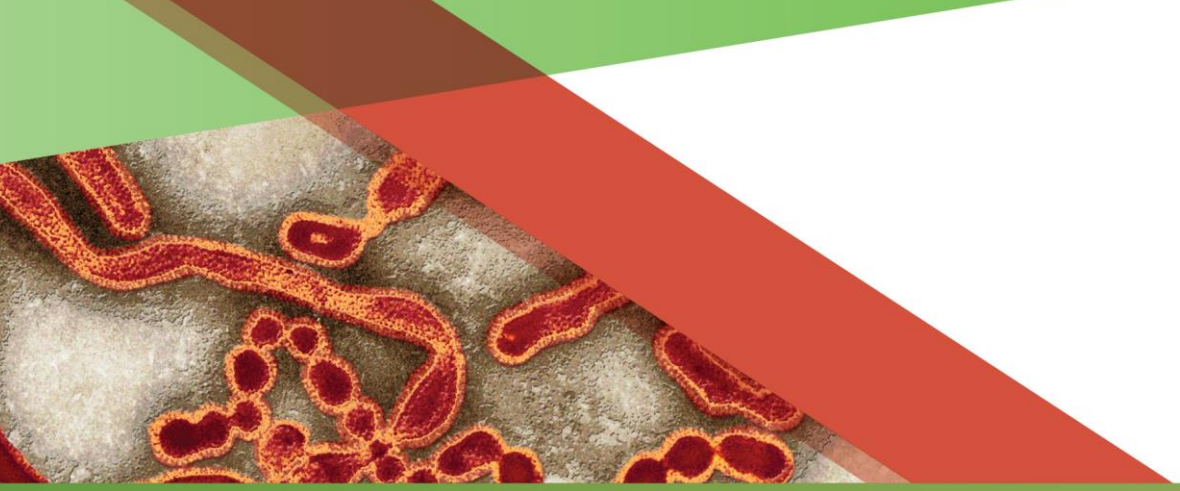

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, April 2019

Summary

This is the sixth report for the 2018–19 influenza season. As of week 18/2019, 203 585 influenza detections across the WHO European Region had been reported. Detections were 99% type A viruses, with A(H1N1)pdm09 prevailing over A(H3N2), and 1% type B viruses, with 80 (65%) of 124 ascribed to a lineage being B/Yamagata-lineage.

Since the March 2019 characterisation report[1], a further shipment of influenza-positive specimens from an EU/EEA country was received at the London WHO CC, the Francis Crick Worldwide Influenza Centre (WIC). A total of 1 057 virus specimens, with collection dates after 31 August 2018, have been received.

All 59 A(H1N1)pdm09 test viruses characterised antigenically since the March 2019 characterisation report showed good reactivity with antiserum raised against the 2018–19 vaccine virus, A/Michigan/45/2015 (clade 6B.1). The 391 test viruses with collection dates from week 40/2018 genetically characterised at the WIC, including an H1N2 reassortant, all fell in a 6B.1 subclade, designated 6B.1A, defined by HA1 amino acid substitutions of S74R, S164T and I295V. Of these recently circulating viruses, 355 also have HA1 S183P substitution, often with additional substitutions in HA1 and/or HA2.

Since the last report, only 26 A(H3N2) viruses successfully recovered had sufficient HA titre to allow antigenic characterisation by HI assay in the presence of oseltamivir. These viruses 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 321 viruses with collection dates from week 40/2018 genetically characterised at the WIC, 267 were clade 3C.2a (with 32 3C.2a2, 13 3C.2a3, six 3C.2a4 and 216 3C.2a1b) and 54 were clade 3C.3a.

No B/Victoria-lineage viruses were 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 five viruses characterised from EU/EEA countries this season, one has been Δ162-163 and four Δ162-164 (three African and one Asian subgroup).

Including the two B/Yamagata-lineage viruses reported on here, a total of 11 from the 2018–19 season have been characterised. 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 the vaccine

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.

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virus 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 40/2018–18/2019). Since week 1/2019, the cumulative number of detections has increased from 18 049 to 20 3585, with type A (99%) predominating over type B (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 = 76 072) and the type B viruses ascribed to a lineage (n = 124), A(H1N1)pdm09 (n = 43 856) have continued to prevail over A(H3N2) (n = 32 216) viruses and 80 of 124 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 March 2019 characterisation report[1]. Overall, the ratio of type A to type B detections dramatically increased compared with the 2017–18 season (0.8:1 to 98:1), 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 (57.7% 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 40/2018–18/2019)[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	**21043**	**180487**	**201530**	**99**	**98:1**	**106003**	**44.1**	**0.8:1**
A(H1N1)pdm09	8739	35117	43856	57.7		23121	50.6	
A(H3N2)	7233	24983	32216	42.3	0.7:1	22568	49.4	1:1
A not subtyped	5071	120387	125458			60314		
Influenza B	**247**	**1807**	**2054**	**1**		**134618**	**55.9**	
Victoria lineage	11	33	44	35.5		301	1.9	
Yamagata lineage	52	28	80	64.5	1.8:1	15701	98.1	52.2:1
Lineage not ascribed	184	1746	1930			118616		
Total detections (total tested	**21290 (53013)**	**182294 (774629)**	**203585 (827642)**			**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).**

Since week 40/2018, 48 shipments of specimens (virus isolates and/or clinical specimens) from 34 centres across 29 EU/EEA countries have been received at the Crick Worldwide Influenza Centre (WIC); they have contained a total of 1 057 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 was presented at the WHO influenza vaccine composition meeting for the northern hemisphere 2019–20 season. Recommendations emerging from this meeting, held 18–21 February 2019, and the subsequent update (21 March 2019) have been published [1, 2].

