	640	1280	1280	2560	1280	5120	1280
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	80	80	160	80	320	160	320	320	640	320	1280	320
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	640	640	640	1280	640	1280	1280	1280	640	2560	1280
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E1	640	1280	320	320	640	320	640	640	1280	1280	2560	640
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	320	640	320	640	640	1280	1280	2560	640
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	1280	640	320	320	1280	320	640	1280	2560	1280	5120	1280
A/Michigan/272/2017		6B.1	2017-07-18	E3/E1	1280	1280	640	640	1280	640	1280	1280	2560	1280	>5120	2560
TEST VIRUSES																
A/Clermont-Ferrand/1873/2017		6B.1	2017-08-19	MDCK2/MDCK1	1280	640	640	320	640	320	1280	640	2560	1280	>5120	1280
A/Annecy/1878/2017		6B.1	2017-09-09	MDCK2/MDCK1	640	640	320	320	640	320	640	1280	2560	1280	2560	1280
A/Lyon-Croix-Rousse/1874/2017		6B.1	2017-09-09	MDCK3/MDCK1	640	640	320	320	640	320	640	640	1280	1280	>5120	1280
A/Lyon/2041/2017		6B.1	2017-11-05	MDCK2/MDCK1	640	320	320	160	640	320	640	640	1280	1280	2560	640
A/Netherlands/03411/2017		6B.1	2017-11-05	SIAT1/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	>5120	1280
A/Clermont Ferrand/2290/2017		6B.1	2017-12-03	MDCK2/MDCK1	640	640	640	320	640	320	640	640	2560	1280	>5120	1280
A/Catalonia/3517716NS/2017		6B.1	2017-12-17	C0/MDCK1	640	640	640	320	640	320	640	1280	2560	1280	2560	1280
A/Hungary/6/2018		6B.1	2018-01-02	MDCK1/MDCK1	1280	1280	640	640	1280	640	1280	2560	2560	2560	>5120	2560
A/Catalonia/3518597NS/2018		6B.1	2018-01-03	C0/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560	1280
A/Catalonia/3518646NS/2018		6B.1	2018-01-04	C0/MDCK1	640	640	640	320	640	320	640	640	2560	1280	2560	1280
A/Norway/205/2018		6B.1	2018-01-08	MDCK1/MDCK1	640	640	640	320	640	320	640	640	2560	1280	>5120	1280
A/Catalonia/2242523NS/2018		6B.1	2018-01-09	C0/MDCK1	640	640	320	160	640	320	640	640	1280	640	1280	640
A/Norway/283/2018		6B.1	2018-01-12	MDCK1/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560	1280
A/Norway/282/2018		6B.1	2018-01-13	MDCK1/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560	1280
					Vaccine											

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)

1 < = <40; 2 < = <80

Table 3-5. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera										
		Passage history			A/Mich 45/15 Egg	A/Cal 7/09 Egg	A/Bayern 69/09 MDCK	A/Lviv N6/09 MDCK	A/Astrak 1/11 MDCK	A/St. P 27/11 Egg	A/HK 5659/12 MDCK	A/Sth Afr 3626/13 Egg	A/Slov 2903/2015 Egg	A/Israel Q-504/15 MDCK	A/Paris 1447/17 MDCK
		Ferret number			NIB F42/16*1	F06/16*1	F09/15*1	F14/13*1	F22/13*1	F26/14*1	F30/12*1	F03/14*1	F02/16*1	F08/16*1	F03/18*2
		Genetic group			6B.1				5	6	6A	6B	6B.1	6B.2	6B.1
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	320	320	640	320	640	640	1280	1280	2560
A/California/7/2009	Clone38-32		2009-04-09	E3/E3	640	640	640	320	640	320	640	640	1280	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	40	640	320	40	40	40	40	80	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	160	1280	1280	80	160	80	80	320	80	640
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK6	640	640	320	320	640	320	640	320	1280	640	1280
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	640	640	640	640	640	320	640	640	1280	1280	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	160	160	160	80	160	160	320	160	320	160	640
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	1280	640	640	640	640	640	640	640	1280	640	2560
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	640	320	160	640	320	640	640	1280	1280	1280
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	1280	640	320	320	640	320	640	640	1280	1280	2560
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	640	640	320	160	640	320	640	640	1280	640	2560
TEST VIRUSES															
A/Baleares/2477/2017			2017-11-07	MDCK1	640	160	320	320	320	160	320	320	1280	640	1280
A/Galicia/2466/2017			2017-12-01	MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	2560	5120
A/Paris/1931/2017			2017-12-22	MDCK1/MDCK1	1280	640	640	320	1280	640	1280	1280	2560	1280	5120
A/Paris/1959/2017			2017-12-24	MDCK2/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Bretagne/1994/2017			2017-12-26	MDCK1/MDCK1	1280	1280	640	640	1280	640	1280	1280	2560	2560	5120
A/Haute Normandie/1945/2017			2017-12-26	MDCK1/MDCK1	640	160	320	320	320	160	320	320	1280	640	1280
A/Bretagne/1939/2017			2017-12-26	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Bretagne/1937/2017			2017-12-26	MDCK1/MDCK1	640	320	160	160	320	160	320	640	1280	640	1280
A/Niedersachsen/5/2018			2018-01-22	C1/MDCK1	1280	1280	640	320	640	320	640	640	2560	1280	2560
A/Rheinland-Pfalz/6/2018			2018-01-24	C1/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Nordrhein-Westfalen/11/2018			2018-01-25	C1/MDCK1	1280	1280	640	320	640	320	640	640	1280	1280	2560
A/Berlin/8/2018			2018-01-26	C1/MDCK1	640	640	320	160	640	160	640	640	1280	640	1280
A/Thuringen/7/2018			2018-01-29	C1/MDCK1	1280	640	320	320	640	320	640	640	1280	1280	2560
A/Hessen/5/2018			2018-01-29	C1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
					Vaccine										

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)

1 < = <40; 2 < = <80

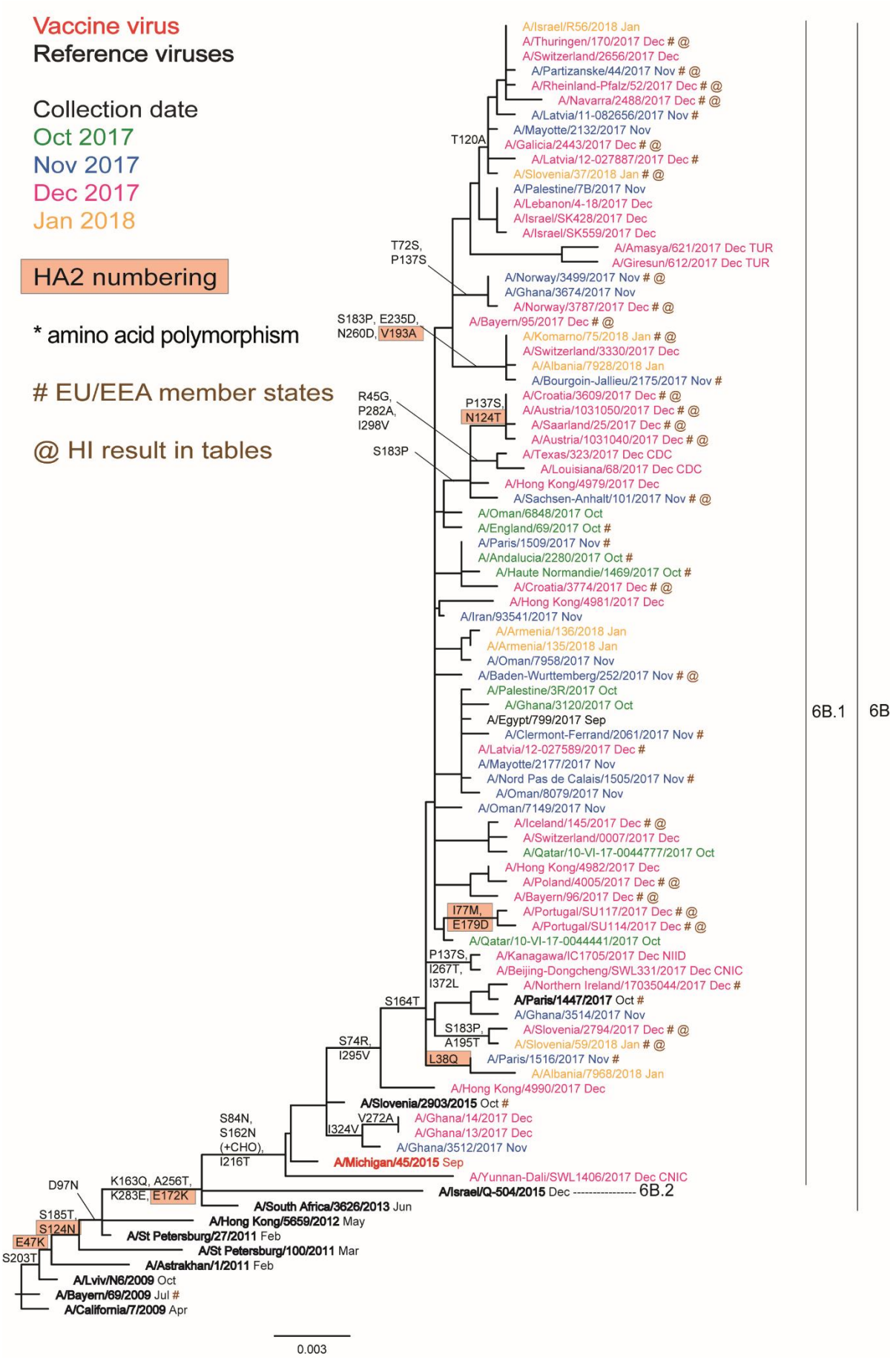
Table 3-6. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
	Passage history			A/Mich 45/15 Egg NIB F42/16[*1]	A/Cal 7/09 Egg F06/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F14/13[*1]	A/Astrak 1/11 MDCK F22/13[*1]	A/St. P 27/11 Egg F26/14[*1]	A/HK 5659/12 MDCK F30/12[*1]	A/Sth Afr 3626/13 Egg F03/14[*1]	A/Slov 2903/2015 Egg F02/16[*1]	A/Israel Q-504/15 MDCK F08/16[*1]	A/Paris 1447/17 MDCK F03/18[*2]	
	Ferret number							5	6	6A	6B	6B.1	6B.2	6B.1	
	Genetic group			6B.1											
REFERENCE VIRUSES															
A/Michigan/45/2015	6B.1	2015-09-07	E3/E3	1280	1280	320	320	640	640	640	640	1280	1280	1280	
A/California/7/2009	clone38-32	2009-04-09	E3/E3	640	640	640	640	1280	640	640	640	2560	1280	2560	
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	40	40	320	320	40	40	40	40	80	40	320	
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK3	80	160	1280	640	80	80	80	80	160	80	640	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK6	1280	1280	640	320	1280	640	1280	640	2560	1280	2560	
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	640	640	640	640	640	640	640	640	1280	640	1280	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	320	160	160	320	160	320	320	640	320	640	
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	1280	640	640	640	640	640	640	640	1280	640	1280	
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	640	320	160	640	320	640	640	1280	1280	1280
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	320	640	320	640	640	1280	1280	1280
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	1280	640	320	160	640	320	640	640	1280	1280	2560
TEST VIRUSES															
A/Austria/1028502/2017			2017-12-11	SIAT1/MDCK1	640	320	160	160	320	320	320	320	1280	640	2560
A/Austria/1029090/2017			2017-12-12	SIAT1/MDCK1	320	320	160	160	320	160	320	320	640	640	1280
A/Austria/1029091/2017			2017-12-12	SIAT1/MDCK1	640	320	320	160	320	320	320	320	1280	640	2560
A/Austria/1029092/2017			2017-12-13	SIAT1/MDCK1	1280	640	320	320	640	320	640	640	2560	1280	2560
A/Austria/1029513/2017			2017-12-15	SIAT1/MDCK1	640	640	320	160	320	160	320	640	1280	640	1280
A/Austria/1029613/2017			2017-12-15	SIAT1/MDCK1	1280	640	640	320	640	640	640	640	2560	1280	2560
A/Austria/1029752/2017			2017-12-18	SIAT1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Austria/1029923/2017			2017-12-18	SIAT2/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Haute Normandie/1852/2017			2017-12-18	MDCK1/MDCK1	1280	640	320	320	640	320	640	640	2560	2560	2560
A/Austria/1030260/2017			2017-12-19	SIAT1/MDCK1	640	320	160	160	320	160	320	320	1280	640	1280
A/Austria/1030262/2017			2017-12-19	SIAT1/MDCK1	640	640	320	160	640	320	640	640	1280	1280	2560
A/Austria/1030575/2017			2017-12-19	SIAT1/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560

