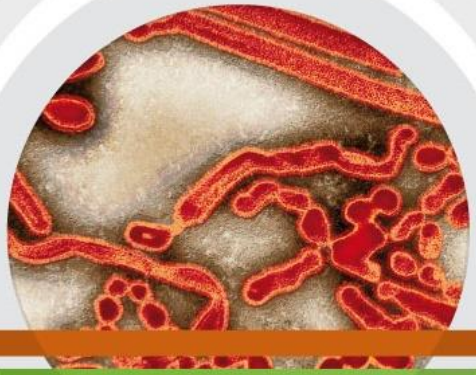

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, May 2018

Summary

This is the fifth report of the 2017–18 influenza season. As of week 20/2018, nearly 240 000 influenza detections across the WHO Europe region have been reported. Types A and B viruses have been detected in the proportions 44% and 56%, respectively, with A(H1N1)pdm09 viruses being slightly more prevalent than A(H3N2) (1:0.98) and B/Yamagata being significantly more prevalent than B/Victoria viruses (52.5:1).

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 1 281 specimens having collection dates after August 2017.

The 49 A(H1N1)pdm09 test viruses characterised antigenically showed good reactivity with antiserum raised against the 2017–18 vaccine virus, A/Michigan/45/2015. The 210 test viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others from the European Region recently deposited in the GISAID EpiFlu database, 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 215 A(H3N2) viruses successfully recovered to date, only 44 (20%) had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir, of which seven were tested since the last report. The majority of these 44 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 251 viruses with collection dates from week 40/2017 genetically characterised at the WIC, 247 were clade 3C.2a (with 144 3C.2a2, 78 3C.2a1, 21 3C.2a3 and four 3C.2a4 subclade viruses) and four were clade 3C.3a. Of the 78 subclade 3C.2a1 viruses 73 and 3, respectively, fell in subgroups 3C.2a1b and 3C.2a1a.

Nine B/Victoria-lineage viruses were tested by HI, and eight reacted well only with post-infection ferret antisera raised against tissue culture-propagated cultivars of B/Norway/2409/2017 and B/Colorado/06/2017, viruses with a deletion of two amino acids in HA1 (Δ162-163). Of the 41 viruses characterised genetically at the WIC with a collection date after week 40/2017, 11 fell within clade 1A and 30 fell within the subgroup (1A(Δ2)) carrying the HA1 double amino acid deletion.

A total of 58 B/Yamagata viruses were characterised antigenically and all 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 2018–2018–19 seasons and for trivalent vaccines in the southern hemisphere 2018 season. The 298 viruses with collection dates from week 40/2017 genetically characterised at the WIC, as others recently circulating in the European region and reported to the GISAID EpiFlu database, fall within genetic clade 3.

This report was prepared by Rod Daniels, 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 40/2017–20/2018), with detections having already exceeded the number for the entire 2016–17 season by over 64%. Nearly 240 000 detections have been reported with type B (56%) predominating over type A (44%) viruses. Of the type A viruses subtyped (n = 45 362) and the type B viruses ascribed to lineage (n = 15 990), A(H3N2) and A(H1N1)pdm09 viruses have been detected in nearly equal proportions, with a ratio of 0.98:1, and B/Yamagata prevailed over B/Victoria, at a ratio of 52.5:1. These ratios represent a decrease and an increase in relative prevalence, respectively, compared to the situation as of week 13/2018 (as summarised in the March 2018 report[1]). Compared to the 2016–17 season, significant numbers of influenza type B viruses were detected early in the 2017–18 season and predominated over type A up to week 11/2018. The dominance of B/Yamagata over B/Victoria has increased from 2.7:1, seen in the 2016–17 winter, to 52.5:1 currently reported; overall, the ratio of type A to type B detections has decreased significantly compared with the 2016–17 season (0.8:1 from 6.5:1), and of the A subtyped viruses a significant increase in the proportion of A(H1N1)pdm09 has been seen (50.6% in 2017–18 compared with 1.1% in 2016–17).

Since week 40/2017, 59 shipments of specimens have been received at the Crick Worldwide Influenza Centre (WIC) from 29 EU/EEA countries. These packages contained 1 281 specimens, a mix of clinical samples and virus isolates, with specimen collection dates after August 2017 (Table 2). The majority (54%) were type A viruses, and A(H3N2) outnumbered A(H1N1)pdm09 at a ratio of 1.3:1. Of the 595 type-B specimens received (47% of the specimens), 71 were B/Victoria-lineage and 468 were B/Yamagata-lineage. The antigenic and genetic properties of influenza viruses, characterised since the March 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 40/2017–20/2018)

	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	**9 156**	**96 353**	**105 509**	**44.0**	**0.8:1**	**126 614**	**86.6**	**6.5:1**
A(H1N1)pdm09	4 987	17 976	22 963	50.6		591	1.1	
A(H3N2)	2 702	19 697	22 399	49.4	0.98:1	53 101	98.9	89.8:1
A not subtyped	1 467	58 680	60 147			**72 922**		
Influenza B	**15 647**	**118 830**	**134 477**	**56.0**		**19 570**	**13.4**	
Victoria lineage	209	90	299	1.9		749	27.1	
Yamagata lineage	7 304	8 387	15 691	98.1	52.5:1	2 016	72.9	2.7:1
Lineage not ascribed	8 134	110 353	118 487			16 805		
Total detections (total tested)	**24 803 (60 658)**	**215 183 (779 071)**	**239 986 (839 729)**			**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, March 2018. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/en/publications-data/influenza-virus-characterisation-march-2018

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

MONTH / Country	Total Number received	A Number received	A Number propagated[1]	H1N1pdm09 Number received	H1N1pdm09 Number propagated[1]	H3N2 Number received	H3N2 Number propagated[2]		B Number received	B Number propagated[1]	B Victoria lineage Number received	B Victoria lineage Number propagated[1]	B Yamagata lineage Number received	B Yamagata lineage 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	1									
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	2	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	1
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	1	2	0	2					2	2
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	11			1	in process	7	in process						3	in process
United Kingdom	5					3	0	3			1	1	1	1
DECEMBER														
Austria	37			18	17	7	0	7					12	12
Belgium	19			7	6	1	0	1					11	6
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			2	2	1	0	1						
Hungary	6			1	1								5	5
Iceland	15			1	1	8	3	5					6	6
Ireland	13			1	1	5	0	5					7	5
Italy	25			12	12	2	0	2					11	11
Latvia	2			2	2									
Lithuania	9			3	1						1	1	5	3
Malta	1			1	0									
Netherlands	16			1	0	1	0	1					14	5
Norway	35			5	1	15	0				2	1	13	7
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	7	7	16	10
Sweden	5			1	in process	4	in process							
United Kingdom	14			1	0	2	0		3	0			8	6

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

MONTH / Country	Total Number received	A Number received	A Number propagated[1]	H1N1pdm09 Number received	H1N1pdm09 Number propagated[1]	H3N2 Number received	H3N2 Number propagated[2]		B Number received	B Number propagated[1]	B Victoria lineage Number received	B Victoria lineage Number propagated[1]	B Yamagata lineage Number received	B Yamagata lineage Number propagated[1]
2018														
JANUARY														
Belgium	25			12	5	5	0	4					8	3
Bulgaria	23			7	6	4	2	0			1	in process	11	6
Cyprus	12	2	0	3	3				2	0			5	5
Czech Republic	1			1	1									
Denmark	4												4	2
Estonia	14	2	0	3	2	3	0	3	1	0			5	4
France	4			2	2	1	0	1					1	1
Germany	25			6	6	6	0	6			5	5	8	8
Greece	26			9	3	3	0	2					14	7
Hungary	7			3	3								4	4
Iceland	6					2	2	0					4	4
Ireland	13			1	1	4	1	2	3	0			5	5
Italy	12			4	3	2	0	2					6	6
Lithuania	16					3	0		2	0	2	1	9	1
Malta	39			3	2	13	1		11	0			12	4
Netherlands	22			5	5	9	7	6			1	1	7	3
Norway	19			5	3	6	2				4	in process	4	0
Poland	2	1	in process								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						
Sweden	4			1	in process	2	in process						1	in process
United Kingdom	37			3	0	22	0		8	0			4	0
FEBRUARY														
Bulgaria	21			8	8						1	in process	12	11
Cyprus	17	1	0			1	0	1	4	0			11	11
France	13			6	in process	1	in process				1	in process	5	in process
Germany	12			3	3	3	0	3			4	4	2	2
Greece	12			3	2	3	1	0					6	5
Netherlands	6			4	4	2	0	2						
Norway	3					1	in process				2	in process		
Poland	34	8	in process	1	in process								25	in process
Spain	8	1	in process	3	in process	3	in process		1	in process				
Sweden	6			2	in process	3	in process						1	in process
United Kingdom	6					6	in process							
MARCH														
Bulgaria	5			3	3						2	in process		
France	31			9	in process	8	in process				1	in process	13	in process
Germany	7			2	2	1	0	1			2	2	2	2
Greece	7			3	1								4	2
Norway	15			5	in process	4	in process				1	in process	5	in process
Poland	10	2	in process	4	in process				4	in process				
Spain	45	1	in process	2	in process	28	in process		3	in process	3	in process	8	in process
Sweden	2												2	in process
United Kingdom	6			2	in process	1	1	0					3	in process
APRIL														
France	12					7	in process						5	in process
Germany	3			1	1	1	1	0					1	1
Norway	21			6	in process	9	in process				2	in process	4	in process
Spain	3					2	in process						1	in process
Sweden	1												1	in process
	1281	24	0	292	205	370	44	171	56	0	71	47	468	296
					22.8%		28.9%					5.5%		36.5%
29 Countries					53.6%							46.4%		

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 2018-05-31

Influenza A(H1N1)pdm09 virus analyses

Results of haemagglutination inhibition (HI) analyses of viruses performed since the March 2018 report are shown in Tables 3-1 to 3-3. All 49 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 but one virus 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 90% to 100% for individual antisera. Eightfold or greater reduced recognition of test viruses compared to homologous titres were observed for antisera raised against two viruses: A/Lviv/N6/2009 – 25 (51%) within twofold, 22 (45%) within fourfold and two (4%) at eightfold; and A/Hong Kong/5659/2012 – 46 (94%) within twofold and three (6%) at sixteenfold.