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, March 2019. Stockholm: ECDC; 2018. Available from: https://ecdc.europa.eu/sites/portal/files/documents/influenza-virus-characterisation-march-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 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	1					1	0	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						
Slovenia	3			1	1						2	2		
Spain	28			15	8	13	2	3						
Sweden	11			7	7	4	3	1						
United Kingdom	8			5	5	3	1							
2019														
JANUARY														
Belgium	47			8	3	39	2	18						
Bulgaria	13			12	in process	1	0	1						
Croatia	2												2	1
Cyprus	17			17	7									
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	4			3	3	1	0	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	6			6	3									
Portugal	5			1	1	4	3	1						
Romania	13			11	6	2	1	1						
Slovenia	14			9	in process	4	in process				1	in process		
Spain	73			32	27	41	19	12						
United Kingdom	38	3	0	31	2	4	1	0						
FEBRUARY														
Bulgaria	42			22	in process	20	in process							
Germany	26			9	9	17	9	8						
Greece	17			11	10	5	1	4					1	1
Latvia	7			1	1	6	5	1						
Malta	8			5	2	3	0	1						
Slovenia	4			3	in process						1	in process		
MARCH														
Bulgaria						1	in process							
Germany	23			7	7	16	12	4						
Greece	15			8	3	6	1	4					1	1
Latvia	2			1	1	1	1	0						
Slovenia	8			4	in process	3	in process		1	in process				
APRIL														
Slovenia	5			2	in process	3	in process							
	1057	6	0	548	358	473	130	208	4	0	9	5	18	13
29 Countries					51.8%		44.7%					0.9%		1.7%
					97.2%							2.9%		

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 was H1N2

As of 2019-05-07

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. Tables 3-1 to 3-3 are repeated from the March 2019 characterisation report but with genetic group data now included, while Tables 3-4 and 3-5 were generated during April 2019. Test viruses in each table are sorted by genetic group (where known at the time of preparing this report) and then by date of collection. A summary of the HI results for all test viruses in Tables 3-1 to 3-5 is shown in Table 3-6, and a summary for viruses sorted by genetic group is shown in Table 3-7.

The vast majority of A(H1N1)pdm09 test viruses – 126 of 129 (98%) – were antigenically indistinguishable from the egg-propagated vaccine virus for the northern hemisphere 2018–19 influenza season, A/Michigan/45/2015 [3], as assessed with post-infection ferret antisera, being recognised at titres within twofold of the titre of the antiserum with the homologous virus (Table 3-6). The three viruses from England showing greater than twofold titre reductions all contained **HA1** amino acid substitutions at positions known to be associated with antigenic change: A/England/731/2018 (**N156D**), A/England/732/2018 (**N156S**) and A/England/733/2018 (**S157L**).

Antisera raised against six reference viruses (A/Bayern/69/2009, A/Slovenia/2903/2015, A/Paris/1447/2017, A/Switzerland/3330/2017, A/Norway/3433/2018 and A/Ireland/84630/2018) recognised ≥90% of test viruses at titres within twofold of the titres of the antisera with their homologous viruses and over 97% at titres within fourfold of the respective homologous titres (Table 3-6). Similarly good reactivities were seen with antiserum raised against egg-propagated A/Brisbane/02/2018, the vaccine virus recommended for the 2019–20 northern hemisphere influenza season [1, 2]. The antiserum raised against A/Switzerland/2656/2017 recognised 81% of test viruses at titres within twofold of the titre of the antiserum with the homologous virus and 95% within fourfold. The antiserum raised against cell culture-propagated A/Lviv/N6/2009 recognised only 3% of test viruses at titres within twofold of the homologous titre, and 34% within fourfold. The antiserum raised against 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**.

All test viruses for which HA gene sequencing was 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 have remained antigenically similar to A/Michigan/45/2015, as shown in the March 2019 and earlier characterisation reports, as assessed with post-infection ferret antisera.

Figure 1 shows a phylogenetic tree for the HA genes 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 during April 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, 2]; 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 and the recently recommended A/Brisbane/02/2018 for the northern hemisphere 2019–20 influenza season [1, 2], are indicated on the phylogeny (Figure 1).

Table 3-7 shows that test viruses from EU/EEA countries in subclade 6B.1A and viruses in each of the genetic groups 183P-1, -2, -5, -6 and -7 show similar patterns of recognition by the panel of post-infection ferret antisera. Generally, test viruses showed good reactivity, ≥90% reacting within twofold 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 antisera raised against A/Slovenia/2903/2015 (82%) and A/Switzerland/2656/2017 (63%), although 96% and 89% of test viruses reacted within fourfold of the respective homologous titres. While such HI studies conducted with post-infection ferret antisera indicated low levels of antigenic drift in A(H1N1)pdm09 viruses, panels of post-vaccination human antisera recognised viruses containing the HA1 substitution S183P less well. 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, 2].