Vaccine

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80

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



Influenza A(H3N2) virus analyses

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

Most of the 238 A(H3N2) virus specimens with collection dates after week 40/2017 are in process for antigenic and genetic characterisation. However, of those successfully isolated to date (n = 185), as shown by positive neuraminidase activity, only 30 (16%) had sufficient HA activity in the presence of 20nM oseltamivir to allow antigenic analysis by HI assay (Table 2).

Since the December report, 25 viruses were able to be analysed by HI assay (Tables 4-1 to 4-4). None of the tested viruses was recognised by the antiserum raised against the currently used vaccine virus, egg-propagated A/Hong Kong/4801/2014, at titres within fourfold of the titre of the antiserum for the homologous virus. However, the antiserum raised against cell culture-propagated A/Hong Kong/5738/2014, a virus closely related genetically to A/Hong Kong/4801/2014, recognised all 25 viruses at titres within fourfold of the homologous titre of the antiserum, 20 within twofold. An antiserum raised against egg-propagated A/Singapore/INFIMH-16-0019/2016, recommended for use in vaccines for the southern hemisphere 2018, recognised 10 of the 25 test viruses at titres within fourfold of the titre of the antiserum for the homologous virus.

Antisera have been raised against two viruses that fall into subclade 3C2a2 (see below), A/Bretagne/1413/2017 and A/Nantes/1441/2017, and were used in experiments shown in Table 4-2 (A/Bretagne/1413/2017 and A/Nantes/1441/2017) and Table 4-3 and Tables 4-4 (A/Bretagne/1413/2017 only). The antiserum raised against A/Bretagne/1413/2017 recognised 13 of the 23 viruses analysed by this antiserum at titres within fourfold of the titre of the antiserum for the homologous virus, 12 within twofold, and the antiserum raised against A/Nantes/1441/2017 recognised three of the four of the test viruses analysed by this antiserum at titres within fourfold of the homologous titre of the antiserum.

Two antisera for which no homologous titres are given, due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, were used in the HI tests. Both A/Norway/4436/2016 and A/Greece/4/2017 had HA genes that fell into genetic subclade 3C2a1, with A/Greece/4/2017 falling into a genetic subgroup 3C2a1a (see below). The antisera raised against A/Norway/4436/2016 and A/Greece/4/2017 recognised, respectively, 20 and 18 of the 25 tested viruses at titres similar to the titres of the antisera for the majority of the panel of reference viruses.

Antisera raised against the cell culture-propagated cultivars of A/Switzerland/9715293/2013 and A/Stockholm/6/2014, both viruses with HA genes in clade 3C.3a, were also used. The antiserum raised against A/Switzerland/9715293/2013 recognised five of the seven viruses tested at titres within fourfold of the titre of the antiserum for the homologous virus and the antiserum raised against A/Stockholm/6/2014 recognised 23 of the 25 test viruses at titres within fourfold of the homologous titre of the antiserum, eight within twofold.

Phylogenetic analysis of the HA genes of representative A(H3N2) viruses from Europe with recent collection dates, after 31 August 2017 as available in GISAID, is shown in Figure 2. Viruses in clades 3C.2a and 3C.3a have been in circulation since the 2013–14 northern hemisphere influenza season, with clade 3C.2a viruses predominating since the 2014–15 influenza season and continuing to predominate in recent months (Figure 2), but the HA gene sequences continue to diverge. New subclades and new genetic subgroups have been adopted. Amino acid substitutions that define these subdivisions and subclades are:

- 3C.2a: **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) and **Q311H** in **HA1**, and **D160N** in **HA2**, e.g. A/Hong Kong/4801/2014;
- 3C2a1: Those in clade 3C.2a plus: **N171K** in **HA1** and **I77V** and **G155E** in **HA2,** most also carry **N121K** in **HA1**, e.g. A/Singapore/INFIMH-16-0019/2016;
- 3C2a1a: Those in subclade 3C2a1 plus **T135K** in **HA1**, resulting in the loss of a potential glycosylation site, and also **G150E** in **HA2**, e.g. A/Greece/4/2017;
- 3C2a1b: Those in subclade 3C2a1 plus **K92R** and **H311K** in **HA1**, e.g. A/England/74560298/2017;
- 3C2a2: Those in clade 3C.2a plus **T131K**, **R142K** and **R261Q** in **HA1**, e.g. A/Norway/4465/2016;
- 3C2a3: Those in clade 3C.2a plus **N121K** and **S144K** in **HA1**, e.g. A/Norway/4849/2016;
- 3C2a4: Those in clade 3C.2a plus **N31S, D53N, R142G, S144R, N171K, I192T, Q197H** and **A304T** in **HA1** and **S113A** in **HA2**, e.g. A/Valladolid/182/2017;
- 3C.3a: **T128A** (resulting in the loss of a potential glycosylation site), **R142G** and **N145S** in **HA1** which

[2] For example, the September 2013 report: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2013. Stockholm: ECDC; 2014. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/influenza-virus-characterisation-sep-2013.pdf

[3] 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

defined clade 3C.3 plus **A138S**, **F159S** and **N225D** in **HA1**, many with **K326R**, e.g. A/Switzerland/9715293/2013.

The currently circulating viruses have HA genes that fall into genetic groups within clade 3C.2a, with the majority of recently circulating viruses in EU/EEA countries falling in subclade 3C2a2; a sizable proportion had HA genes that fell into genetic group 3C2a1b, and some also had HA genes that fell into other genetic subgroups. The location of A/Singapore/INFIMH-16-0019/2016 (3C2a1), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2018 [2] and the northern hemisphere 2018–2019 influenza seasons [3], is indicated in Figure 2.

The test viruses recognised well by the antisera raised against A/Bretagne/1413/2017 and A/Nantes/1441/2017 for which the HA gene sequence is known all belonged to genetic subclade 3C2a2.

Table 4-1/2. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre						
				Post-infection ferret antisera						
				A/Stock	A/Switz	A/HK	A/HK	A/Nor	A/Greece	A/Sing
				6/14	9715293/13	5738/14	4801/14	4436/16	4/17	0019/16
	Passage history			SIAT	SIAT	MDCK	Egg	SIAT	SIAT	Egg 10^{-4}
	Ferret number			F14/14[-1]	F18/15[1]	F30/14[-1]	F42/15[-1]	F03/17[-1]	F27/17[-1]	F41/17[-1]
	Genetic group			3C.3a	3C.3a	3C.2a	3C.2a	3C.2a1	3C.2a1	3C.2a1
REFERENCE VIRUSES										
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	320	160	160	80	320	320	320
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	320	160	80	40	320	160	160
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	320	80	160	160	320	320	640
A/Hong Kong/4801/2014	3C.2a	2014-02-26	E6/E2	160	80	320	1280	320	640	5120
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-06-14	E5/E2	40	40	40	320	160	320	1280
TEST VIRUSES										
A/Slovenia/2269/2017	3C2a1b	2017-10-06	SIATx/SIAT1	160	40	80	40	160	160	160
A/Slovenia/2792/2017	3C2a2	2017-12-29	SIATx/SIAT1	40	40	80	40	160	80	160