Of the 49 test viruses, 48 were genetically characterised and, as is the case for viruses antigenically characterised in the March 2018 report for which genetic analysis was pending (Tables 3-4 to 3-6), together with EU/EEA A(H1N1)pdm09 viruses characterised throughout the 2016–17 and 2017–18 seasons for which sequences have been submitted to the GISAID EpiFlu database, all carried haemagglutinins (HAs) belonging to genetic 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 a number of subclusters have emerged (Figure 1). These subclusters are defined by HA1 amino acid substitutions, e.g. S183P, E235D and N260D or T120A or V250A or S183P with additional substitutions.

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 [19]. 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	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	1280	1280	320	320	1280	640	1280	640	2560	2560	2560
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	2560	1280	640	640	1280	640	1280	640	2560	1280	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	80	320	320	80	40	40	40	80	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK2	320	160	1280	1280	160	160	320	80	320	160	1280
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	2560	1280	640	640	1280	640	1280	1280	2560	1280	2560
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	2560	1280	640	640	1280	640	640	640	2560	12802	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	640	320	160	160	640	320	640	320	640	640	1280
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	1280	640	320	640	640	320	640	640	640	640	1280
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	640	320	320	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	1280	1280	640	320	1280	640	1280	1280	2560	1280	5120
TEST VIRUSES															
A/Ireland/54260/2017		6B.1	2017-10-13	C1/MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	2560	5120
A/Ireland/71503/2017		6B.1	2017-12-25	MDCK1	2560	1280	640	640	1280	640	1280	1280	2560	2560	5120
A/Thessaloniki/3/2017		6B.1	2017-12-27	MDCK/E1/MDCK1	2560	1280	320	320	1280	640	1280	640	2560	1280	5120
A/Thessaloniki/15/2018		6B.1	2018-01-05	MDCK/E1/MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	2560	5120
A/Netherlands/00737/2018		6B.1	2018-01-16	SIATx/MDCK1	1280	640	320	160	640	320	640	640	1280	1280	2560
A/Netherlands/10081/2018		6B.1	2018-01-23	MDCK-MIX3/MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	1280	5120
A/Netherlands/10066/2018		6B.1	2018-01-23	MDCK-MIX3/MDCK1	2560	640	640	320	1280	640	1280	640	2560	1280	2560
A/Netherlands/10093/2018		6B.1	2018-01-24	MDCK-MIX2/MDCK1	2560	640	640	320	1280	640	1280	640	2560	1280	5120
A/Netherlands/10208/2018		6B.1	2018-02-08	MDCK-MIX2/MDCK1	1280	640	320	160	640	320	640	640	1280	640	2560
A/Netherlands/10218/2018		6B.1	2018-02-12	MDCK-MIX2/MDCK1	2560	1280	640	320	1280	640	1280	640	2560	1280	5120
A/Netherlands/10278/2018		6B.1	2018-02-15	MDCK-MIX1/MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	1280	5120
A/Netherlands/10273/2018		6B.1	2018-02-19	MDCK-MIX1/MDCK1	2560	1280	640	320	1280	640	1280	1280	2560	2560	5120

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

1 < = <40; 2 < = <80

Vaccine

Sequences in phylogenetic trees

Table 3-2. 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/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]
		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	1280	1280	640	320	640	640	1280	640	1280	1280	1280	2560
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	640	640	640	640	1280	640	640	640	1280	1280	1280	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	80	320	320	80	40	40	80	80	40	40	320
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK2	80	80	640	640	80	160	160	80	160	80	80	640
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK5	1280	1280	640	320	1280	640	1280	1280	640	2560	2560	2560
A/St. Petersburg/27/2011		6	2011-02-14	E1/E3	640	640	640	320	1280	640	640	640	1280	1280	1280	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	320	160	160	640	320	640	320	640	640	640	1280
A/South Africa/3626/2013		6B	2013-06-06	E1/E3	640	640	640	640	640	640	640	640	1280	640	640	2560
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	640	320	320	640	320	640	640	1280	1280	2560	2560
A/Israel/Q-504/2015		6B.2	2015-12-15	C1/MDCK2	640	640	320	320	640	320	640	640	1280	640	2560	2560
A/Paris/1447/2017		6B.1	2017-10-20	MDCK1/MDCK3	640	320	320	160	640	320	320	640	1280	1280	1280	2560
TEST VIRUSES																
A/Belgium/G0543/2017		6B.1	2017-10-06	MDCK1/MDCK1	1280	640	320	160	640	640	640	640	1280	1280	1280	2560
A/Ireland/54308/2017		6B.1	2017-10-13	MDCK2	1280	640	320	160	640	320	640	640	1280	1280	1280	2560
A/Ireland/64110/2017		6B.1	2017-11-27	MDCK2	1280	640	320	320	640	320	1280	640	1280	1280	1280	2560
A/Belgium/G0604/2017		6B.1	2017-12-06	MDCK1	2560	2560	1280	1280	2560	1280	1280	2560	2560	5120	5120	5120
A/Belgium/G0603/2017		6B.1	2017-12-06	MDCK1/MDCK1	2560	1280	1280	1280	2560	1280	1280	2560	5120	2560	5120	5120
A/Belgium/G0616/2017		6B.1	2017-12-11	SIAT1	1280	1280	640	320	1280	640	1280	1280	2560	1280	5120	5120
A/Belgium/S0020/2018		6B.1	2017-12-25	MDCK1	1280	640	640	320	1280	320	640	640	2560	1280	2560	2560
A/Belgium/G0034/2018		6B.1	2018-01-08	MDCK1	1280	640	640	320	1280	640	1280	1280	2560	1280	2560	2560
A/Belgium/G0047/2018		6B.1	2018-01-09	MDCK1	1280	640	640	320	1280	640	1280	640	2560	1280	2560	2560
A/Belgium/G0039/2018		6B.1	2018-01-09	MDCK1	2560	1280	640	640	1280	640	1280	1280	2560	2560	2560	5120
A/Malta/33600/2018		6B.1	2018-01-15	MDCK2	1280	640	320	160	640	320	640	640	1280	1280	1280	2560
A/Malta/33680/2018		6B.1	2018-01-16	MDCK2	640	320	160	160	320	320	320	320	640	640	640	1280
A/Cyprus/F93/2018		6B.1	2018-01-25	SIAT1	640	320	160	160	320	320	320	320	640	640	640	1280
A/Athens.GR/521/2018		6B.1	2018-02-14	MDCK1	1280	1280	640	320	1280	640	640	1280	5120	1280	1280	5120
A/Baden-Wurttemberg/77/2018		6B.1	2018-02-15	C1/MDCK1	1280	640	640	320	640	320	640	640	1280	1280	1280	2560
A/Hessen/14/2018		6B.1	2018-02-19	C1/MDCK1	640	320	160	160	320	160	320	320	640	640	640	1280
A/Sachsen/41/2018		6B.1	2018-02-27	C1/MDCK1	640	320	160	160	320	160	320	320	640	640	640	1280
A/Athens.GR/767/2018		6B.1	2018-03-05	MDCK1	1280	1280	640	320	1280	640	640	1280	2560	1280	1280	5120
A/Brandenburg/19/2018		6B.1	2018-03-09	C1/MDCK1	640	640	320	160	640	320	320	640	1280	640	640	2560
A/Rheinland-Pfalz/34/2018		6B.1	2018-03-15	C1/MDCK1	1280	640	640	320	640	640	640	1280	2560	2560	2560	2560
A/Bremen/21/2018		6B.1	2018-04-09	C1/MDCK1	1280	1280	640	640	1280	640	1280	1280	5120	1280	5120	5120

