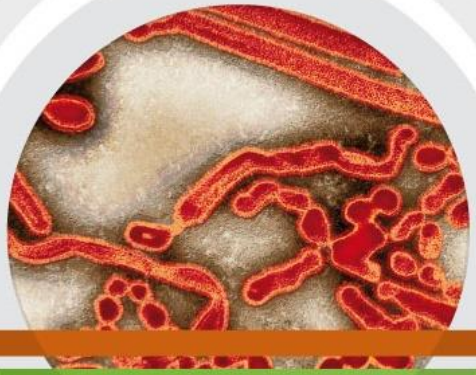

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, March 2018

Summary

This is the fourth report of the 2017–18 influenza season. As of week 13/2018, over 217 000 influenza detections across the WHO European Region have been reported. Types A and B viruses have been detected in the proportions 42% and 58%, respectively, with A(H1N1)pdm09 viruses now being slightly more prevalent than A(H3N2) (1:0.96), and B/Yamagata being significantly more prevalent than B/Victoria viruses (48.7:1).

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 984 specimens having collection dates after August 2017.

The 36 A(H1N1)pdm09 test viruses characterised antigenically showed good reactivity with antiserum raised against the 2017–18 vaccine virus, A/Michigan/45/2015. The 133 test viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others from the WHO European Region with collection dates after 31 August 2017 deposited in GISAID (Global Initiative on Sharing All Influenza Data), all fell 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 191 A(H3N2) viruses successfully recovered to date, only 32 (17%) had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir. The majority of these 32 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 225 viruses with collection dates from week 40/2017 genetically characterised at the WIC, 154 were clade 3C.2a (with 129 3C.2a2, 21 3C.2a3 and four 3C.2a4), 68 fell within clade 3C.2a1 (with two 3C.2a1a and 65 3C.2a1b) and three were clade 3C.3a.

A single B/Victoria-lineage viruses was tested by HI and it reacted well with only one of the panel of post-infection ferret antisera; this antiserum was raised against tissue culture-propagated B/Norway/2409/2017, a virus with a deletion of two amino acids in HA1 (Δ162-163). Of the 29 viruses characterised genetically at the WIC with a collection date after week 40/2017, ten fell within clade 1A, and 19 fell within the subgroup carrying the HA1 double amino acid deletion.

A total of 45 B/Yamagata viruses were characterised antigenically and 98% 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 180 viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others recently circulating in the WHO European Region and reported to GISAID, fall within clade 3.

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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 40/2017–13/2018), with detections having already exceeded the number for the entire 2016–17 season by nearly 50%. Over 217 000 detections have been reported with type B (58%) predominating over type A (42%) viruses. Of the type A viruses subtyped (n = 38 380) and the type B viruses ascribed to lineage (n = 14 747), A(H3N2) no longer prevail over A(H1N1)pdm09, with a ratio of 0.96:1, and B/Yamagata prevailed over B/Victoria, at a ratio of 48.7:1; these ratios represent a decrease and an increase in relative prevalence, respectively, compared to the situation as of week 8/2018 (as summarised in the February 2018 report[1]). Compared with 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 2016–17 winter, to 48.7:1 currently reported; overall, the ratio of type A to type B detections has decreased significantly compared with 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 (50.9% in 2017–18, compared with 1.1% in 2016–17).

Since week 40/2017, 50 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC) from 29 EU/EEA countries. These packages contained 984 specimens, a mix of clinical samples and virus isolates, with specimen collection dates after August 2017 (Table 2). The majority (53%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 1.2:1. Of the 466 type B specimens received (47% of the specimens), 46 were B/Victoria-lineage and 353 were B/Yamagata-lineage. The antigenic and genetic properties of influenza viruses, characterised since the February 2018 report[1], are presented and discussed in this surveillance report. A significant number of the specimens are still undergoing characterisation (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 40/2017-13/2018)

	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	**8 563**	**81 998**	**90 561**	**41.6**	**0.7:1**	**126 614**	**86.6**	**6.5:1**
A(H1N1)pdm09	4 698	14 834	19 532	50.9		591	1.1	
A(H3N2)	2 512	16 336	18 848	49.1	0.96:1	53 101	98.9	89.8:1
A not subtyped	1 353	50 828	52 181			**72 922**		
Influenza B	**15 303**	**111 637**	**126 940**	**58.4**		**19 570**	**13.4**	
Victoria lineage	206	91	297	2.0		749	27.1	
Yamagata lineage	7 093	7 357	14 450	98.0	48.7:1	2 016	72.9	2.7:1
Lineage not ascribed	8 004	104 189	112 193			16 805		
Total detections (total tested)	**23 866 (56 068)**	**193 635 (662 166)**	**217 501 (718 234)**			**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, February 2018. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/sites/portal/files/documents/ERLI-Net_report_20-Feb-2018_0.pdf

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

MONTH / Country		A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
		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	1						
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	0
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	1
Estonia	1					1	0							
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	1
Hungary	1												1	1
Ireland	5			1	in process	2	0	2					2	in process
Italy	1												1	1
Latvia	4			1	1	3	3	0						
Netherlands	3			1	1	2	0	1						
Norway	24			3	3	10	1	9			2	1	9	7
Portugal	4					1	0	1			1	1	2	2
Slovakia	1			1	1									
Slovenia	1												1	1
Spain	30			1	1	9	1	7	1	0	6	5	13	10
Sweden	7					5	1	4					2	2
United Kingdom	5					3	0	3			1	1	1	1
DECEMBER														
Austria	37			18	17	7	0	7					12	12
Belgium	19			7	in process	1	0	1					11	in process
Bulgaria	3			2	1								1	1
Croatia	6			3	3	3	1	2						
Cyprus	3	2	0			1	0	1						
Czech Republic	1												1	1
Denmark	17					9	2	7					8	8
Estonia	5	2	0			2	0						1	1
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	3			1	1	1	0	1					1	in process
Hungary	6			1	1								5	5
Iceland	15			1	1	8	3	5					6	6
Ireland	13			1	in process	5	0	5					7	in process
Italy	25			12	12	2	0	2					11	11
Latvia	2			2	2									
Lithuania	9			3	1						1	1	5	3
Malta	1			1	in process									
Netherlands	16			1	0	1	0	1					14	5
Norway	35			5	1	15	in process				2	1	13	in process
Poland	9	1	0	2	2				3	0	3	3		
Portugal	30			2	2	3	0	3			6	6	19	19
Romania	9			4	4	2	0						3	2
Slovakia	5												5	5
Slovenia	12			4	4	3	1	2			3	2	2	2
Spain	52			18	15	8	0	6	3	0	6	6	17	in process
United Kingdom	14			1	0	2	0		3	0			8	6
2018														
JANUARY														
Belgium	25			12	in process	5	in process						8	in process
Bulgaria	10			3	2	1	0	0					6	2
Cyprus	12	3	in process	2	2				5	in process			2	2
Czech Republic	1			1	1									
Denmark	4												4	2
Estonia	14	2	in process	3	2	3	in process		1	0			5	in process
France	4			2	2	1	0	1					1	1
Germany	23			6	6	5	0	5			5	5	7	7
Greece	26	2	in process	8	2	2	0	1					14	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	3	2	0	2					6	6
Lithuania	16					3	0		2	0	2	1	9	in process
Malta	39			3	in process	13	in process		11	0			12	in process
Netherlands	22			5	in process	9	in process				1	in process	7	in process
Norway	15			5	3	6	in process						4	0
Poland	1										1	1		
Portugal	6												6	6
Romania	9			3	0				4	0			2	2
Slovakia	1			1	1									
Slovenia	19			7	7	2	0	2	3	0			7	6
Spain	5			3	3	2	0	2						
United Kingdom	37			3	0	22	0		8	0			4	0
FEBRUARY														
Cyprus	17	2	in process						15	in process				
Greece	12			3	in process	3	in process						6	in process
Netherlands	6			4	in process	2	in process							
MARCH														
Greece	7			3	in process								4	in process
	984	15	0	225	150	278	30	153	67	0	46	39	353	198
					22.9%		28.3%				4.7%		35.9%	
29 Countries					52.6%						47.4%			

