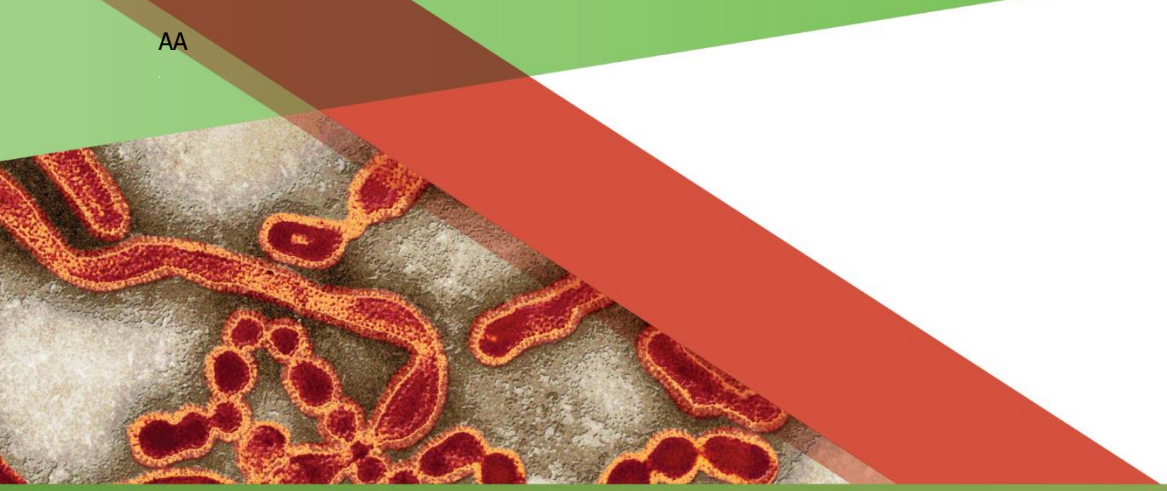
AA



SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, July 2019

Summary

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

Since the June 2019 characterisation report[1], a further four 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 1 432 virus specimens, with collection dates after 31 August 2018, have been received.

A number of the 103 A(H1N1)pdm09 test viruses characterised antigenically since the last report showed better reactivity with antiserum raised against the A/Michigan/45/2015 2018–19 vaccine virus, compared with antiserum raised against the A/Brisbane/02/2018 2019–20 vaccine virus. The 539 test viruses with collection dates from week 40/2018 genetically characterised at the WIC, including two H1N2 reassortants, have all fallen in subclade 6B.1A, defined by S74R, S164T and I295V HA1 substitutions; 493 of these viruses also have HA1 S183P substitution, often with additional substitutions in HA1 and/or HA2.

Since the last report, 21 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 vaccine virus, egg-propagated A/Singapore/INFIMH-16-0019/2016. Of the 446 viruses with collection dates from week 40/2018 genetically characterised at the WIC, 363 were clade 3C.2a (41 3C.2a2, 14 3C.2a3, eight 3C.2a4 and 300 3C.2a1b); 83 were clade 3C.3a.

Four B/Victoria-lineage viruses have been characterised in this reporting period. All recent viruses have HA1 amino acid substitutions of I117V, N129D, and V146I compared to B/Brisbane/60/2008, a previous vaccine virus. 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 Δ162-164 group having subgroups of Asian and African origin. These virus groups are antigenically distinguishable by HI assay. Of 12 viruses characterised from EU/EEA countries this season, one has been Δ162-163 and 11 Δ162-164 (10 African and one Asian subgroup).

Two B/Yamagata-lineage viruses have been characterised in this reporting period, raising the total to 15 for the 2018–19 season. All have HA genes that encode HA1 amino acid substitutions of L172Q and M251V compared to, and remain antigenically similar to, the vaccine virus B/Phuket/3073/2013 (clade 3) recommended for use in quadrivalent vaccines for the next northern hemisphere influenza season.

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

Suggested citation: European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, July 2019. Stockholm: ECDC; 2019.

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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 205 167, with type A (98.9%) predominating over type B viruses (1.1%), 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 prevailed over A(H3N2) (n = 32753) viruses, and 85 of 146 type B viruses have been B/Yamagata-lineage. 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). 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)**		

[a] Numbers taken from Flu News Europe week 20/2019 and weeks 21-25/2019

*** 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, 64 (4 in July) 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 1 432 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].

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 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														
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	1							
Slovenia	3			1	1						2	2		
Spain	28			15	8	13	2	3						
Sweden	14			10	10	4	3	1						
United Kingdom	11			5	5	6	in process							
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	10	1	0	1						
Czech Republic	1			1	1									
Estonia	10	3	in process	5	5	2	0	2						
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	1		
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	5	4	0	0						
Portugal	7			2	2	5	4	1						
Romania	13			11	6	2	1	1						
Slovakia	12			7	7	5	5							
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	42	3	0	32	in process	7	in process	0						

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]
FEBRUARY														
Austria	5			4	4	1	1	0						
Bulgaria	41			22	23	19	13	9						
Cyprus	15			14	13	1	0	1						
Czech Republic	10			10	10									
Denmark	6			3	3	3	0	3						
Estonia	8	2	in process	5	4	1	0	1						
Finland	4			4	4									
Germany	26			9	9	17	9	8						
Greece	17			11	10	5	1	4					1	1
Italy	12			4	4	8	in process							
Latvia	7			1	1	6	5	1						
Malta	8			5	2	3	0	1						
Poland	28	1	0	22	7	5	0	3						
Portugal	13			6	6	7	6	1						
Slovakia	13			10	10	3	3							
Slovenia	7			3	3	3	1	2			1	1		
Sweden	5			1	1	2	2				1	1	1	1
United Kingdom	14			4	in process	10	in process							
MARCH														
Austria	2												2	2
Bulgaria	1			1	1									
Cyprus	1					1	0	0						
Czech Republic	2					2	1	1						
Denmark	16			7	7	9	1	8						
Estonia	7			5	5	2	0	2						
Finland	7			2	2	5	2	3						
France	9			4	in process	4	3	1					1	1
Germany	23			7	7	16	12	4						
Greece	15			8	3	6	1	4					1	1
Iceland	7			4	4	3	2	1						
Italy	15			6	6	9	in process							
Latvia	2			1	1	1	1	0						
Poland	7			7	5									
Portugal	5			3	3	2	1	1						
Slovakia	4			2	2	2	2							
Slovenia	8			4	4	3	0	3			1	1		
Sweden	5			2	2	2	0	2			1	1		
United Kingdom	18			13	in process	5	0							
APRIL														
Cyprus	1			1	1									
Czech Republic	2					2	1	1						
Denmark	1			1	1									
Finland	6			2	2	4	3	1						
France	15			3	in process	12	7	5						
Iceland	7			1	1	4	in process				2	2		
Slovakia	1			1	1									
Slovenia	2			2	2									
United Kingdom	15					15	0							
MAY														
Finland	1					1	0	1						
France	1										1	1		
Iceland	3			2	2	1	4							
Portugal	1										1	0		
JUNE														
Iceland	2					2	1	1						
30 Countries	1432	12	0	744	552	632	200	268	3	0	18	14	23	18
				52.0%		44.1%					1.3%		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 2019-08-05

Influenza A(H1N1)pdm09 virus analyses

Tables 3-1 to 3-5 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 June 2019 characterisation report but with genetic group data now included, while Tables 3-2 to 3-5 were generated during July 2019. Test viruses in each table are sorted by date of collection and genetic group/subgroup (where known). A summary of the HI results for all test viruses in Tables 3-1 to 3-5 is shown in Table 3-6 and is broken down by genetic group/subgroup in Table 3-7.

The proportion of A(H1N1)pdm09 test viruses that were antigenically indistinguishable from the A/Michigan/45/2015 northern hemisphere 2018–19 influenza season vaccine virus [2], being recognised at titres within twofold of the titre of the post-infection ferret antiserum with the homologous virus, was 75% rising to 90% at titres with fourfold (Table 3-6). Similar proportions were seen with antiserum raised against the A/Brisbane/02/2018 northern hemisphere 2019–20 influenza season vaccine virus [1], 74% at twofold and 95% at fourfold compared to the titre with the homologous virus. Similar levels of recognition were observed with antiserum raised against another egg-propagated virus, A/Slovenia/2903/2015, 75% at twofold and 95% at fourfold. Antisera raised against egg-propagated A/Switzerland/2656/2017 and A/Switzerland/3330/2017 performed somewhat better with 88% and 87% recognition within twofold, respectively, rising to 98% and 99% within fourfold of their respective homologous titres.

Of four antisera raised against cell culture-propagated viruses, those against A/Bayern/69/2009, A/Paris/1447/2017 and A/Norway/3433/2018 retained recognition of all but two (99%) test viruses at titres within fourfold of their respective homologous titres. That raised against A/Ireland/84630/2018 showed lower recognition of test viruses at titres within twofold of the titres of the antiserum with the homologous viruses, but retained 98% 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 polymorhism of **G155G/E**, with E predominating, and **D222G** substitution. This antiserum recognised only 17% of test viruses at titres within twofold of the homologous titre, and 44% within fourfold (Table 3-6). Two viruses from Portugal that showed reduced recognition across the panel of antisera both contained HA1 N156K amino acid substitutions (Table 3-2).