Vaccine

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

1 < = <40; 2 < = <80

Sequences in phylogenetic trees

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											
	Passage history			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
	Ferret number			Egg NIB F42/16[*1]	Egg F06/16[*1]	MDCK F09/15[*1]	MDCK F14/13[*1]	MDCK F22/13[*1]	Egg F26/14[*1]	MDCK F30/12[*1]	Egg F03/14[*1]	Egg F02/16[*1]	MDCK F08/17[*1]	MDCK F03/18[*2]
	Genetic group			6B.1				5	6	6A	6B	6B.1	6B.2	6B.1
REFERENCE VIRUSES														
A/Michigan/45/2015		2015-09-07	E3/E2	1280	640	320	320	640	640	1280	640	2560	2560	2560
A/California/7/2009	clone 38-32	2009-04-09	E3/E3	640	1280	320	320	320	320	640	640	1280	640	1280
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	40	40	320	160	40	<	<	40	40	40	160
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK2	80	80	640	640	80	80	160	80	320	160	640
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK5	320	320	320	160	640	320	640	320	1280	640	1280
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	640	640	640	640	640	640	640	2560	640	2560
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	640	320	160	160	640	320	640	320	1280	640	1280
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	320	180	160	160	160	160	160	320	640	320	640
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	640	320	160	160	320	160	320	320	1280	640	1280
A/Israel/Q-504/2015	6B.1	2015-12-15	CJ/MDCK2	640	640	160	320	640	320	640	640	1280	1280	1280
A/Paris/1447/2017	6B.2	2017-10-20	MDCK1/MDCK3	320	160	160	80	320	160	320	320	1280	640	1280
	6B.1													
TEST VIRUSES														
A/Belgium/G0043/2018	6B.1	2018-01-08	MDCK3	320	320	160	160	320	320	320	320	640	640	1280
A/Bulgaria/215/2018	6B.1	2018-01-15	SIAT2/MDCK1	640	640	320	320	640	640	640	640	1280	1280	2560
A/Bulgaria/540/2018		2018-01-23	SIAT2/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Bulgaria/531/2018	6B.1	2018-01-23	SIAT2/MDCK1	640	640	320	320	640	320	640	640	1280	1280	2560
A/Bulgaria/699/2018	6B.1	2018-01-29	SIAT2/MDCK1	1280	640	320	320	320	320	640	640	1280	1280	2560
A/Bulgaria/783/2018	6B.1	2018-02-03	SIAT2/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	>5120
A/Bulgaria/962/2018	6B.1	2018-02-20	SIAT2/MDCK1	640	640	320	160	640	320	40	640	1280	1280	2560
A/Bulgaria/980/2018	6B.1	2018-02-20	SIAT2/MDCK1	1280	640	320	160	640	320	40	640	1280	1280	2560
A/Bulgaria/985/2018	6B.1	2018-02-20	SIAT2/MDCK1	1280	640	640	320	640	640	640	640	1280	2560	2560
A/Bulgaria/987/2018	6B.1	2018-02-20	SIAT2/MDCK1	1280	1280	640	640	1280	640	1280	1280	2560	2560	5120
A/Arta.GR/681/2018	6B.1	2018-02-23	MDCK1	640	320	320	160	640	320	320	320	1280	640	2560
A/Bulgaria/1008/2018	6B.1	2018-02-23	SIAT2/MDCK1	1280	640	640	320	1280	640	40	640	2560	1280	2560
A/Bulgaria/1013/2018	6B.1	2018-02-27	SIAT2/MDCK1	1280	640	320	320	640	320	640	640	1280	2560	2560
A/Bulgaria/1029/2018	6B.1	2018-03-12	SIAT2/MDCK1	1280	640	320	160	640	640	640	640	2560	1280	2560
A/Bulgaria/1039/2018	6B.1	2018-03-15	SIAT2/MDCK1	1280	1280	640	320	1280	640	640	640	2560	1280	2560
A/Bulgaria/1038/2018	6B.1	2018-03-15	SIAT2/MDCK1	1280	640	320	320	640	640	640	640	2560	1280	2560
				Vaccine										

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
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 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	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	6B.1	2015-10-26	E4/E2	640	640	320	320	640	320	640	320	1280	640	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	640	320	320	160	320	320	320	320	640	640	1280
TEST VIRUSES															
A/Bulgaria/892/2017		6B.1	2017-12-15	MDCK2	1280	1280	640	320	640	640	640	640	2560	1280	2560
A/Segovia/226/2017		6B.1	2017-12-19	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Athens.GR/2680/2017		6B.1	2017-12-20	MDCK1	1280	640	640	320	640	320	640	640	1280	1280	2560
A/Segovia/235/2017		6B.1	2017-12-21	MDCK1/MDCK2	640	640	320	160	640	320	320	640	1280	640	2560
A/Segovia/233/2017		6B.1	2017-12-21	MDCK1/MDCK1	1280	1280	640	320	1280	640	640	640	2560	1280	5120
A/Valladolid/236/2017		6B.1	2017-12-22	MDCK1/MDCK1	1280	1280	640	320	1280	640	640	640	2560	1280	5120
A/Valladolid/238/2017		6B.1	2017-12-23	MDCK1/MDCK1	1280	640	320	160	640	320	640	640	1280	1280	2560
A/Valladolid/240/2017		6B.1	2017-12-23	MDCK1/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Valladolid/243/2017		6B.1	2017-12-24	MDCK1/MDCK1	1280	1280	640	320	640	320	640	640	1280	1280	2560
A/Valladolid/242/2017		6B.1	2017-12-24	MDCK1/MDCK1	1280	640	320	320	640	320	640	640	1280	1280	5120
A/Valladolid/260/2017		6B.1	2017-12-26	MDCK1/MDCK1	1280	1280	640	320	640	640	640	640	2560	1280	2560
A/Salamanca/256/2017		6B.1	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		6B.1	2017-12-27	MDCK3/MDCK1	640	80	320	160	320	160	320	160	640	640	1280
A/Roma/10/2017		6B.1	2017-12-27	MDCK2/MDCK1	640	640	320	160	640	320	320	640	1280	640	2560
A/Parma/128/2017		6B.1	2017-12-28	MDCK2/MDCK1	640	640	320	160	640	320	640	640	1280	640	2560
A/Parma/130/2017		6B.1	2017-12-29	MDCK2/MDCK1	640	160	320	160	320	160	320	320	640	640	1280
A/Pavia/21/2017		6B.1	2017-12-29	MDCK2/MDCK1	640	320	320	160	320	160	320	320	640	640	2560
A/Padova/1/2017		6B.1	2017-12-30	MDCK2/MDCK1	640	640	320	320	640	320	640	640	1280	640	2560

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

Vaccine

Sequence in Phylogenetic tree

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	640	640	320	320	640	640	1280	640	1280	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	1280	2560
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	40	80	320	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	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	1280	2560
A/St. Petersburg/27/2011	6	2011-02-14	E1/E3	1280	1280	640	640	1280	640	1280	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	640	1280
A/South Africa/3626/2013	6B	2013-06-06	E1/E3	1280	640	640	640	640	640	640	1280	1280	640	640	2560
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	640	1280	640	320	1280	640	1280	640	2560	1280	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	1280
A/Paris/1447/2017	6B.1	2017-10-20	MDCK1/MDCK3	1280	640	640	320	640	640	640	640	1280	1280	1280	2560
TEST VIRUSES															
A/Firenze/1/2017	6B.1	2017-12-05	MDCK3/MDCK1	1280	640	320	320	640	640	1280	640	2560	1280	1280	2560
A/Firenze/2/2017	6B.1	2017-12-07	MDCK3/MDCK1	640	640	320	160	640	320	320	640	1280	640	1280	2560
A/Roma/7/2017	6B.1	2017-12-11	MDCK2/MDCK1	1280	640	640	320	640	640	1280	640	2560	1280	1280	2560
A/Perugia/45/2017	6B.1	2017-12-14	MDCK2/MDCK1	1280	640	320	320	640	640	640	640	1280	1280	1280	2560
A/Pavia/19/2017	6B.1	2017-12-22	MDCK2/MDCK1	640	160	320	320	320	320	320	320	1280	640	640	2560
A/Pavia/20/2017	6B.1	2017-12-24	MDCK2/MDCK1	1280	640	320	320	640	640	1280	640	1280	1280	1280	2560
A/Slovenia/106/2018	6B.1	2018-01-07	SIATx/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	1280	5120
A/Slovenia/119/2018	6B.1	2018-01-09	SIATx/MDCK1	320	320	160	160	320	320	640	640	640	640	640	1280
A/Slovenia/112/2018	6B.1	2018-01-09	SIATx/MDCK1	640	640	320	160	640	640	640	640	1280	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	1280	2560
A/Slovenia/373/2018		2018-01-17	SIATx/MDCK1	640	640	320	320	640	320	640	640	1280	1280	1280	2560
A/Slovenia/366/2018	6B.1	2018-01-17	SIATx/MDCK1	1280	1280	640	320	1280	640	1280	1280	2560	1280	1280	5120

Vaccine

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

1 < = <40; 2 < = <80

Sequence in Phylogenetic tree

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

Viruses	Other information	Passage history	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		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	320	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		6B.1		SIAT1	5120	2560	1280	640	2560	1280	2560	2560	5120	5120	10240
A/Bucuresti/221625/2017		6B.1	2017-12-15	MDCK1/MDCK1	2560	640	640	320	1280	640	1280	1280	2560	1280	5120
A/Cyprus/F11/2018		6B.1	2018-01-05	MDCK1	1280	640	320	320	640	320	640	640	2560	1280	2560
A/Greece/32/2018		6B.1	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