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

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					A/Mich 45/15	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			NIB F42/16[*1]	F09/15[*1]	F13/18[*2]	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/E2	640	320	320	1280	2560	640	320	1280	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	320	160	<	160	40	40	320	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	640	1280	160	1280	320	320	1280	320	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	320	1280	2560	640	320	2560	1280	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	320	160	40	640	1280	320	160	1280	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	640	320	320	1280	2560	320	320	2560	1280	640
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	160	160	80	320	640	320	160	640	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	160	<	320	1280	160	160	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK2	320	160	80	640	1280	320	160	1280	640	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/IE1	640	320	320	1280	2560	640	320	1280	1280	640
IVR-190(A/Brisbane/02/2018)		6B.1A1	2018-01-04	E3/D8/IE1	1280	640	320	2560	5120	1280	640	2560	2560	1280
TEST VIRUSES														
A/Belgium/G0024/2019		6B.1A5	2019-01-07	MDCK2	320	160	80	320	1280	160	160	2560	640	640
A/Belgium/S0270/2019		6B.1A7	2019-01-15	MDCK2	320	160	80	640	1280	320	160	1280	640	640
A/Luxembourg/2575/2019		6B.1A6	2019-01-13	MDCK2	640	160	80	640	1280	320	320	2560	640	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	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.1	A/Swit 2656/17 Egg F20/18*1 6B.1	A/Swit 3330/17 Egg F23/18*1 6B.1	A/Norway 3433/18 MDCK F04/19*1 6B.1	A/Ire 84630/18 MDCK F08/19*1 6B.1	A/Bris 02/18 Egg F09/19*1 6B.1A1
REFERENCE VIRUSES														
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	320	160	640	1280	640	320	1280	1280	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	80	320	320	40	320	40	40	320	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	1280	1280	160	640	160	160	1280	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	160	1280	1280	640	320	1280	1280	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	160	80	1280	1280	640	320	2560	1280	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	1280	640	320	1280	2560	1280	640	2560	1280	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	80	640	1280	640	320	1280	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	80	40	320	640	160	160	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	320	160	80	640	1280	320	160	1280	640	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	640	320	1280	5120	1280	640	2560	2560	640
TEST VIRUSES														
A/Hamburg/5/2018		6B.1A5	2018-11-28	P2/MDCK1	320	80	80	320	640	160	80	1280	640	320
A/Berlin/58/2018		6B.1A5	2018-12-07	P1/MDCK1	640	320	160	640	1280	320	320	2560	1280	640
A/Hamburg/6/2018		6B.1A5	2018-12-10	P1/MDCK1	320	160	160	320	640	160	160	1280	640	320
A/Hamburg/7/2018		6B.1A5	2018-12-17	P1/MDCK1	640	320	160	640	1280	320	320	2560	1280	640
A/England/733/2018		6B.1A5	2018-12-17	SIAT2/MDCK1	160	80	80	80	320	40	80	640	80	160
A/England/700/2018		6B.1A5	2018-12-21	SIAT1/MDCK1	320	160	160	320	640	160	160	1280	640	320
A/Saint-Etienne/2322/2018		6B.1A5	2018-12-23	MDCK2/MDCK1	320	80	80	320	640	160	160	1280	320	320
A/England/732/2018		6B.1A5	2018-12-26	SIAT1/MDCK1	80	160	40	40	160	40	40	1280	40	160
A/Lyon/4/2019		6B.1A5	2018-12-27	MDCK2/MDCK1	640	160	160	640	1280	320	160	2560	640	640
A/Lyon/CHU/R18.134.99/2018		6B.1A5	2018-12-29	MDCK2/MDCK1	640	160	160	640	1280	320	160	1280	640	640
A/Lyon/CHU/R19.03.40/2019		6B.1A5	2019-01-03	MDCK2/MDCK1	640	320	160	1280	1280	640	320	2560	640	640
A/England/1/2019		6B.1A5	2019-01-03	SIAT1/MDCK1	640	320	160	640	1280	320	320	2560	640	640
A/Lyon/CHU/R19.04.49/2019		6B.1A5	2019-01-05	MDCK2/MDCK1	640	160	40	320	1280	320	160	1280	640	320
A/Annecy/35/2019		6B.1A5	2019-01-06	MDCK2/MDCK1	640	320	160	1280	1280	640	320	2560	1280	1280
A/Gueret/64/2019		6B.1A5	2019-01-07	MDCK2/MDCK1	640	160	80	640	1280	320	160	2560	640	640
A/Lyon/HFME/47/2019		6B.1A5	2019-01-07	MDCK2/MDCK1	640	160	80	640	1280	320	320	2560	640	640
A/England/2/2019		6B.1A5	2019-01-07	SIAT1/MDCK1	640	320	320	640	1280	640	320	2560	1280	1280
A/Bayern/50/2018		6B.1A7	2018-12-06	P1/MDCK1	1280	320	160	1280	2560	640	320	2560	1280	1280
A/Lyon/128/2019		6B.1A7	2019-01-09	MDCK2/MDCK1	1280	320	160	1280	2560	640	320	2560	1280	1280
A/England/620/2018		6B.1A6	2018-11-12	SIAT2/MDCK1	640	160	80	640	1280	640	320	1280	640	640
A/Toulon/2307/2018		6B.1A6	2018-12-18	MDCK2/MDCK1	640	160	80	640	1280	320	160	1280	640	640
A/England/731/2018		6B.1A6	2018-12-24	SIAT1/MDCK1	80	160	80	40	320	80	<	320	40	160
A/Mecklenburg-Vorpommern/5/2018		6B.1A6	2018-12-27	P1/MDCK1	1280	320	160	2560	2560	1280	640	2560	2560	1280
A/Lyon/6/2019		6B.1A6	2018-12-29	MDCK2/MDCK1	640	160	160	1280	2560	640	320	2560	1280	640
A/Lyon/96/2019		6B.1A6	2019-01-08	MDCK2/MDCK1	640	320	80	1280	1280	640	320	2560	1280	1280
A/Grenoble/43/2019		6B.1A2	2018-12-28	MDCK2/MDCK1	1280	320	160	1280	2560	640	320	2560	1280	640
A/Lyon/10/2019		6B.1A2	2018-12-31	MDCK2/MDCK1	1280	320	160	1280	2560	640	640	2560	2560	1280
A/Lyon/CHU/R19.01.51/2019		6B.1A2	2019-01-01	MDCK2/MDCK1	1280	320	320	2560	2560	1280	640	2560	2560	2560
A/Saint-Etienne/137/2019		6B.1A1	2019-01-11	MDCK2/MDCK1	2560	640	160	1280	5120	1280	640	5120	2560	2560
A/Niedersachsen/1/2019		6B.1A	2019-01-02	P1/MDCK1	1280	320	160	1280	2560	1280	320	2560	2560	1280
A/England/708/2018			2018-12-27	SIAT1/MDCK1	640	320	160	640	1280	320	320	1280	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 3-3. Antigenic analysis of A(H1N1)pdm09 viruses by HI