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 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 July 2019, with a focus on those with collection dates in February to May. 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 3-7 summarises the data in Table 3-6 for viruses that had been sequenced at the time of preparing this report, by genetic groups 183P-2, -5, -6 and -7. Generally, 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 seven of the antisera in the panel (Table 3-7). 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	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/1119457/2019		6B.1A	2019-01-23	SIAT1/MDCK1	1280	160	80	640	1280	1280	640	2560	1280	640
A/Austria/1120563/2019		6B.1A	2019-01-28	SIAT1/MDCK1	640	160	80	640	1280	1280	640	2560	640	640
A/Finland/90/2019		6B.1A2	2019-02-25	MDCK1/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
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		6B.1A5	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		6B.1A5	2018-12-28	MDCK0/MDCK1	320	160	80	320	640	320	320	1280	640	640
A/Linkoping/71/2018		6B.1A5	2018-12-31	MDCK1/MDCK1	640	80	80	320	640	640	320	1280	640	640
A/Linkoping/1/2019		6B.1A5	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		6B.1A5	2019-01-03	MDCK0/MDCK1	320	80	80	160	320	320	160	640	320	160
A/Sundsvall/2/2019		6B.1A5	2019-01-23	MDCK0/MDCK1	640	160	80	320	640	640	320	1280	320	320
A/Gavle/2/2019		6B.1A5	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/Gavle/3/2019	S190X	6B.1A5	2019-02-05	MDCK0/MDCK1	160	80	<	160	320	320	160	640	320	160
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		6B.1A5	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/47/2019		6B.1A5	2019-02-28	MDCK1/MDCK1	320	80	40	320	640	320	320	1280	640	320
A/Halmstad/1/2019		6B.1A5	2019-03-16	MDCK0/MDCK1	160	40	<	160	320	160	160	640	160	160
A/Finland/55/2019		6B.1A5	2019-03-19	MDCK1/MDCK1	320	80	40	320	320	320	320	1280	640	320
A/Finland/54/2019		6B.1A5	2019-03-19	MDCK1/MDCK1	320	80	80	320	640	320	160	1280	320	320
A/Sundsvall/3/2019		6B.1A5	2019-03-24	MDCK0/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Finland/103/2019		6B.1A5	2019-04-02	MDCK1/MDCK1	640	160	160	640	640	640	320	1280	640	320
A/Finland/102/2019		6B.1A5	2019-04-02	MDCK1/MDCK1	320	160	80	320	640	320	320	1280	640	320
A/Austria/1122894/2019		6B.1A6	2019-02-05	SIAT1/MDCK1	640	160	80	640	1280	1280	640	2560	1280	640
A/Finland/45/2019		6B.1A6	2019-02-25	MDCK1/MDCK1	640	160	80	640	640	640	320	1280	640	640
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/Sundsvall/1/2019		6B.1A7	2019-01-23	MDCK0/MDCK1	1280	320	160	1280	2560	2560	1280	2560	2560	1280
A/Austria/1124185/2019		6B.1A7	2019-02-11	SIAT1/MDCK1	1280	160	80	640	1280	1280	640	2560	1280	640
A/Bulgaria/1171/2019		6B.1A7	2019-02-24	SIAT2/SIAT1	2560	640	160	2560	2560	2560	1280	5120	1280	2560
A/Bulgaria/1238/2019		6B.1A7	2019-03-05	SIAT2/SIAT1	1280	320	160	1280	2560	1280	1280	5120	1280	1280
					Vaccine NH 2018-19									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: SH 2019

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 F31/16*1 6B.1	A/Bayern 69/09 MDCK F09/15*1	A/Lviv N6/09 MDCK F13/18*1 NIB	A/Slov 2903/2015 Egg 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	640	320	2560	2560	2560	1280	2560	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	160	640	320	80	320	320	160	320	80	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	640	1280	1280	160	640	640	320	1280	160	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	320	320	1280	1280	1280	640	2560	1280	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	1280	320	80	1280	1280	1280	640	2560	1280	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	1280	640	320	2560	2560	2560	1280	2560	1280	2560
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	640	320	160	640	1280	1280	1280	1280	640	1280
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	640	160	80	640	1280	640	640	1280	640	640
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	320	320	2560	2560	2560	1280	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	2560	640	320	2560	2560	2560	1280	2560	1280	2560
TEST VIRUSES														
A/Lisboa/niEVA195/2019	N156K	6B.1A2	2019-01-29	MDCK1/MDCK1	80	80	40	<	<	80	40	160	40	40
A/Cyprus/1165/2019		6B.1A2	2019-02-22	MDCK1	2560	320	160	2560	5120	2560	1280	2560	2560	2560
A/Lisboa/niEVA275/2019	N156K	6B.1A2	2019-02-27	MDCK1/MDCK1	160	160	80	40	80	160	80	320	80	80
A/Cyprus/788/2019		6B.1A5	2019-02-11	MDCK1	640	320	160	640	320	640	640	2560	1280	640
A/Lisboa/78/2019		6B.1A5	2019-02-25	MDCK1/MDCK1	1280	320	320	1280	640	1280	1280	2560	1280	1280
A/Lisboa/80/2019		6B.1A5	2019-03-10	MDCK1/MDCK1	1280	320	160	1280	640	1280	1280	2560	1280	640
A/Lisboa/82/2019		6B.1A5	2019-03-12	MDCK1/MDCK1	1280	320	320	640	640	1280	1280	2560	1280	640
A/Cyprus/1619/2019		6B.1A5	2019-04-09	MDCK1	1280	320	160	640	1280	1280	640	1280	1280	1280
A/Lisboa/74/2019		6B.1A6	2019-02-27	MDCK1/MDCK1	2560	640	320	2560	1280	5120	5120	5120	2560	1280
A/Cyprus/368/2019		6B.1A7	2019-01-29	MDCK1	2560	320	160	1280	320	1280	1280	2560	1280	1280
A/Cyprus/367/2019		6B.1A7	2019-01-29	MDCK1	2560	320	160	2560	1280	2560	1280	2560	1280	1280
A/Cyprus/389/2019		6B.1A7	2019-01-31	MDCK1	1280	640	160	1280	1280	2560	1280	2560	640	1280
A/Cyprus/738/2019		6B.1A7	2019-02-05	MDCK1	1280	320	160	1280	640	1280	640	2560	1280	1280
A/Cyprus/507/2019		6B.1A7	2019-02-05	MDCK1	2560	640	80	2560	1280	2560	1280	5120	2560	2560
A/Cyprus/505/2019		6B.1A7	2019-02-05	MDCK1	640	160	80	640	320	1280	640	1280	1280	640
A/Cyprus/488/2019		6B.1A7	2019-02-05	MDCK1	1280	320	160	640	1280	1280	640	2560	2560	1280
A/Cyprus/774/2019		6B.1A7	2019-02-11	MDCK1	1280	320	160	1280	640	1280	640	2560	1280	640
A/Cyprus/753/2019		6B.1A7	2019-02-11	MDCK1	1280	320	160	1280	640	1280	1280	2560	1280	640
A/Cyprus/740/2019		6B.1A7	2019-02-11	MDCK1	1280	160	160	1280	640	1280	640	2560	1280	640
A/Cyprus/739/2019		6B.1A7	2019-02-11	MDCK1	2560	320	160	1280	1280	2560	640	5120	2560	1280
A/Cyprus/873/2019		6B.1A7	2019-02-12	MDCK1	2560	640	160	2560	1280	2560	2560	5120	1280	1280
A/Cyprus/919/2019		6B.1A7	2019-02-13	MDCK1	1280	320	160	1280	640	1280	640	2560	1280	320
A/Lisboa/73/2019		6B.1A7	2019-02-14	MDCK2/MDCK1	1280	640	320	2560	1280	2560	1280	2560	2560	2560
A/Lisboa/77/2019		6B.1A7	2019-02-18	MDCK2/MDCK1	2560	640	320	2560	1280	2560	1280	2560	2560	2560
A/Lisboa/79/2019		6B.1A7	2019-02-26	MDCK1/MDCK1	2560	640	320	2560	1280	2560	1280	5120	2560	1280
A/Lisboa/81/2019		6B.1A7	2019-03-25	MDCK3/MDCK1	2560	640	320	2560	1280	2560	1280	2560	2560	1280
A/Cyprus/957/2019			2019-02-14	MDCK1	1280	320	80	1280	640	1280	640	2560	1280	640

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1 < = <40; 2 < = <80
Sequences in phylogenetic trees

