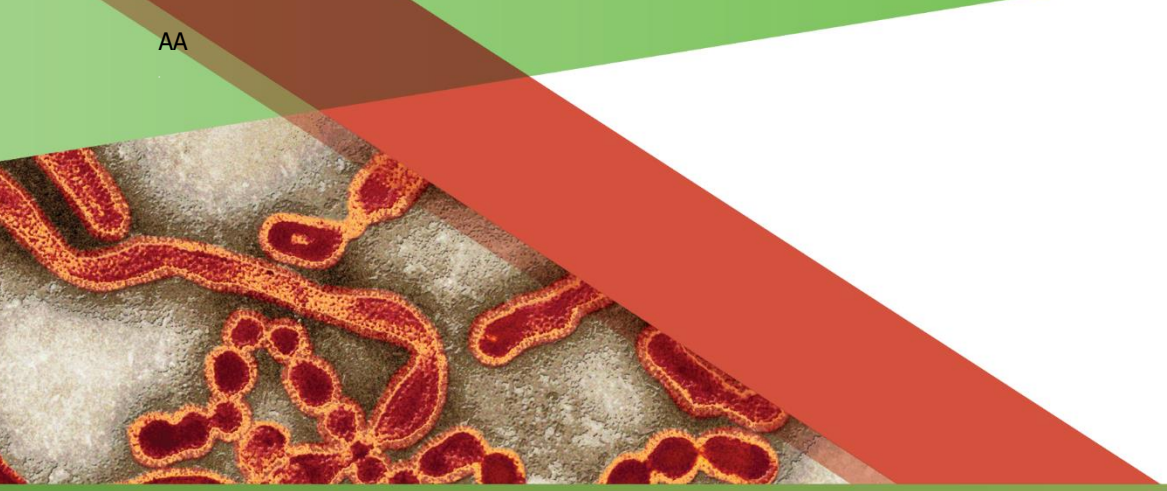
AA



SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, June 2019

Summary

This is the eighth report for the 2018–19 influenza season. As of week 25/2019, 205 167 influenza detections across the WHO European Region had been reported. Detections were 98.9% type A viruses, with A(H1N1)pdm09 prevailing over A(H3N2), and 1.1% type B viruses, with 85 (58%) of 146 ascribed to a lineage being B/Yamagata-lineage.

Since the May 2019 characterisation report[1], a further eight shipments of influenza-positive specimens from EU/EEA countries were received at the London WHO CC, the Francis Crick Worldwide Influenza Centre (WIC). A total of 1 373 virus specimens, with collection dates after 31 August 2018, have been received.

A number of the 69 A(H1N1)pdm09 test viruses characterised antigenically since the May 2019 characterisation report showed reduced reactivity, with antiserum raised against the 2018–19 vaccine virus, A/Michigan/45/2015 (clade 6B.1). The 473 test viruses with collection dates from week 40/2018 genetically characterised at the WIC, including two H1N2 reassortants, have all fallen in a 6B.1 subclade, designated 6B.1A, defined by HA1 amino acid substitutions of S74R, S164T and I295V. Of these recently circulating viruses, 430 also have HA1 S183P substitution, often with additional substitutions in HA1 and/or HA2.

Since the last report, 36 A(H3N2) viruses successfully recovered had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir; all were poorly recognised by antisera raised against the currently used vaccine virus, egg-propagated A/Singapore/INFIMH-16-0019/2016, in HI assays. Of the 386 viruses with collection dates from week 40/2018 genetically characterised at the WIC, 315 were clade 3C.2a (with 38 3C.2a2, 14 3C.2a3, eight 3C.2a4 and 255 3C.2a1b); 71 were clade 3C.3a.

Five B/Victoria-lineage viruses have been characterised in this reporting period. All recent viruses carry HA genes that fall in clade 1A but encode HA1 amino acid substitutions of I117V, N129D, and V146I compared to a previous vaccine virus, B/Brisbane/60/2008. Groups of viruses defined by deletions of two (Δ162-163, 1A(Δ2)) or three (Δ162-164, 1A(Δ3)) amino acids in HA1 have emerged, with the triple deletion group having subgroups of Asian and African origin. HI analyses with panels of post-infection ferret antisera have shown these virus groups to be antigenically distinguishable. Of a total of seven viruses characterised from EU/EEA countries this season, one has been Δ162-163 and six Δ162-164 (five African and one Asian subgroup).

Three B/Yamagata-lineage viruses have been characterised in this reporting period, bringing the total to 13 for the 2018–19 season. All have HA genes that fall in clade 3 and encode HA1 amino acid substitutions of L172Q and M251V compared to the vaccine virus B/Phuket/3073/2013 but remain antigenically similar to

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the vaccine virus which is recommended for use in quadrivalent vaccines for current and subsequent northern hemisphere influenza seasons.

Table 1 shows a summary of influenza virus detections in the WHO European Region reported to ECDC's TESSy database since the start of the 2018–19 season (weeks 40/2018–25/2019), with only 555 detections in weeks 21–25/2019. Since week 1/2019, the cumulative number of detections has increased from 18 049 to 20 5167, with type A (98.9%) predominating over type B (1.1%) viruses which is a common pattern, unlike the 2017–18 season when type B predominated over type A at the start of the season and throughout most of it. Of the type A viruses subtyped (n = 76825) and the type B viruses ascribed to a lineage (n = 146), A(H1N1)pdm09 (n = 44072) have continued to prevail over A(H3N2) (n = 32753) viruses and 85 of 146 type B viruses have been B/Yamagata-lineage; these relative proportions have increased in favour of A(H3N2) and decreased slightly for B/Yamagata-lineage viruses compared to the summary in the May 2019 characterisation report[1]. Overall, the ratio of type A to type B detections is dramatically increased compared with the 2017–18 season (0.8:1 to 89:1), and as the 2018–19 influenza season has progressed the early prevalence of A(H1N1)pdm09 over A(H3N2) viruses has decreased such that levels observed in the two seasons have become comparable (57.4% in 2018–19 compared with 50.6% in 2017–18).

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2018–19 season (weeks 40/2018–25/2019)[a]

	Cumulative number of detections			Totals*		Totals for 2017-18 season*		
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Number	%	Ratios
Influenza A	**21076**	**181812**	**202888**	**98.9**	**89:1**	**106003**	**44.1**	**0.8:1**
A(H1N1)pdm09	8761	35311	44072	57.4		23121	50.6	
A(H3N2)	7258	25495	32753	42.6	0.7:1	22568	49.4	1:1
A not subtyped	5057	121006	126063			60314		
Influenza B	**298**	**1981**	**2279**	**1.1**		**134618**	**55.9**	
Victoria lineage	13	48	61	41.8		301	1.9	
Yamagata lineage	50	35	85	58.2	1.4:1	15701	98.1	52.2:1
Lineage not ascribed	235	1898	2133			118616		
Total detections (total tested)	**21374 (53865)**	**183793 (>793000)**	**205167 (>846865)**			**240621 (903182)**		

*** 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.**

Since week 40/2018, 60 (8 in June) shipments of specimens (virus isolates and/or clinical specimens) from 35 centres across 30 EU/EEA countries have been received at the Crick Worldwide Influenza Centre (WIC). They have contained a total of 1 373 individual virus-related samples with collection dates after 31 August 2018 (Table 2). The proportions of received samples are similar to those reported to TESSy (Table 1) in terms of virus type and virus subtype or lineage. The genetic and antigenic characterisation data generated at the WIC for many of these viruses, with collection dates up to 31 January 2019, were presented at the WHO influenza vaccine composition meeting for the northern hemisphere 2019–20 season. Recommendations emerging from this meeting, held 18–21 February, and the subsequent update (21 March) have been published [1].

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, May 2019. Stockholm: ECDC; 2019. Available from (accessed 01 July 2019): https://ecdc.europa.eu/sites/portal/files/documents/influenza-characterisation-report-May-2019.pdf

Table 2. Summary of clinical samples and virus isolates, contained in packages received from EU/EEA Member States since week 40/2018

MONTH / Country	TOTAL RECEIVED Seasonal viruses	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]
2018														
SEPTEMBER														
France	7					6	3	3					1	1
Spain	1			1	1									
Sweden	1			1	1									
OCTOBER														
Czech Republic	2			2	2									
Denmark	2					2	0	2						
Estonia	3	1	0	1	0	1	0	1						
Finland	2			1	1	1	0	1						
France	11			3	3	7	5	2					1	1
Germany	1					1	0	1						
Iceland	2					1	0	1					1	1
Ireland	3			2	1	1	0	1						
Latvia	1			1	1									
Netherlands	1					1	0	1						
Norway	29			12	8	14	0	8					3	1
Portugal	2			2	2									
Slovenia	1			1	1									
United Kingdom	3			1	1	2	0	2						
NOVEMBER														
Austria	4			1	1	3	1	2						
Belgium	5			3	2	2	0	2						
Bulgaria	1			1	0									
Croatia	1			1	1									
Czech Republic	1			1	1									
Denmark	12			8	8	3	0	3			1	1		
Estonia	3			3	1									
Finland	4			2	2	2	0	2						
France	17			10	10	7	4	2						
Germany	8			4	4	4	0	4						
Iceland	15			4	3	11	7	3						
Ireland	17			12	10	4	0	3					1	1
Italy	10			2	2	8	5	3						
Latvia	2					2	1	1						
Lithuania	5					5	0	4						
Netherlands	3			2	2	1	0	1						
Norway	26			14	13	12	1	10						
Portugal	1												1	0
Spain	8			2	1	6	0	2						
Sweden	1			1	1									
United Kingdom	14			6	6	6	2	1			1	0	1	1
DECEMBER														
Austria	4			2	2	2	1	1						
Belgium	6			2	1	4	0	2						
Bulgaria	9			5	4	4	0	4						
Croatia	8			6	6	2	0	1						
Cyprus	3			3	1									
Denmark	7			5	5	2	0	2						
Estonia	18	1	0	16	11	1	0							
France	33			17	17	14	10	4			1	1	1	1
Germany	11			5	5	6	0	6						
Greece	11			8	5	3	0	1						
Hungary	6			4	4	2	1	1						
Iceland	3			3	3									
Ireland	3			3	3									
Italy	1			1	1									
Latvia	6			5	5	1	1	0						
Lithuania	14	1	0	5	3	8	0	3						
Netherlands	5			4	4	1	0	1						
Norway	15			6	4	7	1	4			2	1		
Poland	1			1	0									
Portugal	18			8	8	9	0	9					1	1
Romania	12			2	2	10	1	9						
Slovakia	1					1	in process							
Slovenia	3			1	1						2	2		
Spain	28			15	8	13	2	3						
Sweden	14			10	10	4	3	1						
United Kingdom	8			5	5	3	1							