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					A/Mich 45/15	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[*2]	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	320	320	1280	2560	640	320	1280	1280	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	320	160	<	160	40	40	320	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	640	1280	160	1280	320	320	1280	320	640
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	320	1280	2560	640	320	2560	1280	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	320	160	40	640	1280	320	160	1280	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	640	320	320	1280	2560	640	320	2560	1280	640
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	160	160	80	320	640	320	320	640	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	160	<	320	1280	160	160	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	320	160	80	640	1280	320	160	1280	640	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	640	320	320	1280	2560	640	320	1280	1280	640
TEST VIRUSES														
A/Greece/1589/2018		6B.1A5		MDCK1/MDCK1	1280	640	320	1280	2560	640	640	2560	2560	1280
A/Bucuresti/238999/2018		6B.1A5	2018-12-07	SIAT2/MDCK1	640	160	160	640	1280	320	640	1280	640	640
A/Bucuresti/239045/2018		6B.1A5	2018-12-10	SIAT1/MDCK1	320	160	80	320	640	160	320	1280	640	320
A/Greece/1607/2018		6B.1A5	2018-12-27	MDCK1/MDCK1	640	320	320	640	1280	640	640	2560	640	640
A/Greece/1619/2018		6B.1A5	2018-12-28	MDCK1/MDCK1	1280	640	320	1280	2560	640	640	2560	2560	1280
A/Greece/1617/2018		6B.1A5	2018-12-28	MDCK1/MDCK1	1280	320	320	640	1280	320	640	2560	1280	640
A/Greece/1616/2018		6B.1A5	2018-12-31	MDCK1/MDCK1	1280	320	320	1280	1280	640	640	2560	1280	640
A/Rheinland-Pfalz/1/2019		6B.1A5	2019-01-10	C1/MDCK1	640	320	320	640	640	320	640	2560	1280	640
A/Bucuresti/239839/2019		6B.1A5	2019-01-11	MDCK2	640	320	160	1280	2560	640	640	2560	1280	640
A/Thuringen/1/2019		6B.1A5	2019-01-11	C1/MDCK1	1280	320	320	640	640	320	640	2560	1280	640
A/Greece/144/2019		6B.1A5	2019-01-14	MDCK1	640	160	40	640	1280	320	320	2560	640	640
A/Berlin/7/2019		6B.1A5	2019-01-14	C1/MDCK1	640	320	320	1280	640	320	640	2560	1280	640
A/Brandenburg/2/2019		6B.1A5	2019-01-15	C1/MDCK1	1280	320	80	1280	2560	640	1280	2560	1280	1280
A/Rheinland-Pfalz/3/2019		6B.1A5	2019-01-17	C1/MDCK1	640	320	160	640	1280	320	640	2560	640	640
A/Greece/232/2019		6B.1A5	2019-01-21	MDCK1	640	320	160	1280	1280	640	320	2560	1280	640
A/Sachsen/5/2019		6B.1A5	2019-01-21	C1/MDCK1	640	320	160	640	1280	320	640	2560	640	640
A/Bremen/7/2019		6B.1A5	2019-01-31	C1/MDCK1	1280	320	160	640	1280	640	640	2560	1280	640
A/Niedersachsen/31/2019		6B.1A5	2019-02-05	C1/MDCK1	1280	320	160	640	1280	320	640	2560	640	640
A/Hamburg/1/2019		6B.1A5	2019-02-11	C1/MDCK1	640	320	320	640	640	320	640	2560	1280	640
A/Nordrhein-Westfalen/63/2019		6B.1A5	2019-02-18	C1/MDCK1	640	320	160	640	640	320	640	1280	640	640
A/Bayern/68/2019		6B.1A5	2019-02-19	C1/MDCK1	640	160	80	320	320	160	160	1280	320	320
A/Croatia/5299/2018		6B.1A7	2018-11-28	MDCKx/MDCK1	640	320	80	640	2560	640	640	1280	1280	640
A/Croatia/5327/2018		6B.1A7	2018-12-03	MDCKx/MDCK1	640	160	80	640	2560	320	640	1280	1280	640
A/Bucuresti/239594/2019		6B.1A7	2019-01-07	MDCK1	1280	320	160	1280	2560	640	640	2560	1280	1280
A/Baden-Wurttemberg/7/2019		6B.1A7	2019-01-21	C1/MDCK1	640	160	80	640	1280	320	640	1280	640	640
A/Sachsen/28/2019		6B.1A7	2019-02-11	C1/MDCK1	640	160	160	640	640	320	640	2560	1280	640
A/Thuringen/16/2019		6B.1A7	2019-02-11	C1/MDCK1	640	160	80	640	640	320	320	1280	1280	640
A/Greece/1519/2018		6B.1A6		MDCK1/MDCK1	640	160	80	640	1280	320	320	2560	640	320
A/Greece/168/2019		6B.1A6	2019-01-17	MDCK1	1280	320	160	640	1280	640	640	1280	1280	640
A/Greece/1585/2018		6B.1A2	2018-12-18	MDCK1/MDCK1	2560	640	320	1280	2560	1280	640	2560	2560	1280
A/Saarland/1/2019		6B.1A2	2019-01-07	C1/MDCK1	640	160	80	640	640	320	320	2560	1280	640
A/Nordrhein-Westfalen/9/2019		6B.1A2	2019-01-17	C1/MDCK1	1280	320	160	1280	1280	640	640	2560	1280	640
A/Greece/199/2019		6B.1A2	2019-01-18	MDCK1	1280	320	160	1280	2560	640	640	2560	1280	640
A/Croatia/5331/2018		6B.1A	2018-12-03	MDCKx/MDCK1	2560	640	320	2560	5120	1280	1280	2560	2560	2560
A/Berlin/26/2019		6B.1A	2019-02-04	C1/MDCK1	2560	640	160	1280	2560	1280	1280	2560	2560	2560
A/Thuringen/8/2019			2019-01-28	C1/MDCK1	640	160	160	640	1280	320	320	1280	640	640