Vaccine NH 2018-19
SH 2019

Vaccine NH 2019-20

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
		Passage history			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	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	2015-09-07	E3/E3	1280	640	320	2560	2560	2560	2560	2560	2560	2560
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	80	320	320	40	320	160	80	320	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	1280	160	640	640	320	1280	160	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	320	320	1280	1280	1280	1280	2560	1280	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	1280	320	160	1280	1280	1280	1280	2560	2560	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	2560	640	640	2560	2560	2560	1280	5120	2560	2560
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	640	320	160	640	640	1280	1280	1280	1280	640
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	640	160	80	640	640	640	640	2560	640	640
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	640	160	2560	2560	2560	1280	2560	2560	2560
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	640	320	2560	2560	2560	2560	5120	2560	2560
TEST VIRUSES														
A/Poland/16714/2019		6B.1A	2019-03-18	MDCK1	1280	320	80	1280	1280	1280	640	2560	1280	1280
A/Poland/6732/2019		6B.1A2	2019-01-21	MDCK2	1280	320	160	2560	1280	2560	1280	2560	2560	1280
A/Poland/1973/2019		6B.1A5	2019-02-08	MDCK1	640	160	160	640	640	640	640	2560	1280	640
A/Poland/6218/2019		6B.1A5	2019-02-13	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Poland/11284/2019		6B.1A5	2019-02-19	MDCK1	640	320	160	640	1280	640	640	2560	640	640
A/Poland/14120/2019		6B.1A5	2019-03-04	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Iceland/17/2019		6B.1A5	2019-03-12	MDCK1/MDCK1	640	160	80	640	640	1280	320	1280	640	640
A/Iceland/16/2019		6B.1A5	2019-03-12	MDCK1/MDCK1	640	80	80	640	640	1280	320	1280	640	640
A/Iceland/20/2019		6B.1A5	2019-03-15	MDCK1/MDCK1	640	160	160	640	1280	1280	320	1280	640	640
A/Poland/866/2019		6B.1A5	2019-03-18	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280
A/Poland/149/2019		6B.1A5	2019-03-19	MDCK1	1280	320	160	1280	2560	1280	1280	2560	2560	1280
A/Iceland/44/2019		6B.1A5	2019-04-03	MDCK1/MDCK1	640	160	80	640	640	1280	320	1280	640	640
A/Poland/349/2019		6B.1A6	2019-01-31	MDCK1	1280	320	160	1280	1280	2560	1280	2560	2560	1280
A/Poland/433/2019		6B.1A6	2019-02-06	MDCK1	1280	320	160	1280	2560	2560	1280	2560	2560	1280
A/Poland/68/2019		6B.1A6	2019-02-11	MDCK1	1280	320	160	1280	2560	2560	1280	2560	2560	2560
A/Poland/100/2019		6B.1A6	2019-02-20	MDCK1	2560	640	320	2560	2560	2560	1280	5120	2560	2560
A/Poland/876/2019		6B.1A6	2019-03-19	MDCK1	2560	640	160	2560	2560	2560	1280	2560	2560	2560
A/Iceland/68/2019		6B.1A6	2019-05-06	MDCK1/MDCK1	640	160	160	640	1280	1280	320	1280	1280	1280
A/Iceland/74/2019		6B.1A6	2019-05-29	MDCK1/MDCK1	640	160	160	640	640	1280	320	1280	640	640
A/Poland/553/2019		6B.1A7	2019-02-14	MDCK1	1280	320	80	1280	1280	1280	640	2560	1280	1280
A/Iceland/11/2019			2019-03-07	MDCK1/MDCK1	320	160	40	640	640	1280	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 3-4. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre													
				Post-infection ferret antisera										NEW	NEW	NEW	
				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	A/HK 110/19	A/Greece 144/19	A/Swit 4217/19
	Passage history			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	Egg	MDCK	Egg	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}	F28/19^{-1}	F27/19^{-1}	F22/19^{-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		2015-09-07	E3/E3	1280	320	320	1280	2560	2560	1280	2560	2560	1280	40	2560	1280	
A/Bayern/69/2009		2009-07-01	MDCK5/MDCK1	160	640	320	80	320	160	160	640	80	320	40	80	80	
A/Lviv/N6/2009	G155E	2009-10-27	MDCK4/SIAT1/MDCK3	320	640	640	160	640	640	320	1280	320	640	40	80	80	
A/Slovenia/2903/2015	G155E, D222G	2015-10-26	E4/E2	1280	640	320	2560	2560	2560	1280	2560	2560	2560	40	1280	2560	
A/Paris/1447/2017	clone 37	2017-10-20	MDCK1/MDCK3	1280	320	160	1280	2560	2560	1280	5120	2560	2560	80	2560	1280	
A/Switzerland/2656/2017	6B.1	2017-12-21	E5/E3	640	320	320	640	640	1280	640	2560	640	640	40	640	640	
A/Switzerland/3330/2017	6B.1A	2017-12-20	E6/E2	640	160	160	640	1280	640	1280	1280	1280	640	<	640	640	
A/Norway/3433/2018	clone 35	2018-10-30	MDCK3	640	160	80	640	1280	640	640	2560	1280	640	40	1280	1280	
A/Ireland/84630/2018	6B.1A5	2018-11-28	MDCK1/MDCK3	1280	320	160	1280	2560	2560	1280	2560	2560	1280	40	1280	2560	
A/Brisbane/02/2018	6B.1A6	2018-01-04	E3/E1	2560	640	640	2560	5120	2560	2560	5120	5120	1280	160	2560	2560	
A/Hong Kong/110/2019	6B.1A1	2019-01-01	MDCK1/MDCK2	160	160	80	<	40	160	80	320	80	80	1280	160	80	
A/Greece/144/2019		2019-01-14	E3	1280	320	160	1280	1280	1280	640	2560	1280	640	40	1280	1280	
A/Switzerland/4217/2019		2019-01-08	E4	1280	320	320	640	1280	1280	640	2560	1280	1280	80	640	1280	
A/Switzerland/4217/2019		2019-01-08	E4/E1	1280	320	320	640	1280	640	640	2560	1280	1280	80	640	1280	
TEST VIRUSES																	
A/Banska Bystrica/115/2019		2019-01-15	MDCKx/MDCK1	1280	640	320	1280	2560	1280	640	2560	2560	1280	80	1280	2560	
A/Piestany/80/2019		2019-01-15	MDCK1/MDCK1	1280	320	160	1280	2560	1280	640	2560	2560	1280	40	1280	1280	
A/Bratislava/76/2019		2019-01-18	MDCK1/MDCK1	640	160	160	640	640	2560	640	5120	2560	1280	40	1280	1280	
A/Bratislava/93/2019		2019-01-21	MDCKx/MDCK1	2560	320	320	1280	2560	5120	1280	5120	2560	2560	80	1280	2560	
A/Trnava/85/2019		2019-01-22	MDCK1/MDCK1	1280	320	160	640	1280	2560	1280	2560	1280	1280	40	1280	1280	
A/Trencin/124/2019		2019-01-28	MDCKx/MDCK1	1280	320	160	640	1280	2560	1280	5120	2560	1280	40	1280	1280	
A/Poprad/134/2019		2019-01-29	MDCKx/MDCK1	1280	320	160	1280	2560	1280	1280	2560	2560	2560	80	1280	2560	
A/Malacky/145/2019		2019-02-01	MDCKx/MDCK1	1280	640	640	1280	1280	2560	2560	5120	2560	2560	80	1280	1280	
A/Lubica/183/2019		2019-02-05	MDCKx/MDCK1	1280	320	320	1280	1280	2560	640	5120	2560	1280	80	1280	1280	
A/Nitra/197/2019		2019-02-08	MDCKx/MDCK1	1280	320	320	640	1280	2560	640	2560	2560	1280	80	1280	1280	
A/Bojnice/225/2019		2019-02-11	MDCKx/MDCK1	640	160	160	640	1280	1280	640	2560	1280	1280	40	640	640	
A/Bratislava/216/2019		2019-02-11	MDCKx/MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	1280	80	1280	2560	
A/Piestany/267/2019		2019-02-12	MDCKx/MDCK1	1280	320	320	1280	1280	1280	640	2560	2560	1280	80	1280	1280	
A/Dunajska Streda/243/2019		2019-02-12	MDCKx/MDCK1	1280	320	160	640	1280	1280	640	2560	2560	1280	40	640	2560	
A/Senica/305/2019		2019-02-18	MDCKx/MDCK1	640	160	80	320	640	640	320	1280	640	640	40	640	2560	
A/Torino/617/2019		2019-02-19	MDCK4/MDCK1	640	160	80	640	1280	640	320	1280	640	640	<	640	640	
A/Padova/22/2019		2019-02-20	MDCK4/MDCK1	1280	320	160	1280	1280	1280	640	1280	1280	1280	40	640	640	
A/Friuli Venezia Giulia/184/2019		2019-02-21	MDCK2/MDCK1	1280	640	640	1280	2560	1280	640	2560	2560	1280	80	1280	1280	
A/Padova/26/2019		2019-02-25	MDCK3/MDCK1	640	320	160	640	1280	640	320	2560	1280	640	40	640	640	
A/Galanta/387/2019		2019-02-27	MDCKx/MDCK1	1280	320	320	1280	2560	1280	1280	2560	1280	1280	80	1280	1280	
A/Kosice/422/2019	6B.1A2	2019-02-28	MDCKx/MDCK1	2560	640	320	2560	5120	2560	1280	2560	2560	2560	80	1280	2560	
A/Trnava/429/2019	6B.1A6	2019-03-04	MDCK4/MDCK1	5120	640	320	2560	5120	5120	2560	5120	5120	2560	80	2560	2560	
A/Torino/779/2019		2019-03-06	MDCK4/MDCK1	2560	640	320	1280	2560	1280	640	2560	2560	1280	80	1280	1280	
A/Torino/778/2019		2019-03-06	MDCK4/MDCK1	640	320	160	640	1280	640	320	160	1280	640	40	320	640	
A/Parma/348/2019		2019-03-06	MDCK2/MDCK1	2560	1280	640	2560	5120	2560	1280	2560	2560	2560	80	2560	2560	
A/Palermo/23/2019		2019-03-08	MDCK5/MDCK1	1280	640	160	1280	1280	1280	640	1280	2560	1280	80	1280	2560	
A/Palermo/26/2019		2019-03-12	MDCK3/MDCK1	1280	320	320	640	1280	1280	640	1280	1280	1280	80	1280	1280	
A/Parma/370/2019		2019-03-12	MDCK4/MDCK1	1280	320	320	640	1280	640	640	1280	1280	640	40	1280	640	
A/Prievidza/518/2019	6B.1A5	2019-03-25	MDCKx/MDCK1	2560	640	640	1280	2560	2560	1280	2560	2560	1280	80	1280	2560	
A/Trnava/535/2019	6B.1A6	2019-04-10	MDCKx/MDCK1	1280	640	160	1280	2560	2560	1280	2560	2560	1280	40	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 3-5. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera									
					A/Mich 45/15	A/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	MDCK	Egg	Egg	MDCK	MDCK	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	2015-09-07	E3/E3	640	160	160	640	1280	640	320	640	640	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	80	320	320	40	160	160	80	320	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	640	640	80	320	320	160	640	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	1280	640	320	1280	2560	2560	1280	2560	1280	2560
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	80	640	1280	1280	640	1280	1280	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	640	320	320	640	640	1280	640	2560	640	640
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	640	160	160	640	1280	640	640	1280	640	640
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK4/SIAT1/MDCK3	320	80	40	640	640	320	320	640	640	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	320	320	1280	2560	2560	640	2560	2560	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	640	320	160	1280	1280	1280	640	1280	1280	640
TEST VIRUSES														
A/Estonia/118748/2019			2019-01-16	SIAT1/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Estonia/118723/2019			2019-01-16	SIAT1/MDCK1	640	320	320	640	1280	1280	640	1280	640	640
A/Estonia/118840/2019			2019-01-21	SIAT2/MDCK1	320	160	80	640	640	640	320	1280	640	320
A/Estonia/118896/2019			2019-01-23	SIAT2/MDCK1	640	320	320	1280	1280	640	640	2560	1280	640
A/Estonia/118882/2019			2019-01-23	SIAT2/MDCK1	1280	320	160	1280	2560	1280	1280	2560	1280	1280
A/Czech Republic/1250/2019			2019-01-30	MDCK3/MDCK1	1280	320	160	640	1280	640	640	5120	1280	640
A/Czech Republic/761/2019			2019-02-04	MDCK3/MDCK1	640	160	80	320	640	320	320	2560	640	640
A/Estonia/119176/2019			2019-02-06	MDCK1	1280	320	320	1280	1280	2560	1280	2560	1280	640
A/Estonia/119338/2019			2019-02-11	SIAT2/MDCK1	1280	640	640	1280	2560	2560	1280	2560	2560	2560
A/Czech Republic/1254/2019			2019-02-11	MDCK3/MDCK1	1280	320	160	640	1280	1280	640	2560	1280	1280
A/Czech Republic/1253/2019			2019-02-11	MDCK3/MDCK1	640	160	40	320	640	320	320	1280	640	320
A/Czech Republic/1255/2019			2019-02-13	MDCK3/MDCK1	640	160	80	640	640	640	320	2560	640	640
A/Czech Republic/1257/2019			2019-02-14	MDCK3/MDCK1	640	160	160	640	1280	640	320	1280	640	640
A/Czech Republic/1256/2019			2019-02-14	MDCK3/MDCK1	1280	640	640	1280	2560	1280	640	5120	2560	1280
A/Czech Republic/1258/2019			2019-02-17	MDCK3/MDCK1	640	160	160	640	1280	640	320	1280	640	640
A/Estonia/119487/2019			2019-02-18	SIAT2/SIAT1	640	320	320	640	1280	1280	640	2560	1280	640
A/Estonia/119483/2019			2019-02-19	SIAT2/SIAT1	640	320	160	640	1280	640	640	2560	1280	640
A/Czech Republic/1259/2019			2019-02-21	MDCK3/MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Czech Republic/1262/2019			2019-02-26	MDCK3/MDCK1	640	320	160	1280	1280	640	1280	2560	1280	640
A/Czech Republic/1261/2019			2019-02-27	MDCK3/MDCK1	640	160	40	640	1280	640	640	1280	640	640
A/Estonia/119738/2019			2019-03-04	SIAT2/MDCK1	1280	640	320	1280	2560	2560	640	2560	1280	1280
A/Estonia/120012/2019			2019-03-18	SIAT2/MDCK2	1280	320	160	1280	1280	2560	640	2560	1280	1280
A/Estonia/119976/2019			2019-03-18	SIAT2/SIAT1	640	160	80	640	1280	640	320	1280	640	640
A/Estonia/120077/2019			2019-03-20	SIAT2/MDCK1	640	160	80	640	1280	640	640	1280	640	640
A/Estonia/120189/2019			2019-03-27	SIAT2/SIAT1	1280	640	320	1280	1280	1280	640	2560	1280	640
					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 3-6. Antigenic analysis of A(H1N1)pdm09 viruses by HI – Summary all test viruses