1. Propagated to sufficient titre to perform HI assay (the totalled number does not include any from batches that are in process)
2. Propagated to sufficient titre to perform HI assay in 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

Numbers highlighted in blue show the number of viruses subjected to HI assay for 'completed' sample sets. Under a 'sequence first' virus characterisation scheme: (i) sequencing only was possible for some clinical specimens that had been collected in lysis buffer; (ii) where sequencing failed, despite samples having good Ct values, virus propagation was attempted for only a few samples; and (iii) where multiple viruses shared the same HA sequence only a selection were propagated to allow assay by HI

* As of 2018-04-06

Influenza A(H1N1)pdm09 virus analyses

Results of haemagglutination inhibition (HI) analyses of viruses performed since the February 2018 report are shown in Tables 3-1 to 3-3. All 36 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 twofold of the titre of the antiserum for the homologous virus. Of the other 10 antisera used, eight recognised all test viruses at titres within fourfold of their respective homologous titres, with recognition within twofold being in the range of 92% to 100% for individual antisera. Eightfold or greater reduced recognition of test viruses compared with homologous titres were observed for antisera raised against two viruses: A/Lviv/N6/2009 – 14 (39%) within twofold, 19 (53%) within fourfold, and three (8%) at eightfold or greater; and A/California/7/2009 (the former vaccine virus) – 32 (89%) within twofold, 2 (5.5%) within fourfold, and two (5.5%) at eightfold or greater.

Genetic analyses of the 36 test viruses are in process but viruses antigenically characterised in the February 2018 report, for which genetic analysis was pending, are now known to all carry haemagglutinins (HAs) belonging to genetic subclade 6B.1 (Tables 3-4 to 3-5), 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 The majority of HA genes of recently circulating viruses from EU/EAA countries cluster in a genetic subgroup defined by HA1 amino acid substitutions of S74R, S164T and I295V within which at least four subclusters have emerged (Figure 1). These subclusters are defined by HA1 amino acid substitutions: S183P, E235D and N260D; T120A; P137S and S183P; and V250A.

Recently, an A(H1N2) reassortant virus was detected in the Netherlands which had acquired genes from recently circulating seasonal influenza viruses; HA and NS genes from an A(H1N1)pdm09 virus and the other six genes from an A(H3N2) virus [17]. As all genes were from recently circulating seasonal influenza viruses, this virus was considered to pose no increased risk to humans.

Table 3-1. 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 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}
Passage history				6B.1				5	6	6A	6B	6B.1	6B.2	6B.1
Ferret number														
Genetic group														
REFERENCE VIRUSES														
A/Michigan/45/2015	6B.1	2015-09-07	E3/E3	1280	640	320	320	640	320	640	640	1280	1280	1280
A/California/7/2009	clone 38-32	2009-04-09	E3/E3	1280	1280	640	640	1280	640	640	640	1280	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	640	640	80	80	80	80	160	80	640
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK6	640	640	640	320	640	320	640	640	1280	640	1280
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	640	640	640	640	640	640	1280	1280	2560
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	640	160	160	640	320	640	320	640	320	1280
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	640	640	320	320	640	320	320	640	1280	640	1280
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	640	640	320	320	640	320	640	320	1280	640	1280
A/Israel/Q-504/2015	6B.1	2015-12-15	C1/MDCK2	640	640	320	320	640	320	640	640	1280	1280	1280
A/Paris/1447/2017	6B.2	2017-10-20	MDCK1/MDCK3	640	320	320	160	320	320	320	320	640	640	1280
	6B.1													
TEST VIRUSES														
A/Bulgaria/892/2017		2017-12-15	MDCK2	1280	1280	640	320	640	640	640	640	2560	1280	2560
A/Segovia/226/2017		2017-12-19	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Athens.GR/2680/2017		2017-12-20	MDCK1	1280	640	640	320	640	320	640	640	1280	1280	2560
A/Segovia/235/2017		2017-12-21	MDCK1/MDCK2	640	640	320	160	640	320	320	640	1280	640	2560
A/Segovia/233/2017		2017-12-21	MDCK1/MDCK1	1280	1280	640	320	1280	640	640	640	2560	1280	5120
A/Valladolid/236/2017		2017-12-22	MDCK1/MDCK1	1280	1280	640	320	1280	640	640	640	2560	1280	5120
A/Valladolid/238/2017		2017-12-23	MDCK1/MDCK1	1280	640	320	160	640	320	640	640	1280	1280	2560
A/Valladolid/240/2017		2017-12-23	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Valladolid/243/2017		2017-12-24	MDCK1/MDCK1	1280	1280	640	320	640	320	640	640	1280	1280	2560
A/Valladolid/242/2017		2017-12-24	MDCK1/MDCK1	1280	640	320	320	640	320	640	640	1280	1280	5120
A/Valladolid/260/2017		2017-12-26	MDCK1/MDCK1	1280	1280	640	320	640	640	640	640	2560	1280	2560
A/Salamanca/256/2017		2017-12-26	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Valladolid/287/2017		2017-12-26	MDCK1/MDCK2	1280	1280	640	320	1280	640	640	640	2560	1280	2560
A/Parma/127/2017		2017-12-27	MDCK3/MDCK1	640	80	320	160	320	160	320	160	640	640	1280
A/Roma/10/2017		2017-12-27	MDCK2/MDCK1	640	640	320	160	640	320	320	640	1280	640	2560
A/Parma/128/2017		2017-12-28	MDCK2/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Parma/130/2017		2017-12-29	MDCK2/MDCK1	640	160	320	160	320	160	320	320	640	640	1280
A/Pavia/21/2017		2017-12-29	MDCK2/MDCK1	640	320	320	160	320	160	320	320	640	640	2560
A/Padova/1/2017		2017-12-30	MDCK2/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