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

Vaccine NH 2018-19 SH 2019

Vaccine NH 2019-20

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera									
					A/Mich 45/15	A/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*2	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	1280	640	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	160	320	40	160	80	80	320	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	320	640	1280	160	640	320	160	1280	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	160	160	640	1280	640	320	1280	640	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	160	80	640	2560	640	320	1280	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	1280	640	640	1280	2560	1280	640	2560	1280	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	160	640	1280	640	640	1280	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	160	40	320	640	320	160	1280	320	320
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	640	320	160	1280	2560	640	320	2560	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	320	320	1280	2560	1280	640	2560	1280	1280
TEST VIRUSES														
A/Valladolid/12/2019		6B.1A5	2019-01-09	SIAT1/SIAT1	1280	640	320	1280	2560	1280	1280	2560	1280	1280
A/Cyprus/F68/2019		6B.1A5	2019-01-12	MDCK2	320	80	<	320	640	320	160	640	320	320
A/Cyprus/F33/2019		6B.1A7	2019-01-04	MDCK1	640	320	160	640	1280	1280	640	1280	1280	640
A/Cyprus/F96/2019		6B.1A7	2019-01-14	MDCK1	640	320	160	1280	1280	640	640	2560	1280	640
A/Latvia/01-040279/2019		6B.1A7	2019-01-14	MDCK2/MDCK1	640	160	80	320	640	640	320	640	640	320
A/Valladolid/23/2019		6B.1A7	2019-01-14	SIAT1/SIAT1	640	160	80	640	1280	640	640	1280	640	640
A/Latvia/01-042924/2019		6B.1A6	2019-01-14	MDCK2/MDCK1	1280	320	160	640	1280	1280	640	1280	1280	640
A/Latvia/01-035913/2019		6B.1A6	2019-01-14	MDCK2/MDCK1	640	160	80	640	1280	640	320	1280	1280	640
A/Latvia/01-078881/2019		6B.1A6	2019-01-28	MDCK2/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Latvia/01-075097/2019		6B.1A6	2019-01-28	MDCKx/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Latvia/19-090472/2019		6B.1A6	2019-01-31	MDCKx/MDCK1	640	320	160	1280	1280	1280	640	1280	1280	640
A/Latvia/02-033557/2019		6B.1A6	2019-02-11	MDCK1/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	640
A/Latvia/03-012374/2019		6B.1A6	2019-03-04	MDCK1/MDCK1	640	320	160	640	1280	1280	640	1280	640	640
A/Cyprus/FA13/2019		6B.1A1	2019-01-11	MDCK1	320	80	40	320	640	640	320	640	640	320
					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