Viruses	Other information	Passage history	Ferret number	Genetic group	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	A/HK 110/19	A/Greece 144/19	A/Swit 4217/19
			Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	Egg	MDCK	Egg	Egg
			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]	F28/19[*1]	F27/19[*1]	F22/19[*1]
			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	40	2560	1280
A/Bayern/69/2009	G155E		80	320	160	40	160	160	80	160	40	160	40	80	80
A/Lviv/N6/2009	G155E, D222G		320	640	640	160	320	320	320	1280	160	640	40	80	160
A/Slovenia/2903/2015	clone 37	6B.1	640	320	160	1280	640	1280	640	1280	1280	640	40	1280	2560
A/Paris/1447/2017		6B.1A	640	320	40	640	640	640	320	1280	640	640	80	2560	1280
A/Switzerland/2656/2017		6B.1A	1280	640	160	1280	1280	1280	640	2560	1280	1280	40	< 640	640
A/Switzerland/3330/2017	clone 35	6B.1A5	320	160	80	320	640	640	320	1280	640	640	40	640	640
A/Norway/3433/2018		6B.1A5	320	160	40	640	640	1280	640	2560	1280	640	40	1280	1280
A/Ireland/84630/2018		6B.1A6	640	160	160	1280	1280	1280	640	2560	1280	1280	160	1280	2560
A/Brisbane/02/2018		6B.1A1	1280	320	160	1280	1280	1280	1280	2560	1280	1280	160	2560	2560
A/Hong Kong/110/2019			160	160	80	< 40	160	160	80	320	80	80	1280	160	80
A/Greece/144/2019			1280	320	160	1280	1280	1280	640	2560	1280	640	40	1280	1280
A/Switzerland/4217/2019			1280	320	320	640	1280	1280	640	2560	1280	1280	80	640	1280
A/Switzerland/4217/2019			1280	320	320	640	1280	640	640	2560	1280	1280	80	640	1280
TEST VIRUSES															
Number of viruses tested*			138	138	138	138	138	138	138	138	138	138	30	30	30
No with titre reduction ≤2-fold			104	120	23	104	131	121	120	135	108	102		29	30
%			*75.4*	*87.0*	*16.7*	*75.4*	*94.9*	*87.7*	*87.0*	*97.8*	*78.3*	*73.9*		*96.7*	*100.0*
No with titre reduction =4-fold			20	16	38	28	5	14	16	1	27	29		1	
%			*14.5*	*11.6*	*27.5*	*20.3*	*3.6*	*10.1*	*11.6*	*0.8*	*19.6*	*21.0*		*3.3*	
No with titre reduction ≥8-fold			14	2	77	6	2	3	2	2	3	7	30		
%			*10.1*	*1.4*	*55.8*	*4.3*	*1.5*	*2.2*	*1.4*	*1.4*	*2.1*	*5.1*	*100.0*		
			Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20			