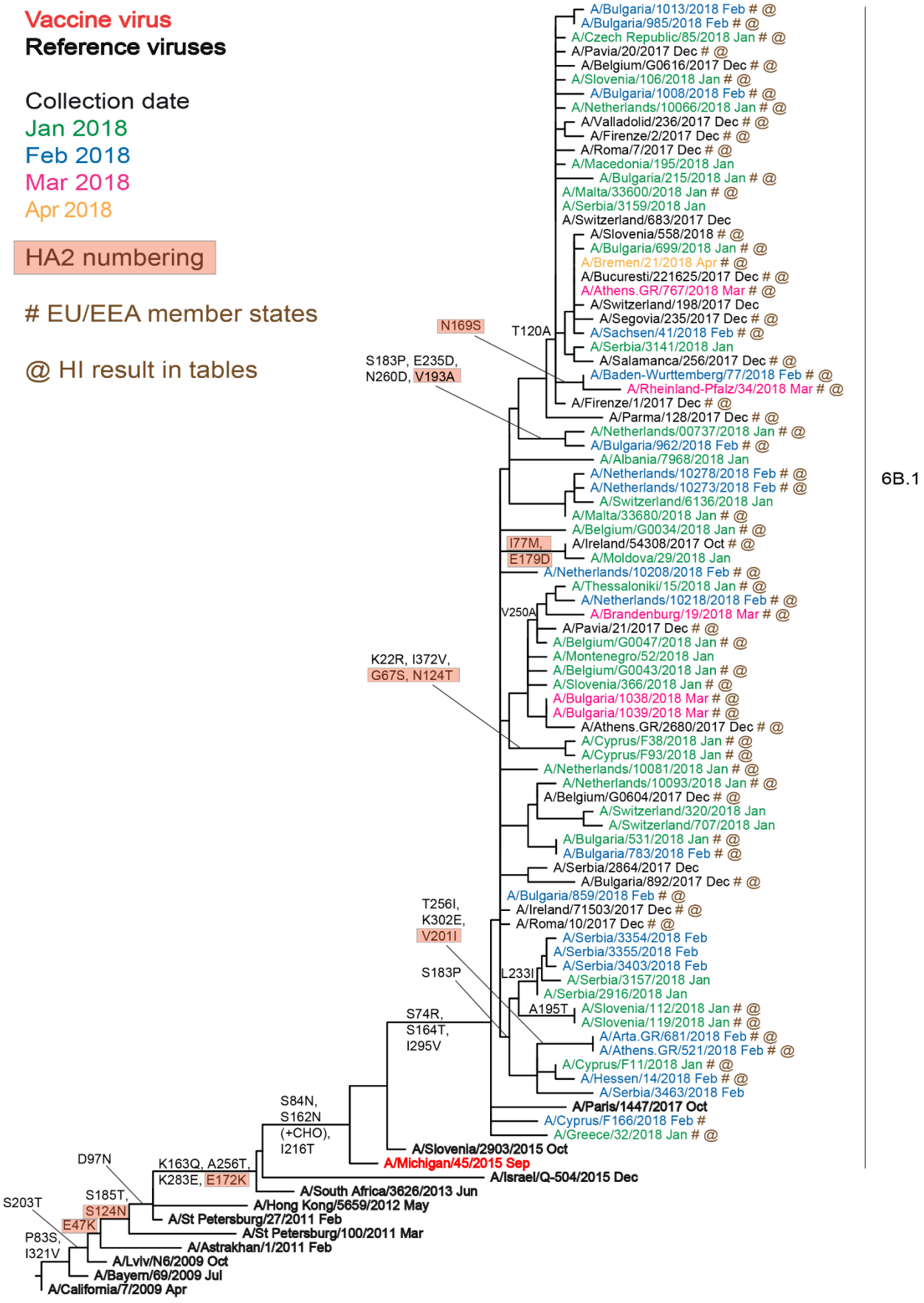
Vaccine

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

1 < = <40; 2 < = <80

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 370 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 = 215), as shown by positive neuraminidase activity, only 44 (20%) had sufficient HA activity in the presence of 20nM oseltamivir to allow antigenic analysis by HI assay. Since the March 2018 report only seven viruses recovered, based on positive neuraminidase activity, retained sufficient HA activity to allow antigenic analysis by HI (Table 4). Only one 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 six of the viruses at titres within fourfold of the homologous titre of the antiserum, four within twofold. An antiserum raised against egg-propagated A/Singapore/INFIMH-16-0019/2016, recommended for use in vaccines for the southern hemisphere 2018 and northern hemisphere 2018–19, recognised three of the seven test viruses at titres within fourfold of the titre of the antiserum for the homologous virus.

An antiserum raised against A/Bretagne/1413/2017, a 3C.2a2 subclade virus (see below), recognised two test viruses (both subclade 3C.2a2) at titres equivalent to the homologous titre of the antiserum, while the other five test viruses, including a subclade 3C.2a2 virus were recognised at titres at least eightfold reduced compared to the homologous titre. The low reacting subclade 3C.2a2 virus, A/Athens.GR/341/2018, carried additional HA1 amino acid substitutions of S21P, R92K, S144R, K160T (gain of a N-linked glycosylation motif at residues 158-160), N216S and F219R, compared to A/Bretagne/1413/2017.

Three 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. All three, A/Oman/2585/2016, A/Norway/4436/2016 and A/Greece/4/2017, had HA genes that fell into genetic subclade 3C.2a1, with A/Greece/4/2017 falling into a genetic subgroup 3C.2a1a (see below). The antisera raised against A/Oman/2585/2016, A/Norway/4436/2016 and A/Greece/4/2017 recognised, respectively, 5, 6 and 6 of the 7 test viruses at titres similar to the titres of the antisera for the majority of the panel of reference viruses.

Antiserum raised against the cell culture-propagated cultivar of A/Stockholm/6/2014, a clade 3C.3a virus, was also used. This antiserum recognised four of the seven test viruses at titres within fourfold of the titre of the antiserum with the homologous virus. However, the only clade 3C.3a test virus in the panel, A/Bayern/47/2018, showed a sixteenfold reduction in HI titre compared to the homologous titre and carried additional HA1 amino acid substitutions of L3I, S91N, N144K (loss of a N-linked glycosylation motif at residues 144-146), F193S, V204I, R261Q and K326R, compared to A/Stockholm/6/2014.

Phylogenetic analysis of the HA genes of representative A(H3N2) viruses from Europe with recent collection dates, after 31 August 2017 as available in the GISAID EpiFlu database, 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 subclades and subgroups are:

- Clade 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.
- Subclade 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.
- Subgroup 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.
- Subgroup 3C.2a1b: Those in subclade 3C.2a1 plus **K92R** and **H311K** in **HA1**, e.g. A/England/74560298/2017.
- Subclade 3C.2a2: Those in clade 3C.2a plus **T131K**, **R142K** and **R261Q** in **HA1**, e.g. A/Norway/4465/2016.
- Subclade 3C.2a3: Those in clade 3C.2a plus **N121K** and **S144K** in **HA1**, e.g. A/Norway/4849/2016.

[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

- Subclade 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.
- Clade 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 great majority of recently circulating viruses have HA genes that fall into genetic groups within clade 3C.2a, with a low number of viruses falling in clade 3C.3a. Within EU/EEA countries recently circulating viruses have fallen in approximately equal proportions into subclades 3C.2a2 and 3C.2a1, with the majority of viruses in the latter subclade having HA genes that fell into genetic subgroup 3C.2a1b (Figure 2). 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.