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: A/Michigan/45/2015 (6B.1)	A/Bayern/69/2009 (6B.1)	A/Lviv/N6/2009 (6B.1)	A/Slovenia/2903/2015 (6B.1)	A/Paris/1447/2017 (6B.1A)	A/Switzerland/2656/2017 (6B.1A)	A/Switzerland/3330/2017 (6B.1A5)	A/Norway/3433/2018 (6B.1A5)	A/Ireland/84630/2018 (6B.1A6)	A/Brisbane/02/2018 (6B.1A1)
					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 Egg 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	640	320	160	1280	1280	1280	640	1280	640	640
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	160	160	160	160	80	40	160	40	80
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	160	640	640	160	640	320	160	640	160	320
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	160	160	640	1280	640	320	1280	640	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK3/MDCK3	640	160	80	640	1280	640	320	1280	640	640
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E2	1280	640	320	1280	1280	1280	640	1280	1280	640
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	80	640	1280	640	640	640	640	320
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	160	80	40	320	640	320	160	640	320	160
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK3/MDCK2	320	80	40	320	640	320	320	640	640	320
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	320	320	1280	2560	1280	640	2560	1280	1280
TEST VIRUSES														
A/Navarra/2907/2018		6B.1A5	2018-11-15	MDCK1	640	160	80	640	1280	640	320	1280	640	320
A/Baleares/3014/2018		6B.1A5	2018-12-07	MDCK1	320	160	80	320	640	320	160	1280	320	320
A/Galicia/296/2019		6B.1A5	2019-01-04	MDCK1	640	160	80	640	640	640	320	1280	640	640
A/Extremadura/280/2019		6B.1A5	2019-01-04	SIAT1/MDCK1	640	320	160	640	1280	640	320	1280	640	640
A/Andalucia/268/2019		6B.1A5	2019-01-05	SIAT1/MDCK1	640	160	80	640	1280	640	320	1280	640	320
A/Andalucia/271/2019		6B.1A5	2019-01-07	SIAT1/MDCK1	640	160	160	640	1280	640	320	1280	640	640
A/Galicia/174/2019		6B.1A5	2019-01-07	MDCK1	640	320	160	640	1280	640	320	1280	1280	640
A/Galicia/173/2019		6B.1A5	2019-01-07	MDCK1	640	320	160	640	1280	640	640	2560	640	640
A/Andalucia/276/2019		6B.1A5	2019-01-10	SIAT1/MDCK1	640	160	160	640	1280	640	320	1280	640	640
A/Malta/53463/2019		6B.1A5	2019-01-23	MDCK1	320	160	80	320	640	320	320	1280	1280	640
A/Greece/261/2019		6B.1A5	2019-01-30	MDCK1	1280	320	320	1280	2560	1280	640	2560	1280	1280
A/Malta/54659/2019		6B.1A5	2019-02-02	MDCK1	640	160	80	640	1280	640	320	1280	640	320
A/Malta/51615/2019		6B.1A5	2019-02-03	MDCK1	1280	160	160	1280	2560	640	640	2560	1280	640
A/PaisVasco/3139/2018		6B.1A7	2018-12-11	SIAT1/MDCK2	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/PaisVasco/3135/2018		6B.1A7	2018-12-13	MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/PaisVasco/3130/2018		6B.1A7	2018-12-17	SIAT1/MDCK2	640	160	80	640	1280	640	320	1280	640	640
A/Extremadura/282/2019		6B.1A7	2019-01-03	SIAT1/MDCK1	640	320	160	640	1280	640	320	1280	1280	640
A/Extremadura/278/2019		6B.1A7	2019-01-03	SIAT1/MDCK1	640	320	160	640	1280	640	320	1280	640	640
A/Madrid/209/2019		6B.1A7	2019-01-13	MDCK1	1280	320	160	640	1280	640	640	1280	1280	640
A/Aragon/190085/2018		6B.1A6	2018-12-30	SIAT1/MDCK2	1280	160	160	1280	2560	1280	1280	>5120	2560	1280
A/Greece/311/2019		6B.1A6	2019-02-04	MDCK1	640	160	80	640	1280	640	320	1280	1280	640
A/Greece/237/2019		6B.1A2	2019-01-30	MDCK2	640	160	160	640	2560	1280	640	2560	1280	640
A/Greece/324/2019		6B.1A2	2019-02-03	MDCK1	1280	320	160	1280	2560	1280	1280	2560	1280	1280
A/Greece/351/2019		6B.1A2	2019-02-05	MDCK1	640	160	160	640	1280	640	320	1280	640	640
A/Andalucia/190267/2018		6B.1A	2018-12-14	SIAT1/MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	640
A/Malta/53336/2019		6B.1A	2019-01-21	MDCK1	320	160	80	320	640	320	320	640	320	640
A/Malta/53480/2019		6B.1A	2019-01-23	MDCK1	640	160	80	640	640	640	640	1280	1280	640
A/Malta/53465/2019		6B.1A	2019-01-23	MDCK1	1280	320	160	1280	2560	1280	640	2560	1280	1280
A/Greece/341/2019		6B.1A	2019-02-04	MDCK2	1280	320	160	1280	2560	1280	640	2560	2560	1280
A/Greece/1046/19/2019			2019-02-20	MDCK1	320	80	40	320	640	320	320	1280	640	320
A/Greece/1078/19/2019			2019-02-21	MDCK1	640	320	160	640	1280	640	640	1280	1280	640
A/Greece/1063/19/2019			2019-02-21	MDCK1	2560	320	160	1280	2560	2560	1280	2560	1280	2560
A/Greece/1092/19/2019			2019-02-22	MDCK3	1280	640	320	1280	1280	1280	640	2560	1280	640
A/Greece/1170/19/2019			2019-02-25	MDCK1	640	160	80	640	1280	640	320	1280	640	640
A/Greece/1125/19/2019			2019-02-25	MDCK1	1280	640	320	1280	2560	1280	640	2560	2560	640
A/Thuringen/61/2019			2019-03-05	C1/MDCK1	640	160	160	640	1280	1280	320	1280	640	1280
A/Greece/1383/19/2019			2019-03-07	MDCK1	1280	640	320	1280	2560	1280	640	5120	1280	640
A/Niedersachsen/116/2019			2019-03-07	C1/MDCK1	640	320	160	640	1280	1280	320	1280	640	640
A/Greece/1428/19/2019			2019-03-10	MDCK1	1280	320	160	1280	1280	1280	640	2560	1280	640
A/Greece/1387/19/2019			2019-03-12	MDCK1	640	160	80	1280	1280	640	320	1280	640	640
A/Sachsen-Anhalt/43/2019			2019-03-12	C1/MDCK1	640	160	160	640	640	640	320	1280	640	640
A/Nordrhein-Westfalen/90/2019			2019-03-14	C1/MDCK1	640	160	80	640	1280	640	320	1280	640	640
A/Bremen/19/2019			2019-03-18	C1/MDCK1	640	160	80	640	1280	640	320	1280	640	640
A/Niedersachsen/150/2019			2019-03-19	C1/MDCK1	640	160	160	640	640	640	320	1280	640	640
A/Bayern/104/2019			2019-03-26	C1/MDCK1	640	160	160	640	1280	640	320	2560	640	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		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	640	320	160	1280	1280	1280	640	1280	640	640
A/Bayern/69/2009	G155E		40	160	160	40	160	80	40	160	40	80
A/Lviv/N6/2009	G155E, D222G		160	640	640	160	640	320	160	640	160	320
A/Slovenia/2903/2015	clone 37	6B.1	640	160	160	640	1280	640	320	1280	640	640
A/Paris/1447/2017		6B.1A	640	160	80	640	1280	640	320	1280	640	640
A/Switzerland/2656/2017		6B.1A	1280	640	320	1280	1280	1280	640	1280	1280	640
A/Switzerland/3330/2017	clone 35	6B.1A5	320	160	80	640	1280	640	640	640	640	320
A/Norway/3433/2018		6B.1A5	160	80	40	320	640	320	160	640	320	160
A/Ireland/84630/2018		6B.1A6	320	80	40	320	640	320	320	640	640	320
A/Brisbane/02/2018		6B.1A1	1280	320	320	1280	2560	1280	640	2560	1280	1280
TEST VIRUSES												
Number of viruses tested*			129	129	129	129	129	129	129	129	129	129
No with titre reduction ≤2-fold			126	126	4	118	122	104	123	128	125	118
%			*97.7*	*97.7*	*3.1*	*91.5*	*94.6*	*80.6*	*95.3*	*99.3*	*97.0*	*91.5*
No with titre reduction =4-fold			1	3	40	8	6	18	4	1	1	11
%			*0.7*	*2.3*	*31.0*	*6.2*	*4.7*	*14.0*	*3.1*	*0.7*	*0.7*	*8.5*
No with titre reduction ≥8-fold			2		85	3	1	7	2		3	
%			*1.6*		*65.9*	*2.3*	*0.7*	*5.4*	*1.6*		*2.3*	
			Vaccine NH 2018-19 SH 2019									Vaccine NH 2019-20