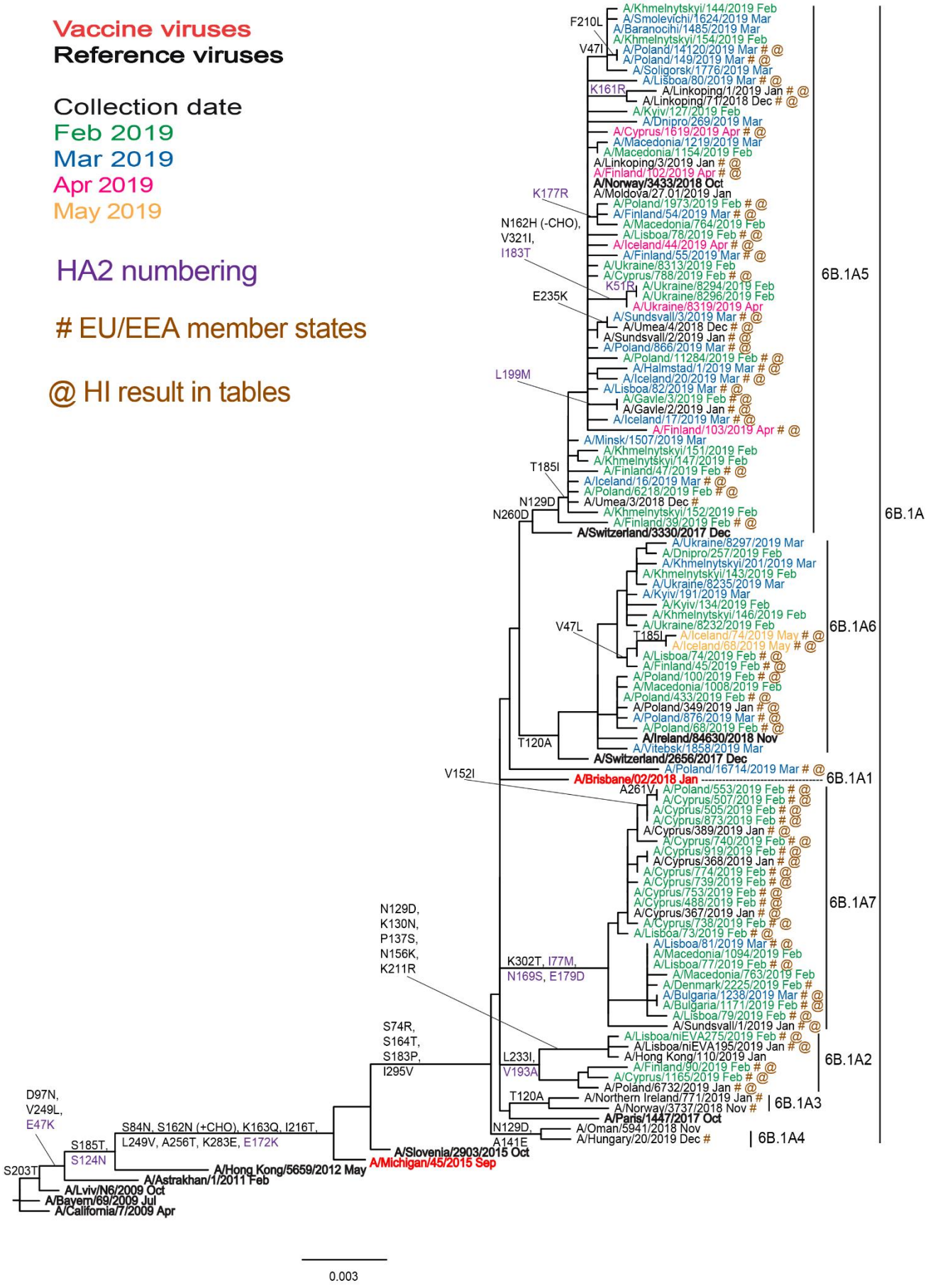
* Of those with available HA sequence, all were clade 6B.1A

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 3-7. 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	MDCK	Egg	Egg	MDCK	MDCK	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
TEST VIRUSES											
Number tested	6B.1A	85	85	85	85	85	85	85	85	85	85
No with titre reduction ≤2-fold		52	71	3	65	80	70	72	83	70	51
No with titre reduction =4-fold		19	12	18	15	3	12	11		12	28
No with titre reduction ≥8-fold		14	2	64	5	2	3	2	2	3	6
Number tested	6B.1A2	6	6	6	6	6	6	6	6	6	6
No with titre reduction ≤2-fold		4	4	1	4	4	4	4	4	4	4
No with titre reduction =4-fold			1	1							
No with titre reduction ≥8-fold		2	1	4	2	2	2	2	2	2	2
Number tested	6B.1A5	40	40	40	40	40	40	40	40	40	40
No with titre reduction ≤2-fold		15	30	1	23	39	27	31	40	28	14
%		*37.5*	*75.0*	*2.5*	*57.5*	*97.5*	*67.5*	*77.5*	*100.0*	*70.0*	*35.0*
No with titre reduction =4-fold		13	9	7	14	1	12	9		11	23
%		*32.5*	*22.5*	*17.5*	*35.00*	*2.5*	*30.0*	*22.5*		*27.5*	*57.5*
No with titre reduction ≥8-fold		12	1	32	3		1			1	3
%		*30.0*	*2.5*	*80.0*	*7.5*		*2.5*			*2.5*	*7.5*
Number tested	6B.1A6	12	12	12	12	12	12	12	12	12	12
No with titre reduction ≤2-fold		10	12	1	12	12	12	10	12	11	11
		83.3	*100.0*	8.3	*100.0*	*100.0*	*100.0*	83.3	*100.0*	91.7	91.7
No with titre reduction =4-fold		2		3				2		1	1
		16.7		25.0				16.7		8.3	8.3
No with titre reduction ≥8-fold				8							
				66.7							
Number tested	6B.1A7	24	24	24	24	24	24	24	24	24	24
No with titre reduction ≤2-fold		21	22		23	22	24	24	24	24	19
%		*87.5*	*91.7*		*95.8*	*91.7*	*100.0*	*100.0*	*100.0*	*100.0*	*79.2*
No with titre reduction =4-fold		3	2	7	1	2					4
%		*12.5*	*8.3*	*29.2*	*4.2*	*8.3*					*16.6*
No with titre reduction ≥8-fold				17							1
%				*70.8*							*4.2*
		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[1], 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[2], this is a particular problem for most viruses that fall in genetic clade 3C.2a.

Since the June 2019 characterisation report of the viruses recovered, based on positive neuraminidase activity, 21 retained sufficient HA activity to allow antigenic analysis by HI (Tables 4-2 to 4-4) and Table 4-1 is repeated from the June report, now with clade information completed; the test virus results for all four tables are summarised in Table 4-5. All test viruses but one, A/Iceland/12621/2019 for which gene sequence is pending, 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, an antiserum raised against cell culture-propagated A/Bretagne/1413/2017 (subclade 3C.2a2) recognised only 2/32 (6%) test viruses at titres within fourfold of homologous titres, while antisera raised against two cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, fared somewhat better, recognising 47% and 44% of test viruses 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 13 and 11 test viruses, respectively, at titres of ≥160. Antiserum raised against cell-culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised 75% 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 show: (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 six antisera raised against cell culture-propagated viruses, the one raised against A/Hong Kong/5738/2014 (clade 3C.2a) gives the broadest cross-clade/subclade reactivity.

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**, and **D160N** in **HA2**, 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 June 2019 (Figure 2). Notably, a significant number of the subgroup

[1] 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

[2] 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

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								
					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	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	Ex/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/Skovde/1/2019		3C.2a1b	2019-02-11	MDCK1/SIAT1	40	<	40	80	40	40	160	<	40
A/Eskilstuna/6/2019		3C.2a1b	2019-02-13	MDCK0/SIAT1	160	160	80	80	160	80	320	40	40
A/Denmark/2785/2019		3C.2a1b	2019-03-13	SIAT2/SIAT1	40	<	40	160	<	<	80	<	<
A/Lisboa/100/2019		3C.3a	2019-01-28	SIAT3/SIAT1	40	<	40	<	40	320	<	160	320
A/Lisboa/93/2019		3C.3a	2019-02-08	SIAT2/SIAT1	40	<	40	<	40	320	<	160	320
A/Lisboa/92/2019		3C.3a	2019-02-15	MDCK2/SIAT1	40	40	80	<	40	320	40	160	320
A/Lisboa/91/2019		3C.3a	2019-02-20	SIAT1/SIAT1	40	40	80	40	40	640	40	160	320
A/Lisboa/97/2019		3C.3a	2019-02-25	SIAT2/SIAT1	40	40	80	40	40	640	40	160	320
A/Lisboa/94/2019		3C.3a	2019-02-26	SIAT1/SIAT1	40	40	80	<	40	320	<	160	320
A/Lisboa/95/2019		3C.3a	2019-02-27	SIAT2/SIAT1	40	<	40	<	40	320	<	160	320
A/Lisboa/98/2019		3C.3a	2019-03-08	SIAT1/SIAT1	<	<	40	<	<	160	<	40	40
							Vaccine SH 2018		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	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/Kansas/14 Egg	A/Kansas 14/17 SIAT	A/Norway 3275/18 Egg
	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]	F21/19 [-1]
	Genetic group			3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a	3C.2a1b
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	320	320	320	160	320	320	320	320	160	80
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	320	1280	320	160	640	320	320	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	160	80	1280	320	320	80	80	40	<	320
A/Switzerland/8060/2017	clone 57 3C.2a2	2017-12-12	E7/E1	320	2560	640	320	2560	160	80	80	<	640
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	40	40	<	80	1280	<	320	640	<
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	ExE1	<	<	80	<	40	640	40	1280	320	40
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	160	80	160	40	160	1280	40	640	640	<
A/Norway/3275/2018	3C.2a1b	2018-10-04	E6(Am3AI3)	160	160	640	160	320	40	80	<	<	640
TEST VIRUSES													
A/Finland/92/2019	3C.2a1b	2019-03-06	SIAT1/SIAT1	80	<	<	160	<	<	320	<	<	<
A/Finland/105/2019	3C.2a1b	2019-04-09	SIAT1/SIAT1	320	640	320	320	320	640	1280	160	160	320
A/Finland/99/2019	3C.3a	2019-03-26	SIAT1/SIAT1	80	80	160	40	320	640	80	320	320	<
A/Finland/104/2019	3C.3a	2019-04-03	SIAT1/SIAT1	80	40	40	<	80	1280	<	320	640	<
A/Finland/114/2019	3C.3a	2019-04-30	SIAT1/SIAT1	160	80	160	40	80	1280	<	320	640	<
					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