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
				A/Stock	A/Switz	A/HK	A/HK	A/Nor	A/Greece	A/Sing	A/Bretagne	A/Nantes
				6/14	9715293/13	5738/14	4801/14	4436/16	4/17	0019/16	1413/17	1441
	Passage history			SIAT	SIAT	MDCK	Egg	SIAT	SIAT	Egg 10^{-4}	SIAT	SIAT
	Ferret number			F14/14[-1]	F18/15[1]	F30/14[-1]	F42/15[-1]	F03/17[-1]	F27/17[-1]	F41/17[-1]	F01/18[-1]	F02/18[-1]
	Genetic group			3C.3a	3C.3a	3C.2a	3C.2a	3C.2a1	3C.2a1	3C.2a1	3C.2a	3C.2a
REFERENCE VIRUSES												
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	320	80	160	80	160	160	160	80	80
A/Switzerland/9715293/2013	3C.3a	2013-12-06	SIAT1/SIAT3	320	80	80	40	160	80	80	80	80
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	160	40	160	80	160	160	80	160	160
A/Hong Kong/4801/2014	3C.2a	2014-02-26	E6/E2	40	40	320	640	160	320	2560	640	320
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-06-14	E5/E2	<	<	40	160	80	160	640	80	80
A/Bretagne/1413/2017	3C.2a	2017-10-09	MDCK1/SIAT4	160	40	160	80	160	160	320	1280	640
A/Nantes/1441/2017	3C.2a	2017-10-10	MDCK2/SIAT3	320	80	160	160	320	160	320	1280	1280
TEST VIRUSES												
A/Croatia/3608/2017	3C2a2	2017-12-12	MDCKx/SIAT2	80	40	80	40	160	160	160	640	320
A/Toulon/2533/2017	3C2a3	2017-12-18	MDCK2/SIAT2	80	ND	40	<	80	160	80	40	ND
A/Iceland/136/2017	3C2a2	2017-12-27	MDCK1/SIAT1	160	40	80	40	160	160	160	640	320
A/Iceland/03/2018	3C2a2	2018-01-02	MDCK1/SIAT1	80	40	80	40	160	80	160	640	640
A/Iceland/08/2018	3C2a2	2018-01-04	MDCK1/SIAT1	80	<	40	<	160	80	80	320	160
							Vaccine NH 2017-18			Vaccine SH 2018		

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) [1] < = <40

Sequences in phylogenetic trees

ND = Not Done

Table 4-3/4. Antigenic analysis of A(H3N2) viruses by HI

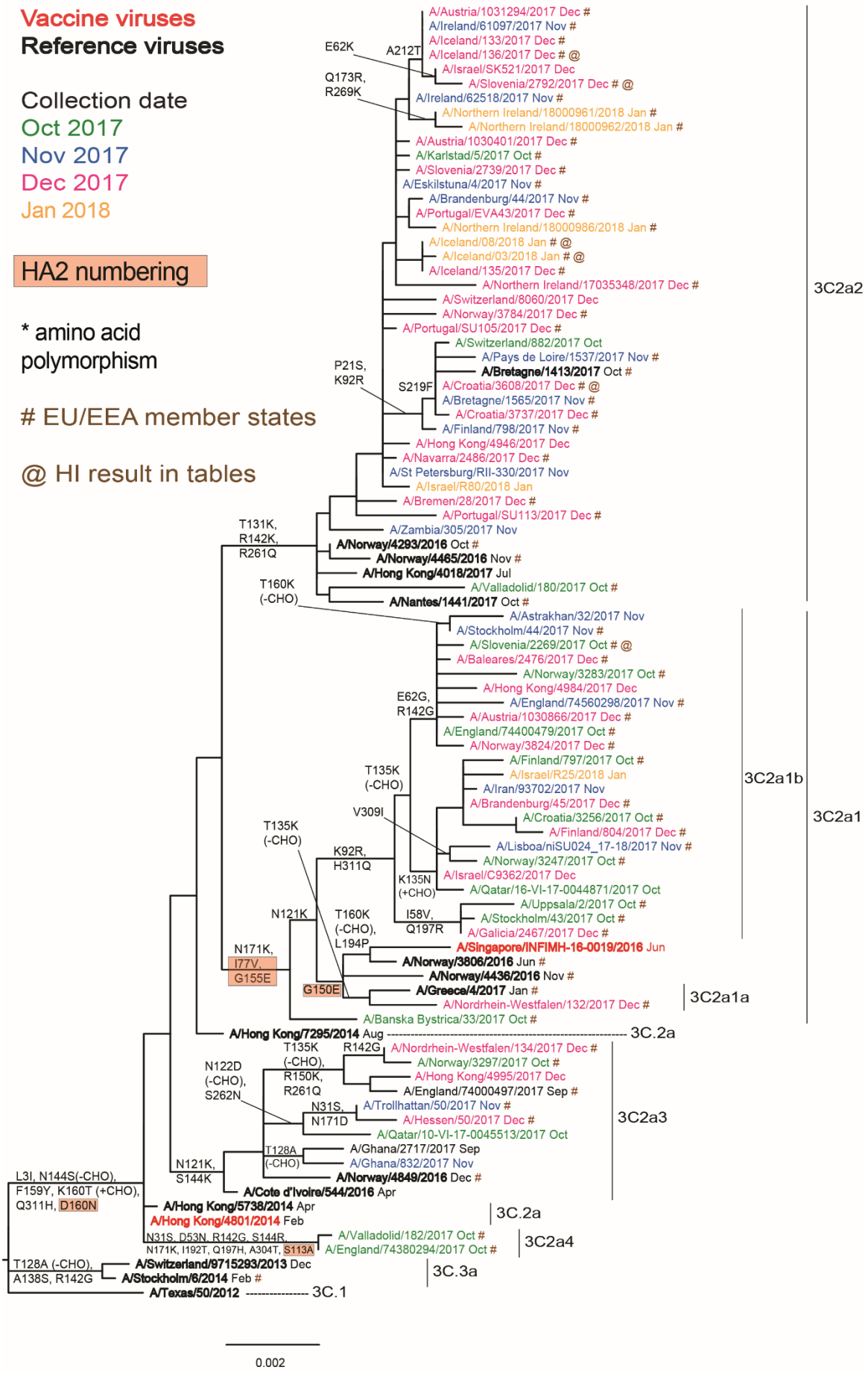
Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
	Passage history			B/Bris 60/08 Egg	B/Mal 2506/04 Egg	B/Bris 60/08 Egg	B/Malta 636714/11 Egg	B/Jhb 3964/12 Egg	B/For V2367/12 MDCK	B/Sth Aus 81/12 Egg	B/HK 514/09 MDCK	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Nor 2409/17 MDCK
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F41/14[*2]	NIB F52/16[*2]	F29/13[*2]	F04/16[*2]	F09/16[*2]	F25/16[*2]	F09/13[*2]	F15/16[*2]	F16/16[*2]	F40/17[*2]
	Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A	1A(Δ2)
REFERENCE VIRUSES														
B/Malaysia/2506/2004		2004-12-06	E3/E6	2560	320	160	160	40	160	160	20	<	<	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	160	640	320	160	320	640	80	40	40	<
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	80	320	320	80	320	320	40	20	40	<
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E2	5120	320	1280	1280	640	1280	1280	160	80	160	<
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	40	320	320	80	320	640	80	80	80	<
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	160	640	320	160	320	640	80	40	40	<
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	5120	10	40	160	160	320	40	160	80	160	<
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	5120	<	20	40	10	80	40	80	160	160	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	2560	<	20	40	40	80	<	80	80	80	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK2	80	<	<	<	<	<	<	<	<	<	80
TEST VIRUSES														
B/Valladolid/185/2017		2017-11-10	MDCK1/MDCK1	40	<	<	10	<	<	<	<	<	<	40
B/Norway/3574/2017	1A	2017-11-23	MDCK1/MDCK1	2560	10	40	80	80	160	40	80	80	160	<
B/England/103/2017	1A(Δ2)	2017-11-23	SIAT2/MDCK1	80	<	<	<	<	<	<	<	<	<	80
B/Spain/106811/2017	1A(Δ2)	2017-11-29	MDCK1	80	10	<	<	<	<	<	<	<	<	80
B/Lithuania/36282/2017	1A	2017-12-17	MDCK1	2560	<	20	80	40	80	40	80	80	160	<
B/Lyon/2452/2017	1A(Δ2)	2017-12-18	MDCK3/MDCK1	80	<	<	<	<	<	<	<	<	<	80
B/Poland/31392/2017	1A(Δ2)	2017-12-18	MDCK2	80	<	<	<	<	<	<	<	<	<	40
B/Poland/7/2018	1A(Δ2)	2018-01-02	MDCK2	80	<	<	<	<	<	<	<	<	<	80
B/Lithuania/1547/2018	1A(Δ2)	2018-01-15	MDCK1	40	<	<	<	<	<	<	<	<	<	80
B/Bayern/4/2018		2018-01-10	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Bayern/14/2018		2018-01-16	C1/MDCK1	80	<	<	<	<	<	10	<	<	<	40
B/Niedersachsen/34/2018		2018-01-25	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Niedersachsen/32/2018		2018-01-25	C1/MDCK1	320	<	<	40	<	10	20	<	<	<	40
B/Niedersachsen/33/2018		2018-01-26	C1/MDCK1	160	<	<	<	<	<	10	<	<	<	40
						Vaccine[#]								Vaccine[$]

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum;

[#] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2017-18 and quadravalent vaccines SH 2018

[$] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2018-19 (like B/Colorado/06/2017)

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



Influenza B virus analyses

A total of 416 influenza type B-positive specimens with collection dates after August 2017 have been received, with 369 being ascribed to a lineage: 43 are B/Victoria-lineage and 326 belong to B/Yamagata (Table 2).

Influenza B – Victoria lineage

HI results for tissue culture-propagated test viruses analysed since the December 2017 report are shown in Tables 5-1 to 5-2. The post-infection ferret antiserum raised against the egg-propagated vaccine virus B/Brisbane/60/2008 recognised none of the test viruses at a titre within fourfold of the titre of the serum for the homologous virus. Post-infection ferret antisera raised against other egg-propagated reference viruses (B/Malaysia/2506/2004, B/Malta/636714/2011, B/Johannesburg/3964/2012 and B/South Australia/81/2012) similarly recognised the test viruses poorly, although the antiserum raised against B/Malta/636714/2011 recognised nine of the 31 test viruses at titres within fourfold of the homologous titre of the antiserum, but only one at a titre within twofold of the homologous titre. Antisera raised against clade 1A viruses propagated in tissue culture B/Formosa/V2367/2012, B/Ireland/3154/2016 and B/Nordrhein-Westfalen/1/2016 recognised nine of the 31 test viruses better but failed to recognise the other 22 test viruses at all well. The same nine test viruses showed reactivity with an antiserum raised against a cell culture-propagated clade 1B virus, B/Hong Kong/514/2009, at titres equal to or within twofold of the homologous titre of the antiserum, but this antiserum also recognised the other 22 test viruses poorly. The 22 test viruses that had been poorly recognised by these antisera were recognised well by an antiserum raised against cell culture-propagated B/Norway/2409/2017 which, in turn, recognised the other nine viruses poorly. B/Norway/2409/2017 is a virus carrying a double amino acid deletion in HA1, Δ(K162, N163) (Table 5). These results show that viruses with the two amino acid deletions in HA1 are antigenically distinct from those without the deletion, and previously we have shown that they are also antigenically distinct from those with a deletion of three amino acids in HA1 [4].