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

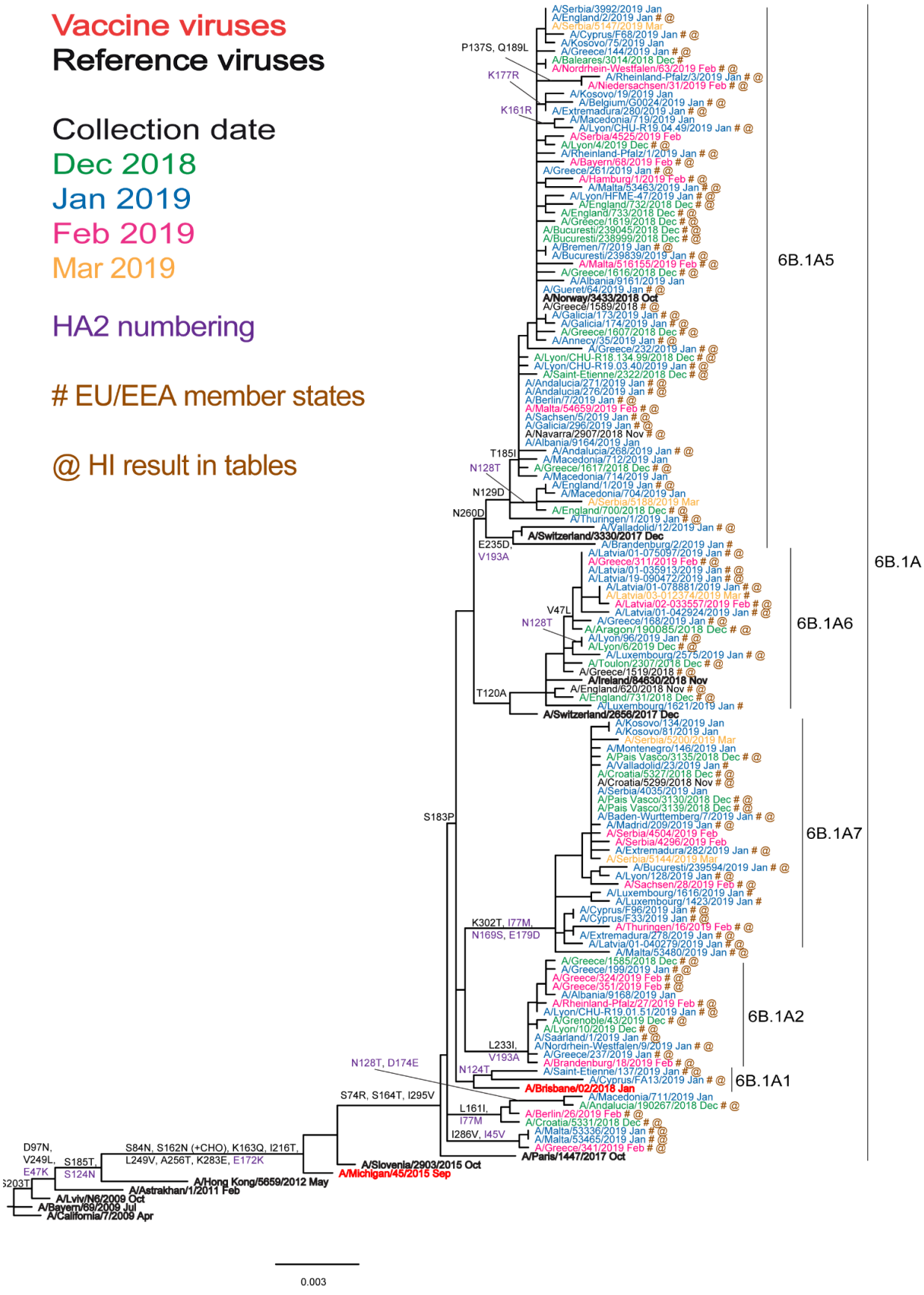
ND = Not Done

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 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		111	111	111	111	111	111	111	111	111	111
Number tested	6B.1A	8	8	8	8	8	8	8	8	8	8
No with titre reduction ≤2-fold		8	8		8	8	7	8	8	8	8
No with titre reduction =4-fold				4			1				
No with titre reduction ≥8-fold				4							
Number tested	6B.1A1	2	2	2	2	2	2	2	2	2	2
No with titre reduction ≤2-fold		2	2		2	1	2	2	2	2	1
No with titre reduction =4-fold						1					1
No with titre reduction ≥8-fold				2							
Number tested	6B.1A2	10	10	10	10	10	10	10	10	10	10
No with titre reduction ≤2-fold		10	10		10	10	10	10	10	10	10
No with titre reduction =4-fold				5							
No with titre reduction ≥8-fold				5							
Number tested	6B.1A5	54	54	54	54	54	54	54	54	54	54
No with titre reduction ≤2-fold		52	51	1	44	50	34	49	54	51	47
%		*96.4*	*94.4*	*1.8*	*81.5*	*92.6*	*63.0*	*90.7*	*100*	*94.4*	*87.0*
No with titre reduction =4-fold		1	3	17	8	3	14	4		1	7
%		*1.8*	*5.6*	*31.5*	*14.7*	*5.6*	*25.9*	*7.5*		*1.8*	*13.0*
No with titre reduction ≥8-fold		1		36	2	1	6	1		2	
%		*1.8*		*66.7*	*3.8*	*1.8*	*11.1*	*1.8*		*3.8*	
Number tested	6B.1A6	18	18	18	18	18	18	18	18	18	18
No with titre reduction ≤2-fold		17	18		17	17	16	17	17	17	17
%		*94.4*	*100*		*94.4*	*94.4*	*88.8*	*94.4*	*94.4*	*94.4*	*94.4*
No with titre reduction =4-fold				1		1	1		1		1
%				*5.6*		*5.6*	*5.6*		*5.6*		*5.6*
No with titre reduction ≥8-fold		1		17	1		1	1		1	
%		*5.6*		*94.4*	*5.6*		*5.6*	*5.6*		*5.6*	
Number tested	6B.1A7	19	19	19	19	19	19	19	19	19	19
No with titre reduction ≤2-fold		19	19		19	18	19	19	19	19	18
%		*100*	*100*		*100*	*94.7*	*100*	*100*	*100*	*100*	*94.7*
No with titre reduction =4-fold				5		1					1
%				*26.3*		*5.3*					*5.3*
No with titre reduction ≥8-fold				14							
%				*73.7*							
	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 March 2019 characterisation report of the viruses recovered, based on positive neuraminidase activity, only 26 retained sufficient HA activity to allow antigenic analysis by HI (Tables 4-4 to 4-5). Tables 4-1 to 4-3 are repeated from the March 2019 characterisation report but with genetic group data now included. Of the 26 test viruses, only one was recognised at a titre within fourfold of the homologous titre by the antiserum raised against the currently used vaccine virus, egg-propagated A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1). Test viruses were analysed with antisera raised against two cell culture-propagated subgroup 3C.2a1b viruses for which no homologous titres are given due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs. The antisera raised against A/La Rioja/2202/2018 and A/Norway/3275/2018 recognised, respectively, 6/26 (23%) and 4/26 (15%) test viruses at titres of ≥160.