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										
					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
		Passage history							5	6	6A	6B	6B.1	6B.2	6B.1
		Ferret number													
		Genetic group			6B.1										
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	320	320	640	640	1280	640	1280	1280	2560
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	640	640	640	640	1280	640	1280	640	1280	1280	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	80	320	320	80	40	80	80	80	40	320
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	160	1280	1280	160	160	160	160	160	160	640
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK6	640	1280	640	640	1280	640	1280	1280	2560	1280	2560
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	1280	1280	1280	1280	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	640	640	320	160	640	320	640	640	1280	640	1280
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	1280	640	640	640	640	640	640	1280	1280	640	2560
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	1280	640	320	1280	640	1280	640	2560	1280	2560
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	160	640	320	640	640	1280	1280	1280
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	1280	640	640	320	640	640	640	640	1280	1280	2560
TEST VIRUSES															
A/Firenze/1/2017			2017-12-05	MDCK3/MDCK1	1280	640	320	320	640	640	1280	640	2560	1280	2560
A/Firenze/2/2017			2017-12-07	MDCK3/MDCK1	640	640	320	160	640	320	320	640	1280	640	2560
A/Roma/7/2017			2017-12-11	MDCK2/MDCK1	1280	640	640	320	640	640	1280	640	2560	1280	2560
A/Perugia/45/2017			2017-12-14	MDCK2/MDCK1	1280	640	320	320	640	640	640	640	1280	1280	2560
A/Pavia/19/2017			2017-12-22	MDCK2/MDCK1	640	160	320	320	320	320	320	320	1280	640	2560
A/Pavia/20/2017			2017-12-24	MDCK2/MDCK1	1280	640	320	320	640	640	1280	640	1280	1280	2560
A/Slovenia/106/2018			2018-01-07	SIATx/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	5120
A/Slovenia/119/2018			2018-01-09	SIATx/MDCK1	320	320	160	160	320	320	640	640	640	640	1280
A/Slovenia/112/2018			2018-01-09	SIATx/MDCK1	640	640	320	160	640	640	640	640	1280	1280	2560
A/Czech Republic/85/2018		6B.1	2018-01-09	E1/E1	640	640	320	320	640	640	1280	640	1280	1280	2560
A/Slovenia/373/2018			2018-01-17	SIATx/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Slovenia/366/2018			2018-01-17	SIATx/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	5120
						Vaccine									

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

Table 3-3. 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 F-42/16[-1] 6B.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] 5	A/St. P 27/11 Egg F26/14[-1] 6	A/HK 5659/12 MDCK F30/12[-1] 6A	A/Sth Afr 3626/13 Egg F03/14[-1] 6B	A/Slov 2903/2015 Egg F02/16[-1] 6B.1	A/Israel Q-504/15 MDCK F08/16[-1] 6B.2	A/Paris 1447/17 MDCK F03/18[-2] 6B.1
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	1280	1280	320	320	1280	640	1280	1280	2560	1280	5120
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	1280	640	320	320	1280	640	1280	640	2560	1280	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	40	320	320	40	40	80	80	80	40	320
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	80	640	640	80	80	160	80	160	80	640
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK6	1280	1280	640	640	1280	640	1280	1280	2560	1280	5120
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	1280	640	640	640	640	640	640	640	2560	1280	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	640	320	160	160	640	320	640	640	640	320	1280
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	1280	640	320	640	640	640	640	640	1280	640	2560
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	640	320	320	640	320	640	640	1280	1280	2560
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	1280	640	320	320	640	320	640	640	2560	1280	2560
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	1280	640	320	160	640	320	640	640	1280	640	2560
TEST VIRUSES															
A/Slovenia/558/2018				SIAT1	5120	2560	1280	640	2560	1280	2560	2560	5120	5120	10240
A/Bucuresti/221625/2017			2017-12-15	MDCK1/MDCK1	2560	640	640	320	1280	640	1280	1280	2560	1280	5120
A/Cyprus/F11/2018			2018-01-05	MDCK1	1280	640	320	320	640	320	640	640	2560	1280	2560
A/Greece/32/2018			2018-01-11	MDCK2	2560	1280	640	640	1280	640	1280	1280	2560	2560	5120
A/Cyprus/F38/2018		6B.1	2018-01-12	MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	2560	5120
					Vaccine										

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

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 Egg NIB F42/16[+1] 6B.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] 5	A/St. P 27/11 Egg F26/14[+1] 6	A/HK 5659/12 MDCK F30/12[+1] 6A	A/Sth Afr 3626/13 Egg F03/14[+1] 6B	A/Slov 2903/2015 Egg F02/16[+1] 6B.1	A/Israel Q-504/15 MDCK F08/16[+1] 6B.2	A/Paris 1447/17 MDCK F03/18[+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	clone 38-32		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		6B.1	2017-11-07	MDCK1	640	160	320	320	320	160	320	320	1280	640	1280
A/Galicia/2466/2017		6B.1	2017-12-01	MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	2560	5120
A/Paris/1931/2017		6B.1	2017-12-22	MDCK1/MDCK1	1280	640	640	320	1280	640	1280	1280	2560	1280	5120
A/Paris/1959/2017		6B.1	2017-12-24	MDCK2/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Bretagne/1994/2017		6B.1	2017-12-26	MDCK1/MDCK1	1280	1280	640	640	1280	640	1280	1280	2560	2560	5120
A/Haute Normandie/1945/2017		6B.1	2017-12-26	MDCK1/MDCK1	640	160	320	320	320	160	320	320	1280	640	1280
A/Bretagne/1939/2017		6B.1	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		6B.1	2018-01-24	C1/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Nordrhein-Westfalen/11/2018		6B.1	2018-01-25	C1/MDCK1	1280	1280	640	320	640	320	640	640	1280	1280	2560
A/Berlin/8/2018		6B.1	2018-01-26	C1/MDCK1	640	640	320	160	640	160	640	640	1280	640	1280
A/Thuringen/7/2018		6B.1	2018-01-29	C1/MDCK1	1280	640	320	320	640	320	640	640	1280	1280	2560
A/Hessen/5/2018		6B.1	2018-01-29	C1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560