MONTH	TOTAL RECEIVED	A		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
Country	Seasonal viruses	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]
2019														
JANUARY														
Austria	17			6	6	10	10						1	1
Belgium	47			8	3	39	2	18						
Bulgaria	13			12	9	1	0	1						
Croatia	2												2	1
Cyprus	22			21	in process	1	0	1						
Estonia	10	5	in process	3	in process	2	in process							
Finland	1					1	0	1						
France	26			11	11	15	13	2						
Germany	34			15	15	19	5	14						
Greece	30			19	8	8	0	4	3	0				
Hungary	2					2	2							
Italy	6			3	3	1	0	1			2	in process		
Latvia	6			6	6									
Lithuania	1			1	1									
Luxembourg	25			10	8	14	3	6					1	1
Malta	42			23	4	19	1	0						
Netherlands	12			8	8	4	2	2						
Norway	19			10	9	7	0	6					2	1
Poland	17			13	in process	4	0	0						
Portugal	7			2	in process	5	4	1						
Romania	13			11	6	2	1	1						
Slovakia	12			7	in process	5	in process							
Slovenia	14			9	9	4	0	4			1	1		
Spain	73			32	27	41	19	12						
Sweden	6			5	5	1	0	1						
United Kingdom	38	3	0	31	2	4	1	0						
FEBRUARY														
Austria	5			4	4	1	1	0						
Bulgaria	41			22	23	19	13	9						
Cyprus	15			14	in process	1	0	1						
Denmark	6			3	3	3	0	3						
Estonia	8	6	in process	2	in process									
Finland	4			4	4									
Germany	26			9	9	17	9	8						
Greece	17			11	10	5	1	4					1	1
Italy	12			4	in process	8	in process							
Latvia	7			1	1	6	5	1						
Malta	8			5	2	3	0	1						
Poland	28	1	0	22	in process	5	0	3						
Portugal	13			6	in process	7	6	1						
Slovakia	13			10	in process	3	in process							
Slovenia	7			3	3	3	1	2			1	1		
Sweden	5			1	1	2	2				1	1	1	in process
MARCH														
Austria	2												2	2
Bulgaria	1			1	1									
Cyprus	1					1	in process							
Denmark	16			7	7	9	1	8						
Estonia	7	3	in process	3	in process	1	in process							
Finland	7			2	2	5	in process							
Germany	23			7	7	16	12	4						
Greece	15			8	3	6	1	4					1	1
Iceland	7			4	in process	3	in process							
Italy	15			6	in process	9	in process							
Latvia	2			1	1	1	1	0						
Poland	7			7	in process									
Portugal	5			3	in process	2	1	1						
Slovakia	4			2	in process	2	in process							
Slovenia	8			4	4	3	0	3			1	1		
Sweden	5			2	2	2	0	2			1	1		
United Kingdom	16			11	0	5	0							
APRIL														
Cyprus	1					1	in process							
Denmark	1			1	1									
Finland	6			2	2	4	in process							
Iceland	7			1	in process	4	in process		2	in process				
Slovakia	1			1	in process									
Slovenia	2			2	2									
United Kingdom	15					15	0							
MAY														
Finland	1					1	0	1						
Iceland	7			2	in process	5	in process							
Portugal	1										1	0		
MAY														
Iceland	2					2	in process							
	1373	21	0	711	440	599	167	249	5	0	15	10	22	16
30 Countries					51.8%		43.6%					1.1%		1.6%
					96.9%							3.1%		

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

One virus each from Denmark and Sweden were A(H1N2)pdm09 reassortants

As of 2019-07-02

Influenza A(H1N1)pdm09 virus analyses

Tables 3-1 to 3-4 show the results of haemagglutination inhibition (HI) assays of A(H1N1)pdm09 viruses performed with a panel of post-infection ferret antisera. Table 3-1 is repeated from the May 2019 characterisation report but with genetic group data now included, while Tables 3-2 to 3-4 were generated during June 2019. Test viruses in each table are sorted by date of collection. A summary of the HI results for all test viruses in Tables 3-1 to 3-4 is shown in Table 3-5 and is broken down by genetic subgroup in Table 3-6.

Compared with the May 2019 characterisation report, the proportion of A(H1N1)pdm09 test viruses that were antigenically indistinguishable from the egg-propagated vaccine virus for the northern hemisphere 2018–19 influenza season, A/Michigan/45/2015 [2], has dropped from 98% (53 of 54) to 42% (33 of 78), as assessed with post-infection ferret antisera, being recognised at titres within twofold of the titre of the antiserum with the homologous virus (Table 3-5). The proportion recognised within fourfold has also dropped from 100% to 76%. This may be related to a degree of antigenic drift as the viruses analysed over the last month have circulated more recently, with the majority having collection dates from 1 February 2019. Loss of recognition was somewhat less with antiserum raised against A/Brisbane/02/2018, the vaccine virus recommended for the 2019–20 northern hemisphere influenza season [1]; 74% of test viruses were recognised at titres within twofold of the respective homologous titres and 96% within fourfold (Table 3-5), compared to 91% and 100% respectively in the May 2019 characterisation report. Similar loss of recognition was observed with antiserum raised against another egg-propagated virus, A/Slovenia/2903/2015, 100% to 68% at twofold and 100% to 96% at fourfold. Antisera raised against egg-propagated A/Switzerland/2656/2017 and A/Switzerland/3330/2017 performed somewhat better and retained a greater level of recognition of test viruses at twofold and 100% recognition within fourfold of their respective homologous titres.

Of four antisera raised against cell culture-propagated viruses, those for A/Paris/1447/2017 and A/Norway/3433/2018 retained recognition of all test viruses at titres within twofold of their respective homologous titres. Those raised against A/Bayern/69/2009 and A/Ireland/84630/2018 showed lower recognition of test viruses at titres within twofold of the titres of the antisera with their homologous viruses, but retained 99% recognition within fourfold.

The antiserum raised against cell culture-propagated A/Lviv/N6/2009 is an unusual virus/antiserum combination with A/Lviv/N6/2009 encoding HA1 amino acid substitutions of **G155G/E**, with E predominating, and **D222G**. This antiserum recognised only 2% of test viruses at titres within twofold of the homologous titre, and 28% within fourfold (Table 3-5), compared to 11% and 72% in the May 2019 characterisation report.

All test viruses for which HA gene sequencing had been completed fell into clade 6B.1, which is defined by the amino acid substitutions **S84N**, **S162N** (introducing a potential N-linked glycosylation site) and **I216T** in **HA1**, with all recently circulating viruses clustering in a genetic subclade designated as 6B.1A and defined by the HA1 amino acid substitutions **S74R**, **S164T** (which alters the glycosylation motif at residues 162 to 164) and **I295V**. A number of genetic subgroups defined by specific amino acid substitutions have emerged, but the great majority of viruses in the various subgroups had remained antigenically similar to A/Michigan/45/2015 as shown in the April 2019 and earlier characterisation reports, as assessed with post-infection ferret antisera.

Figure 1 shows a phylogenetic tree for the HA genes of a selection of A(H1N1)pdm09 viruses from the European Region, all with collection dates since the start of the 2018–19 influenza season, that were sequenced at the Francis Crick Institute between April and June 2019. Within subclade 6B.1A clusters of viruses (genetic groups) encoding a range of **HA1** amino acid substitutions have emerged, e.g. **T120A**, or **N260D** in combination with **N129D,** many with **T185I**, or **N260D** with **E235D** and **V193A** in **HA2,** or **N129D** with **A141E**, or **K302T** and **N169S** and **E179D** in **HA2,** or **L161I** and **I77M** in **HA2**. The HA of most recently circulating viruses carry the substitution **S183P** in **HA1**, although this is not retained in all genetic groups, and the phylogenetic tree is annotated with **HA1 S183P** substitution groups assigned for the February 2019 WHO Vaccine Consultation Meeting [1]; 6B.1A/183P-1 to -7, abbreviated to 6B.1A1 to 6B.1A7 in Figure 1. The location of vaccine viruses, A/Michigan/45/2015 [2] and the recently recommended A/Brisbane/02/2018 for the northern hemisphere 2019–20 influenza season [1], are indicated on the phylogeny (Figure 1).

Table 3-6 summarises the data in Table 3-5 for viruses that had been sequenced at the time of preparing this report, by genetic groups 183P-2, -5, -6 and -7. Generally, despite some fall-off in recognition compared with the levels observed at the time of the May 2019 characterisation report, test viruses reacted within fourfold of respective homologous titres with all antisera but for that raised against A/Lviv/N6/2009. However, group 6B.1A5 test viruses (defined by **HA1 S183P** and **N260D** amino acid substitutions, with the great majority also having **N129D** and **T185I** substitutions) showed lower proportions reacting within twofold of homologous titres with six of the antisera in the panel (Table 3-6). While such HI studies conducted with post-infection ferret antisera indicated low levels of antigenic drift in A(H1N1)pdm09 viruses up to February 2019, panels of post-vaccination human antisera recognised viruses containing the HA1 substitution S183P less well and, based on these results, A/Brisbane/02/2018 was recommended as the A(H1N1)pdm09 vaccine component for the northern hemisphere 2019–20 influenza season [1].

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera: A/Mich 45/15 Egg F31/16[*1] 6B.1	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F13/18[*1]	A/Slov 2903/2015 Egg NIB F48/16[*1] 6B.1	A/Paris 1447/17 MDCK F03/18[*2] 6B.1A	A/Swit 2656/17 Egg F20/18[*1] 6B.1A	A/Swit 3330/17 Egg F23/18[*1] 6B.1A5	A/Norway 3433/18 MDCK F04/19[*1] 6B.1A5	A/Ire 84630/18 MDCK F08/19[*1] 6B.1A6	A/Bris 02/18 Egg F09/19[*1] 6B.1A1
REFERENCE VIRUSES														
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	2560	320	320	1280	1280	1280	640	1280	1280	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	320	160	<	160	80	80	160	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	640	640	160	640	320	320	1280	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	320	160	640	1280	1280	640	1280	640	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	160	40	640	640	640	320	1280	640	320
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	2560	640	320	1280	2560	2560	1280	2560	2560	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	640	160	80	640	640	640	640	1280	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	80	40	160	320	320	320	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	2560	320	160	1280	2560	2560	1280	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	2560	320	320	1280	2560	1280	1280	2560	1280	1280
TEST VIRUSES														
A/Slovenia/382/2019		6B.1A7	2019-01-18	MDCKx/MDCK1	1280	320	160	1280	640	1280	640	2560	1280	1280
A/Slovenia/888/2019		6B.1A7	2019-02-05	MDCKx/MDCK1	1280	320	160	640	640	1280	640	1280	1280	640
A/Slovenia/999/2019		6B.1A7	2019-02-09	SIATx/SIAT1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Slovenia/1170/2019		6B.1A5	2019-02-18	MDCKx/MDCK1	640	320	160	640	640	640	640	2560	640	640
A/Slovenia/1377/2019		6B.1A2	2019-03-02	MDCKx/MDCK1	1280	320	160	1280	1280	2560	1280	2560	2560	1280
A/Slovenia/1424/2019		6B.1A7	2019-03-05	MDCKx/MDCK1	1280	320	160	1280	640	1280	640	2560	1280	1280
A/Slovenia/1489/2019		6B.1A7	2019-03-10	MDCKx/MDCK1	2560	640	320	2560	2560	2560	2560	2560	2560	2560
A/Slovenia/1512/2019		6B.1A7	2019-03-12	MDCKx/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Slovenia/1772/2019		6B.1A7	2019-04-10	MDCKx/MDCK1	2560	320	320	1280	1280	1280	1280	2560	1280	1280
					Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