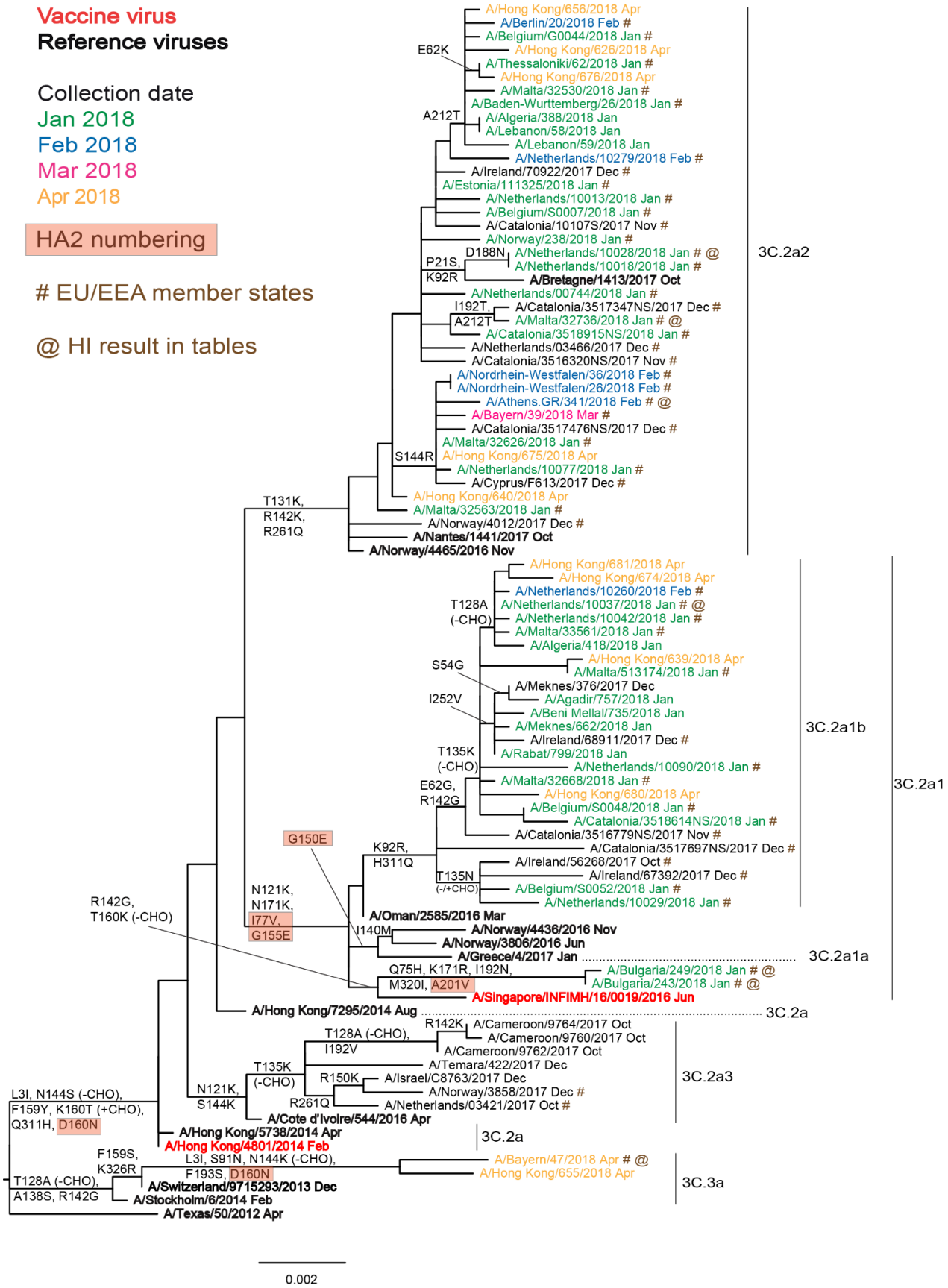
Table 4. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
				A/Stock 6/14 SIAT F14/14*1 3C.3a	A/HK 5738/14 MDCK F30/14*1 3C.2a	A/HK 4801/14 Egg F42/15*1 3C.2a	A/Bretagne 1413/17 SIAT F01/18 3C.2a2	A/Oman 2585/16 SIAT NIB F50/16*1 3C.2a1	A/Nor 4436/16 SIAT F03/17*1 3C.2a1	A/Greece 4/17 SIAT F27/17*1 3C.2a1a	A/Sing 0019/16 Egg 10^{-4} F41/17*1 3C.2a1
Passage history											
Ferret number											
Genetic group											
REFERENCE VIRUSES											
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT2	640	160	160	160	160	320	320	160
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT3	320	320	160	320	320	640	320	640
A/Hong Kong/4801/2014	isolate 1 3C.2a	2014-02-26	E6/E2	80	320	1280	640	320	320	640	1280
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	80	1280	160	320	320	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-06-14	E5/E1	40	40	320	80	160	160	160	1280
TEST VIRUSES											
A/Malta/32736/2018	3C.2a2	2018-01-05	SIAT1	320	320	320	1280	320	640	320	320
A/Netherlands/10028/2018	3C.2a2	2018-01-08	MDCK-MIX2/SIAT1	160	160	80	1280	320	320	320	160
A/Bulgaria/249/2018	3C.2a1	2018-01-12	SIAT2/SIAT1	160	160	80	160	160	320	160	320
A/Netherlands/10037/2018	3C.2a1b	2018-01-15	MDCK-MIX2/SIAT1	80	80	40	80	160	160	320	320
A/Bulgaria/243/2018	3C.2a1	2018-01-16	SIAT2/SIAT1	80	80	40	160	80	160	160	160
A/Athens.GR/341/2018	3C.2a2	2018-02-02	SIAT1	320	160	80	160	320	320	320	80
A/Bayern/47/2018	3C.3a	2018-04-06	C2/SIAT1	40	40	<	80	80	80	80	40
						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

Sequences in phylogenetic trees

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



Influenza B virus analyses

A total of 595 influenza type B-positive specimens with collection dates after August 2017 have been received, with 539 being ascribed to a lineage: 71 B/Victoria-lineage and 468 B/Yamagata (Table 2).

Influenza B – Victoria lineage

Nine tissue culture-propagated test viruses have been antigenically characterised since the March 2018 report (Table 5-1). Eight of the nine test viruses were poorly recognised by the six antisera raised against clade 1A viruses, which included the antiserum raised against the current vaccine virus, egg-propagated B/Brisbane/60/2008. A single virus, A/Berlin/40/2018, showed good reactivity (within twofold) with antisera raised against cell culture-propagated cultivars of B/Hong Kong/514/2009, B/Ireland/3154/2016 and B/Nordrhein-Westfalen/1/2016, which had homologous titres of 80, 160 and 40, respectively. Antiserum raised against cell culture-propagated B/Norway/2409/2017, a virus carrying a double amino acid deletion in HA1, Δ(K162, N163), recognised eight of the test viruses at titres within twofold of the homologous titre, which was only 40. Eight of the test viruses were also tested against cell culture- and egg-propagated cultivars (the B/Victoria lineage vaccine component recommended for northern hemisphere 2018–19 vaccines) of B/Colorado/06/2017, a Δ(K162, N163) virus: the antiserum raised against the cell culture-propagated cultivar recognised seven test viruses at titres within twofold of its homologous titre while that raised against the egg-propagated cultivar recognised only three within fourfold of its homologous titre. All three antisera raised against Δ(K162, N163) viruses recognised A/Berlin/40/2018 poorly. 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, 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**. Eight of the recently characterised test viruses are double deletion viruses (1A(Δ2) in Table 5-1 and Δ(K162, N163) in Figure 3) as is the case for the seven viruses that were characterised antigenically in the March 2018 report (Table 5-2 and Figure 3). 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 58 B/Yamagata-lineage test viruses analysed since the March 2018 report are shown in Tables 6-1 to 6-4. The 298 viruses analysed genetically to date, with collection dates since week 40/2017, all 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 all test viruses at titres within fourfold of the titre of the antiserum with the homologous virus and 57 (98%) within twofold. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 similarly recognised all test viruses at titres within fourfold of the homologous titre of the antiserum and 44 (76%) within twofold. Antisera raised against two other egg-propagated clade 3 viruses, B/Wisconsin/1/2010 (a former vaccine virus) and B/Stockholm/12/2011, recognised all (100%) and 56 (97%) test viruses, respectively, at titres within fourfold of the homologous titres with 52 (90%) and 22 (38%) being recognised within twofold. An antiserum raised against a recently circulating clade 3 cell culture-propagated virus, B/Mauritius/1791/2017, recognised 50 (34%) test viruses at titres within fourfold of the homologous titre, with 34 (59%) 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 25 (43%), 36 (62%) and 26 (45%) test viruses, respectively, at titres within fourfold of the titres of the antisera with their homologous viruses. Similarly, an antiserum raised an older egg-propagated clade 2 virus, B/Brisbane/3/2007, recognised only 3 (12%) of 26 test viruses at titres within fourfold of the homologous titre.

Of the 58 recently characterised viruses, 57 have been sequenced and all fell in genetic clade 3 (Tables 6-1 to 6-4) as did those for which genetic characterisation had not been completed at the time of the March 2018 report (Tables 6-5 to 6-7). 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 the GISAID EpiFlu database, 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 Q122K with T181A, D229N, D232N [introducing a potential N-linked glycosylation site], K253N or P254T), is occurring but with no obvious antigenic effects (Tables 6-1 to 6-7).

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/Bris 60/08 Egg NIB F52/16[*2]	B/Malta 636714/11 Egg F29/13[*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]	B/Colarado 06/17 MDCK F09/18[*2]	B/Colarado 06/17 Egg F10/18[*2]
		Passage history													
		Ferret number													
		Genetic group		1A	1A	1A	1A	1B	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)
REFERENCE VIRUSES													
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	1280	320	160	160	40	20	20	<	20	40
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	320	320	320	40	40	20	<	20	80
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	640	320	640	40	40	40	<	40	80
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	80	80	40	80	80	80	<	10	<
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	40	40	20	80	160	80	<	10	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	1280	20	40	10	40	40	40	<	10	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK2	80	<	<	10	<	20	<	40	160	40
B/Colarado/06/2017	1A(Δ2)	2017-02-05	MDCK1/MDCK2	80	<	<	10	<	10	<	40	80	40
B/Colarado/06/2017	1A(Δ2)	2017-02-05	E5/E1	640	80	80	40	10	10	<	40	160	320
TEST VIRUSES													
B/Valladolid/192/2017	1A(Δ2)	2017-12-01	MDCK1/MDCK1	80	<	<	10	<	20	<	40	160	40
B/Netherlands/00302/2018	1A(Δ2)	2018-01-17	SIAT1/MDCK1	80	<	10	10	<	20	<	40	ND	ND
B/Baden-Wurttemberg/108/2018	1A(Δ2)	2018-02-12	C1/MDCK1	80	<	<	10	<	10	<	40	160	40
B/Hamburg/10/2018	1A(Δ2)	2018-02-19	C1/MDCK1	80	<	<	10	<	10	<	40	160	80
B/Nordrhein-Westfalen/65/2018	1A(Δ2)	2018-02-22	C1/MDCK1	80	<	<	10	<	20	<	40	160	40
B/Hessen/33/2018	1A(Δ2)	2018-02-26	C1/MDCK1	160	<	<	20	<	20	<	80	160	80
B/Berlin/40/2018	1A	2018-03-01	C1/MDCK1	1280	40	40	20	40	80	40	<	10	<
B/Baden-Wurttemberg/137/2018	1A(Δ2)	2018-03-01	C1/MDCK1	80	<	<	10	<	10	<	40	160	80
B/Bulgaria/1021/2018	1A(Δ2)	2018-03-07	SIAT2/MDCK1	160	<	<	10	<	10	<	40	160	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
ND = Not Done
Sequences in phylogenetic trees