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/Kansas/14 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	320	160	160	320	160	320	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	320	80	640	160	160	160	80
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	160	80	640	160	320	160	40	40	80
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	160	1280	640	160	1280	160	80	80	80
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	40	80	40	40	40	640	40	160	320
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	Ex/E1	40	40	80	40	40	320	40	1280	640
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	80	80	80	40	80	640	40	320	320
TEST VIRUSES													
A/Komarno/58/2018		3C.2a1b	2018-12-28	MDCK1/SIAT1	40	<	40	80	<	40	80	<	40
A/Trencin/74/2019		3C.2a1b	2019-01-16	MDCK1/SIAT1	40	<	<	40	<	40	40	<	40
A/Trnava/70/2019		3C.2a1b	2019-01-16	MDCK1/SIAT1	40	<	40	80	40	40	80	<	40
A/Nove Zamky/81/2019		3C.2a1b	2019-01-21	MDCK2/SIAT1	80	<	40	160	40	40	80	<	40
A/Nitra/106/2019		3C.2a1b	2019-01-24	MDCKx/SIAT1	80	<	160	320	80	80	160	80	40
A/Prievidza/126/2019		3C.2a1b	2019-01-29	MDCKx/SIAT1	80	<	40	160	40	80	160	<	40
A/PJovazska Bystrica/177/2019		3C.2a1b	2019-02-05	MDCKx/SIAT1	80	<	80	160	80	80	160	40	40
A/Bratislava/328/2019		3C.2a1b	2019-02-20	MDCKx/SIAT1	<	<	<	80	<	40	80	<	40
A/Skalica/339/2019		3C.2a1b	2019-02-21	MDCKx/SIAT1	80	<	40	160	40	80	160	<	40
A/Bratislava/446/2019		3C.2a1b	2019-03-08	MDCKx/SIAT1	40	<	40	160	40	80	80	<	40
A/Galanta/473/2019		3C.2a1b	2019-03-12	MDCKx/SIAT1	40	<	<	160	40	<	80	<	40
							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 4-4. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
				A/HK 5738/14 MDCK St Judes F60/17[-1] 3C.2a	A/Bretagne 1413/17 SIAT F01/18[-1] 3C.2a2	A/Singapore 0019/16 Egg 10[-4] F46/17[-1] 3C.2a1	A/La Rioja 2202/18 SIAT F26/18[-1] 3C.2a1b	A/Switz 8060/17 Egg F27/18[-1] 3C.2a2	A/Eng 538/18 SIAT F31/18[-1] 3C.3a	A/Norway 3275/18 SIAT F03/19[-1] 3C.2a1b	NYMC X-327 A/Kansas/14 Egg F16/19[-1] 3C.3a	A/Kansas 14/17 SIAT F17/19[-1] 3C.3a
Passage history												
Ferret number												
Genetic group												
REFERENCE VIRUSES												
A/Hong Kong/5738/2014		2014-04-30	MDCK1/MDCK2/SIAT1	320	160	640	160	320	640	320	320	160
A/Bretagne/1413/2017		2017-10-09	MDCK1/SIAT4	320	1280	320	160	1280	320	320	320	160
A/Singapore/INFIMH-16-0019/2016		2016-04-14	E5/E2	160	80	640	320	160	80	40	40	80
A/Switzerland/8060/2017	clone 57	2017-12-12	E7/E1	160	1280	640	160	1280	160	80	80	80
A/England/538/2018		2018-02-26	MDCK1/SIAT3	80	80	40	80	80	640	80	320	640
NYMC X-327 (A/Kansas/14/17)		2017-12-14	E×/E1	40	40	40	40	40	320	40	1280	320
A/Kansas/14/2017		2017-12-14	SIAT3/SIAT2	160	80	80	80	80	640	80	320	640
TEST VIRUSES												
A/Iceland/23/2019		2019-03-18	MDCK1/SIAT1	160	40	160	160	80	160	160	160	160
A/Iceland/12621/2019		2019-06-15	SIAT1	640	640	640	640	640	640	640	640	320
A/Iceland/4/2019	3C.2a1b	2019-03-04	MDCK1/SIAT1	40	<	40	80	<	40	80	<	40
A/Iceland/71/2019	3C.2a1b	2019-05-19	MDCK1/SIAT1	80	40	160	320	40	80	160	80	80
A/Iceland/59/2019	3C.3a	2019-04-15	MDCK1/SIAT1	80	40	160	80	40	640	40	160	320
						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

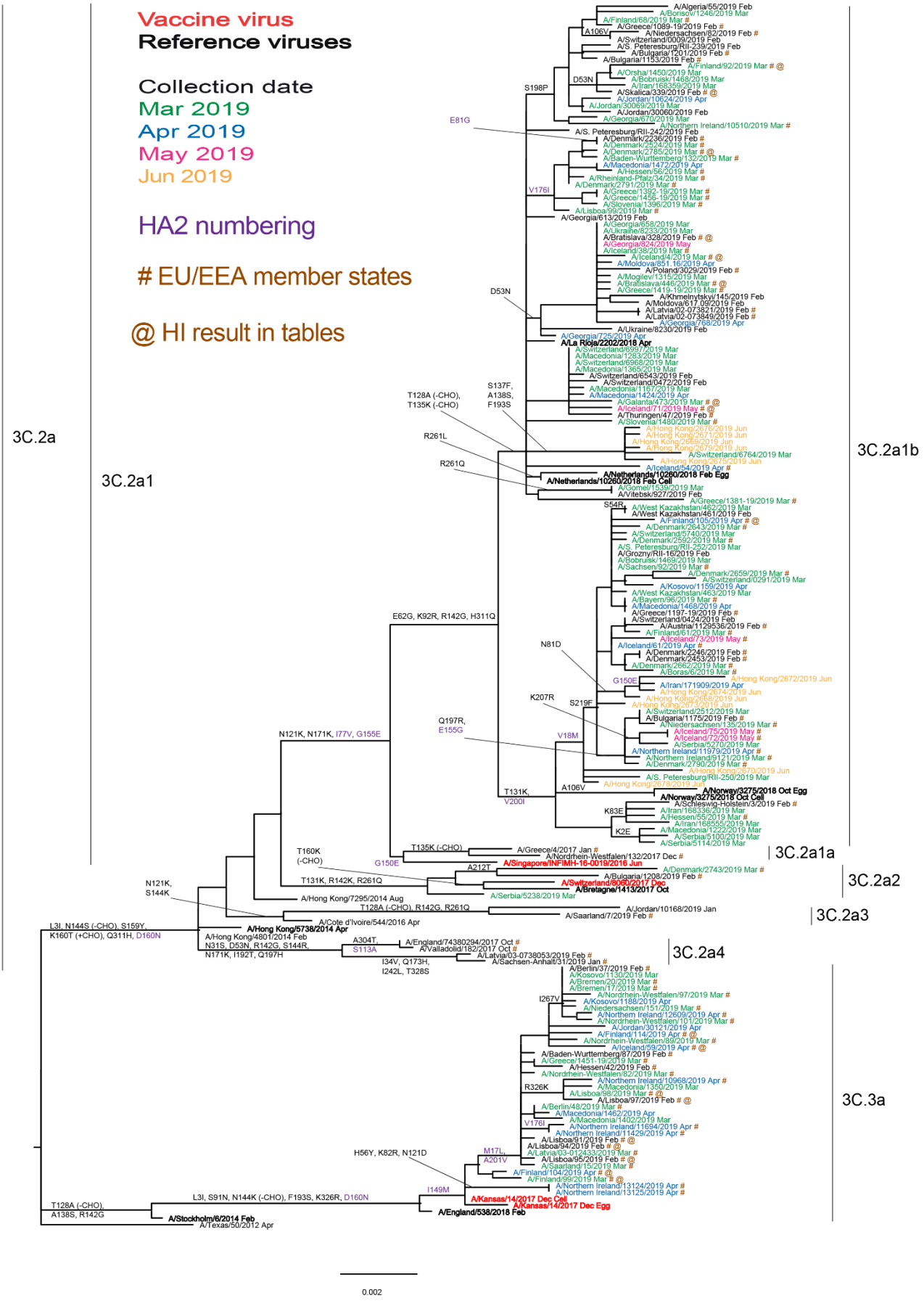
Table 4-5. Antigenic analysis of A(H3N2) viruses by HI - Summary