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

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
	Passage history			A/Mich 45/15	A/Bayern 69/09	A/Lviv N6/09	A/Slov 2903/2015	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18	A/Ire 84630/18	A/Bris 02/18
				Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	Egg
	Ferret number			F31/16-1	F09/15-1	F13/18-1	F48/16-1	F03/18-2	F20/18-1	F23/18-1	F04/19-1	F08/19-1	F09/19-1
	Genetic group			6B.1			6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5	6B.1A6	6B.1A1
REFERENCE VIRUSES													
A/Michigan/45/2015	6B.1	2015-09-07	E3/E3	2560	320	320	1280	1280	2560	640	2560	1280	640
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	160	320	160	40	160	160	80	320	40	80
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK2	320	640	1280	160	640	640	320	1280	160	320
A/Slovenia/2903/2015	clone 37	2015-10-26	E4/E2	1280	320	160	1280	1280	1280	640	1280	640	640
A/Paris/1447/2017	6B.1A	2017-10-20	MDCK1/MDCK3	640	160	40	320	640	640	320	640	640	320
A/Switzerland/2656/2017	6B.1A	2017-12-21	E5/E2	1280	320	320	1280	1280	1280	640	2560	1280	640
A/Switzerland/3330/2017	clone 35 6B.1A5	2017-12-20	E6/E2	640	160	80	640	640	640	640	1280	640	320
A/Norway/3433/2018	6B.1A5	2018-10-30	MDCK3	640	80	40	320	640	320	320	1280	320	320
A/Ireland/84630/2018	6B.1A6	2018-11-28	MDCK1/MDCK3	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Brisbane/02/2018	6B.1A1	2018-01-04	E3/E1	2560	320	160	1280	2560	2560	1280	2560	1280	640
TEST VIRUSES													
A/Bulgaria/863/2019		2019-01-28	SIAT2/MDCK1	1280	640	320	1280	2560	2560	1280	5120	2560	1280
A/Bulgaria/856/2019	6B.1A6	2019-01-29	SIAT2/MDCK1	1280	320	160	1280	2560	1280	1280	2560	2560	1280
A/Bulgaria/869/2019	6B.1A7	2019-01-31	SIAT2/MDCK1	1280	320	160	640	1280	1280	640	2560	1280	1280
A/Bulgaria/904/2019	6B.1A	2019-02-01	SIAT2/MDCK1	640	320	160	1280	1280	1280	640	2560	1280	640
A/Bulgaria/905/2019		2019-02-01	SIAT2/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Bulgaria/865/2019	6B.1A6	2019-02-01	SIAT2/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Bulgaria/981/2019	6B.1A6	2019-02-04	SIAT2/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Bulgaria/936/2019	6B.1A	2019-02-04	SIAT2/MDCK1	1280	320	80	1280	2560	1280	640	2560	1280	1280
A/Bulgaria/923/2019	6B.1A	2019-02-04	SIAT2/MDCK1	640	160	80	640	1280	640	320	1280	640	640
A/Bulgaria/913/2019	6B.1A	2019-02-04	SIAT2/MDCK1	1280	320	160	1280	2560	1280	1280	2560	1280	1280
A/Bulgaria/1041/2019	6B.1A2	2019-02-07	SIAT2/MDCK1	640	320	160	1280	2560	1280	640	1280	1280	640
A/Bulgaria/1044/2019		2019-02-08	SIAT2/MDCK1	1280	640	160	1280	2560	2560	1280	2560	2560	1280
A/Bulgaria/1145/2019	6B.1A2	2019-02-18	SIAT2/MDCK1	1280	320	160	640	1280	1280	640	1280	1280	640
A/Bulgaria/1143/2019	6B.1A	2019-02-18	SIAT2/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Bulgaria/1154/2019	6B.1A2	2019-02-19	SIAT2/MDCK1	1280	640	160	1280	2560	2560	1280	2560	2560	1280
A/Bulgaria/1128/2019		2019-02-19	SIAT2/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Bulgaria/1149/2019	6B.1A2	2019-02-20	SIAT2/MDCK1	1280	320	160	1280	1280	1280	640	1280	1280	640
A/Bulgaria/1158/2019	6B.1A7	2019-02-22	SIAT2/MDCK1	2560	640	320	2560	2560	2560	1280	2560	2560	1280
A/Bulgaria/1174/2019	6B.1A7	2019-02-25	SIAT2/MDCK1	2560	640	320	2560	2560	2560	1280	2560	2560	1280
A/Bulgaria/1172/2019	6B.1A7	2019-02-25	SIAT2/MDCK1	640	320	80	640	1280	1280	640	1280	640	640
A/Bulgaria/1163/2019	6B.1A5	2019-02-25	SIAT2/MDCK1	1280	320	160	640	1280	640	640	2560	1280	640
A/Bulgaria/1200/2019	6B.1A5	2019-02-26	SIAT2/MDCK1	1280	640	320	1280	2560	1280	1280	2560	2560	1280
A/Bulgaria/1197/2019	6B.1A2	2019-02-26	SIAT2/MDCK1	2560	640	320	1280	2560	2560	1280	2560	2560	1280
A/Bulgaria/1216/2019	6B.1A7	2019-02-28	SIAT2/MDCK1	1280	320	160	1280	5120	2560	640	2560	2560	1280
A/Slovenia/1719/2019	6B.1A5	2019-04-01	SIATx/MDCK3	320	160	80	320	640	320	320	1280	320	320
				Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

* 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/Bayern 69/09	A/Lviv N6/09	A/Slov 2903/2015	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18	A/Ire 84630/18	A/Bris 02/18
		Ferret number			Egg F31/16[*1]	MDCK F09/15[*1]	MDCK F13/18[*1]	Egg NIB F48/16[*1]	MDCK F03/18[*2]	Egg F20/18[*1]	Egg F23/18[*1]	MDCK F04/19[*1]	MDCK F08/19[*1]	Egg F09/19[*1]
		Genetic group			6B.1			6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5	6B.1A6	6B.1A1
REFERENCE VIRUSES														
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	2560	320	320	1280	1280	2560	640	2560	1280	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	80	320	160	40	160	80	80	160	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	1280	160	640	640	320	640	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	320	160	1280	1280	1280	640	1280	640	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	40	640	640	640	320	640	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	1280	640	320	1280	1280	1280	640	2560	1280	640
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	80	320	640	640	640	640	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	80	40	320	640	320	320	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	320	160	1280	1280	1280	1280	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	320	160	1280	2560	2560	1280	2560	1280	1280
TEST VIRUSES														
A/Denmark/2276/2019		6B.1A2	2019-02-26	MDCK4/MDCK1	320	80	40	320	640	640	320	1280	640	640
A/Denmark/2225/2019			2019-02-26	MDCK3/MDCK1	640	160	160	640	1280	640	640	1280	640	640
A/Denmark/2336/2019		6B.1A6	2019-02-28	MDCK4/MDCK1	640	320	80	1280	1280	1280	640	2560	1280	1280
A/Denmark/2373/2019		6B.1A5	2019-03-01	MDCK2/MDCK1	320	80	80	320	640	640	320	1280	640	320
A/Denmark/2398/2019		6B.1A5	2019-03-05	MDCK3/MDCK1	320	80	80	320	640	320	320	1280	320	320
A/Denmark/2434/2019		6B.1A6	2019-03-06	MDCK3/MDCK1	640	160	80	640	1280	1280	640	1280	1280	640
A/Denmark/2653/2019		6B.1A7	2019-03-12	MDCK4/MDCK1	320	80	40	320	640	640	320	640	640	320
A/Denmark/2697/2019		6B.1A5	2019-03-14	MDCK3/MDCK1	640	320	320	640	1280	1280	640	2560	1280	640
A/Denmark/2729/2019		6B.1A5	2019-03-18	MDCK2/MDCK1	320	80	80	320	640	320	320	1280	320	320
A/Denmark/2728/2019		6B.1A2	2019-03-19	MDCK3/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Denmark/3176/2019	H1N2	6B.1A5	2019-04-15	SIAT2/SIAT1	320	160	160	320	640	640	320	1280	1280	320
					Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