Recently circulating viruses of the B/Victoria lineage continue to have HA genes that fall in the B/Brisbane/60/2008 clade (clade 1A; Figure 3) and fall in a subcluster defined by **HA1** amino acid substitutions **I117V**, **N129D** and **V146I** within clade 1A. Two new groups within this cluster have deletions in the HA gene. A major group seen in Europe and in the Americas have HA genes encoding an HA the deletion of residues 162 and 163 of HA1 (Δ(K162, N163) in Figure 3. These viruses have additional substitutions **D129G, I180V** in **HA1** and **R151K** in **HA2**. Less common are viruses with HA genes encoding a deletion of three amino acids Δ(K162, N163, D164) which have been detected in the Far East, many of which share the substitutions I180T and K209N in HA1.

Influenza B – Yamagata lineage

HI results for 163 B/Yamagata-lineage test viruses analysed since the December 2017 report are shown in Tables 6-1 to 6-6. The 137 viruses collected since week 40/2017 analysed genetically to date belong to genetic clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade.

The antiserum raised against egg-propagated B/Phuket/3073/2013, recommended for inclusion in quadrivalent vaccines for the 2017–18 [1] and 2018–19 [3] northern hemisphere seasons and trivalent vaccines for the southern hemisphere 2018 season [2], recognised 136 (83.4%) test viruses at titres within fourfold of the titre of the antiserum with the homologous virus, and 93 (57.1%) within twofold. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised 153 (93.9%) test viruses at titres within fourfold of the homologous titre of the antiserum and 111 (68.1%) within twofold. An antiserum raised against a former vaccine virus, egg-propagated B/Wisconsin/1/2010 with a homologous titre of 160, recognised all test viruses at titres within fourfold of the homologous titre of the antiserum. Antisera raised against two other egg-propagated clade 3 viruses, B/Stockholm/12/2011 and B/Hong Kong/3417/2014, recognised 148 (90.8%) and 42 (93.3%) test viruses, respectively, at titres within fourfold of the homologous titre, with 89 (54.6%) and 29 (64.4%), respectively, being recognised within twofold. An antiserum raised against a recently circulating clade 3 cell culture-propagated virus, B/Mauritius/1791/2017, recognised 118 (85.5%) test viruses at titres within fourfold of the homologous titre, with 83 (60.1%) being recognised at titres within twofold.

Generally, antisera raised against both egg- and cell culture-propagated clade 2 viruses recognised the test viruses less well (most were recognised at titres at least eightfold reduced compared to the respective homologous titres of the antisera). However, the antisera raised against cell culture-propagated B/Estonia/55669/2011 and B/Massachusetts/02/2012, and egg-propagated B/Massachusetts/02/2012 recognised 42 (25.8%), 72 (44.2%) and 61 (37.4%) test viruses, respectively, at titres within fourfold of the titres of the antisera with the homologous viruses.

Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses, including recently circulating ones. Worldwide, all HA genes from viruses collected in 2017–18 have fallen in clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade. The vast majority of viruses, including those with collection dates after 31 August 2017 from Europe as deposited in GISAID, fall in a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions.

Table 5-1. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera											
				B/Bris 60/08 Egg Sh 539, 540, 543, 544, 570, 571, 574[-1,3]	B/Mal 2506/04 Egg F41/14[-2]	B/Bris 60/08 Egg NIB F52/16[-2]	B/Malta 636714/11 Egg F29/13[-2]	B/Jhb 3964/12 Egg F04/16[-2]	B/For V2367/12 MDCK F09/16[-2]	B/Sth Aus 81/12 Egg F25/16[-2]	B/HK 514/09 MDCK F09/13[-2]	B/Ireland 3154/16 MDCK F15/16[-2]	B/Nord-West 1/16 MDCK F16/16[-2]	B/Nor 2409/17 MDCK F40/17[-2]
Passage history				1A	1A	1A	1A	1A	1A	1A	1B	1A	1A	1A(Δ2)
Ferret number														
Genetic group														
REFERENCE VIRUSES														
B/Malaysia/2506/2004		2004-12-06	E3/E6	2560	640	160	80	40	80	80	20	<	<	<
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	160	640	320	160	320	640	80	40	40	<
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	80	640	320	160	320	320	40	40	40	<
B/Johannesburg/3964/2012	1A	2012-08-03	E1/E3	5120	320	1280	1280	640	640	1280	160	80	80	<
B/Formosa/V2367/2012	1A	2012-08-06	MDCK1/MDCK3	5120	40	320	320	80	320	640	80	80	80	<
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	320	640	320	320	320	640	80	80	40	<
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	20	80	80	40	320	80	80	80	80	<
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	<	40	20	40	80	20	40	80	80	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	1280	<	40	20	20	80	20	40	80	80	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK2	40	<	<	<	<	<	<	<	<	<	40
TEST VIRUSES														
B/Galicia/2407/2017	1A(Δ2)	2017-11-17	MDCK3	80	<	<	<	<	<	<	<	<	<	20
B/Castilla La Mancha/2439/2017	1A(Δ2)	2017-12-04	MDCK1	160	<	<	<	<	<	20	<	10	10	80
B/Spain/107178/2017	1A(Δ2)	2017-12-04	MDCK1	40	<	<	<	<	<	<	<	<	<	40
B/Spain/107764/2017	1A(Δ2)	2017-12-04	MDCK2	40	<	<	<	<	<	<	<	10	10	40
B/Spain/108127/2017	1A(Δ2)	2017-12-07	MDCK1	40	<	<	<	<	<	<	<	<	<	40
B/Slovenia/2654/2017	1A(Δ2)	2017-12-12	SIATx/MDCK1	40	<	<	<	<	<	<	<	<	<	40
B/Valladolid/183/2017	1A(Δ2)	2017-11-13	MDCK1/MDCK1	40	<	<	<	<	<	<	<	<	<	80
B/Lisboa/miSU039_17-18/2017	1A	2017-11-29	MDCK3/MDCK1	2560	80	20	80	40	80	40	40	80	80	<
B/Valladolid/196/2017	1A(Δ2)	2017-12-07	MDCK1/MDCK1	40	<	<	<	<	<	<	<	<	<	80
B/Poland/31396/2017	1A(Δ2)	2017-12-19	MDCK2	40	<	<	<	<	<	<	<	<	<	40
B/Portugal/SU121/2017	1A	2017-12-27	SIAT1/MDCK1	2560	10	20	160	40	80	40	80	80	80	<
B/Slovenia/2786/2017	1A(Δ2)	2017-12-28	MDCK2	80	<	<	10	<	<	<	<	<	<	40
B/Portugal/SU131/2017	1A	2017-12-28	SIAT1/MDCK1	2560	<	20	80	40	80	40	40	80	80	<
B/Portugal/SU130/2017	1A	2017-12-28	SIAT1/MDCK1	2560	10	20	80	40	160	40	80	80	80	<
B/Portugal/SU146/2017	1A	2017-12-29	SIAT1/MDCK1	2560	<	40	80	40	160	40	80	80	80	<
B/Portugal/SU144/2017	1A	2017-12-29	SIAT1/MDCK1	2560	<	40	80	40	160	40	80	80	80	<
B/Portugal/SU138/2017	1A	2017-12-29	SIAT2/MDCK1	2560	<	20	80	40	160	40	80	80	80	<
						Vaccine[#]								Vaccine[$]

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum;
[#] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2017-18 and quadravalent vaccines SH 2018
[$] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2018-19 (like B/Colorado/06/2017)
Sequences in phylogenetic trees

Table 5-2/3. Antigenic analysis of influenza B/Victoria-lineage viruses by HI

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					B/Bris 60/08	B/Mal 2506/04	B/Bris 60/08	B/Malta 636714/11	B/Jhb 3964/12	B/For V2367/12	B/Sth Aus 81/12	B/HK 514/09	B/Ireland 3154/16	B/Nord-West 1/16	B/Nor 2409/17
		Passage history			Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK	MDCK
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F41/14[*2]	NIB F52/16[*2]	F29/13[*2]	F04/16[*2]	F09/16[*2]	F25/16[*2]	F09/13[*2]	F15/16[*2]	F16/16[*2]	F40/17[*2]
		Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A	1A(Δ2)
REFERENCE VIRUSES															
B/Malaysia/2506/2004			2004-12-06	E3/E6	2560	320	160	160	40	160	160	20	<	<	<
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	160	640	320	160	320	640	80	40	40	<
B/Malta/636714/2011		1A	2011-03-07	E4/E1	1280	80	320	320	80	320	320	40	20	40	<
B/Johannesburg/3964/2012		1A	2012-08-03	E1/E2	5120	320	1280	1280	640	1280	1280	160	80	160	<
B/Formosa/V2367/2012		1A	2012-08-06	MDCK1/MDCK3	5120	40	320	320	80	320	640	80	80	80	<
B/South Australia/81/2012		1A	2012-11-28	E4/E2	2560	160	640	320	160	320	640	80	40	40	<
B/Hong Kong/514/2009		1B	2009-10-11	MDCK1/MDCK2	5120	10	40	160	160	320	40	160	80	160	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	5120	<	20	40	10	80	40	80	160	160	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	2560	<	20	40	40	80	<	80	80	80	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK2	80	<	<	<	<	<	<	<	<	<	80
TEST VIRUSES															
B/Norway/3574/2017		1A	2017-11-23	MDCK1/MDCK1	2560	10	40	80	80	160	40	80	80	160	<
B/England/103/2017		1A(Δ2)	2017-11-23	SIAT2/MDCK1	80	<	<	<	<	<	<	<	<	<	80
B/Spain/106811/2017		1A(Δ2)	2017-11-29	MDCK1	80	10	<	<	<	<	<	<	<	<	80
B/Lithuania/36282/2017		1A	2017-12-17	MDCK1	2560	<	20	80	40	80	40	80	80	160	<
B/Lyon/2452/2017		1A(Δ2)	2017-12-18	MDCK3/MDCK1	80	<	<	<	<	<	<	<	<	<	80
B/Poland/31392/2017		1A(Δ2)	2017-12-18	MDCK2	80	<	<	<	<	<	<	<	<	<	40
B/Poland/7/2018		1A(Δ2)	2018-01-02	MDCK2	80	<	<	<	<	<	<	<	<	<	80
B/Lithuania/1547/2018		1A(Δ2)	2018-01-15	MDCK1	40	<	<	<	<	<	<	<	<	<	80