Table 5-2. 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	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	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	1A(Δ2)	2018-01-10	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Bayern/14/2018	1A(Δ2)	2018-01-16	C1/MDCK1	80	<	<	<	<	<	10	<	<	<	40
B/Niedersachsen/34/2018	1A(Δ2)	2018-01-25	C1/MDCK1	160	<	<	10	<	<	10	<	<	<	40
B/Niedersachsen/32/2018	1A(Δ2)	2018-01-25	C1/MDCK1	320	<	<	40	<	10	20	<	<	<	40
B/Niedersachsen/33/2018	1A(Δ2)	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

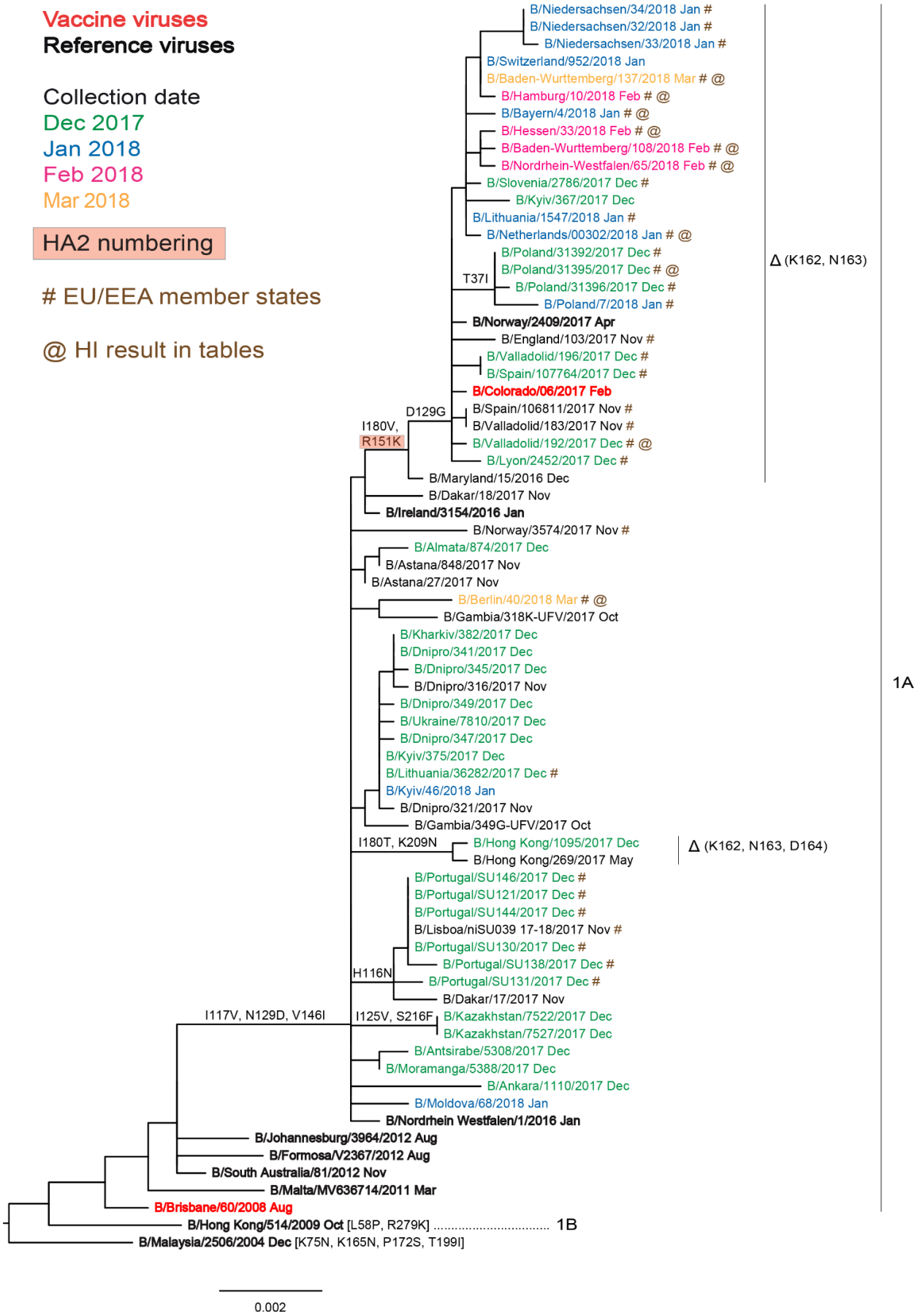


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

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]	F10/16[*2]	F16/14[*2]	F36/15[*2]	F06/15[*2]	F27/15[*2]	F25/17[*2]	F04/18[*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	40	1280	320	320	80	320	20
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	1280	160	640	80	160	80	80	80	80	80
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	2560	640	640	160	1280	320	160	160	320	80
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	1280	640	160	40	1280	160	160	80	160	20
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	320	80	20	640	320	160	80	160	80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	2560	160	40	10	320	160	160	80	80	40
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	160	160	80	320	160	160
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	40	10	320	160	160	40	160	40
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK3	5120	320	320	320	640	320	160	320	320	320
TEST VIRUSES													
B/Ireland/70681/2017	3	2017-12-14	MDCK1	2560	160	80	20	160	160	80	80	80	160
B/Estonia/111081/2017	3	2017-12-19	MDCK1/MDCK1	1280	80	40	20	80	80	40	80	80	80
B/Ireland/71508/2017	3	2017-12-23	MDCK1	2560	160	160	40	160	160	80	160	160	160
B/Ireland/00264/2017	3	2017-12-29	MDCK1	2560	160	160	40	160	160	80	160	160	160
B/Ireland/01654/2018	3	2018-01-03	MDCK1	2560	160	160	40	160	160	80	160	160	160
B/Estonia/111204/2018	3	2018-01-03	MDCK1/MDCK1	2560	160	160	40	160	160	80	160	80	160
B/Ireland/02196/2018	3	2018-01-04	MDCK1	5120	160	160	40	160	160	80	160	160	160
B/Thessaloniki/76/2018	3	2018-01-15	MDCK/E1/MDCK1	5120	640	80	40	160	160	80	160	160	160
B/Thessaloniki/88/2018	3	2018-01-18	MDCK/E1/MDCK1	2560	80	80	20	160	80	80	80	80	80
B/Netherlands/01131/18		2018-01-21	SIAT1/MDCK1	5120	160	160	40	320	160	160	160	160	160
B/Thessaloniki/114/2018	3	2018-01-24	MDCK/E1/MDCK1	2560	80	80	20	160	160	80	80	80	160
B/Thessaloniki/159/2018	3	2018-02-01	MDCK/E1/MDCK2	2560	80	80	40	160	160	80	160	80	160
B/Thessaloniki/163/2018	3	2018-02-02	MDCK/E1/MDCK1	5120	320	320	320	640	640	320	640	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