* 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 F31/16*1 6B.1	A/Bayern 69/09 MDCK F09/15*1	A/Lviv N6/09 MDCK F13/18*1	A/Slov 2903/2015 Egg NIB F48/16*1 6B.1	A/Paris 1447/17 MDCK F03/18*2 6B.1A	A/Swit 2656/17 Egg F20/18*1 6B.1A	A/Swit 3330/17 Egg F23/18*1 6B.1A5	A/Norway 3433/18 MDCK F04/19*1 6B.1A5	A/Ire 84630/18 MDCK F08/19*1 6B.1A6	A/Bris 02/18 Egg F09/19*1 6B.1A1
REFERENCE VIRUSES														
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	2560	320	320	1280	1280	1280	1280	2560	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	80	320	160	40	160	160	80	160	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	640	160	320	320	320	1280	160	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	160	1280	640	1280	640	1280	1280	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	40	640	640	640	320	1280	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	1280	640	160	1280	1280	1280	640	2560	1280	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	80	320	640	640	640	1280	640	640
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	160	40	640	640	640	320	1280	640	640
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	640	160	160	1280	1280	1280	640	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	320	160	1280	1280	1280	1280	2560	1280	1280
TEST VIRUSES														
A/Austria/1113414/2018		6B.1A5	2018-12-26	SIAT1/MDCK1	640	160	80	320	640	640	320	1280	640	320
A/Umea/3/2018			2018-12-26	MDCK0/MDCK1	640	160	160	640	1280	640	640	2560	640	640
A/Austria/1113546/2018		6B.1A5	2018-12-27	SIAT1/MDCK1	640	160	160	640	1280	640	640	2560	1280	640
A/Austria/1113762/2019		6B.1A5		SIAT1/MDCK1	640	160	80	320	640	640	640	1280	640	640
A/Umea/4/2018			2018-12-28	MDCK0/MDCK1	320	160	80	320	640	320	320	1280	640	640
A/Linkoping/71/2018			2018-12-31	MDCK1/MDCK1	640	80	80	320	640	640	320	1280	640	640
A/Linkoping/1/2019			2019-01-02	MDCK1/MDCK1	640	160	160	640	640	640	320	1280	640	640
A/Austria/1114707/2019		6B.1A5	2019-01-03	SIAT1/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Linkoping/3/2019			2019-01-03	MDCK0/MDCK1	320	80	80	160	320	320	160	640	320	160
A/Austria/1115871/2019		6B.1A7	2019-01-08	SIAT1/MDCK1	640	160	80	320	640	640	320	1280	640	640
A/Austria/1119591/2019		6B.1A7	2019-01-23	SIAT1/MDCK1	640	160	80	640	1280	1280	640	1280	640	640
A/Austria/1119457/2019		6B.1A	2019-01-23	SIAT1/MDCK1	1280	160	80	640	1280	1280	640	2560	1280	640
A/Sundsvall/2/2019			2019-01-23	MDCK0/MDCK1	640	160	80	320	640	640	320	1280	320	320
A/Sundsvall/1/2019			2019-01-23	MDCK0/MDCK1	1280	320	160	1280	2560	2560	1280	2560	2560	1280
A/Austria/1120563/2019		6B.1A	2019-01-28	SIAT1/MDCK1	640	160	80	640	1280	1280	640	2560	640	640
A/Gavle/2/2019			2019-01-28	MDCK0/MDCK1	320	80	40	320	640	320	320	640	320	320
A/Austria/1121448/2019		6B.1A5	2019-01-31	SIAT1/MDCK1	320	160	80	320	640	640	320	2560	640	320
A/Austria/1122894/2019		6B.1A6	2019-02-05	SIAT1/MDCK1	640	160	80	640	1280	1280	640	2560	1280	640
A/Gavle/3/2019			2019-02-05	MDCK0/MDCK1	160	80	<	160	320	320	160	640	320	160
A/Austria/1124185/2019		6B.1A7	2019-02-11	SIAT1/MDCK1	1280	160	80	640	1280	1280	640	2560	1280	640
A/Austria/1123857/2019		6B.1A5	2019-02-11	SIAT1/MDCK1	640	160	160	640	640	640	320	1280	640	320
A/Finland/39/2019			2019-02-17	MDCK2/MDCK1	320	80	40	320	320	320	160	1280	320	320
A/Austria/1125761/2019		6B.1A5		SIAT1/MDCK1	640	160	80	320	640	640	320	1280	640	640
A/Austria/1126231/2019		6B.1A5	2019-02-18	SIAT1/MDCK1	320	160	80	320	640	640	320	1280	640	320
A/Finland/90/2019			2019-02-25	MDCK1/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Finland/45/2019			2019-02-25	MDCK1/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Finland/47/2019			2019-02-28	MDCK1/MDCK1	320	80	40	320	640	320	320	1280	640	320
A/Halmstad/1/2019			2019-03-16	MDCK0/MDCK1	160	40	<	160	320	160	160	640	160	160
A/Finland/55/2019			2019-03-19	MDCK1/MDCK1	320	80	40	320	320	320	320	1280	640	320
A/Finland/54/2019			2019-03-19	MDCK1/MDCK1	320	80	80	320	640	320	160	1280	320	320
A/Sundsvall/3/2019			2019-03-24	MDCK0/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Finland/103/2019			2019-04-02	MDCK1/MDCK1	640	160	160	640	640	640	320	1280	640	320
A/Finland/102/2019			2019-04-02	MDCK1/MDCK1	320	160	80	320	640	320	320	1280	640	320
					Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

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

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

Viruses	Other information		Haemagglutination inhibition titre: Post-infection ferret antisera									
		Passage history	A/Mich 45/15 Egg	A/Bayern 69/09 MDCK	A/Lviv N6/09 MDCK	A/Slov 2903/2015 Egg	A/Paris 1447/17 MDCK	A/Swit 2656/17 Egg	A/Swit 3330/17 Egg	A/Norway 3433/18 MDCK	A/Ire 84630/18 MDCK	A/Bris 02/18 Egg
		Ferret number	F31/16[*1]	F09/15[*1]	F13/18[*1]	NIB F48/16[*1]	F03/18[*2]	F20/18[*1]	F23/18[*1]	F04/19[*1]	F08/19[*1]	F09/19[*1]
		Genetic group	6B.1			6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5	6B.1A6	6B.1A1
REFERENCE VIRUSES												
A/Michigan/45/2015		6B.1	2560	320	320	1280	1280	1280	1280	2560	1280	1280
A/Bayern/69/2009	G155E		80	320	160	40	160	160	80	160	40	160
A/Lviv/N6/2009	G155E, D222G		320	640	640	160	320	320	320	1280	160	640
A/Slovenia/2903/2015	clone 37	6B.1	640	320	160	1280	640	1280	640	1280	1280	640
A/Paris/1447/2017		6B.1A	640	320	40	640	640	640	320	1280	640	640
A/Switzerland/2656/2017		6B.1A	1280	640	160	1280	1280	1280	640	2560	1280	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	320	160	80	320	640	640	640	1280	640	640
A/Norway/3433/2018		6B.1A5	320	160	40	640	640	640	320	1280	640	640
A/Ireland/84630/2018		6B.1A6	640	160	160	1280	1280	1280	640	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	1280	320	160	1280	1280	1280	1280	2560	1280	1280
TEST VIRUSES												
Number of viruses tested*			78	78	78	78	78	78	78	78	78	78
No with titre reduction ≤2-fold			33	64	2	53	78	64	73	78	68	58
%			*42.3*	*82.1*	*2.6*	*67.9*	*100*	*82.1*	*93.6*	*100*	*87.3*	*74.3*
No with titre reduction =4-fold			26	13	20	22		13	5		9	17
%			*33.3*	*16.7*	*25.6*	*28.2*		*16.7*	*6.4*		*11.5*	*21.8*
No with titre reduction ≥8-fold			19	1	56	3		1			1	3
%			*24.4*	*1.2*	*71.8*	*3.9*		*1.2*			*1.2*	*3.9*
			Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

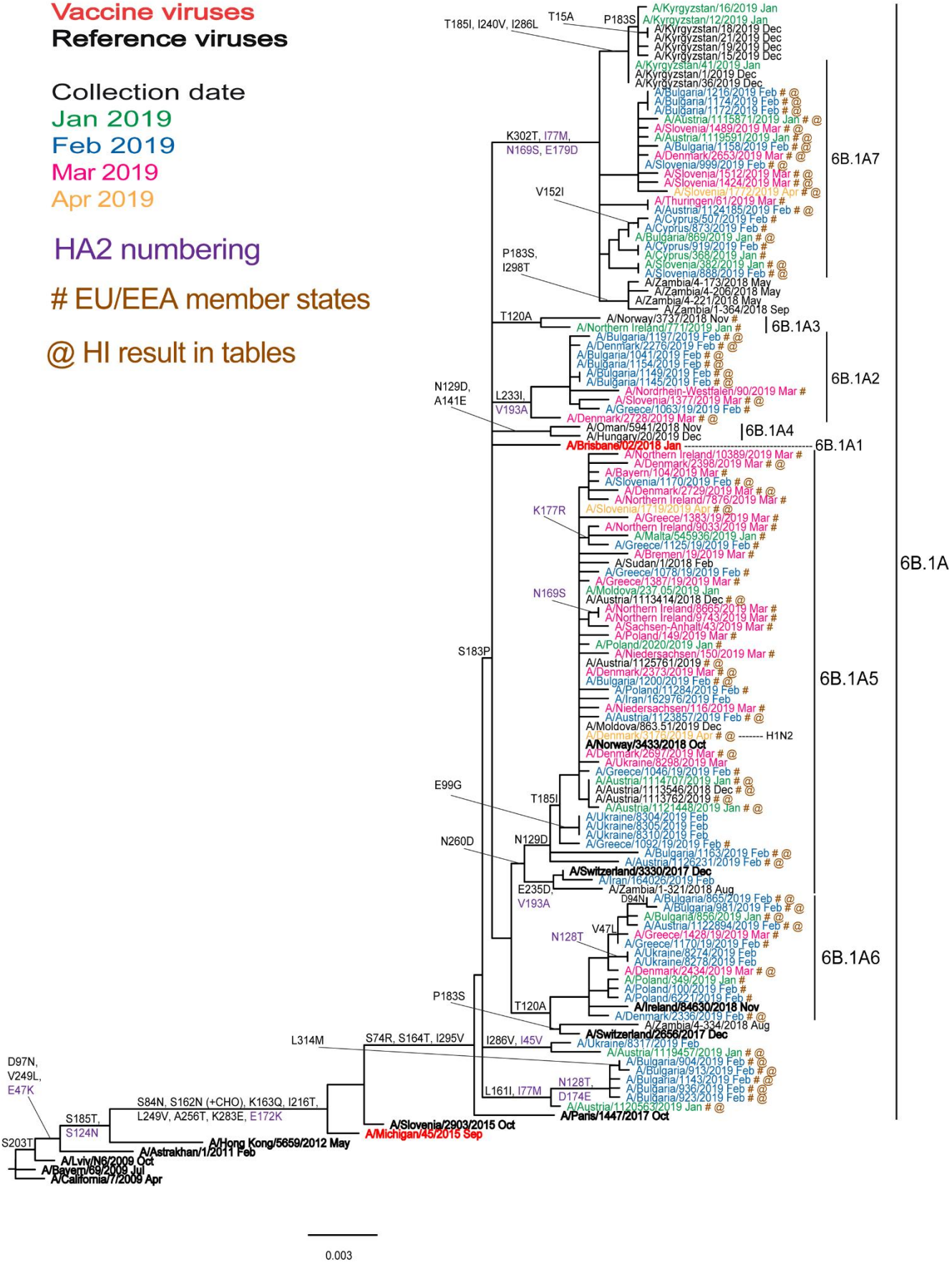
* Of those with available HA sequence, all were clade 6B.1A

Reference virus results are taken from an individual table as an example. Summaries for each antiserum are based on fold-reductions observed on the days that HI assays were performed.