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					B/Bris 60/08	B/Mal 2506/04	B/Bris 60/08	B/Malta 636714/11	B/Jhb 3964/12	B/For V2367/12	B/Sth Aus 81/12	B/HK 514/09	B/Ireland 3154/16	B/Nord-West 1/16	B/Nor 2409/17
		Passage history			Egg	Egg	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK	MDCK	MDCK
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F41/14[*2]	NIB F52/16[*2]	F29/13[*2]	F04/16[*4]	F09/16[*2]	F25/16[*2]	F09/13[*2]	F15/16[*2]	F16/16[*2]	F40/17[*2]
		Genetic group			1A		1A	1A	1A	1A	1A	1B	1A	1A	1A(Δ2)
REFERENCE VIRUSES															
B/Malaysia/2506/2004			2004-12-06	E3/E6	2560	320	160	160	40	80	80	10	<	<	<
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	160	320	320	160	160	320	80	40	40	<
B/Malta/636714/2011		1A	2011-03-07	E4/E1	1280	80	320	320	160	160	320	40	20	40	<
B/Johannesburg/3964/2012		1A	2012-08-03	E1/E2	5120	320	1280	1280	640	640	1280	160	80	160	40
B/Formosa/V2367/2012		1A	2012-08-06	MDCK1/MDCK3	5120	80	320	320	80	320	320	80	80	80	<
B/South Australia/81/2012		1A	2012-11-28	E4/E2	2560	160	640	320	160	320	640	80	40	40	<
B/Hong Kong/514/2009		1B	2009-10-11	MDCK1/MDCK2	2560	20	80	160	40	320	40	80	80	160	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	2560	<	20	80	20	160	40	80	80	160	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	1280	<	20	40	20	160	20	40	80	80	<
B/Norway/2409/2017		1A(Δ2)		MDCK1/MDCK2	40	<	<	<	<	<	<	<	<	<	40
TEST VIRUSES															
B/Valladolid/185/2017			2017-11-10	MDCK1/MDCK1	40	<	<	10	<	<	<	<	<	<	40
B/Bayern/4/2018			2018-01-10	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Bayern/14/2018			2018-01-16	C1/MDCK1	80	<	<	<	<	<	10	<	<	<	40
B/Niedersachsen/34/2018			2018-01-25	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Niedersachsen/32/2018			2018-01-25	C1/MDCK1	320	<	<	40	<	10	20	<	<	<	40
B/Niedersachsen/33/2018			2018-01-26	C1/MDCK1	160	<	<	<	<	<	10	<	<	<	40

Vaccine[#] Vaccine[$]

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20

[#] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2017-18 and quadravalent vaccines SH 2018

[$] B/Victoria-lineage virus recommended for use in trivalent vaccines NH 2018-19 (like B/Colorado/06/2017)

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

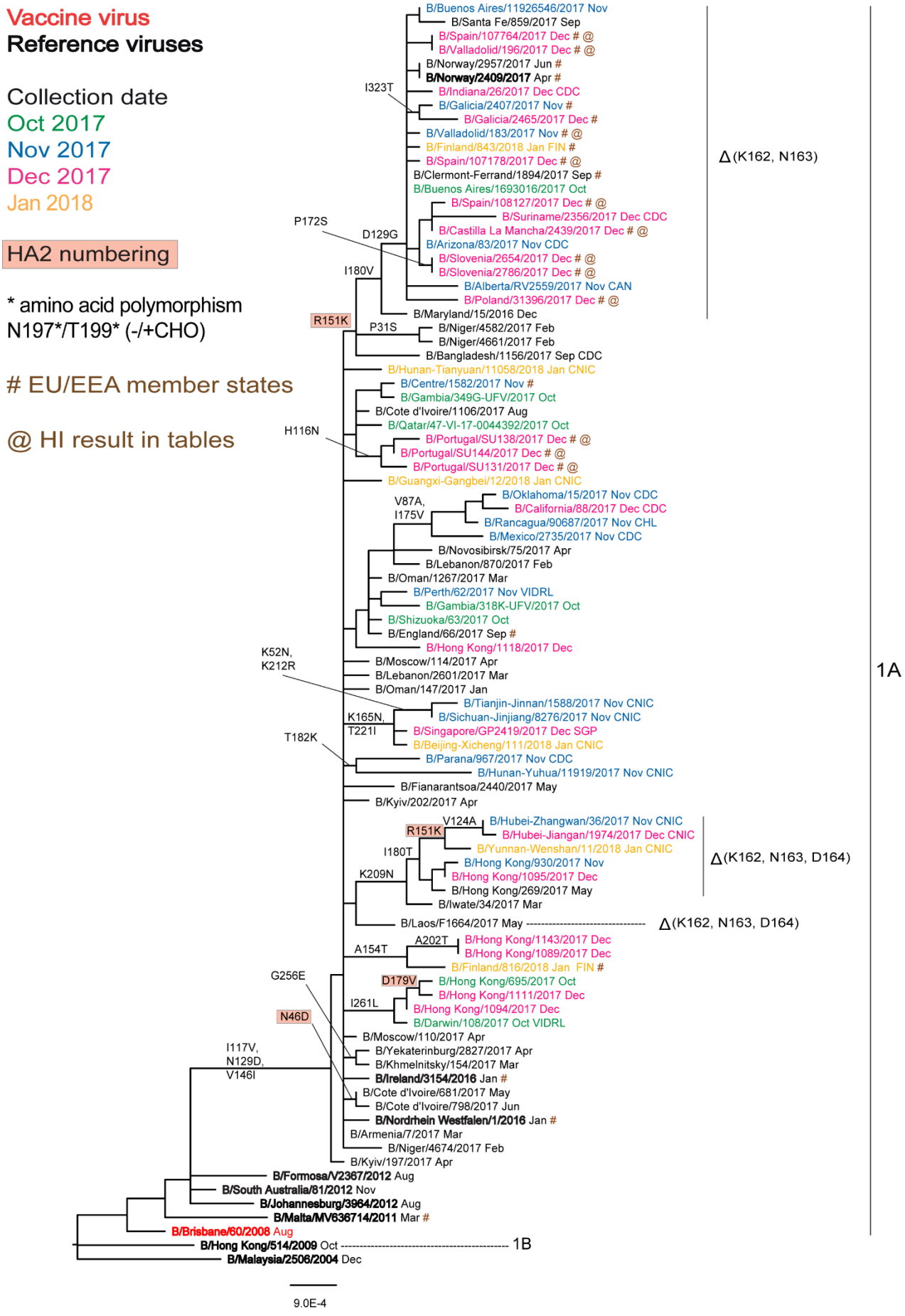


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
		Passage history			B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg	B/HK 3417/14 Egg
		Ferret number			SH614*1,3	F38/14*2	F27/13*2	F05/15*2	F16/14*2	F36/15*2	F06/15*2	F27/15*2	NIB F51/16*2	St Judes F716/14*2
		Genetic Group			3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	1280	320	160	1280	320	320	40	1280	320
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	1280	160	640	320	80	80	20	40	40	10
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	640	640	320	640	160	80	40	640	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	2560	640	160	80	1280	160	160	20	640	160
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	320	40	20	320	160	80	40	320	80
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	160	40	10	160	80	80	20	160	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	80	160	80	80	80	40	80	80	80
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	160	40	10	160	160	80	40	320	80
B/Hong Kong/3417/2014		3	2014-06-04	E4/E3	2560	80	40	20	80	80	40	20	160	160
TEST VIRUSES														
B/Rheinland-Pfalz/4/2017		3	2017-09-29	C1/MDCK1	2560	160	160	160	160	160	40	160	160	80
B/Finland/811/2017		3	2017-11-20	MDCK1	2560	160	160	80	80	160	80	160	320	160
B/Nordrhein-Westfalen/15/2017		3	2017-11-21	C1/MDCK1	2560	80	80	40	80	80	40	80	160	20
B/Niedersachsen/54/2017		3	2017-11-27	C2/MDCK1	2560	80	80	40	80	80	40	40	160	80
B/Slovenia/2558/2017		3	2017-11-30	SIATx/MDCK1	5120	160	160	320	160	160	80	160	320	80
B/Norway/3817/2017		3	2017-12-08	MDCK1	5120	160	80	80	80	160	40	80	320	160
B/Castilla La Mancha/2485/2017		3	2017-12-09	MDCK1	2560	160	80	80	80	80	40	80	160	160
B/Navarra/2487/2017		3	2017-12-11	MDCK1	5120	80	80	80	80	160	40	80	160	160
B/Bayern/25/2017		3	2017-12-11	C1/MDCK1	5120	320	160	160	160	320	80	160	320	160
B/Navarra/2489/2017		3	2017-12-12	MDCK1	2560	80	80	40	80	80	40	80	160	80
B/Austria/1028919/2017		3	2017-12-13	SIAT1/MDCK1	5120	320	160	160	160	320	80	160	320	160
B/Sachsen-Anhalt/8/2017		3	2017-12-14	C2/MDCK1	2560	80	80	80	80	160	40	80	160	80
B/Bayern/26/2017		3	2017-12-15	C1/MDCK1	2560	80	80	80	80	80	40	80	80	80
B/Austria/1029615/2017		3	2017-12-15	SIAT1/MDCK1	5120	320	320	1280	320	640	160	320	640	320
B/Slovenia/2678/2017		3	2017-12-15	SIATx/MDCK1	5120	160	160	320	160	320	80	160	320	80
B/Austria/1029652/2017		3	2017-12-16	SIAT2/MDCK1	5120	320	320	640	320	320	160	320	640	320
B/Hessen/3/2017		3	2017-12-18	C1/MDCK1	2560	80	80	80	80	80	40	80	80	160
B/Austria/1029753/2017		3	2017-12-18	SIAT1/MDCK1	5120	160	80	80	80	80	40	80	320	40
B/Austria/1029757/2017		3	2017-12-18	SIAT2/MDCK1	2560	80	80	80	80	80	40	80	160	40
B/Austria/1029921/2017		3	2017-12-18	SIAT1/MDCK1	5120	160	160	80	80	160	80	80	320	80
B/Baden-Wurttemberg/11/2017		3	2017-12-21	C1/MDCK1	2560	80	80	40	80	80	40	80	80	10
B/Niedersachsen/55/2017		3	2017-12-21	C1/MDCK1	5120	80	80	40	80	80	40	80	80	40
B/Sachsen/12/2017		3	2017-12-21	C1/MDCK1	2560	160	80	40	80	160	40	80	160	80
B/Slovenia/2799/2017		3	2017-12-29	SIATx/MDCK1	1280	40	40	20	40	40	20	40	40	20
B/Slovenia/34/2018		3	2018-01-04	SIATx/MDCK1	5120	160	320	640	320	320	160	320	320	160
													Vaccine#	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
1 < = <40; 2 < = <10; 3 hyperimmune sheep serum