Sequences in phylogenetic trees

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	B/Bris	B/Estonia	B/Mass	B/Mass	B/Wis	B/Stock	B/Phuket	B/Phuket	B/Maur
	Ferret number			3073/13	3/07	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13	1791/17
	Genetic Group			Egg	Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	MDCK
				SH614[-1,3]	F38/14[-2]	F27/13[-2]	F10/16[-2]	F16/14[-2]	F36/15[-2]	F06/15[-2]	F27/15[-2]	F25/17*[-2]	F04/18*[-2]
				3	2	2	2	2	3	3	3	3	3
REFERENCE VIRUSES													
B/Brisbane/3/2007	2	2007-09-03	E2/E2	1280	640	160	40	1280	320	160	160	320	20
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	160	640	80	160	80	40	40	80	40
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	320	640	80	640	160	80	80	160	40
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	640	320	80	20	640	80	80	40	160	10
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	1280	160	40	10	160	80	160	40	160	40
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	2560	80	160	80	160	160	80	160	160	320
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	160	40	10	320	80	80	40	160	40
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK3	5120	320	640	640	320	640	160	320	640	640
TEST VIRUSES													
B/Ireland/65465/2017	3	2017-11-30	MDCK2	1280	80	40	20	80	80	40	80	160	80
B/Norway/3718/2017	3	2017-12-01	MDCK2	1280	40	40	10	80	40	20	40	80	80
B/Ireland/67111/2017	3	2017-12-05	MDCK2	1280	80	80	40	80	80	40	80	80	160
B/Norway/3687/2017	3	2017-12-05	MDCK1	1280	80	80	40	80	80	40	80	160	160
B/Norway/3863/2017	3	2017-12-06	MDCK1	1280	80	40	20	80	80	40	40	80	40
B/Ireland/70751/2017	3	2017-12-15	MDCK2	1280	80	40	20	80	80	40	80	80	80
B/Ireland/00263/2018	3	2018-01-02	MDCK2	1280	80	40	20	80	40	40	40	80	80
B/Ireland/02602/2018	3	2018-01-06	MDCK2	1280	80	80	40	80	80	40	80	160	160
B/Ireland/02600/2018	3	2018-01-06	MDCK2	1280	80	40	20	80	80	40	80	80	80
B/Malta/33570/2018	3	2018-01-15	MDCK1	2560	80	80	80	160	160	40	160	160	160
B/Malta/33535/2018	3	2018-01-15	MDCK1	2560	80	80	20	80	80	40	80	80	160
B/Malta/33611/2018	3	2018-01-16	MDCK1	2560	80	80	40	160	80	40	80	160	160
B/Malta/33776/2018	3	2018-01-17	MDCK1	5120	160	160	80	160	160	80	160	320	320
Sequences in phylogenetic trees												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 6-3. 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/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
		Passage history											
		Ferret number			SH614*1,3	F27/13*2	F10/16*2	F16/14*2	F36/15*2	F06/15*2	F27/15*2	F25/17*2	F04/18*2
		Genetic Group			3	2	2	2	3	3	3	3	3
REFERENCE VIRUSES													
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	1280	640	80	160	160	40	80	80	40
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK3	1280	640	160	640	320	160	80	320	40
B/Massachusetts/02/2012		2	2012-03-13	E3/E3	1280	160	20	640	160	160	20	160	10
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	80	20	320	160	160	80	320	80
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	40	10	160	160	160	40	160	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	160	80	160	160	80	160	160	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	40	10	160	160	80	40	160	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK3	5120	320	320	320	320	160	320	320	320
TEST VIRUSES													
B/Belgium/G0593/2017		3	2017-11-21	MDCK1/MDCK1	2560	80	20	320	160	40	80	80	80
B/Belgium/G0629/2017		3	2017-12-18	SIAT1/MDCK1	2560	160	40	160	160	80	80	160	160
B/Belgium/G0634/2017		3	2017-12-19	MDCK1/MDCK1	2560	80	20	160	80	40	80	80	80
B/Belgium/S0023/2018		3	2017-12-26	MDCK1	2560	80	40	160	80	80	80	160	160
B/Belgium/G0011/2018		3	2017-12-28	SIAT1/MDCK1	1280	80	<	40	40	20	40	40	40
B/Belgium/S0037/2018		3	2018-01-08	MDCK1	1280	80	10	80	80	40	40	80	80
B/Belgium/H0008/2018		3	2018-01-11	MDCK1	2560	80	10	80	80	40	80	80	80
B/Cyprus/F89/2018		3	2018-01-24	MDCK1	2560	160	10	80	160	40	80	80	160
B/Cyprus/F103/2018		3	2018-01-29	MDCK1	1280	40	10	40	80	40	40	80	40
B/Cyprus/F102/2018		3	2018-01-29	MDCK1	2560	160	<	160	160	40	80	160	160
B/Cyprus/F136/2018		3	2018-02-01	MDCK1	2560	160	10	160	160	40	80	80	160
B/Cyprus/F130/2018		3	2018-02-01	MDCK1	2560	160	20	160	160	40	80	160	160
B/Cyprus/F127/2018		3	2018-02-01	MDCK1	2560	160	<	160	160	40	80	160	160
B/Cyprus/F121/2018		3	2018-02-01	MDCK1	2560	160	40	160	160	40	80	160	160
B/Cyprus/F140/2018		3	2018-02-02	MDCK1	2560	160	10	160	160	40	80	160	160
B/Cyprus/F161/2018		3	2018-02-08	MDCK1	2560	160	10	160	160	40	80	80	80
B/Ioannina.GR/528/2018		3	2018-02-12	MDCK1	2560	160	10	160	160	40	80	160	160
B/Niedersachsen/78/2018		3	2018-02-12	C1/MDCK1	1280	80	20	160	160	80	80	160	80
B/Cyprus/F222/2018		3	2018-02-14	MDCK1	2560	160	<	80	80	40	80	80	160
B/Cyprus/F221/2018		3	2018-02-14	MDCK1	2560	80	40	160	80	40	80	80	160
B/Cyprus/F216/2018		3	2018-02-14	MDCK1	2560	160	40	160	160	80	80	160	160
B/Bayern/64/2018		3	2018-02-19	C1/MDCK1	2560	80	40	160	160	40	80	160	160
B/Sachsen-Anhalt/66/2018		3	2018-03-01	C1/MDCK1	2560	160	40	160	160	40	80	160	160
B/Ftiotida.GR/744/2018		3	2018-03-02	MDCK1	2560	160	40	160	160	80	160	160	160
B/Nordrhein-Westfalen/91/2018		3	2018-03-20	C2/MDCK1	2560	160	40	160	160	80	160	160	160
B/Bayern/99/2018		3	2018-04-09	C1/MDCK1	2560	80	40	160	160	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

Sequences in phylogenetic trees

Table 6-4. 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 SH614[-1,3]	B/Estonia 55669/11 MDCK F27/13[*2]	B/Mass 02/12 MDCK F10/16[*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 F25/17[*2]	B/Maur 1791/17 MDCK F04/18[*2]
	Ferret number			3	2	2	2	3	3	3	3	3
	Genetic Group											
REFERENCE VIRUSES												
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	640	80	160	160	20	40	40	20
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	320	80	640	160	80	80	320	40
B/Massachusetts/02/2012	2	2012-03-13	E3/E3	1280	160	40	1280	160	160	40	320	10
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	80	20	320	320	160	80	320	80
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	40	10	160	160	160	40	160	40
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	5120	160	160	160	320	80	320	320	320
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	40	10	160	160	80	40	160	40
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK3	5120	160	160	160	320	160	320	320	320
TEST VIRUSES												
B/Berlin/16/2018	3	2018-01-22	C2/MDCK1	2560	160	40	160	160	80	80	160	160
B/Cyprus/F165/2018	3	2018-02-08	MDCK2	2560	80	10	160	160	40	80	80	80
B/Cyprus/F204/2018	3	2018-02-13	MDCK2	2560	80	20	160	160	40	80	160	160
A/Athens.GR/625/2018	3	2018-02-22	MDCK1	2560	80	40	160	160	80	160	160	160
B/Chios Island.GR/698/2018	3	2018-02-26	MDCK1	2560	80	40	160	80	40	80	160	80
B/Larisa.GR/825/2018	3	2018-03-05	MDCK1/MDCK1	5120	160	160	320	320	80	320	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

Sequences in phylogenetic trees

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	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	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	3	2017-12-11	MDCK1/MDCK1	5120	160	160	160	320	320	160	320	320	320
B/Trencin/56/2017	3	2017-12-12	MDCK1/MDCK1	2560	160	160	80	160	160	80	160	160	320
B/Netherlands/3534/2017	3	2017-12-20	(MDCK/SIAT)2/MDCK1	5120	160	80	80	320	320	80	160	160	320
B/Bulgaria/915/2017	3	2017-12-21	MDCK1	2560	160	40	20	160	160	80	80	80	160
B/Netherlands/3543/2017	3	2017-12-27	(MDCK/SIAT)2/MDCK1	2560	80	80	40	160	160	80	80	80	160
B/Parma/22/2017	3	2017-12-27	MDCK2/MDCK1	5120	160	160	80	320	320	160	320	320	320
B/Parma/20/2017	3	2017-12-28	MDCK2/MDCK1	5120	160	160	80	320	320	80	160	160	320
B/Roma/5/2017	3	2017-12-29	MDCK2/MDCK1	2560	160	160	80	320	320	80	320	160	320
B/Pavia/1/2018	3	2018-01-01	MDCK2/MDCK1	2560	80	80	40	160	160	40	80	80	160
B/Bulgaria/010/2018	3	2018-01-02	MDCK1	1280	80	40	40	80	80	40	80	80	160
B/Pavia/4/2018	3	2018-01-03	MDCK2/MDCK1	2560	160	80	40	160	160	80	160	160	160
B/Pavia/3/2018	3	2018-01-03	MDCK2/MDCK1	2560	80	80	40	160	160	40	80	80	160
B/Pavia/5/2018	3	2018-01-04	MDCK2/MDCK1	5120	160	160	160	320	320	160	160	320	320
B/Athens.GR/63/2018	3	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