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Haemagglutination inhibition titre – Post-infection ferret antisera: A/HK 5738/14 (MDCK; St Judes F60/17[*1]; 3C.2a)	A/Bretagne 1413/17 (SIAT; F01/18[*1]; 3C.2a2)	A/Singapore 0019/16 (Egg 10^{-4}; F46/17[*1]; 3C.2a1)	A/La Rioja 2202/18 (SIAT; F26/18[*1]; 3C.2a1b)	A/Switz 8060/17 (Egg; F27/18[*1]; 3C.2a2)	A/Eng 538/18 (SIAT; F31/18[*1]; 3C.3a)	A/Norway 3275/18 (SIAT; F03/19[*1]; 3C.2a1b)	NYMC X-327 A/Kansas/14 (Egg; F16/19[*1]; 3C.3a)	A/Kansas 14/17 (SIAT; F17/19[*1]; 3C.3a)
REFERENCE VIRUSES												
A/Hong Kong/5738/2014		3C.2a	2014-04-30	320	160	640	160	320	640	320	320	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	320	1280	320	160	1280	320	320	320	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	160	80	640	320	160	80	40	40	80
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	160	1280	640	160	1280	160	80	80	80
A/England/538/2018		3C.3a	2018-02-26	80	80	40	80	80	640	80	320	640
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	40	40	40	40	40	320	40	1280	320
A/Kansas/14/2017		3C.3a	2017-12-14	160	80	80	80	80	640	80	320	640
TEST VIRUSES												
Number of viruses tested*				32	32	32	32*	32	32	32*	32	32
No with titre reduction ≤2-fold				5	2	1	13	1	14	11	1	12
%				*15.6*	*6.2*	*3.1*		*3.1*	*43.8*		*3.1*	*37.5*
No with titre reduction =4-fold				19		4			1		3	2
%				*59.4*		*12.5*			*3.1*		*9.4*	*6.2*
No with titre reduction ≥8-fold				8	30	27		31	17		28	18
%				*25.0*	*93.8*	*84.4*		*96.9*	*53.1*		*87.5*	*56.3*
Subgroup 3C.2a1b viruses												
Number of viruses tested*				18	18	18	18*	18	18	18*	18	18
No with titre reduction ≤2-fold				2	1		11		1	9		
%				*11.1*	*5.6*				*5.6*			
No with titre reduction =4-fold				9		3						1
%				*50.0*		*16.7*						*5.6*
No with titre reduction ≥8-fold				7	17	15		18	17		18	17
%				*38.9*	*94.4*	*83.3*		*100.0*	*94.4*		*100.0*	*94.4*
Clade 3C.3a viruses												
Number of viruses tested*				12	12	12	12*	12	12	12*	12	12
No with titre reduction ≤2-fold				1					4			11
%				*8.4*					*33.3*			*91.7*
No with titre reduction =4-fold				10		1			7		3	
%				*83.2*		*8.3*			*58.3*		*25.0*	
No with titre reduction ≥8-fold				1	12	11		12	1		9	1
%				*8.4*	*100.0*	*91.7*		*100.0*	*8.4*		*75.0*	*8.3*
						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, 23 were B/Yamagata-lineage and 18 were B/Victoria-lineage.

Influenza B/Victoria-lineage

Four B/Victoria-lineage viruses, two from Iceland and one each from France and Italy, have been tested by HI since the June 2019 characterisation report (Tables 5-1 to 5-2). The four viruses gave similar patterns of reactivity in HI profiles and all belong to the HA triple amino acid deletion group, 1A(Δ3), of African origin (see below).

A relatively small number (1 718 in total of which 1 486 were full length, as of 11 August 2019) 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 63 (42 full length) from countries in Europe. All recent viruses, those with collection dates from 1 May to 7 August 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, with the most recently circulating viruses having been reported mainly from the USA and Madagascar, 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[3], 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

Two B/Yamagata-lineage viruses, one each from France and Sweden, have been tested by HI since the June 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), recognised both test viruses at titres within fourfold of the respective homologous titres, with the virus from France being recognised within twofold. Antisera raised against cell culture-propagated B/Mauritius/I-762/2018 and egg-propagated B/Massachusetts/02/2012 recognised both viruses within twofold of homologous titres. Antisera raised against four additional cell culture-propagated viruses, two clade 2 (B/Estonia/55669/2011 and a former vaccine virus, B/Massachusetts/02/2012) and two clade 3 (B/Phuket/3073/2013 and B/Mauritius/1791/2017), recognised the test viruses less well (Figure 6).

A smaller number (855 in total of which 791 were full length, as of 11 August 2019) 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 64 (44 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 1 April to 7 August 2019 that have data deposited in GISAID and those analysed at the London WHO CC with collection dates from 1 January 2019; there are only nine from EU/EEA countries with collection dates falling within these periods. 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.

[3] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, September 2018. Stockholm: ECDC; 2018. Available from: 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	2560	640	320	640	320	40	40	<	40	80	<
B/Malta/636714/2011		1A	2011-03-07	E4/E1	5120	640	640	320	320	40	40	<	20	80	<
B/South Australia/81/2012		1A	2012-11-28	E4/E2	1280	640	160	320	160	20	40	<	20	40	<
B/Hong Kong/514/2009		1B	2009-10-11	MDCK1/MDCK2	2560	160	80	40	160	80	80	<	<	20	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	2560	80	<	10	80	80	80	<	<	20	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	2560	80	<	10	80	80	160	<	<	20	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	40	20	<	<	<	<	<	40	80	20	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	MDCK1/MDCK2	80	20	<	<	<	<	<	40	80	40	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	320	40	80	<	<	<	40	80	160	<
B/Cote D'Ivoire/1662/2018		1A(Δ3)	2018-07-25	P0/MDCK3	80	40	<	20	<	<	<	<	<	<	20
TEST VIRUSES															
B/Iceland/7775/2019		1A(Δ3)	2019-04-03	MDCK1	160	20	<	<	<	<	10	10	40	<	<
B/Iceland/60/2019		1A(Δ3)	2019-04-19	MDCK1/MDCK1	160	20	<	<	<	<	10	<	<	<	<
						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]	F15/19[*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	320	640	320	40	40	<	20	80	10
B/Malta/636714/2011		1A	2011-03-07	E4/E1	2560	1280	640	640	320	40	80	<	20	80	10
B/South Australia/81/2012		1A	2012-11-28	E4/E2	2560	640	320	640	320	40	80	<	40	80	10
B/Hong Kong/514/2009		1B	2009-10-11	MDCK1/MDCK2	2560	160	80	80	160	80	160	<	<	<	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	2560	80	<	40	80	80	160	<	<	<	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	2560	80	40	40	160	80	160	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	160	20	<	<	<	<	<	80	80	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	MDCK1/MDCK2	320	40	<	<	<	<	<	80	80	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	160	40	40	20	<	<	40	80	160	<
B/Cote D'Ivoire/1662/2018		1A(Δ3)	2018-07-25	P0/MDCK3	160	80	<	20	<	<	<	<	<	<	40
TEST VIRUSES															
B/Sicilia/3/2019		1A(Δ3)	2019-01-19	MDCK1	640	40	<	10	<	<	<	<	<	<	80
B/Paris/2038/2019		1A(Δ3)	2019-05-16	MDCK2/MDCK1	640	80	<	<	<	<	<	<	<	<	80
						Vaccine[#]								Vaccine[$]	