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

1 < = <40; 2 < = <80

Sequence in Phylogenetic tree

Vaccine

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

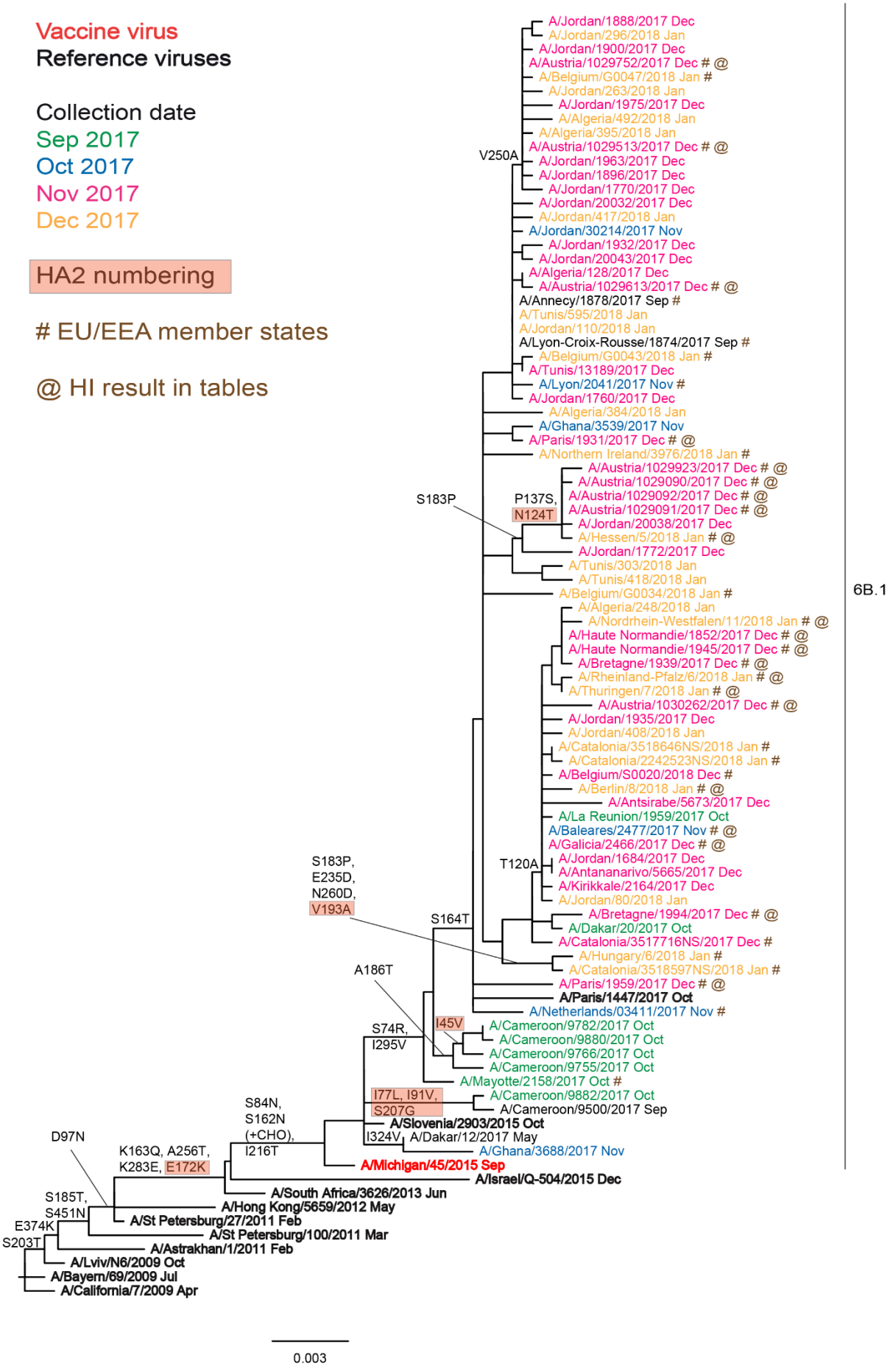
Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera										
				A/Mich 45/15 Egg NIB F42/16[-1]	A/Cal 7/09 Egg F06/16[-1]	A/Bayern 69/09 MDCK F09/15[-1]	A/Lviv N6/09 MDCK F14/13[+1]	A/Astrak 1/11 MDCK F22/13[+1]	A/St. P 27/11 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]
	Passage history													
	Ferret number							5	6	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	320	320	640	640	640	640	1280	1280	1280
A/California/7/2009	clone 38-32	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	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	6B.1	2017-12-12	SIAT1/MDCK1	320	320	160	160	320	160	320	320	640	640	1280
A/Austria/1029091/2017	6B.1	2017-12-12	SIAT1/MDCK1	640	320	320	160	320	320	320	320	1280	640	2560
A/Austria/1029092/2017	6B.1	2017-12-13	SIAT1/MDCK1	1280	640	320	320	640	320	640	640	2560	1280	2560
A/Austria/1029513/2017	6B.1	2017-12-15	SIAT1/MDCK1	640	640	320	160	320	160	320	640	1280	640	1280
A/Austria/1029613/2017	6B.1	2017-12-15	SIAT1/MDCK1	1280	640	640	320	640	640	640	640	2560	1280	2560
A/Austria/1029752/2017	6B.1	2017-12-18	SIAT1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Austria/1029923/2017	6B.1	2017-12-18	SIAT2/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Haute Normandie/1852/2017	6B.1	2017-12-18	MDCK1/MDCK1	1280	640	320	320	640	320	640	640	2560	2560	2560
A/Austria/1030260/2017	6B.1	2017-12-19	SIAT1/MDCK1	640	320	160	160	320	160	320	320	1280	640	1280
A/Austria/1030262/2017	6B.1	2017-12-19	SIAT1/MDCK1	640	640	320	160	640	320	640	640	1280	1280	2560
A/Austria/1030575/2017	6B.1	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

Sequence in Phylogenetic tree

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



Influenza A(H3N2) virus analyses

As described in many previous reports[2], influenza A(H3N2) viruses 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.

A number of the 278 A(H3N2) virus specimens with collection dates after week 40/2017, 24 of which were lysed specimens, are in process for antigenic and genetic characterisation (Table 2). However, of those successfully isolated to date (n = 191), as shown by positive neuraminidase activity, only 32 (17%) had sufficient HA activity in the presence of 20nM oseltamivir to allow antigenic analysis by HI assay. Since the February 2018 report, no virus recovered, based on positive neuraminidase activity, retained sufficient HA activity to allow antigenic analysis by HI.

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;
- 3C.2a1: 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;
- 3C.2a1a: Those in subclade 3C.2a1 plus **T135K** in **HA1**, resulting in the loss of a potential glycosylation site, and also **G150E** in **HA2**, e.g. A/Greece/4/2017;
- 3C.2a1b: Those in subclade 3C.2a1 plus **K92R** and **H311K** in **HA1**, e.g. A/England/74560298/2017;
- 3C.2a2: Those in clade 3C.2a plus **T131K**, **R142K** and **R261Q** in **HA1**, e.g. A/Norway/4465/2016;
- 3C.2a3: Those in clade 3C.2a plus **N121K** and **S144K** in **HA1**, e.g. A/Norway/4849/2016;
- 3C.2a4: 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 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 3C.2a2. A sizable proportion had HA genes that fell into genetic group 3C.2a1b, and some also had HA genes that fell into other genetic subgroups. The location of A/Singapore/INFIMH-16-0019/2016 (3C.2a1), 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.

Table 4 shows HI results on a set of test viruses for which genetic analysis had not been completed at the time of the February 2018 report. Five of the eight test viruses fell in subclade 3C.2a2 and generally were recognised well by antiserum raised against A/Bretagne/1413/2017, a genetic subclade 3C.2a2 virus, as was the case for antisera raised against other cell-culture-propagated viruses: A/Stockholm/6/2014 (3C.3a); A/Hong Kong/4801/2014 (3C.2a); A/Oman/2585/2016 and A/Norway/4436/2016 (3C.2a1); and A/Greece/4/2017 (3C.2a1a), although homologous titres were not available for the last three viruses.