Table 3-6. Antigenic analysis of A(H1N1)pdm09 viruses by HI – Summary by test virus genetic group

Viruses		Haemagglutination inhibition titre										
		Post-infection ferret antisera										
		A/Mich 45/15	A/Bayern 69/09	A/LViv N6/09	A/Slov 2903/2015	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18	A/Ire 84630/18	A/Bris 02/18
	Passage history	Egg	MDCK	MDCK	Egg NIB	MDCK	Egg	Egg	MDCK	MDCK	Egg
	Ferret number	F31/16*1	F09/15*1	F13/18*1	F48/16*1	F03/18*2	F20/18*1	F23/18*1	F04/19*1	F08/19*1	F09/19*1
	Genetic group	6B.1			6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5	6B.1A6	6B.1A1
TEST VIRUSES											
Total number tested		54	54	54	54	54	54	54	54	54	54
Number tested	6B.1A	7	7	7	7	7	7	7	7	7	7
No with titre reduction ≤2-fold		4	7		7	7	7	7	7	7	7
No with titre reduction =4-fold		3									
No with titre reduction ≥8-fold				7							
Number tested	6B.1A2	8	8	8	8	8	8	8	8	8	8
No with titre reduction ≤2-fold		6	7		7	8	8	8	8	8	8
No with titre reduction =4-fold		1	1	2	1						
No with titre reduction ≥8-fold		1		6							
Number tested	6B.1A5	17	17	17	17	17	17	17	17	17	17
No with titre reduction ≤2-fold		2	14		7	17	13	17	17	14	9
%		*11.7*	*82.4*		*41.2*	*100*	*76.5*	*100*	*100*	*82.4*	*52.9*
No with titre reduction =4-fold		8	3	5	10		4			3	8
%		*47.1*	*17.6*	*29.4*	*58.8*		*23.5*			*17.6*	*47.1*
No with titre reduction ≥8-fold		7		12							
%		*41.2*		*70.6*							
Number tested	6B.1A6	6	6	6	6	6	6	6	6	6	6
No with titre reduction ≤2-fold		3	6		6	6	6	6	6	6	6
No with titre reduction =4-fold		3									
No with titre reduction ≥8-fold				6							
Number tested	6B.1A7	16	16	16	16	16	16	16	16	16	16
No with titre reduction ≤2-fold		12	15	2	14	16	16	16	16	16	15
%		*75.0*	*93.8*	*12.4*	*87.5*	*100*	*100*	*100*	*100*	*100*	*93.8*
No with titre reduction =4-fold		3	1	7	2						1
%		*18.8*	*6.2*	*43.8*	*12.5*						*6.2*
No with titre reduction ≥8-fold		1		7							
%		*6.2*		*43.8*							
		Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

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.

Since the May 2019 characterisation report of the viruses recovered, based on positive neuraminidase activity, 36 retained sufficient HA activity to allow antigenic analysis by HI (Tables 4-1 to 4-2); the results are summarised in Table 4-3. All test viruses were poorly recognised by the antiserum raised against the currently used vaccine virus, egg-propagated A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1). This was also the case with antisera raised against other egg-propagated vaccine viruses, A/Switzerland/8060/2017 (subclade 3C.2a2) and A/Kansas/14/2017 (clade 3C.3a).

Similarly, antisera raised against cell culture-propagated reference viruses for which homologous titres were available, A/Bretagne/1413/2017 (subclade 3C.2a2), A/England/538/2018 (clade 3C.3a) and A/Kansas/14/2017 (clade 3C.3a), recognised the test virus poorly; 14%, 42% and 28% respectively at titres within fourfold of homologous titres. The two antisera raised against cell culture-propagated subgroup 3C.2a1b viruses, A/La Rioja/2202/2018 and A/Norway/3275/2018, for which no homologous titres are given due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, recognised 14 and 17 test viruses, respectively, at titres of ≥160. Antiserum raised against cell culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised over 80% of test viruses at titres within fourfold of homologous titres.

Overall, the HI data show poor recognition of test viruses by post-infection ferret antisera raised against egg-propagated vaccine/reference viruses. Further, for test viruses of known genetic clade/subclade the data shows: (i) poor cross-reactivity of antisera raised against a subclade 3C.2a2 virus, (ii) clade specificity of the antisera raised against cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, and (iii) of the antisera raised against cell culture-propagated viruses that raised against A/Hong Kong/5738/2014 (clade 3C.2a) gives the broadest cross-clade/subclade reactivity.

The HA gene sequences of all test viruses in Table 4-1 are included in the HA phylogenetic analysis (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 having been dominant since the 2014–15 influenza season, notably subclade 3C.2a2 viruses, though subgroup 3C.2a1b viruses have predominated over the course of the 2018–19 season (Figure 2). The HA gene sequences of viruses in both clades continue to diverge. Notably, clade 3C.3a viruses have evolved to carry **HA1** amino acid substitutions of **L3I, S91N**, **N144K** (loss of a N-linked glycosylation motif at residues 144-146), **F193S** and **K326R**, compared with A/Stockholm/6/2014, and levels of detection since January 2019 have increased in a number of WHO European Region countries (Figure 2) and North America. New genetic groups have also emerged among the clade 3C.2a viruses, designated as subclades/subgroups. Amino acid substitutions that define these subclades/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/7295/2014 a cell culture-propagated surrogate for A/Hong Kong/4801/2014 (a former vaccine virus)
- 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 (2018–19 northern hemisphere vaccine virus)
- 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 **H311Q** in **HA1**, e.g. A/La Rioja/2202/2018, with many viruses in this subgroup carrying additional HA1 amino acid substitutions
- Subclade 3C.2a2: those in clade 3C.2a plus **T131K**, **R142K** and **R261Q** in **HA1**, e.g. A/Switzerland/8060/2017 (2019 southern hemisphere vaccine virus)
- Subclade 3C.2a3: those in clade 3C.2a plus **N121K** and **S144K** in **HA1**, e.g. A/Cote d'Ivoire/544/2016
- 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/England/538/2018.

Globally, the great majority of viruses with collection dates from 1 September 2018 have HA genes that continue to fall into genetic groups within clade 3C.2a, with those in subgroup 3C.2a1b having been more numerous than those in subclade 3C.2a2 for the period September 2018 to April 2019 (Figure 2). Notably, a significant number of the subgroup

[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 (accessed 02 July 2019): 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 (accessed 02 July 2019): http://www.ecdc.europa.eu/en/publications/Publications/ERLI-Net report November 2014.pdf

3C.2a1b viruses have fallen in two recently emerged clusters; one defined by amino acid substitutions **T131K** in **HA1** with **V200I** in **HA2** and the other by **T128A** and **T135K** substitutions in **HA1** (both resulting in loss of potential glycosylation sequons). Further, as indicated above, numbers of clade 3C.3a virus detections have increased over the course of the 2018–19 season in a number of countries/regions.

The locations of A/Singapore/INFIMH-16-0019/2016 (3C.2a1), the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2018–19 influenza season [2], A/Switzerland/8060/2017 (3C.2a2), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2019 influenza season [3], and A/Kansas/14/2017, the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2019–20 influenza season [1], are indicated in Figure 2.

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
	Passage history			A/HK 5738/14 MDCK	A/Bretagne 1413/17 SIAT	A/Singapore 0019/16 Egg 10^{-4}	A/La Rioja 2202/18 SIAT	A/Switz 8060/17 Egg	A/Eng 538/18 SIAT	A/Norway 3275/18 SIAT	NYMC X-327 A/Kans/14/17 Egg	A/Kansas 14/17 SIAT
	Ferret number			St Judes F60/17^{+1}	F01/18^{+1}	F46/17^{+1}	F26/18^{+1}	F27/18^{+1}	F31/18^{+1}	F03/19^{+1}	F16/19^{+1}	F17/19^{+1}
	Genetic group			3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a
REFERENCE VIRUSES												
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	320	160	160	320	160	160	160	80
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	160	80	640	160	160	80
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	160	40	640	160	160	80	40	<
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	160	1280	640	80	1280	80	80	40
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	40	<	40	40	40	320	<	160
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	E x/E1	40	40	40	<	40	320	<	1280
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	80	40	80	40	80	640	40	320
TEST VIRUSES												
A/Austria/1113943/2018		3C.2a1b	2018-12-31	SIAT1/SIAT1	80	<	80	160	80	40	160	80
A/Austria/1114682/2019		3C.2a1b	2019-01-02	SIAT1/SIAT1	160	80	40	160	80	80	320	80
A/Austria/1114171/2019		3C.2a1b	2019-01-03	SIAT1/SIAT1	80	160	40	160	160	80	320	80
A/Austria/1115877/2019		3C.2a1b	2019-01-08	SIAT1/SIAT1	80	<	<	80	40	<	80	<
A/Austria/1115342/2019		3C.3a	2019-01-08	SIAT1/SIAT1	160	80	160	80	160	320	160	320
A/Austria/1117352/2019		3C.2a3	2019-01-14	SIAT1/SIAT1	80	<	40	80	80	40	40	80
A/Austria/1117700/2019		3C.2a1b	2019-01-16	SIAT1/SIAT1	80	<	40	160	40	<	160	80
A/Austria/1120261/2019		3C.2a1b	2019-01-25	SIAT1/SIAT1	80	<	40	160	80	40	80	<
A/Austria/1121455/2019		3C.2a4	2019-01-29	SIAT1/SIAT1	40	40	40	40	40	40	80	40
A/Austria/1121454/2019		3C.2a1b	2019-01-31	SIAT1/SIAT1	80	<	80	40	40	<	40	<
A/Austria/1121450/2019		3C.2a2	2019-01-31	SIAT1/SIAT1	80	160	40	160	80	80	160	80
A/Bulgaria/958/2019		3C.2a1b	2019-02-01	SIAT2/SIAT1	80	40	80	160	80	80	160	80
A/Bulgaria/949/2019		3C.2a1b	2019-02-01	SIAT2/SIAT1	80	<	40	160	40	40	80	40
A/Bulgaria/902/2019		3C.2a2	2019-02-01	SIAT2/SIAT1	160	320	80	80	320	80	160	160
A/Bulgaria/900/2019		3C.2a2	2019-02-01	SIAT2/SIAT1	160	320	80	80	320	80	160	160
A/Bulgaria/896/2019		3C.2a1b	2019-02-01	SIAT2/SIAT1	80	80	<	80	80	40	160	80
A/Bulgaria/947/2019		3C.2a1b	2019-02-03	SIAT2/SIAT1	<	<	<	40	<	<	40	<
A/Bulgaria/909/2019		3C.2a1b	2019-02-03	SIAT2/SIAT1	80	40	80	160	80	40	160	40
A/Bulgaria/1052/2019		3C.2a1b	2019-02-05	SIAT2/SIAT1	40	<	40	160	<	<	80	<
A/Bulgaria/1051/2019		3C.2a1b	2019-02-06	SIAT2/SIAT1	40	40	40	320	<	<	160	<
A/Bulgaria/1134/2019		3C.2a1b	2019-02-12	SIAT2/SIAT2	80	<	40	640	40	<	320	<
A/Bulgaria/1129/2019		3C.2a1b	2019-02-16	SIAT2/SIAT1	80	<	40	160	<	<	160	<
A/Slovenia/1213/2019		3C.2a1b	2019-02-19	MDCKx/MDCK1	40	<	<	160	40	<	80	40
A/Bulgaria/1153/2019		3C.2a1b	2019-02-21	SIAT2/SIAT1	40	<	40	80	<	<	<	<
A/Austria/1129536/2019		3C.2a1b	2019-02-27	SIAT1/SIAT1	160	160	40	80	80	40	160	<
							Vaccine SH 2018 NH 2018-19		Vaccine SH 2019			Vaccine NH 2019-20