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

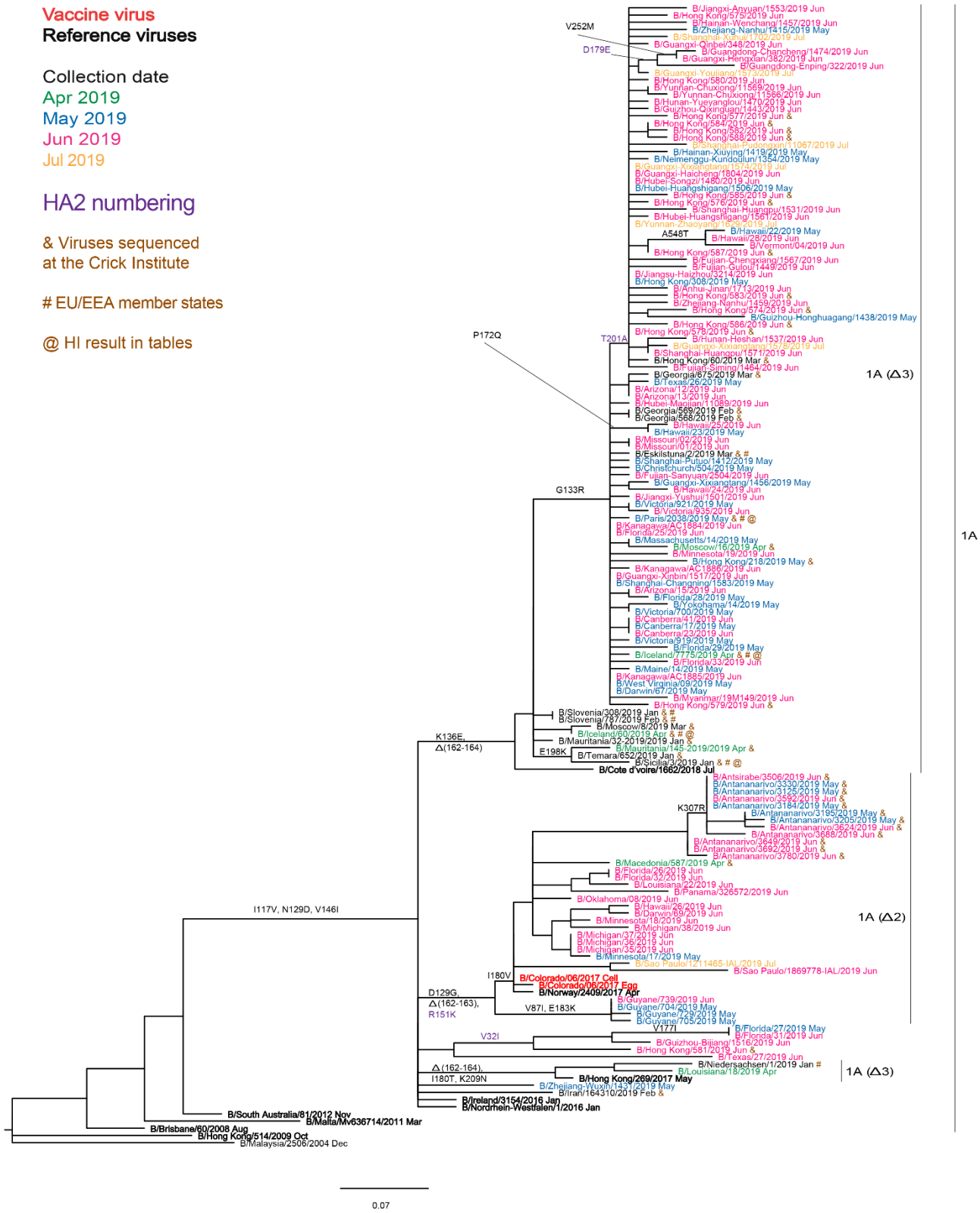


Table 6-1. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

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 MDCK F05/19[*2]
		3			3	2	2	2	3	3	3	3	3	3
REFERENCE VIRUSES														
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	640	160	80	80	20	40	<	160	<	80
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK4	1280	320	320	320	80	160	80	160	80	160
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	320	20	20	160	20	40	<	80	<	20
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	1280	10	10	160	40	80	<	160	20	40
B/Stockholm/12/2011		3	2011-03-28	E4/E1	640	<	10	80	20	80	<	80	<	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	320	320	160	80	320	160	160	80	320
B/Phuket/3073/2013		3	2013-11-21	E4/E3	640	10	10	80	20	40	<	160	<	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK4	1280	20	40	80	20	40	10	80	20	160
B/Mauritius/I-762/2018		3	2018-09-02	MDCK1/MDCK3	1280	20	40	40	20	40	10	80	20	80
TEST VIRUSES														
B/Stockholm/2/2019		3	2019-02-14	MDCK0/MDCK1	640	10	20	80	10	40	40	40	<	160
												Vaccine[#]		

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

[#] B/Yamagata-lineage virus recommended for use in quadravalent vaccines NH 2018-19, SH 2019 and NH 2019-20

Sequences in phylogenetic trees

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

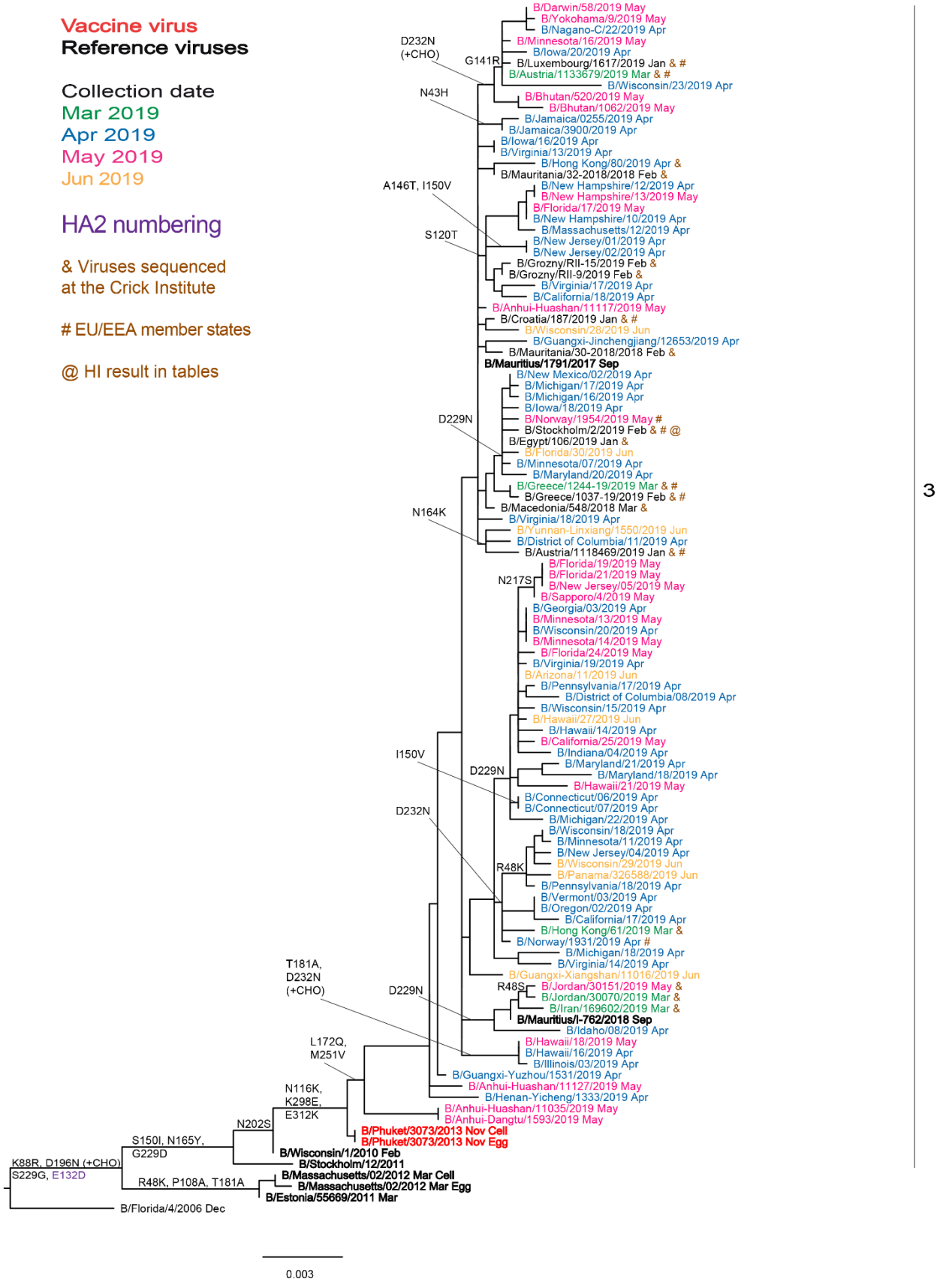
Viruses	Other information	Passage history / Ferret number / Genetic Group	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					B/Phuket 3073/13 Egg SH614[*1,3]	B/Estonia 55669/11 MDCK F39/17[*2]	B/Mass 02/12 MDCK F10/16[*2]	B/Mass 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 MDCK F05/19[*2]
		3			3	2	2	2	3	3	3	3	3	3
REFERENCE VIRUSES														
B/Estonia/55669/2011		2	2011-03-14	MDCK2/MDCK3	1280	160	80	160	40	40	<	160	<	160
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK4	2560	320	640	640	160	160	80	320	80	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	640	40	20	320	40	80	<	160	<	40
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	2560	10	20	320	80	160	10	320	40	160
B/Stockholm/12/2011		3	2011-03-28	E4/E1	1280	<	20	160	40	160	<	160	<	80
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	160	320	320	160	160	160	160	160	640
B/Phuket/3073/2013		3	2013-11-21	E4/E3	1280	10	10	160	40	80	<	320	<	80
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK4	1280	20	40	160	40	80	20	160	40	160
B/Mauritius/I-762/2018		3	2018-09-02	MDCK1/MDCK3	2560	40	80	80	40	80	20	160	40	320
TEST VIRUSES														
B/Brest/1993/2019			2019-03-24	MDCK1/MDCK1	2560	20	40	160	40	80	20	160	40	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 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, 1 016 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 542 A(H1N1)pdm09, 442 A(H3N2), 15 B/Victoria-lineage and 17 B/Yamagata-lineage. All but five viruses showed normal inhibition (NI) by the two neuraminidase inhibitors. B/Norway/3241/2018 (Victoria-lineage) showed 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 polymorphism and V165I amino acid substitution. Two A(H1N1)pdm09 viruses, A/Cyprus/919/2019 and A/Trnava/535/2019, showed HRI by oseltamivir and their NA genes encoded N295S and H275Y amino acid substitutions, respectively. A third A(H1N1)pdm09 virus, A/Denmark/2697/2019, showed RI by zanamivir and sequencing revealed NA Q136K/Q and D151D/E amino acid polymorphisms.

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]. In Nepal, where there have been reports of A(H5N1) infection in domestic birds since February 2019, no new human cases of A(H5N1) infection have been detected since the fatal case in March 2019 that marked 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.

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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