[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

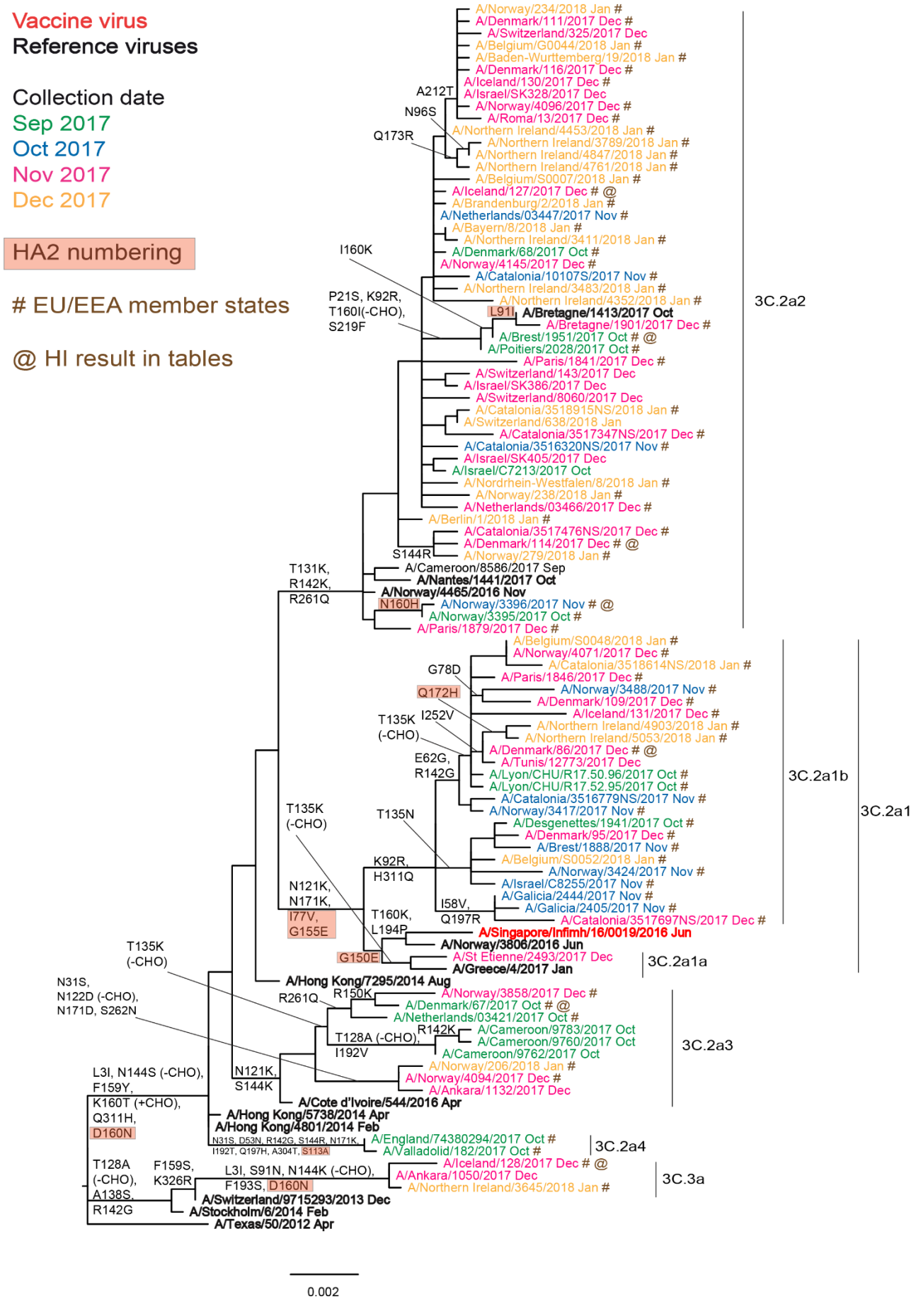
Table 4. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre							
				Post-infection ferret antisera							
				A/Stock	A/HK	A/HK	A/Bretagne	A/Oman	A/Nor	A/Greece	A/Sing
				6/14	5738/14	4801/14	1413/17	2585/16	4436/16	4/17	0019/16
				SIAT	MDCK	Egg	SIAT	SIAT	SIAT	SIAT	Egg 10^{-4}
	Passage history			F14/14*1	F30/14*1	F42/15*1	F01/18 NIB	F50/16*1	F03/17*1	F27/17*1	F41/17*1
	Ferret number			3C.3a	3C.2a	3C.2a	3C.2a2	3C.2a1	3C.2a1	3C.2a1a	3C.2a1
	Genetic group										
REFERENCE VIRUSES											
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	640	160	160	320	320	320	320	320
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	320	160	160	320	320	320	320	640
A/Hong Kong/4801/2014 isolate 1	3C.2a	2014-02-26	E6/E2	80	320	1280	640	640	320	640	2560
A/Bretagne/1413/2017	3C.2a2		MDCK1/SIAT4	320	160	80	1280	320	320	160	320
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-06-14	E5/E1	40	80	320	80	160	160	160	1280
TEST VIRUSES											
A/Brest/1951/2017	3C.2a2	2017-10-22	MDCK1/SIAT1	160	160	80	1280	160	320	160	160
A/Norway/3396/2017	3C.2a2	2017-11-02	SIAT1/SIAT1	320	160	80	640	640	320	320	160
A/Catalonia/2228981NS/2017	3C.2a2	2017-11-23	C0/SIAT1	320	160	80	640	320	320	320	160
A/Iceland/127/2017	3C.2a2	2017-12-01	MDCK1/SIAT1	160	160	80	640	320	320	320	160
A/Iceland/128/2017	3C.3a	2017-12-11	MDCK1/SIAT1	80	40	<	80	80	160	80	40
A/Denmark/67/2017	3C.2a3	2017-10-08	SIAT3/SIAT1	160	160	40	80	160	320	160	80
A/Denmark/86/2017	3C.2a1b	2017-12-11	SIAT3/SIAT1	160	80	40	80	160	160	160	80
A/Denmark/114/2017	3C.2a2	2017-12-28	SIAT1	160	80	40	160	160	320	160	80
						Vaccine NH 2017-18					Vaccine SH 2018 NH 2018-19

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

Sequence in Phylogenetic tree

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



Influenza B virus analyses

A total of 466 influenza type B-positive specimens with collection dates after August 2017 have been received, with 399 being ascribed to a lineage: 46 were B/Victoria lineage and 353 were B/Yamagata (Table 2).

Influenza B – Victoria lineage

A single-tissue culture-propagated test virus, B/Poland/31395/2017, has been antigenically characterised since the February 2018 report (Table 5). The HI profiles of the other test viruses in Table 5 were presented in the February 2018 report, at which time genetic information was not available. All seven test viruses were poorly recognised by nine of ten post-infection ferret antisera raised against a range of viruses encompassing both egg- and cell-culture-propagated reference viruses and the current vaccine virus, egg-propagated B/Brisbane/60/2008.The antiserum raised against cell-culture-propagated B/Norway/2409/2017, a virus carrying a double amino acid deletion in HA1, Δ(K162, N163), recognised all seven test viruses at titres within twofold of the homologous titre, which was only 40. These results show that viruses with the two amino acid deletions in HA1 are antigenically distinct from those without the deletion. 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, the Americas and Japan have HA genes encoding an HA with 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**. The antigenic profiles of the seven test viruses indicate that they are all double deletion viruses and this has been confirmed for two of them (1A(Δ2) in Table 5 and Δ(K162, N163) in Figure 3). Less common are viruses with HA genes encoding a deletion of three amino acids Δ(K162, N163, D164). These viruses were detected in the Far East and many share the substitutions I180T and K209N in HA1.