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

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
	Passage history			A/HK 5738/14 MDCK St Judes	A/Bretagne 1413/17 SIAT	A/Singapore 0019/16 Egg 10^{-4}	A/La Rioja 2202/18 SIAT	A/Switz 8060/17 Egg	A/Eng 538/18 SIAT	A/Norway 3275/18 SIAT	NYMC X-327 A/Kans/14/17 Egg	A/Kansas 14/17 SIAT
	Ferret number			F60/17 [-1]	F01/18 [-1]	F46/17 [-1]	F26/18 [-1]	F27/18 [-1]	F31/18 [-1]	F03/19 [-1]	F16/19 [-1]	F17/19 [-1]
	Genetic group			3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a
REFERENCE VIRUSES												
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	160	160	160	80	160	160	160	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	1280	160	80	640	160	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	160	80	640	160	160	80	40	40	<
A/Switzerland/8060/2017	clone 57 3C.2a2	2017-12-12	E7/E1	160	1280	640	160	1280	80	80	80	<
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	40	80	40	40	640	<	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	E4/E1	40	40	80	40	40	320	40	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	160	80	160	80	160	640	40	320	320
TEST VIRUSES												
A/Lisboa/100/2019		2019-01-28	SIAT3/SIAT1	40	<	40	<	40	320	<	160	320
A/Lisboa/93/2019		2019-02-08	SIAT2/SIAT1	40	<	40	<	40	320	<	160	320
A/Skovde/1/2019		2019-02-11	MDCK1/SIAT1	40	<	40	80	40	40	160	<	40
A/Eskilstuna/6/2019		2019-02-13	MDCK0/SIAT1	160	160	80	80	160	80	320	40	40
A/Lisboa/92/2019		2019-02-15	MDCK2/SIAT1	40	40	80	<	40	320	40	160	320
A/Lisboa/91/2019		2019-02-20	SIAT1/SIAT1	40	40	80	40	40	640	40	160	320
A/Lisboa/97/2019		2019-02-25	SIAT2/SIAT1	40	40	80	40	40	640	40	160	320
A/Lisboa/94/2019		2019-02-26	SIAT1/SIAT1	40	40	80	<	40	320	<	160	320
A/Lisboa/95/2019		2019-02-27	SIAT2/SIAT1	40	<	40	<	40	320	<	160	320
A/Lisboa/98/2019		2019-03-08	SIAT1/SIAT1	<	<	40	<	<	160	<	40	40
A/Denmark/2785/2019		2019-03-13	SIAT2/SIAT1	40	<	40	160	<	<	80	<	<
						Vaccine SH 2018 NH 2018-19		Vaccine SH 2019			Vaccine NH 2019-20	

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

Sequences in phylogenetic trees

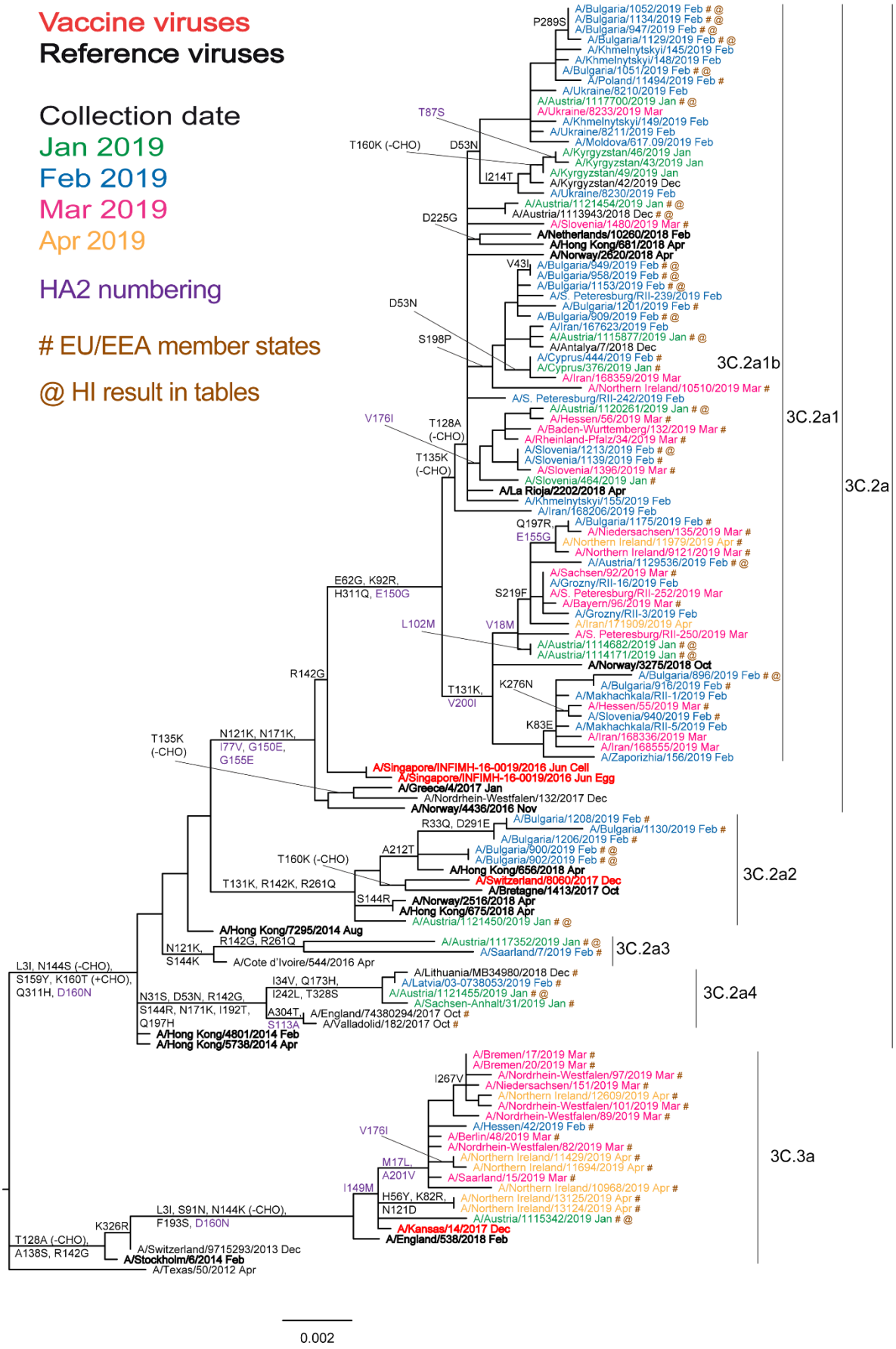
Table 4-3. Antigenic analysis of A(H3N2) viruses by HI - Summary

Viruses	Other information	Collection date	Haemagglutination inhibition titre								
			Post-infection ferret antisera								
			A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/La Rioja 2202/18	A/Switz 8060/17	A/Eng 538/18	A/Norway 3275/18	NYMC X-327 A/Kans/14/17	A/Kansas 14/17
	Passage history		MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	SIAT	Egg	SIAT
	Ferret number		St Judes F60/17[*1]	F01/18[*1]	F46/17[*1]	F26/18[*1]	F27/18[*1]	F31/18[*1]	F03/19[*1]	F16/19[*1]	F17/19[*1]
	Genetic group		3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a
REFERENCE VIRUSES											
A/Hong Kong/5738/2014	3C.2a	2014-04-30	320	160	160	160	320	160	160	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	160	640	160	80	640	160	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	160	40	640	160	160	80	40	<	<
A/Switzerland/8060/2017 clone 57	3C.2a2	2017-12-12	160	1280	640	80	1280	80	80	40	<
A/England/538/2018	3C.3a	2018-02-26	40	<	40	40	40	320	<	160	160
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	40	40	40	<	40	320	<	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	80	40	80	40	80	640	40	320	320
TEST VIRUSES											
Number of viruses tested*			36	36	36	36*	36	36	36*	36	36
No with titre reduction ≤2-fold			6	2		14		8	17		8
%			*16.7*	*5.6*				*22.3*			*22.3*
No with titre reduction =4-fold			23	3	1		2	7		1	2
%			*63.9*	*8.3*	*2.8*		*5.6*	*19.4*		*2.8*	*5.6*
No with titre reduction ≥8-fold			7	31	35		34	21		35	26
%			*19.4*	*86.1*	*97.2*		*94.4*	*58.3*		*97.2*	*72.1*
Subgroup 3C.2a1b viruses											
Number of viruses tested*			19	19	19	19*	19	19	19*	19	19
No with titre reduction ≤2-fold			2			13			11		
%			*10.5*								
No with titre reduction =4-fold			12	2				3			
%			*63.2*	*10.5*				*15.8*			
No with titre reduction ≥8-fold			5	17	19		19	16		19	19
%			*26.3*	*89.5*	*100*		*100*	*84.2*		*100*	*100*
			Vaccine SH 2018 NH 2018-19				Vaccine SH 2019			Vaccine NH 2019-20	

* Homologous HI titres not available - only results for viruses yielding HI titres of ≥160 with the respective antisera are shown

Reference virus results are taken from Table 4-1. Summaries for each antiserum are based on fold-reductions observed on the days that HI assays were performed.

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



Influenza B virus analyses

Influenza B viruses represented only 3.1% of the samples received with collection dates after 31 August 2018 and were received from NICs in 14 countries: Austria, Croatia, Denmark, France, Greece, Iceland, Ireland, Italy, Luxembourg, Norway, Portugal, Slovenia, Sweden and the United Kingdom (Table 1). Of the small number received, 22 were B/Yamagata-lineage and 15 were B/Victoria-lineage.

Influenza B/Victoria-lineage

Five B/Victoria-lineage viruses, three from Slovenia and two from Sweden, have been tested by HI since the May 2019 characterisation report (Tables 5-1 to 5-2). The viruses from individual countries showed the same patterns of reactivity in HI profiles, but the profiles for viruses from the two countries were different, despite the viruses belonging to the HA triple amino acid deletion group (1A(Δ3) of African origin (see below).