B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg	B/HK 3417/14 Egg	B/Maur 1791/17 MDCK
		Ferret number			SH614[*1,3]	F38/14[*2]	F27/13[*2]	F05/15[*2]	F16/14[*2]	F36/15[*2]	F06/15[*2]	F27/15[*2]	NIB F51/16[*2]	St Judes F716/14[*4]	F04/18[*1]
		Genetic Group			3	2	2	2	2	3	3	3	3	3	3
REFERENCE VIRUSES															
B/Brisbane/3/2007		2	2007-09-03	E2/E2		640	160	80	1280	160	160	20	640	80	<
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	2560	160	1280	640	160	160	40	160	160	<	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	320	640	320	160	160	320	160	160
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	1280	640	160	80	1280	160	160	40	640	80	<
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	160	40	20	320	160	80	40	320	40	20
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	80	20	10	160	80	80	40	160	20	20
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	80	80	80	80	80	40	160	80	20	160
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	160	20	10	320	80	80	40	320	40	20
B/Hong Kong/3417/2014		3	2014-06-04	E4/E3	1280	80	20	<	80	40	20	10	40	40	20
B/Mauritius/1791/2017		3		MDCK1/C2/MDCK2	5120	160	80	80	160	80	40	160	160	40	320
TEST VIRUSES															
B/Ireland/56404/2017		3	2017-10-24	C2/MDCK1	1280	20	40	20	40	40	10	80	20	<	80
B/Croatia/3314/2017		3	2017-11-15	MDCKx/MDCK2	2560	80	160	160	160	160	80	320	160	80	320
B/Ireland/61801/2017		3	2017-11-16	C2/MDCK2	1280	40	40	20	40	40	20	80	40	<	80
B/Croatia/3341/2017		3	2017-11-21	MDCKx/MDCK1	1280	40	40	20	80	40	20	40	40	<	<
B/Croatia/3350/2017		3	2017-11-22	MDCKx/MDCK1	1280	40	40	20	40	40	20	40	40	<	<
B/Croatia/3393/2017		3	2017-11-29	MDCKx/MDCK1	1280	40	40	20	40	40	20	40	40	<	<
B/Trencin/62/2017		3	2017-12-18	MDCK1/MDCK1	1280	40	40	20	80	40	20	80	40	20	80
B/Trencin/66/2017		3	2017-12-21	MDCK2/MDCK1	1280	40	40	20	80	40	20	80	40	20	80
B/Trencin/68/2017		3	2017-12-27	MDCK1/MDCK1	2560	40	40	20	40	40	20	80	40	<	80
B/Paris/2001/2017		3	2017-12-27	MDCK1/MDCK1	1280	40	40	20	40	40	20	40	40	<	80
B/Alsace/1989/2017		3	2017-12-28	MDCK1/MDCK1	1280	40	40	20	80	40	20	80	80	20	80
B/Portugal/EVA63/2018		3	2018-01-03	SIAT1/MDCK1	2560	40	80	40	80	40	20	160	80	20	160
B/Portugal/EVA61/2018		3	2018-01-03	SIAT1/MDCK1	2560	40	80	40	80	40	20	160	80	20	160
B/Iceland/05/2018		3	2018-01-03	MDCK1/MDCK1	2560	80	80	80	160	160	80	160	160	80	320
B/Paris/013/2018		3	2018-01-03	MDCK1/MDCK1	1280	40	40	20	40	40	20	40	40	<	80
B/Iceland/06/2018		3	2018-01-04	MDCK1/MDCK1	2560	80	80	40	80	80	40	160	80	20	160
B/Iceland/13/2018		3	2018-01-05	MDCK1/MDCK1	2560	160	80	40	160	80	40	160	160	20	320
B/Bulgaria/048/2018		3	2018-01-08	MDCK1	1280	40	40	20	40	40	20	40	40	20	<
B/Hungary/10/2018		3	2018-01-08	MDCK1/MDCK1	1280	40	40	20	40	40	20	80	40	<	80
B/Hungary/7/2018		3	2018-01-09	MDCK1/MDCK1	1280	40	40	20	40	40	20	80	40	<	80
													Vaccine[#]		

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
1 < = <40; 2 < = <10; 3 hyperimmune sheep serum; 4 < = <20

[#] B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
	Passage history			B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg	B/Phuket 3073/13 NIB	B/Maur 1791/17 MDCK
	Ferret number			SH614[*1,3]	F38/14[*2]	F27/13[*2]	F05/15[*2]	F16/14[*2]	F36/15[*2]	F06/15[*2]	F27/15[*2]	F51/16[*2]		F04/18[*1]
	Genetic Group			3	2	2	2	2	3	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007	2	2007-09-03	E2/E2	2560	640	160	160	1280	320	160	40	640		<
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	2560	160	640	1280	320	320	40	160	80		160
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	320	640	320	80	80	320		<
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	1280	640	160	160	1280	160	160	40	320		<
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	320	40	40	640	160	80	80	320		80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	2560	160	40	20	320	160	160	40	160		<
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	5120	80	160	160	160	160	40	160	80		160
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	40	20	320	160	80	40	160		<
B/Mauritius/1791/2017	3	2017-10-13	MDCK1/C2/MDCK2	5120	160	160	160	320	160	80	160	320		320
TEST VIRUSES														
B/Czech Republic/28/2018	3	2017-12-02	MDCK1/MDCK1	1280	40	80	40	80	80	20	80	40		80
B/Lyon/2319/2017	3	2017-12-05	MDCK2/MDCK1	2560	80	80	40	80	80	40	80	80		160
B/Grenoble/2382/2017	3	2017-12-07	MDCK2/MDCK1	1280	40	80	20	80	80	20	80	40		80
B/Lyon/2369/2017	3	2017-12-11	MDCK2/MDCK1	2560	40	80	40	80	80	20	80	80		80
B/Denmark/11/2017	3	2017-12-13	SIAT3/MDCK1	2560	80	160	80	80	80	40	160	80		320
B/Lithuania/36447/2017	3	2017-12-18	MDCK2/MDCK1	1280	20	40	40	40	40	20	160	40		80
B/Lithuania/36278/2017	3	2017-12-19	MDCK2/MDCK1	5120	160	160	160	160	160	40	160	160		320
B/Denmark/21/2017	3	2017-12-19	SIAT3/MDCK1	5120	80	160	160	160	160	40	160	160		320
B/Iasi/221737/2017	3	2017-12-20	MDCK1/MDCK1	2560	80	80	80	80	80	20	160	80		160
B/Denmark/23/2017	3	2017-12-20	SIAT3/MDCK1	2560	40	80	40	80	80	20	80	80		160
B/Denmark/45/2017	3	2017-12-24	SIAT3/MDCK1	5120	80	160	160	160	160	40	160	160		320
B/Belgium/G0013/2018	3	2017-12-29	MDCK1/MDCK1	2560	40	80	40	80	80	20	80	80		80
B/Belgium/G0012/2018	3	2017-12-29	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80		80
B/Parma/26/2017	3	2017-12-29	MDCK2/MDCK1	2560	80	80	80	160	160	80	160	160		320
B/Belgium/G0019/2018	3	2018-01-02	MDCK1/MDCK1	2560	40	80	40	80	80	20	80	80		160
B/Estonia/111255/2018	3	2018-01-03	MDCK1/MDCK1	1280	40	40	20	40	80	20	40	40		80
B/Padova/3/2018	3	2018-01-03	MDCK2/MDCK1	2560	80	80	80	160	80	40	80	80		160
B/Netherlands/10011/2018	3	2018-01-04	(MDCK/SIAT)1/MDCK1	5120	160	160	320	160	160	40	320	80		320
B/Padova/2/2018	3	2018-01-04	MDCK2/MDCK1	5120	320	320	640	320	640	160	320	320		640
B/Estonia/111203/2018	3	2018-01-05	MDCK1/MDCK1	2560	40	80	40	80	80	20	80	80		80
B/Olt/222073/2018	3	2018-01-08	MDCK1/MDCK1	2560	80	80	40	80	80	20	160	80		80
B/Estonia/111442/2018	3	2018-01-12	SIAT1/MDCK1	1280	40	80	40	80	80	20	80	40		80
B/Athens.GR/132/2018	3	2018-01-16	MDCK1	1280	40	80	40	80	80	20	80	80		80
B/Athens.GR/131/2018	3	2018-01-16	MDCK1	1280	80	80	40	80	80	20	80	80		80
													Vaccine[#]	