Influenza B – Yamagata lineage

HI results for 45 B/Yamagata-lineage test viruses analysed since the February 2018 report are shown in Tables 6-1 to 6-2. The 180 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 44 (97.8%) test viruses at titres within fourfold of the titre of the antiserum with the homologous virus, and 33 (73.3%) within twofold. An antiserum raised against the cell-culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised all 45 test viruses at titres within fourfold of the homologous titre of the antiserum and 38 (84.4%) within twofold. Antisera with homologous titres of 160 raised against two other egg-propagated clade 3 viruses, B/Wisconsin/1/2010 (a former vaccine virus) and B/Stockholm/12/2011, both recognised all test viruses at titres within fourfold of the homologous titres, with 44 (97.8%) viruses (B/Wisconsin/1/2010) and 23 (51.1%) viruses (B/Stockholm/12/2011) being recognised within twofold. An antiserum raised against a recently circulating clade 3 cell-culture-propagated virus, B/Mauritius/1791/2017, recognised 35 (77.8%) test viruses at titres within fourfold of the homologous titre, with 16 (35.6%) 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 (significant numbers were recognised at titres at least eightfold reduced compared with 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 11 (24.4%), 32 (71.1%) and 23 (51.1%) test viruses, respectively, at titres within fourfold of the titres of the antisera with the homologous viruses.

Since the February 2018 report, and at the time of preparing this report, genetic analysis was complete for only seven of the 45 test viruses (Table 6-2) and for 30 of 68 test viruses for which antigenic characterisation was presented in the February 2018 report (Tables 6-3 to 6-4). 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. Some subclustering of sequences, defined by specific amino acid substitutions (e.g. HA1 G183E, D229N, D232N or P254T), is occurring but with no obvious antigenic effects (Tables 6-2 to 6-4).

Table 5. 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[*4]	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	Egg	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	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	1A(Δ2)	2017-11-10	MDCK1/MDCK1	40	<	<	10	<	<	<	<	<	<	40
B/Poland/31395/2017	1A(Δ2)	2017-12-18	MDCK2	160	<	<	10	<	10	10	<	20	<	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; [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)

Sequence in Phylogenetic tree

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

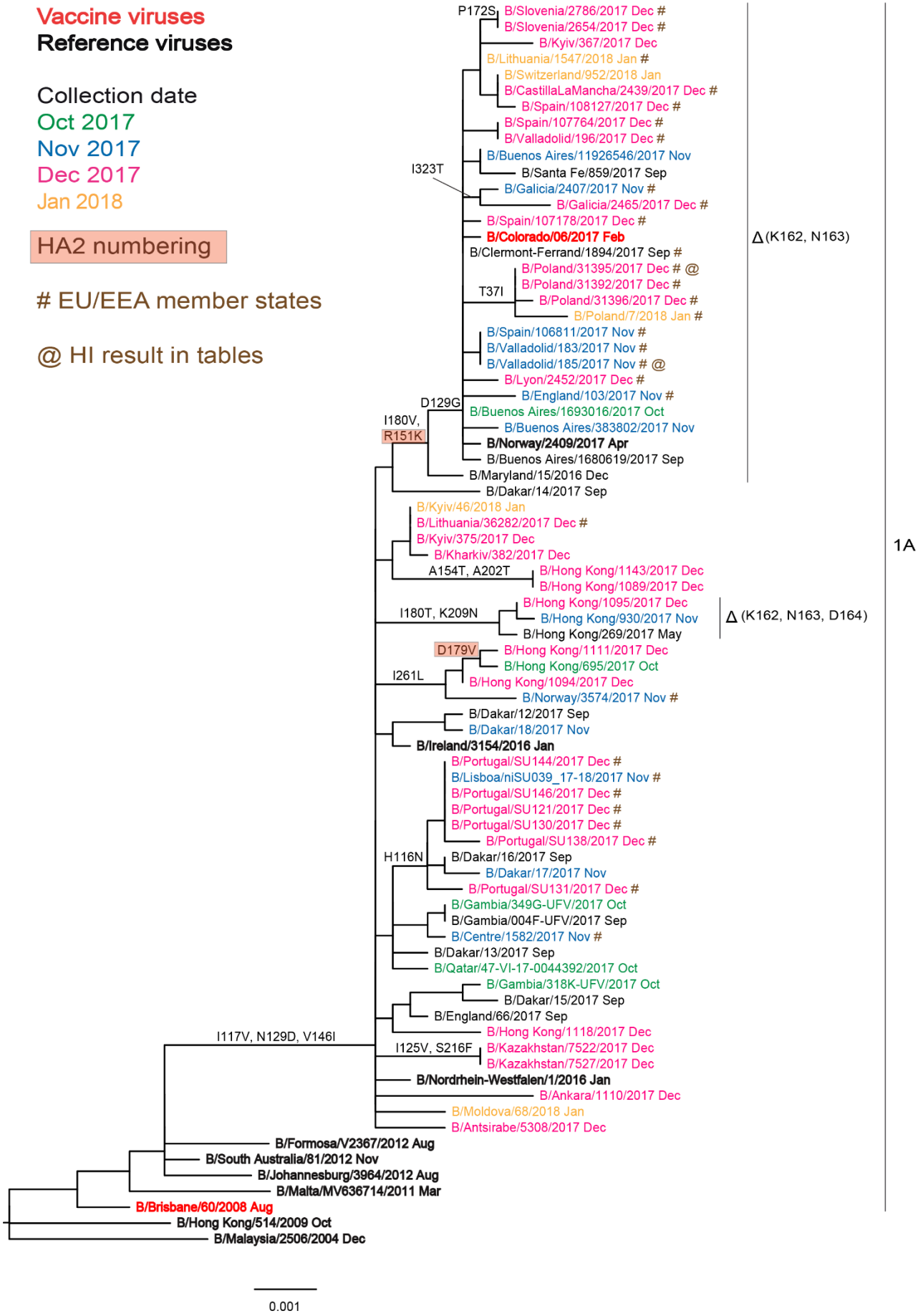


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	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/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]	F37/15[x2]	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	640	320	160	1280	320	320	80	320	40
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	2560	320	640	640	320	320	160	320	160	320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	320	320	160	640	320	160	80	160	40
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	640	320	160	40	640	80	80	20	80	<
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	320	40	20	320	160	160	80	160	80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	160	40	10	160	160	160	40	80	40
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	5120	160	320	320	320	320	160	320	160	640
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	40	10	160	160	80	40	160	40
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK3	5120	320	320	640	640	640	160	640	320	640
TEST VIRUSES													
B/Trencin/55/2017		2017-12-11	MDCK1/MDCK1	5120	160	160	160	320	320	160	320	320	320
B/Trencin/56/2017		2017-12-12	MDCK1/MDCK1	2560	160	160	80	160	160	80	160	160	320
B/Netherlands/3534/2017		2017-12-20	(MDCK/SIAT)2/MDCK1	5120	160	80	80	320	320	80	160	160	320
B/Bulgaria/915/2017		2017-12-21	MDCK1	2560	160	40	20	160	160	80	80	80	160
B/Netherlands/3543/2017		2017-12-27	(MDCK/SIAT)2/MDCK1	2560	80	80	40	160	160	80	80	80	160
B/Parma/22/2017		2017-12-27	MDCK2/MDCK1	5120	160	160	80	320	320	160	320	320	320
B/Parma/20/2017		2017-12-28	MDCK2/MDCK1	5120	160	160	80	320	320	80	160	160	320
B/Roma/5/2017		2017-12-29	MDCK2/MDCK1	2560	160	160	80	320	320	80	320	160	320
B/Pavia/1/2018		2018-01-01	MDCK2/MDCK1	2560	80	80	40	160	160	40	80	80	160
B/Bulgaria/010/2018		2018-01-02	MDCK1	1280	80	40	40	80	80	40	80	80	160
B/Pavia/4/2018		2018-01-03	MDCK2/MDCK1	2560	160	80	40	160	160	80	160	160	160
B/Pavia/3/2018		2018-01-03	MDCK2/MDCK1	2560	80	80	40	160	160	40	80	80	160
B/Pavia/5/2018		2018-01-04	MDCK2/MDCK1	5120	160	160	160	320	320	160	160	320	320
B/Athens.GR/63/2018		2018-01-09	MDCK1	5120	160	160	80	160	320	80	160	80	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