A relatively small number (1 233 in total of which 1 040 were full length, as of 5 July) of HA sequences for viruses collected from 1 September 2018 have been deposited in the GISAID EpiFlu database and the great majority of these have been from China and the USA, with only 46 (29 full length) from countries in Europe. All recent viruses, those with collection dates from 21 March to 3 July 2019 that have data deposited in GISAID, continue to have HA genes that fall in the B/Brisbane/60/2008 clade (clade 1A; Figure 3), with all falling in a subclade defined by **HA1** amino acid substitutions **I117V**, **N129D** and **V146I** within clade 1A. Two groups within this subclade have deletions in the HA gene. A group that has spread worldwide, though the most recently circulating viruses have been reported from the USA, have HA genes encoding an **HA1** with deletion of residues **K162** and **N163** (1A(Δ2) in Figure 3). These viruses have additional substitutions of **D129G** and **I180V** in **HA1**, and **R151K** in **HA2**. The second group of B/Victoria-lineage viruses detected recently have HA genes encoding a deletion of three **HA1** amino acids, **K162**, **N163** and **D164** (1A(Δ3) in Figure 3); this group splits into an Asian subgroup with viruses carrying additional substitutions of **I180T** and **K209N** in **HA1** and a West African subgroup with viruses carrying the **HA1** substitution **K136E**, often with additional HA1 substitutions of **G74E** and **E198G** (within the **197-199** glycosylation site) or **G133R**. The majority of recently collected B/Victoria-lineage viruses fall in the 1A(Δ3) West African subgroup and have been detected in countries worldwide, as is the case for all those reported from EU/EEA countries (Figure 3).

It was noted in the September 2018 characterisation report[4], and earlier ones, that the clade 1A viruses without deletions, the 1A(Δ2) group and the 1A(Δ3) subgroups are antigenically distinct from one another. Following the emergence and spread of viruses in the 1A(Δ2) group a representative, B/Colorado/06/2017, has been recommended for use in trivalent influenza vaccines for the 2018–19 and 2019-20 northern hemisphere [1, 2] and 2019 southern hemisphere [3] seasons.

Influenza B/Yamagata-lineage

Three B/Yamagata-lineage viruses from Austria have been tested by HI since the May 2019 characterisation report. Antisera raised against three egg-propagated viruses, B/Wisconsin1/2010 (former vaccine virus), B/Stockholm/12/2011 and B/Phuket/3073/2013 (current vaccine virus), all recognised the test viruses at titres within twofold of the respective homologous titres, as did an antiserum raised against cell culture-propagated B/Mauritius/I-762/2018. Antisera raised against two additional cell culture-propagated clade 3 viruses, B/Phuket/3073/2013 and B/Mauritius/1791/2017, recognised the test viruses less well, as was the case with antisera raised against clade 2 viruses, B/Estonia/55669/2011 and B/Massachusetts/02/2012 (former vaccine virus) (Figure 6).

A smaller number (767 in total of which 706 were full length, as of 5 July) of B/Yamagata-lineage HA sequences for viruses collected from 1 September 2018 have been deposited in the GISAID EpiFlu database, and the great majority of these have been from China and the USA, with only 52 (35 full length) from countries in Europe. Figure 4 shows a phylogenetic analysis of the HA genes of recently circulating B/Yamagata-lineage viruses, those with collection dates from 21 March to 3 July2019 that have data deposited in GISAID, with just five being from EU/EEA countries. HA sequences of all viruses collected in the 2017–2018 season, and since, carry HA genes in genetic clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade, with those from viruses collected after 31 August 2018 falling in a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions compared to B/Phuket/3073/2013. Some subclustering of sequences, defined by specific amino acid substitutions (e.g. **HA1 S120T** or **D229N** or **D232N** [introducing a potential N-linked glycosylation site]), is occurring. It has been noted in previous characterisation reports for 2018 that none of these amino acid substitutions have any obvious antigenic effects based on HI assays using post-infection ferret antisera raised against egg-propagated B/Phuket/3073/2013 which has been recommended for inclusion in quadrivalent vaccines for the 2018–2019 and 2019–20 [1, 2] northern hemisphere and the 2019 [3] southern hemisphere seasons.

[4] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2018. Stockholm: ECDC; 2018. Available from (accessed 5 July 2019): https://ecdc.europa.eu/sites/portal/files/documents/ECDC-Flu-Characterisation-Report-Sep-2018.pdf

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													
	Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Malta 636714/11 Egg	B/Sth Aus 81/12 Egg	B/HK 514/09 MDCK	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Norway 2409/17 MDCK	B/Colorado 06/17 MDCK	B/Colorado 06/17 Egg	B/CIV 1662/18 MDCK	
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[1,3]	F44/17[*2]	F29/13[*2]	F25/16[*2]	NIB F47/16[*2]	F15/16[*2]	F16/16[*2]	F40/17[*2]	F09/18[*4]	F10/18[*2]	F37/18[*2]	
	Genetic group			1A	1A	1A	1A	1B	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)	
REFERENCE VIRUSES															
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	1280	160	160	320	80	20	20	<	20	40	<	
B/Malta/636714/2011	1A	2011-03-07	E4/E1	1280	160	160	160	80	20	20	<	10	20	<	
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	160	160	320	80	20	20	<	20	20	<	
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	1280	20	40	20	80	40	40	<	<	<	<	
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	10	20	10	40	40	40	<	<	<	<	
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	1280	10	20	10	40	40	40	<	<	<	<	
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	<	<	<	<	<	<	40	40	10	<	
B/Colorado/06/2017	1A(Δ2)	2017-02-05	MDCK1/MDCK2	160	<	<	10	<	<	<	40	80	20	<	
B/Colorado/06/2017	1A(Δ2)	2017-02-05	E5/E2	640	160	40	40	10	<	<	20	80	80	<	
B/Cote D'Ivoire/1662/2018	1A(Δ3)	2018-07-25	P0/MDCK3	160	10	20	20	<	<	<	<	20	10	20	
TEST VIRUSES															
B/Slovenia/308/2019	1A(Δ3)	2019-01-15	MDCKx/MDCK1	320	<	20	10	<	<	<	20	20	10	20	
B/Slovenia/787/2019	1A(Δ3)	2019-02-01	MDCKx/MDCK1	320	<	20	10	<	<	<	20	20	20	20	
B/Slovenia/1654/2019		2019-03-25	MDCKx/MDCK1	320	<	20	10	<	<	<	20	20	10	20	
					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; ND = Not Done
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, SH 2019 and NH 2019-20

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									
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Malta 636714/11 Egg	B/Sth Aus 81/12 Egg	B/HK 514/09 MDCK	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Norway 2409/17 MDCK	B/Colorado 06/17 MDCK	B/Colorado 06/17 Egg	B/CIV 1662/18 MDCK
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*2]	F29/13[*2]	F25/16[*2]	NIB F47/16[*2]	F15/16[*2]	F16/16[*2]	F40/17[*2]	F09/18[*4]	F10/18[*2]	F37/18[*2]
		Genetic group			1A	1A	1A	1A	1B	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)
REFERENCE VIRUSES															
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	640	160	320	320	20	40	<	20	40	<
B/Malta/636714/2011		1A	2011-03-07	E4/E1	2560	640	320	320	320	40	40	<	20	40	<
B/South Australia/81/2012		1A	2012-11-28	E4/E2	1280	320	160	320	160	20	20	<	20	40	<
B/Hong Kong/514/2009		1B	2009-10-11	MDCK1/MDCK2	1280	80	40	20	80	40	40	<	<	<	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	1280	80	20	10	40	40	40	<	<	<	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	1280	80	20	20	80	40	80	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	40	<	<	<	<	<	<	40	40	10	<
B/Colorado/06/2017		1A(Δ2)		MDCK1/MDCK2	80	<	<	<	<	<	<	40	40	10	<
B/Colorado/06/2017		1A(Δ2)		E5/E2	1280	320	40	40	20	<	<	40	80	160	<
B/Cote D'Ivoire/1662/2018		1A(Δ3)	2018-07-25	P0/MDCK3	80	20	10	10	<	<	<	<	20	<	10
TEST VIRUSES															
B/Stockholm/1/2019		1A(Δ3)	2019-02-24	MDCK1/MDCK1	640	80	<	10	<	<	<	<	<	10	<
B/Eskilstuna/2/2019		1A(Δ3)	2019-03-06	MDCK1/MDCK1	640	80	<	10	<	<	<	<	<	20	<
						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; ND = Not Done

[#] 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, SH 2019 and NH 2019-20