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

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

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg	B/Maur 1791/17 MDCK
		Ferret number			SH614*1,3	F38/14*2	F27/13*2	F05/15*2	F16/14*2	F36/15*2	F06/15*2	F27/15*2	NIB F51/16*2	F04/18*1
		Genetic Group			3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	1280	320	160	1280	320	160	80	640	<
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	2560	320	640	640	160	160	40	160	80	320
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	640	320	320	640	160	80	80	320	<
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	640	160	80	640	160	80	40	320	<
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	320	40	20	320	160	80	40	320	80
B/Stockholm/12/2011		3	2011-03-28	Ex/E2	1280	160	40	10	160	80	80	40	160	<
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	160	160	80	320	160	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	160	40	20	160	160	80	40	320	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/C2/MDCK2	5120	160	160	160	160	160	40	160	160	320
TEST VIRUSES														
B/Hungary/824/2017		3		MDCK1/MDCK1	5120	320	160	80	320	320	160	320	320	640
B/Catalonia/10082S/2017		3	2017-11-22	C0/MDCK1	5120	320	160	160	320	320	80	320	320	640
B/Lyon/2239/2017		3	2017-11-25	MDCK2/MDCK1	2560	160	160	40	160	160	40	80	160	160
B/Catalonia/2229675NS/2017		3	2017-11-25	C0/MDCK1	5120	160	160	80	160	160	40	160	160	320
B/Hungary/825/2017		3	2017-11-27	MDCK1/MDCK1	5120	320	160	160	320	320	80	320	320	320
B/Toulouse/2224/2017		3	2017-11-28	MDCK2/MDCK1	2560	80	80	20	80	80	40	80	80	80
B/Norway/3632/2017		3	2017-11-30	MDCK1/MDCK1	5120	320	320	640	320	640	160	320	320	640
B/Catalonia/2233004NS/2017		3	2017-12-06	C0/MDCK1	2560	160	80	40	160	160	40	80	160	160
B/Hungary/826/2017		3	2017-12-14	MDCK1/MDCK1	5120	320	320	320	320	320	160	320	320	640
B/Catalonia/3517603NS/2017		3	2017-12-14	C0/MDCK1	2560	80	80	40	80	80	20	80	80	160
B/Hungary/828/2017		3	2017-12-18	MDCK1/MDCK1	5120	160	160	160	160	160	40	160	160	320
B/Hungary/827/2017		3	2017-12-20	MDCK1/MDCK1	5120	160	160	160	160	160	80	320	320	320
B/England/158/2017		3	2017-12-20	SIAT1/MDCK1	2560	160	80	40	160	160	40	80	160	160
B/England/151/2017		3	2017-12-20	SIAT2/MDCK1	2560	80	160	80	160	80	40	160	80	320
B/Hungary/3/2018		3	2017-12-21	MDCK1/MDCK1	2560	80	80	40	160	80	40	80	80	160
B/Norway/4039/2017		3	2017-12-26	MDCK1/MDCK1	5120	320	320	320	320	320	160	320	320	640
B/Hungary/1/2018		3	2017-12-27	MDCK1/MDCK1	2560	160	160	80	160	160	40	160	160	320
B/England/179/2017		3	2017-12-27	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/England/174/2017		3	2017-12-27	MDCK1/MDCK1	2560	160	160	80	160	160	40	160	160	320
B/Netherlands/04136/2017		3	2017-12-27	SIAT1/MDCK1	2560	160	160	80	160	160	40	160	160	320
B/Netherlands/04135/2017		3	2017-12-27	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Norway/4155/2017		3	2017-12-27	MDCK1/MDCK1	5120	320	320	640	320	320	160	320	320	640
B/England/166/2017		3	2017-12-29	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/England/165/2017		3	2017-12-29	MDCK1/MDCK1	2560	160	160	80	160	160	40	80	80	160
B/Hungary/9/2018		3	2018-01-02	MDCK1/MDCK1	2560	160	160	80	160	160	40	160	160	320
B/Hungary/8/2018		3	2018-01-03	MDCK1/MDCK1	2560	80	80	40	80	80	40	80	80	160
													Vaccine#	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

Table 6-5. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
		Passage history			B/Phuket 3073/13 Egg	B/Bris 3/07 Egg	B/Estonia 55669/11 MDCK	B/Mass 02/12 MDCK	B/Mass 02/12 Egg	B/Wis 1/10 Egg	B/Stock 12/11 Egg	B/Phuket 3073/13 MDCK	B/Phuket 3073/13 Egg NIB F51/16*[2]	B/Maur 1791/17 MDCK
		Ferret number			SH614[*1,3]	F38/14[*2]	F27/13[*2]	F05/15[*2]	F16/14[*2]	F36/15[*2]	F06/15[*2]	F27/15[*2]		F04/18[*1]
		Genetic Group			3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	1280	160	320	1280	320	320	160	640	20
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	5120	160	640	640	320	320	80	320	160	320
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	320	640	320	160	160	640	80
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	320	80	40	640	80	80	40	320	<
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	320	40	20	640	160	160	80	640	80
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	160	40	10	320	80	80	40	160	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	320	320	160	320	320	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	80	40	10	160	80	40	40	320	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK3	5120	320	320	320	320	320	160	320	320	640
TEST VIRUSES														
B/Navarra/2279/2017			2017-10-28	MDCK1	1280	80	80	40	160	80	20	160	80	160
B/Norway/3438/2017			2017-11-03	MDCK1	1280	160	160	80	320	320	40	320	320	320
B/Norway/3482/2017			2017-11-15	MDCK2	1280	80	80	40	160	80	20	80	160	160
B/Norway/3510/2017			2017-11-15	MDCK2	1280	80	80	40	160	160	40	320	320	320
B/Pais Vasco/2384/2017			2017-11-20	SIAT1/MDCK1	2560	80	160	80	160	160	20	320	160	320
B/Valladolid/184/2017			2017-11-21	MDCK1/MDCK1	1280	40	40	20	80	40	20	80	40	80
B/Valladolid/186/2017			2017-11-22	MDCK1/MDCK1	2560	80	40	20	80	80	20	80	80	160
B/Norway/3557/2017			2017-11-23	MDCK1MDCK1	1280	80	80	20	80	80	20	80	160	160
B/Melilla/2412/2017			2017-11-28	MDCK1	2560	80	80	40	160	80	20	160	160	320
B/Valladolid/188/2017			2017-11-29	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Valladolid/189/2017			2017-11-29	MDCK1/MDCK1	1280	80	40	20	80	80	20	40	80	160
B/Melilla/2452/2017			2017-12-04	MDCK1	1280	80	80	20	160	80	20	160	80	160
B/Valladolid/193/2017			2017-12-04	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Leon/194/2017			2017-12-04	MDCK1/MDCK1	1280	80	40	20	80	40	20	40	40	80
B/Norway/3752/2017			2017-12-06	MDCK2	2560	80	80	40	160	160	20	160	320	160
B/Iceland/129/2017			2017-12-13	MDCK1/MDCK1	1280	80	40	20	80	40	20	80	40	80
B/Iceland/132/2017			2017-12-18	MDCK1/MDCK1	5120	160	80	80	160	160	80	160	160	320
B/Haute Normandie/1878/2017			2017-12-19	MDCK1/MDCK1	1280	40	40	20	40	40	20	40	40	80
B/Dijon/053/2018			2017-12-22	MDCK1/MDCK1	1280	40	40	20	80	80	20	80	80	80
B/Bretagne/1991/2017			2017-12-26	MDCK1/MDCK1	2560	80	80	80	160	80	40	160	80	320
B/Picardie/1963/2017			2017-12-27	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Paris/1961/2017			2017-12-27	MDCK1/MDCK1	2560	80	40	20	80	80	20	80	80	80
B/Iceland/138/2017			2017-12-28	MDCK1/MDCK1	2560	160	80	40	160	80	40	80	160	160
B/Iceland/142/2017			2017-12-30	MDCK1/MDCK1	2560	160	160	320	160	160	80	320	160	320
B/Iceland/141/2017			2017-12-30	MDCK1/MDCK1	2560	80	80	40	160	80	20	80	80	160
B/Iceland/144/2017			2017-12-31	MDCK1/MDCK1	1280	80	80	20	80	40	20	80	80	80
B/Iceland/04/2018			2018-01-03	MDCK1/MDCK1	2560	160	160	320	160	160	40	160	160	160
B/Nordrhein-Westfalen/28/2018			2018-01-22	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Berlin/8/2018			2018-01-24	C1/MDCK1	1280	40	40	20	80	40	20	80	40	80
B/Rheinland-Pfalz/15/2018			2018-01-29	C1/MDCK1	2560	80	80	40	80	80	20	80	80	80
B/Niedersachsen/39/2018			2018-01-29	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Saarland/3/2018			2018-01-29	C1/MDCK1	1280	40	40	20	80	80	20	40	40	80
B/Bayern/29/2018			2018-01-29	C1/MDCK1	1280	40	80	40	80	80	20	80	40	160
B/Hessen/12/2018			2018-01-30	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80
													Vaccine[#]	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