Sequence in Phylogenetic tree

Table 6-6. 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/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	320	80	20	320	160	160	40	160	80
B/Stockholm/12/2011	3	2011-03-28	Ex/E2	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	3	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	3	2017-11-28	MDCK2/MDCK1	1280	80	80	40	80	160	80	80	80	160
B/Athens.GR/2601/2017	3	2017-11-30	MDCK2	1280	80	80	40	80	80	40	160	40	160
B/Firenze/7/2017	3	2017-12-04	MDCK3/MDCK1	2560	160	160	40	160	160	80	160	160	320
B/Bolzano/4/2017	3	2017-12-04	MDCK3/MDCK1	5120	320	320	320	160	320	160	320	160	320
B/Denmark/12/2017	3	2017-12-11	SIAT3/MDCK1	1280	80	80	40	80	80	40	80	80	80
B/Perugia/8/2017	3	2017-12-15	MDCK2/MDCK1	1280	80	40	10	80	80	40	80	40	80
B/Perugia/7/2017	3	2017-12-15	MDCK2/MDCK1	2560	80	40	10	80	160	40	40	80	80
B/Perugia/5/2017	3	2017-12-18	MDCK3/MDCK1	5120	160	160	160	160	320	160	320	160	320
B/Denmark/25/2017	3	2017-12-18	SIAT3/MDCK1	5120	320	160	80	160	160	80	160	160	320
B/Parma/13/2017	3	2017-12-21	MDCK2/MDCK1	5120	320	320	320	320	320	160	320	320	320
B/Parma/18/2017	3	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	3	2017-12-25	MDCK1	2560	160	80	40	80	80	40	80	80	160
B/Netherlands/3540/2017	3	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	3	2018-01-02	MDCK2	5120	320	320	640	320	320	160	320	320	320
B/Denmark/13/2018	3	2018-01-02	MDCK1	2560	160	80	40	80	80	40	80	40	160
B/Athens.GR/16/2018	3	2018-01-03	MDCK2	1280	80	80	20	80	80	40	80	40	80
B/Denmark/16/2018	3	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	3	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	3	2018-01-17	MDCKx/MDCK1	2560	80	80	20	80	80	40	80	40	80
B/Slovenia/419/2018	3	2018-01-18	MDCKx/MDCK1	1280	80	80	20	80	80	40	40	40	80
B/Slovenia/431/2018	3	2018-01-18	SIATx/MDCK1	2560	160	80	40	80	80	40	80	40	160
Sequence in Phylogenetic tree												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 6-7. 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 F51/16*[2]	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]		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		3	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		3	2017-12-19	MDCK1/MDCK1	1280	40	40	20	40	40	20	40	40	80
B/Dijon/053/2018		3	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		3	2018-01-22	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Berlin/8/2018		3	2018-01-24	C1/MDCK1	1280	40	40	20	80	40	20	80	40	80
B/Rheinland-Pfalz/15/2018		3	2018-01-29	C1/MDCK1	2560	80	80	40	80	80	20	80	80	80
B/Niedersachsen/39/2018		3	2018-01-29	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80
B/Saarland/3/2018		3	2018-01-29	C1/MDCK1	1280	40	40	20	80	80	20	40	40	80
B/Bayern/29/2018		3	2018-01-29	C1/MDCK1	1280	40	80	40	80	80	20	80	40	160
B/Hessen/12/2018		3	2018-01-30	C1/MDCK1	1280	40	40	20	80	40	20	40	40	80

Vaccine[#]

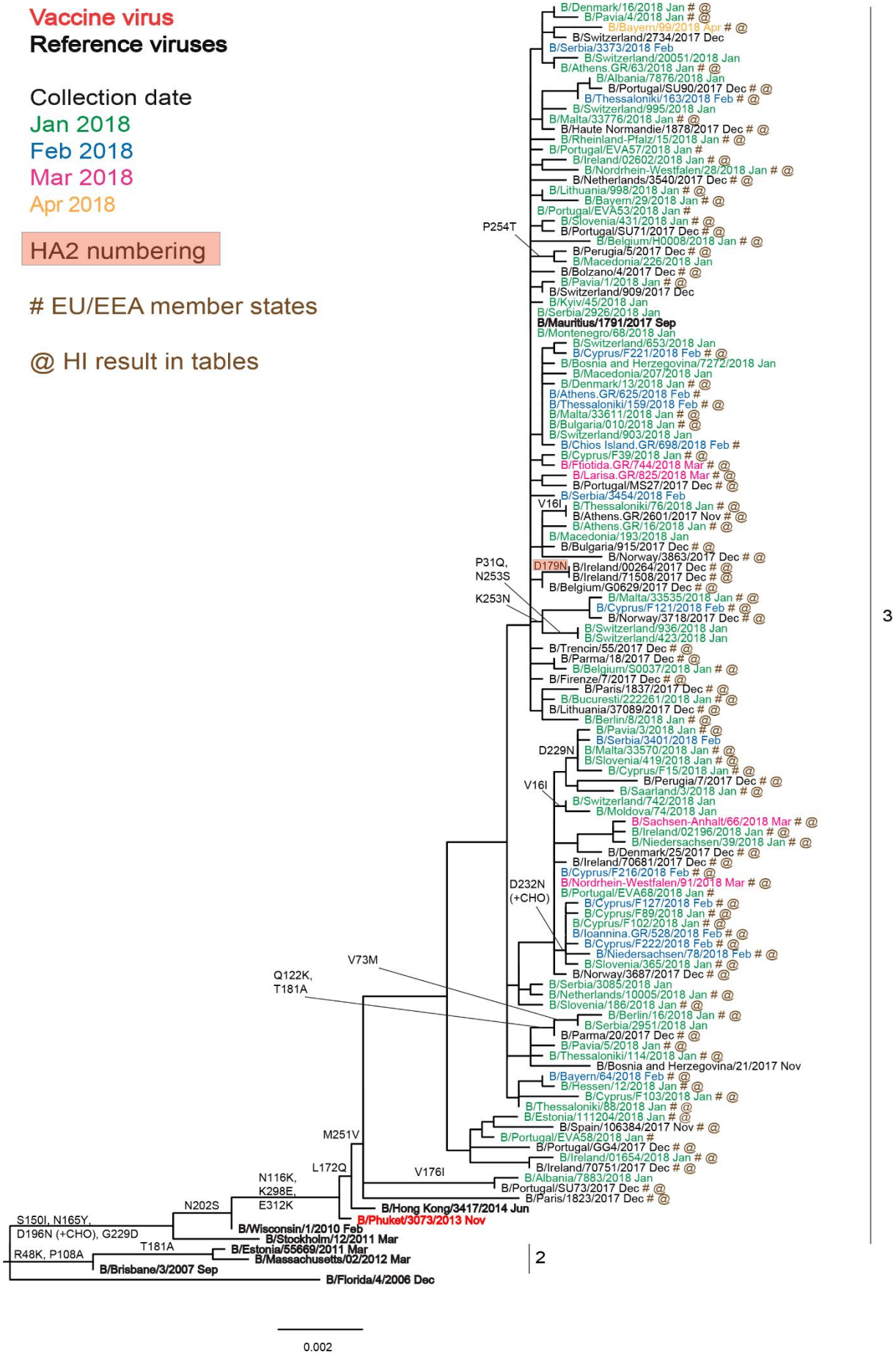
* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):

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

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—20/2018, 3 363 viruses have been characterised genetically:

- 613 were defined as A(H1N1)pdm09 subclade 6B.1, as represented by A/Michigan/45/2015.
- 585 were A(H3N2) clade 3C.2a, represented by A/Hong Kong/4801/2014; 440 were subclade 3C.2a1, represented by A/Singapore/INFIMH-16-0019/2016; and eight were clade 3C.3a, represented by A/Switzerland/9715293/2013; five viruses were not attributed to a clade in TESSy reporting guidance.
- 152 were B/Victoria-lineage clade 1A, represented by B/Brisbane/60/2008, with 68 (45%) falling in the 1A Δ162-163 subclade.
- 1 559 were B/Yamagata-lineage clade 3, represented by B/Phuket/3073/2013; and one was B/Yamagata-lineage clade 2, represented by B/Massachusetts/02/2012.

Antiviral susceptibility

Phenotypic testing for susceptibility to oseltamivir and zanamivir has been conducted on 721 viruses at the WIC, with collection dates from week 40/2017: 196 A(H1N1)pdm09, 215 A(H3N2), 43 B/Victoria-lineage and 267 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 40/2017–20/2018 of the 2017–18 influenza season, countries reported to TESSy on the antiviral susceptibility of 2 192 viruses: 566 A(H1N1)pdm09 viruses, 610 A(H3N2) viruses, and 1 016 influenza type B viruses from sentinel and non-sentinel sources:

- 11 A(H1N1)pdm09 viruses carried neuraminidase (NA) amino acid substitution H275Y and showed highly reduced inhibition (HRI) by oseltamivir.
- 2 A(H3N2) viruses carried NA amino acid substitution R292K and showed reduced inhibition (RI) by both oseltamivir and zanamivir, while another virus showed RI by oseltamivir only.
- 3 type B viruses carried NA amino acid substitution D197N and showed RI by oseltamivir and zanamivir, while another 2 viruses showed RI by oseltamivir only.

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 have been 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 were reported during the 2017–18 season [7]. A revised rapid risk assessment [8] for A(H7N9) viruses was carried out by ECDC, published 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 28 May 2018 indicates that A(H7N9) avian influenza viruses continue to be detected by agricultural authorities in China [11], with the latest human case having occurred early in February 2018 [12]. On 14 February 2018, China notified WHO of the first recorded case of human infection with an avian H7N4 virus [13].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 28 May 2018, indicating that various A(H5Nx) subtypes continue to be detected in birds in Africa, Europe and Asia: notably A(H5N6) viruses, though these viruses differ from A(H5N6) viruses that previously infected humans in China [11]. There have been no cases on human infection by A(H5N1) viruses reported to WHO in 2018 as of 28 May 2018 [14]. ECDC published an updated rapid risk assessment on the situation in Egypt on 13 March 2015 [15] and an epidemiological update on 10 April 2015 [16]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [17]. 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 [18], can be found on the ECDC website[4].

[4] https://ecdc.europa.eu/en/publications-data/ecdcefsa-joint-report-avian-influenza-overview-november-2017-february-2018

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 (i) The Peter Doherty Institute, University of Melbourne, 25-27 September 2017, and (ii) 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 the GISAID EpiFlu database. 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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