Sequences in phylogenetic trees

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

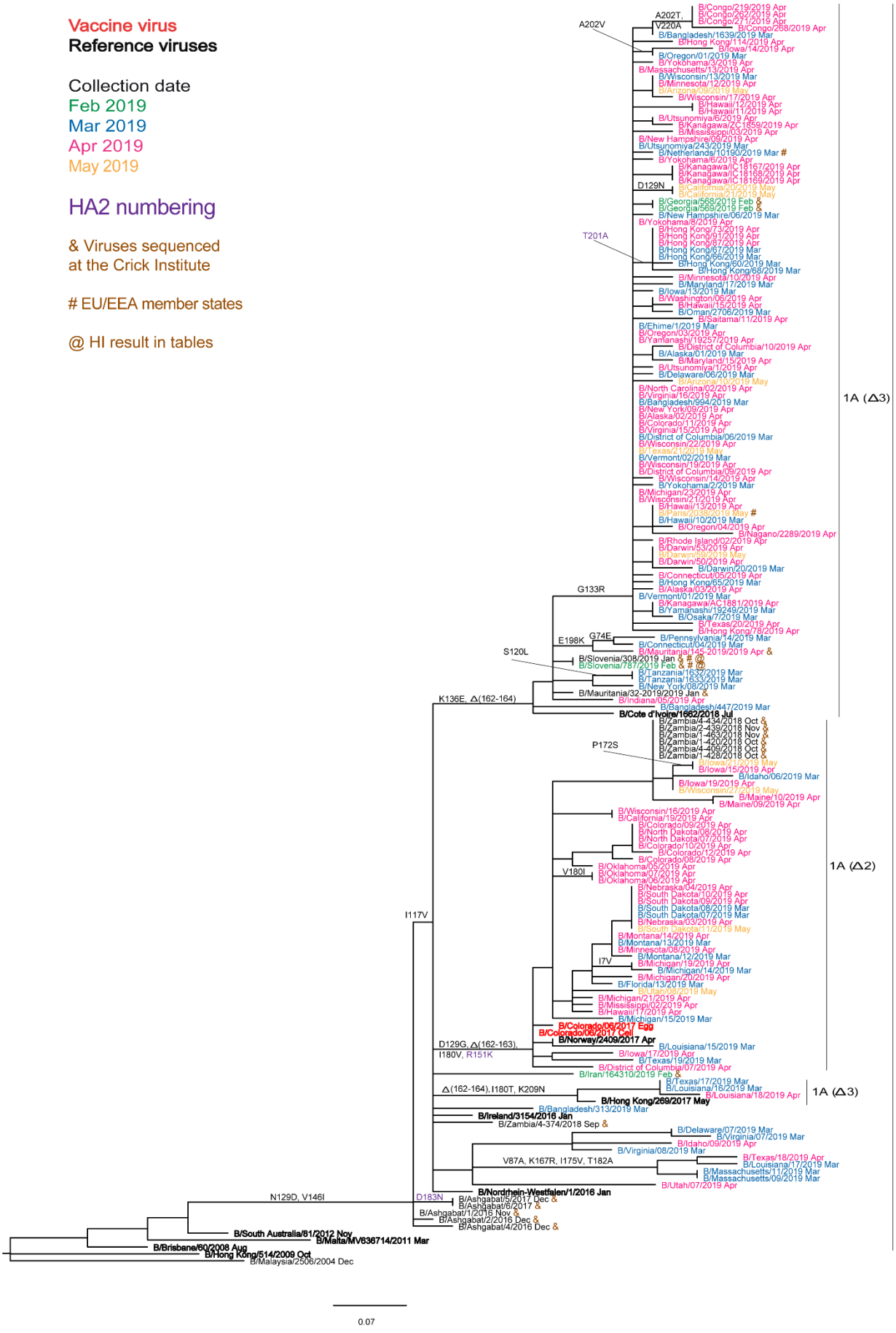


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

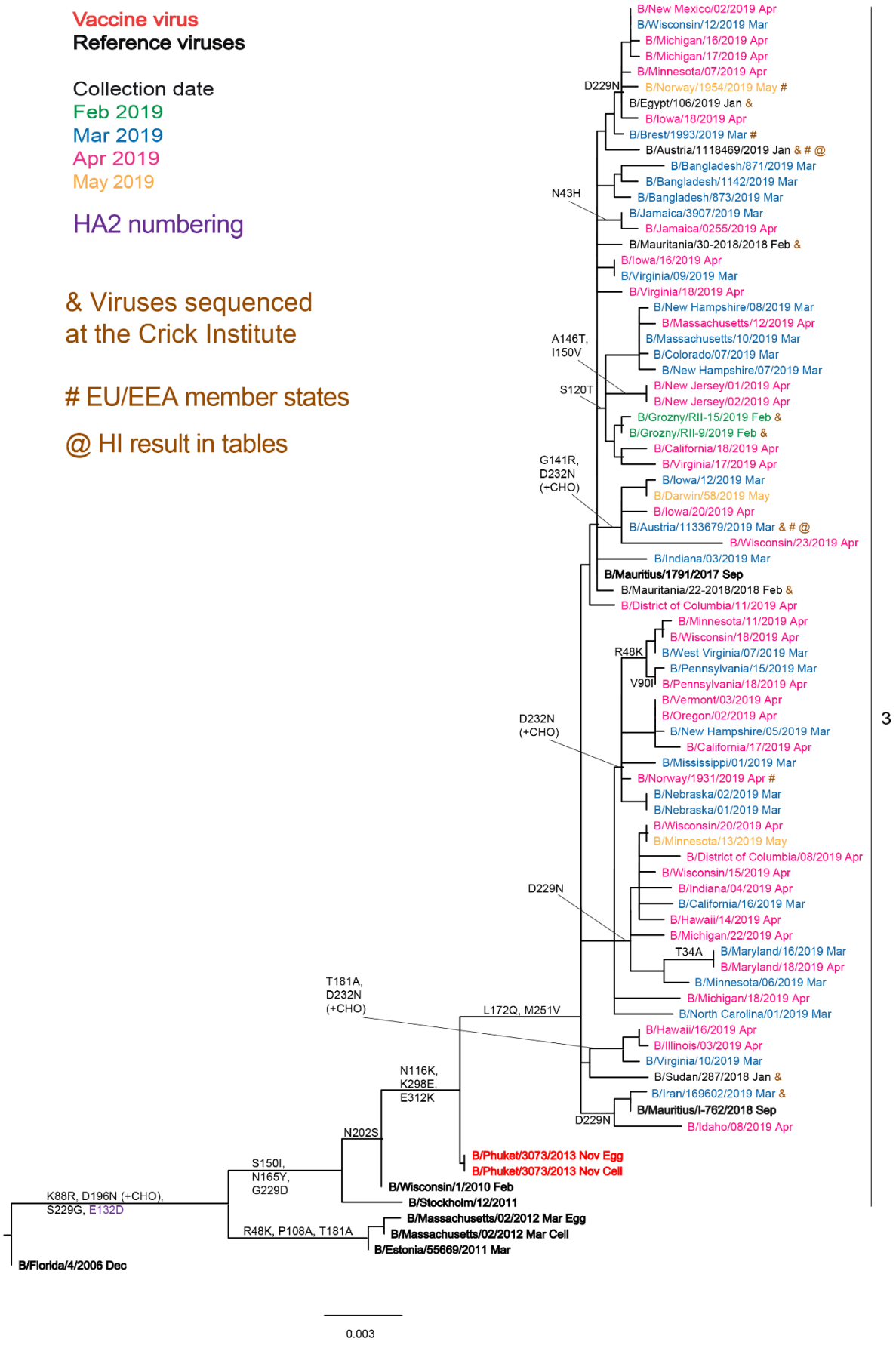
Viruses	Other information	Passage history / Ferret number / Genetic Group	Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
					B/Phuket 3073/13 Egg SH614*1,3	B/Estonia 55669/11 MDCK F39/17*2	B/Mass 02/12 MDCK F10/16*2	B/Mass 02/12 Egg F06/17*2	B/Wis 1/10 Egg F36/15*2	B/Stock 12/11 Egg F05/17*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	B/Maur I-762/18 MDCK F05/19*2
		Genetic Group			3	2	2	2	3	3	3	3	3	3
REFERENCE VIRUSES														
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	640	80	40	160	40	20	<	40	<	80
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK4	2560	160	160	640	80	160	20	160	40	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	640	20	10	320	20	40	<	40	<	10
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	<	10	160	20	40	<	80	10	40
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	<	10	80	20	80	<	80	<	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	5120	160	320	320	80	160	80	160	80	640
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	<	<	80	20	40	<	40	<	20
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK4	2560	10	20	80	20	40	<	40	20	80
B/Mauritius/I-762/2018		3	2018-09-02	MDCK1/MDCK3	1280	10	20	80	20	40	<	40	20	160
TEST VIRUSES														
B/Austria/1118469/2019		3	2019-01-21	MDCK1	640	10	20	80	20	40	10	80	<	160
B/Austria/1130261/2019			2019-03-04	SIAT1/MDCK1	2560	40	80	160	80	160	40	160	80	320
B/Austria/1133679/2019		3	2019-03-14	SIAT1/MDCK1	1280	20	10	80	40	40	10	40	20	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 quadravalent vaccines NH 2018-19, SH 2019 and NH 2019-20

Sequences in phylogenetic trees

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



Summaries of data submitted to TESSy

Genetic characterisation

For the 2018–19 season, as of week 25/2019, 4102 viruses had been characterised genetically and ascribed to a genetic clade, none of which were characterised in weeks 21-25/2019:

- 1 882 A(H1N1)pdm09 were subclade 6B.1, represented by the vaccine virus A/Michigan/45/2015, with a further three attributed to a subgroup not listed
- 2 163 were A(H3N2) viruses, with 1 435 being subgroup 3C.2a1b represented by A/Alsace/1746/2018, 70 being subclade 3C.2a2 represented by A/Switzerland/8060/2017, 33 being subclade 3C.2a3 represented by A/Cote d'Ivoire/544/2016, 548 being clade 3C.3a represented by A/England/538/2018, 57 being subclade 3C.2a1 represented by A/Singapore/16-0019/2016, five being clade 3C.2a represented by A/Hong Kong/4801/2014, nine being subgroup 3C.2a1a represented by A/Greece/4/2017, and six were attributed to a subgroup not listed in current TESSy reporting categories
- 29 were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013
- 25 were B/Victoria-lineage viruses, with five being clade 1A represented by B/Brisbane/60/2008, five being subclade 1A.Δ2 with a two amino acid deletion in HA represented by the vaccine virus B/Colorado/06/2017, and 15 being subclade 1A.Δ3 with a three amino acid deletion in HA represented by B/Hong Kong/269/2017.

Antiviral susceptibility

For viruses collected in the course of the 2018–19 season, as of week 20/2019, 1668 A(H1N1)pdm09, 1121 A(H3N2), and 35 type B have been tested for susceptibility to neuraminidase inhibitors. Eight A(H1N1)pdm09 viruses carried NA H275Y amino acid substitution indicative of highly reduced inhibition (HRI; confirmed phenotypically for three) and an additional three showed evidence of reduced inhibition (RI) by oseltamivir in phenotypic assays. One type B virus showed evidence of RI by oseltamivir and zanamivir. There was no update for the period week 21-25/2019.

At the WIC for this season, 762 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 393 A(H1N1)pdm09, 349 A(H3N2), 7 B/Victoria-lineage and 13 B/Yamagata-lineage. All but two viruses showed normal inhibition (NI) by the two neuraminidase inhibitors. B/Norway/3241/2018 (Victorialineage) showed reduced inhibition (RI) by the inhibitors and the NA gene encoded D197N amino acid substitution. A/Latvia/03-0738053/2019 (H3N2) showed RI by zanamivir and sequencing revealed NA D151D/N and V165I amino acid substitutions.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [4] 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 [5]. Increased numbers of cases were reported over the course of the following seasons and cases were reported in 2017, including the fifth (2016–17) and largest wave to date, which included the emergence of highly pathogenic avian influenza (HPAI) strains that have caused some zoonoses, though few human cases were reported during the 2017–18 season [6]. WHO posted an analysis of information on A(H7N9) viruses on 10 February 2017 [7]; a summary and assessment of influenza viruses at the human-animal interface on 24 June 2019 reports that no new cases of human infection had been detected since the 11 May report and indicates that there have been no publicly available reports from animal health authorities in China of influenza A(H7N9) virus detections in animals in recent months [8]. The most recent human case was detected in mid-March 2019 [9]. The latest overview of avian influenza by ECDC in collaboration with the European Food Safety Authority and the EU Reference Laboratory for Avian Influenza was published on 28 March 2019 and can be found on the ECDC website [10].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 24 June 2019, indicating that various A(H5Nx) subtypes continue to be detected in birds in Africa, Europe and Asia [8]. No new human cases of A(H5N1) infection have been detected since that in Nepal in March, where there have been reports of A(H5N1) infection in domestic birds since February 2019, this being the first human case of A(H5N1) infection reported to WHO since 2017 [11]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [12]. As described above, the EU Reference Laboratory for Avian Influenza, in collaboration with ECDC and the European Food Standards Agency, published on 28 March 2019 the latest overview of avian influenza, which can be found on the ECDC website [10].

WHO CC reports

A description of results generated by the London WHO CC at the WIC and used at the most recent WHO vaccine composition meeting (held in Beijing, China 18–20 February 2019), and previous ones, can be found at:

https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports (accessed 1 July 2019)

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 most 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 the GISAID 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 WHO CC London.

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