Table 6-2. 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/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]	F37/15[*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	320	160	1280	320	320	80	320	20
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	5120	320	1280	640	160	320	80	160	160	320
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	640	640	160	320	160	80	80	80	40
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	1280	640	160	80	640	160	160	40	80	10
B/Wisconsin1/2010	3	2010-02-20	E3/E2	2560	320	80	20	320	160	160	40	160	80
B/Stockholm/12/2011	3	2011-03-28	ExIE2	1280	160	40	10	160	80	160	40	80	20
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	160	160	80	160	80	320
B/Phuket/3073/2013	3	2013-11-21	E4/E3	2560	320	40	10	160	160	80	40	160	40
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK3	5120	320	320	640	320	320	160	320	320	640
TEST VIRUSES													
B/Denmark/06/2017		2017-11-27	SIAT3/MDCK1	2560	160	160	80	160	160	80	160	80	320
B/Spain/106385/2017	3	2017-11-27	MDCK1/MDCK1	1280	80	80	20	160	40	80	80	20	160
B/Firenze/1/2017		2017-11-28	MDCK2/MDCK1	1280	80	80	40	80	160	80	80	80	160
B/Athens.GR/2601/2017		2017-11-30	MDCK2	1280	80	80	40	80	80	40	160	40	160
B/Firenze/7/2017		2017-12-04	MDCK3/MDCK1	2560	160	160	40	160	160	80	160	160	320
B/Bolzano/4/2017		2017-12-04	MDCK3/MDCK1	5120	320	320	320	160	320	160	320	160	320
B/Denmark/12/2017		2017-12-11	SIAT3/MDCK1	1280	80	80	40	80	80	40	80	80	80
B/Perugia/8/2017		2017-12-15	MDCK2/MDCK1	1280	80	40	10	80	80	40	80	40	80
B/Perugia/7/2017		2017-12-15	MDCK2/MDCK1	2560	80	40	10	80	160	40	40	80	80
B/Perugia/5/2017		2017-12-18	MDCK3/MDCK1	5120	160	160	160	160	320	160	320	160	320
B/Denmark/25/2017		2017-12-18	SIAT3/MDCK1	5120	320	160	80	160	160	80	160	160	320
B/Parma/13/2017		2017-12-21	MDCK2/MDCK1	5120	320	320	320	320	320	160	320	320	320
B/Parma/18/2017		2017-12-22	MDCK2/MDCK1	2560	160	80	20	80	80	40	80	80	160
B/Bucuresti/221842/2018	3	2017-12-25	MDCK1	1280	80	80	20	80	80	40	80	40	80
B/Denmark/44/2017		2017-12-25	MDCK1	2560	160	80	40	80	80	40	80	80	160
B/Denmark/52/2017		2017-12-25	MDCK1	2560	160	80	40	80	80	40	80	80	160
B/Netherlands/3540/2017		2017-12-27	MDCK2	5120	320	320	320	160	320	160	320	320	320
B/Lithuania/37089/2017	3	2017-12-28	MDCK1	1280	80	80	20	80	80	40	160	40	80
B/Netherlands/10005/2018		2018-01-02	MDCK2	5120	320	320	640	320	320	160	320	320	320
B/Denmark/13/2018		2018-01-02	MDCK1	2560	160	80	40	80	80	40	80	40	160
B/Athens.GR/16/2018		2018-01-03	MDCK2	1280	80	80	20	80	80	40	80	40	80
B/Denmark/16/2018		2018-01-03	MDCK1	2560	160	80	40	80	160	40	80	80	160
B/Lithuania/998/2018	3	2018-01-08	MDCK1	2560	80	80	20	80	80	40	80	80	80
B/Cyprus/F15/2018	3	2018-01-08	MDCK1	1280	160	80	20	80	80	40	80	40	80
B/Slovenia/186/2018		2018-01-10	SIATx/MDCK1	2560	80	80	20	80	80	40	80	40	160
B/Bucuresti/222261/2018	3	2018-01-11	MDCK1	2560	160	80	40	80	80	40	80	80	160
B/Slovenia/210/2018		2018-01-11	SIATx/MDCK1	2560	160	160	40	80	160	80	160	80	160
B/Cyprus/F39/2018	3	2018-01-12	MDCK1	2560	160	160	40	160	160	80	160	80	160
B/Slovenia/365/2018		2018-01-17	MDCKx/MDCK1	2560	80	80	20	80	80	40	80	40	80
B/Slovenia/419/2018		2018-01-18	MDCKx/MDCK1	1280	80	80	20	80	80	40	40	40	80
B/Slovenia/431/2018		2018-01-18	SIATx/MDCK1	2560	160	80	40	80	80	40	80	40	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

Sequence in Phylogenetic tree

Table 6-3. 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	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	B/Maur 1791/17 MDCK
		Passage history												
		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
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		3	2017-10-28	MDCK1	1280	80	80	40	160	80	20	160	80	160
B/Norway/3438/2017		3	2017-11-03	MDCK1	1280	160	160	80	320	320	40	320	320	320
B/Norway/3482/2017		3	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		3	2017-11-20	SIAT1/MDCK1	2560	80	160	80	160	160	20	320	160	320
B/Valladolid/184/2017		3	2017-11-21	MDCK1/MDCK1	1280	40	40	20	80	40	20	80	40	80
B/Valladolid/186/2017		3	2017-11-22	MDCK1/MDCK1	2560	80	40	20	80	80	20	80	80	160
B/Norway/3557/2017		3	2017-11-23	MDCK1MDCK1	1280	80	80	20	80	80	20	80	160	160
B/Melilla/2412/2017		3	2017-11-28	MDCK1	2560	80	80	40	160	80	20	160	160	320
B/Valladolid/188/2017		3	2017-11-29	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Valladolid/189/2017		3	2017-11-29	MDCK1/MDCK1	1280	80	40	20	80	80	20	40	80	160
B/Melilla/2452/2017		3	2017-12-04	MDCK1	1280	80	80	20	160	80	20	160	80	160
B/Valladolid/193/2017		3	2017-12-04	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Leon/194/2017		3	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		3	2017-12-13	MDCK1/MDCK1	1280	80	40	20	80	40	20	80	40	80
B/Iceland/132/2017		3	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		3	2017-12-26	MDCK1/MDCK1	2560	80	80	80	160	80	40	160	80	320
B/Picardie/1963/2017		3	2017-12-27	MDCK1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Paris/1961/2017		3	2017-12-27	MDCK1/MDCK1	2560	80	40	20	80	80	20	80	80	80
B/Iceland/138/2017		3	2017-12-28	MDCK1/MDCK1	2560	160	80	40	160	80	40	80	160	160
B/Iceland/142/2017		3	2017-12-30	MDCK1/MDCK1	2560	160	160	320	160	160	80	320	160	320
B/Iceland/141/2017		3	2017-12-30	MDCK1/MDCK1	2560	80	80	40	160	80	20	80	80	160
B/Iceland/144/2017		3	2017-12-31	MDCK1/MDCK1	1280	80	80	20	80	40	20	80	80	80
B/Iceland/04/2018		3	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