[#] B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

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

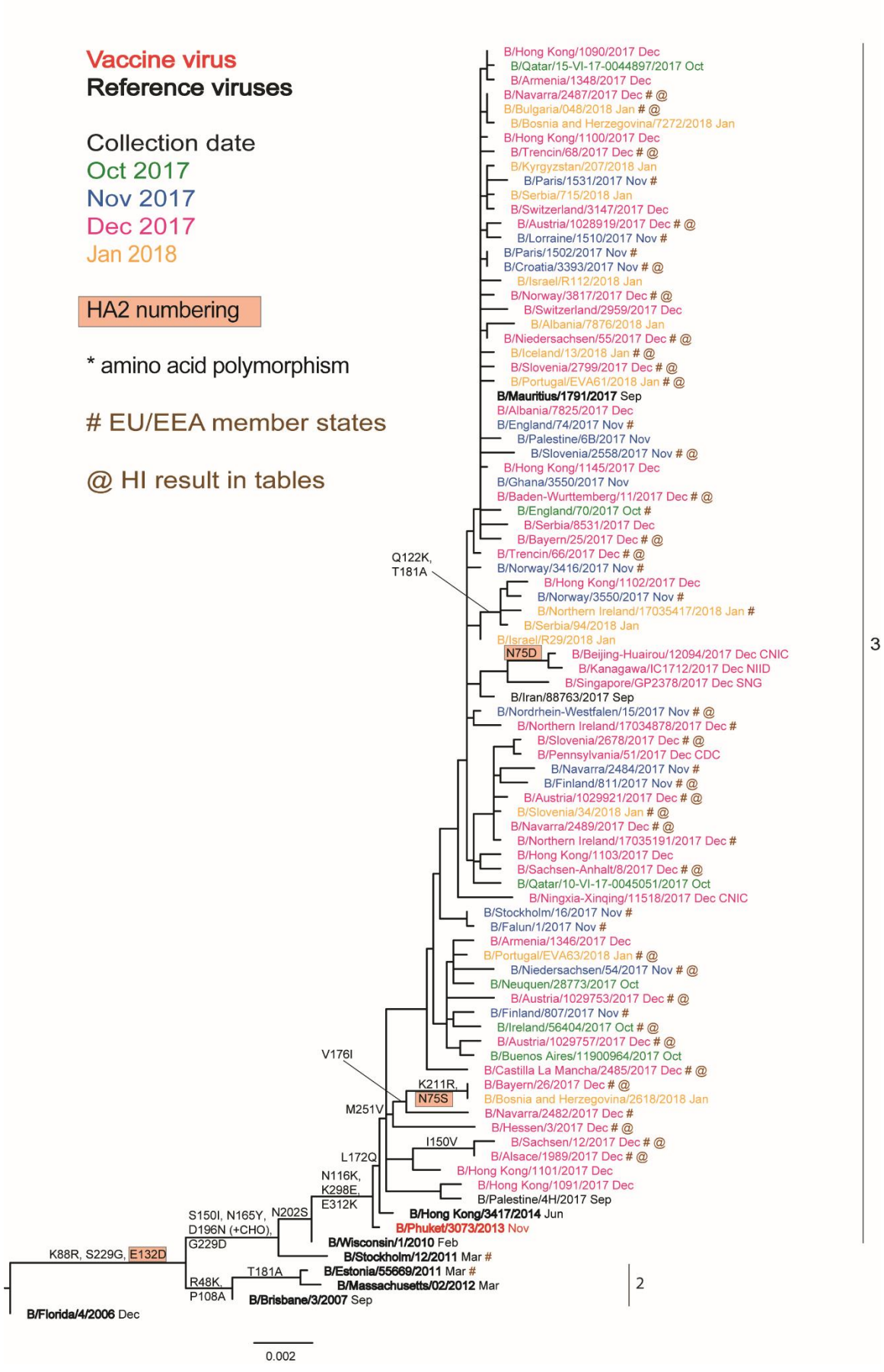
Viruses	Other information	Passage history / Ferret number / Genetic Group	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					B/Phuket 3073/13 Egg SH614*1,3	B/Bris 3/07 Egg F38/14*2	B/Estonia 55669/11 MDCK F27/13*2	B/Mass 02/12 MDCK F05/15*2	B/Mass 02/12 Egg F16/14*2	B/Wis 1/10 Egg F36/15*2	B/Stock 12/11 Egg F06/15*2	B/Phuket 3073/13 MDCK F27/15*2	B/Phuket 3073/13 Egg NIB F51/16*2	B/Maur 1791/17 MDCK F04/18*1
		3			3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES														
B/Brisbane/3/2007		2	2007-09-03	E2/E2	2560	1280	320	160	1280	320	640	80	640	<
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	2560	160	1280	640	160	160	80	320	80	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	320	640	320	640	160	160	80	320	<
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	320	160	80	640	80	160	40	160	<
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	320	40	20	320	160	160	80	320	80
B/Stockholm/12/2011		3	2011-03-28	E4/E1	2560	160	40	10	160	80	160	40	160	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	160	160	80	320	160	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	2560	160	40	20	320	160	80	40	320	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK3	5120	320	320	320	320	320	320	320	320	320
TEST VIRUSES														
B/Lisboa/niRL006 17-18/2017			2017-11-16	MDCK2/MDCK1	5120	160	160	80	160	160	80	160	160	320
B/Lisboa/niMS017 17-18/2017			2017-11-23	SIAT2/MDCK1	2560	80	80	40	80	80	80	80	80	160
B/Spain/106384/2017			2017-11-27	MDCK1	2560	80	40	20	80	80	40	80	80	160
B/Austria/1027579/2017			2017-12-05	SIAT2/MDCK1	5120	320	320	640	320	320	160	320	320	320
B/Portugal/GG4/2017			2017-12-05	MDCK2/MDCK1	2560	80	80	40	80	160	80	80	80	160
B/Portugal/SU48/2017			2017-12-06	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Austria/1028491/2017			2017-12-07	SIAT1/MDCK1	2560	160	80	160	320	320	160	160	320	320
B/Austria/1028735/2017			2017-12-11	SIAT1/MDCK1	5120	320	320	320	320	640	160	320	320	320
B/Austria/1028736/2017			2017-12-12	SIAT1/MDCK1	5120	320	320	640	320	640	160	320	320	640
B/Austria/1028826/2017			2017-12-12	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Austria/1029093/2017			2017-12-12	SIAT1/MDCK1	5120	320	160	320	320	320	160	320	320	320
B/Portugal/SU59/2017			2017-12-12	SIAT1/MDCK2	2560	80	160	80	160	160	80	160	160	320
B/Portugal/SU70/2017			2017-12-13	SIAT1/MDCK1	2560	80	80	40	80	80	80	80	80	160
B/Portugal/SU73/2017			2017-12-15	MDCK2/MDCK1	5120	160	160	160	160	160	160	320	160	320
B/Portugal/SU71/2017			2017-12-15	MDCK2/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Paris/1823/2017			2017-12-18	MDCK1/MDCK1	2560	80	40	40	80	80	40	80	80	80
B/Portugal/MS26/2017			2017-12-19	SIAT1/MDCK1	2560	160	160	160	160	320	160	160	160	320
B/Portugal/SU90/2017			2017-12-19	SIAT1/MDCK1	2560	160	160	80	160	160	80	160	160	320
B/Paris/1837/2017			2017-12-19	MDCK1/MDCK1	2560	80	80	40	80	80	80	80	80	160
B/Portugal/SU98/2017			2017-12-21	SIAT1/MDCK1	5120	160	160	160	160	160	160	160	160	320
B/Portugal/MS27/2017			2017-12-21	SIAT1/MDCK1	2560	160	160	80	160	160	80	160	160	320
B/Portugal/SU110/2017			2017-12-22	SIAT1/MDCK1	2560	80	80	40	160	160	80	160	160	160
B/Portugal/SU120/2017			2017-12-27	SIAT1/MDCK1	2560	160	80	80	160	160	80	160	160	320
B/Portugal/SU119/2017			2017-12-27	SIAT1/MDCK1	5120	160	320	320	320	320	160	320	320	320
B/Portugal/SU134/2017			2017-12-28	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Portugal/SU127/2017			2017-12-28	SIAT1/MDCK2	2560	80	80	80	80	80	40	160	80	160
B/Portugal/EVA46/2017			2017-12-29	SIAT1/MDCK1	5120	160	160	80	160	320	160	320	320	320
B/Portugal/EVA45/2017			2017-12-29	SIAT1/MDCK1	2560	80	80	40	160	80	80	80	160	160
B/Portugal/EVA44/2017			2017-12-29	SIAT1/MDCK1	5120	160	160	160	320	320	160	320	320	320
B/Portugal/MS31/2017			2017-12-29	SIAT1/MDCK1	2560	80	80	80	160	160	80	160	160	320
B/Portugal/EVA58/2018			2018-01-02	SIAT1/MDCK1	2560	160	80	40	160	160	80	160	160	160
B/Portugal/EVA57/2018			2018-01-02	SIAT1/MDCK1	5120	320	320	320	320	320	160	320	320	640
B/Portugal/EVA53/2018			2018-01-02	SIAT1/MDCK1	2560	160	160	80	160	160	80	160	160	320
B/Portugal/EVA68/2018			2018-01-04	SIAT1/MDCK1	5120	160	160	80	160	160	160	160	320	320
													Vaccine#	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

B/Yamagata-lineage virus recommended for use in trivalent vaccines SH 2018 and quadravalent vaccines NH 2017-18 & 2018-19

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



Summary of genetic data submitted to TESSy

For the 2017–18 season, weeks 40/2017–8/2018, 1 715 viruses have been characterised genetically:

- 230 were defined as A(H1N1)pdm09 subclade 6B.1 as represented by A/Michigan/45/2015, with one not attributed to a clade;
- 329 were A(H3N2) clade 3C.2a represented by A/Hong Kong/4801/2014, 202 were subclade 3C.2a1 represented by A/Singapore/INFIMH-16-0019/2016 and 19 were clade 3C.3a represented by A/Switzerland/9715293/2013, with one not attributed to a clade;
- 93 were B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008, with 42 falling in the 1A Δ162-163 subclade;
- 842 were B/Yamagata-lineage clade 3 represented by B/Phuket/3073/2013.

Antiviral susceptibility

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 486 viruses with collection dates from week 40/2017 at the WIC: 117 A(H1N1)pdm09, 162 A(H3N2), 33 B/Victoria-lineage and 141 B/Yamagata-lineage viruses. Of these only two A(H1N1)pdm09 viruses (A/Bretagne/002/2018: I223R and A/Catalonia/2242523NS/2018: H275Y>H) showed RI by oseltamivir.

For weeks 40/2017–8/2018 of the 2017–18 influenza season, countries reported on the antiviral susceptibility of 280 A(H1N1)pdm09 viruses, 413 A(H3N2) viruses and 563 influenza type B viruses from sentinel and non-sentinel sources to TESSy. One A(H1N1)pdm09 virus showed reduced inhibition (RI) by oseltamivir, one A(H3N2) virus showed RI by both oseltamivir and zanamivir, and three type B viruses showed RI by zanamivir, with one also showing RI by oseltamivir.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [5] reported that the China Health and Family Planning Commission notified the WHO of three cases of human infection with influenza A(H7N9). A description of the characteristics of H7N9 viruses can be found on the WHO website [6]. Increased numbers of cases have been reported over the course of the following seasons, and cases were reported in 2017, including the fifth (2016–17) and largest wave to date which included the emergence of Highly Pathogenic Avian Influenza (HPAI) strains that have caused some zoonoses, though few human cases have been reporting during the 2017–18 season [7]. A revised rapid risk assessment [8] for these A(H7N9) viruses was carried out by ECDC and posted on 11 February 2015 and most recently updated on 3 July 2017 [9]. WHO posted an analysis of recent information on A(H7N9) viruses on 10 February 2017 [10] and a summary and assessment of influenza viruses at the human-animal interface on 25 January 2018 [11], with the latest cases being reported on 26 October 2017 [6]. On 14 February 2018, China notified WHO of the first recorded case of human infection with an avian H7N4 virus [16].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 25 January 2018 [11]. ECDC published a rapid risk assessment update on the situation in Egypt on 13 March 2015 [12] and an epidemiological update on 10 April 2015 [13]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [14]. The latest overview of avian influenza by ECDC in collaboration with the European Food Safety Authority and the EU Reference Laboratory for Avian Influenza published on 23 March 2018 can be found on the ECDC website [17].

WHO CC reports

A description of results generated by the London WHO CC at the WIC and used at the WHO vaccine composition meetings and held at The Peter Doherty Institute, University of Melbourne, 25–27 September 2017, and held at WHO Geneva, 19–21 February 2017, can be found at:

https://www.crick.ac.uk/media/393884/crick_sh2017_vcm_report_to_post.pdf

and

https://crick.ac.uk/media/409431/crick_feb2018_report_for_the_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 some 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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