Sequence in Phylogenetic tree

Table 6-4. 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]
		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	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		3	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		3	2017-12-11	SIAT1/MDCK1	5120	320	320	320	320	640	160	320	320	320
B/Austria/1028736/2017		3	2017-12-12	SIAT1/MDCK1	5120	320	320	640	320	640	160	320	320	640
B/Austria/1028826/2017		3	2017-12-12	SIAT1/MDCK1	2560	80	80	40	80	80	40	80	80	160
B/Austria/1029093/2017		3	2017-12-12	SIAT1/MDCK1	5120	320	160	320	320	320	160	320	320	320
B/Portugal/SU59/2017		3	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		3	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[#]	

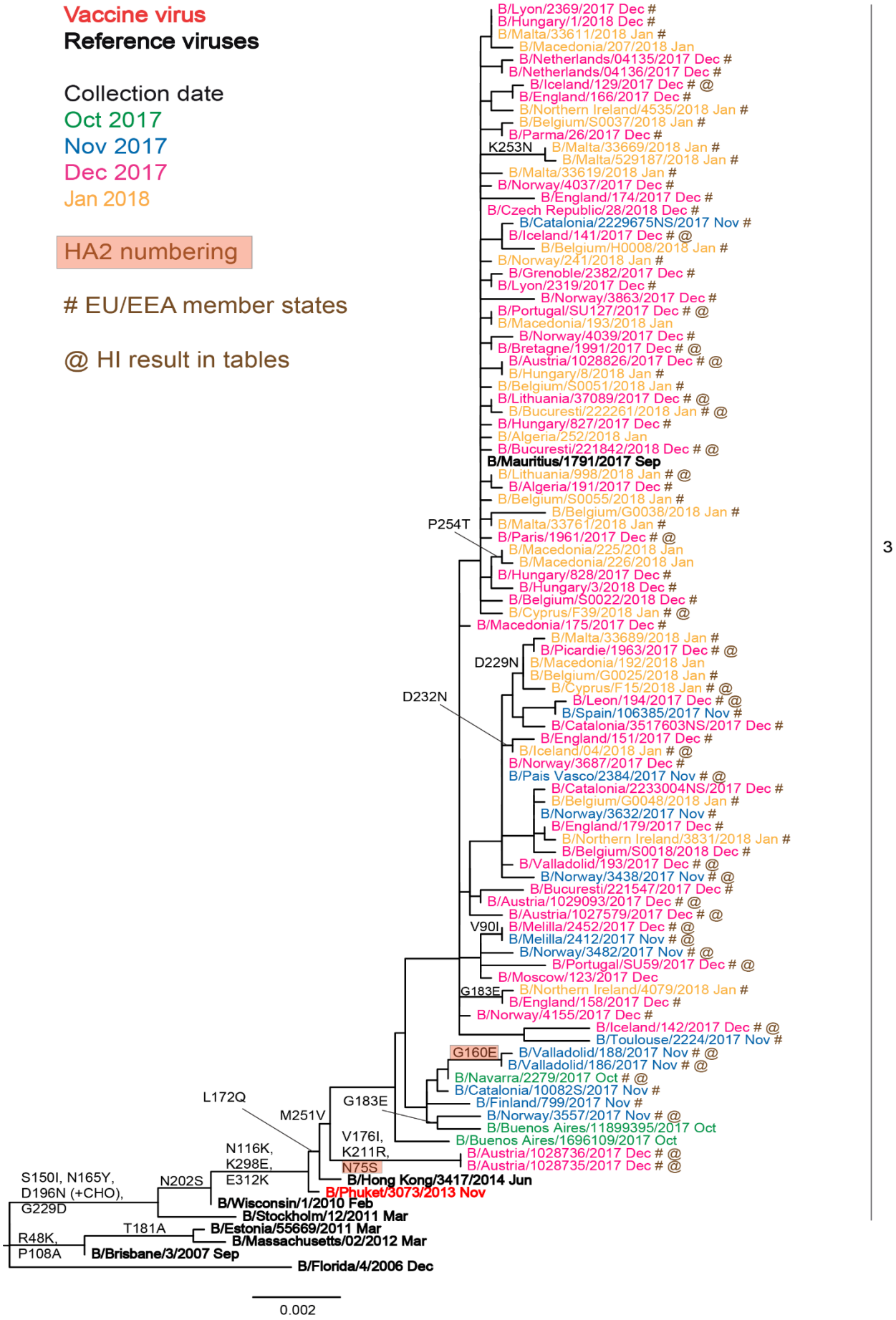
***** Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

Sequence in Phylogenetic tree

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—13/2018, 2 302 viruses have been characterised genetically:

- 354 were defined as A(H1N1)pdm09 subclade 6B.1 as represented by A/Michigan/45/2015;
- 437 were A(H3N2) clade 3C.2a represented by A/Hong Kong/4801/2014, 328 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 3 not attributed to a clade in TESSy reporting guidance;
- 100 were B/Victoria-lineage clade 1A represented by B/Brisbane/60/2008, with 49 falling in the 1A Δ162-163 subclade;
- 1061 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 530 viruses, with collection dates from week 40/2017, at the WIC: 146 A(H1N1)pdm09, 151 A(H3N2), 34 B/Victoria-lineage and 199 B/Yamagata-lineage viruses. Of these only two A(H1N1)pdm09 viruses (A/Bretagne/002/2018: I223R and A/Catalonia/2242523NS/2018: H275Y>H) and one A(H3N2) virus (A/Poitiers/2028/2017: S334R) showed RI by oseltamivir, with the neuraminidases of the viruses carrying the amino acid substitutions indicated.

For weeks 40/2017–10/2018 of the 2017–18 influenza season, countries reported on the antiviral susceptibility of 320 A(H1N1)pdm09 viruses, 449 A(H3N2) viruses and 667 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 only a few human cases were reported 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; the last update was published on 3 July 2017 [9]. WHO posted an analysis of A(H7N9) viruses on 10 February 2017 [10]. In addition, WHO published a summary and assessment of influenza viruses at the human-animal interface on 2 March 2018. The most recent human case occurred early in February 2018 [11]. On 14 February 2018, China notified WHO of the first recorded case of human infection with an avian H7N4 virus [12].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human-animal interface was published by WHO on 2 March 2018 [11]. ECDC updated an earlier rapid risk assessment on the situation in Egypt on 13 March 2015 [13] and posted an epidemiological update on 10 April 2015 [14]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [15]. The latest ECDC overview of avian influenza, produced in collaboration with the European Food Safety Authority and the EU Reference Laboratory for Avian Influenza, was published on 23 March 2018 [16].

WHO CC reports

A description of results generated by the London WHO CC at the WIC and used at WHO vaccine composition meetings held at a) The Peter Doherty Institute, University of Melbourne, 25–27 September 2017, and b) WHO Geneva, 19–21 February 2018, 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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