Antisera raised against subclade 3C.2a2 viruses generally recognised the test viruses poorly. The antisera raised against cell culture-propagated A/Bretagne/1413/2017 and egg-propagated A/Switzerland/8060/2017, the vaccine virus recommended for use in the 2019 southern hemisphere season, recognised none of the 26 test viruses at titres within fourfold of the respective homologous titres.

Antiserum raised against a cell culture-propagated clade 3C.2a virus, A/Hong Kong/5738/2014, recognised 24/26 (92%) test viruses at titres within fourfold of the homologous titre and 10 (38%) within twofold. Antisera raised against the cell culture-propagated cultivar of A/England/538/2018 (clade 3C.3a) recognised 18/26 (69%) test viruses at titres within twofold of the titres of the antisera with the homologous virus, the remaining eight test viruses were poorly recognised (titres reduced by at least eightfold compared to the homologous titre).

Antisera raised against egg-propagated A/Kansas/14/2017, the virus recommended for use in northern hemisphere 2019–20 influenza vaccines, recognised only 1/26 (4%) test viruses at titres within twofold, and 7/26 (27%) within fourfold, of the homologous titre. An antiserum raised against cell culture-propagated A/Kansas/14/2017 recognised 9/13 (69%) test viruses at titres within twofold of the homologous titre (Table 4-5).

A summary of the HI data presented in Tables 4-1 to 4-5 is presented in Table 4-6 and, for those test viruses with known HA sequences at the time this report was prepared, these results are broken down by virus clade/subclade in Table 4-7. The Table shows (i) the poor recognition of test viruses by post-infection ferret antisera raised against egg-propagated vaccine/reference viruses, (ii) poor cross-reactivity of antisera raised against subclade 3C.2a2 viruses, (iii) antigenic drift in the clade 3C.3a viruses from 2014 to 2018 with the response to A/England/538/2018 being more clade 3C.3a specific and (iv) of the antisera raised against cell culture-propagated viruses that raised against A/Hong Kong/5738/2014 gives the broadest cross-clade/subclade reactivity.

HA gene sequences of the test viruses characterised antigenically in the March 2019 report are now available and the genetic clades are shown in Tables 4-1 to 4-3 and most 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 in recent months (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 to A/Stockholm/6/2014, and levels of detection since January 2019 have been increasing 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

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

[3] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, November 2014. Stockholm: ECDC; 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/ERLI-Net report November 2014.pdf

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 March 2019 (Figure 2). Notably, a significant number of the subgroup 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 been increasing in recent weeks 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 [3], A/Switzerland/8060/2017 (3C.2a2), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2019 influenza season [4], and A/Kansas/14/2017, the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2019–20 influenza season [1, 2], 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/Stock 6/14	A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/La Rioja 2202/18	A/Swit 8060/17	A/Eng 538/18	A/Neth 10260/18	A/Neth	A/Norway 3275/18
	Ferret number			SIAT	MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	Egg	SIAT	SIAT
	Genetic group			F14/14[1] 3C.3a	St J F60/17[1] 3C.2a	F01/18[1] 3C.2a2	F46/17[1] 3C.2a1	F26/18[1] 3C.2a1b	F27/18[1] 3C.2a2	F31/18[1] 3C.3a	F02/19[1] 3C.2a1b	F07/19[1] 3C.2a1b	F03/19[1] 3C.2a1b
REFERENCE VIRUSES													
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	160	160	80	160	80	160	160	<	40	80
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	160	160	160	80	160	160	40	80	160
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	320	1280	320	160	1280	320	40	80	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	<	80	40	640	160	160	80	40	40	40
A/Switzerland/8060/2017 clone 57	3C.2a2	2017-12-12	E7/E1	<	160	640	320	80	640	80	40	80	40
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	<	40	40	40	40	320	<	40	<
A/Netherlands/10260/2018	3C.2a1b	2018-02-15	E5/E1	<	160	80	80	320	80	80	1280	320	160
TEST VIRUSES													
A/Greece/1430/2018	3C.2a1b		SIAT1/SIAT1	<	40	80	<	<	40	<	<	40	160
A/Saint-Etienne/1998/2018		2018-10-15	MDCK3/SIAT1	40	40	40	40	160	40	40	40	80	80
A/Lyon/CHU-R18.116.67/2018	3C.2a1b	2018-11-26	MDCK4/SIAT1	40	40	<	40	160	40	40	40	160	160
A/Lyon/CHU-R18.128.2/2018	3C.2a1b	2018-12-17	MDCK3/SIAT1	80	80	80	80	80	160	40	<	80	320
A/Lyon/2296/2018	3C.2a3	2018-12-20	MDCK3/SIAT1	160	160	80	160	160	160	160	<	80	80
A/EHPAD-Montpellier/2320/2018	3C.2a3	2018-12-21	MDCK2/SIAT1	160	160	80	160	160	160	160	<	160	80
A/Lyon/2335/2018	3C.3a	2018-12-27	MDCK2/SIAT1	40	40	40	40	<	40	320	<	40	<
A/Lyon/CHU-R18.133.93/2018	3C.3a	2018-12-28	MDCK2/SIAT1	80	80	40	80	<	40	320	40	40	<
A/Lyon/CHU-R19.02.59/2019		2019-01-02	MDCK2/SIAT1	160	80	80	80	160	160	80	<	80	160
A/Lyon/CHU-R19.03.77/2019	3C.3a	2019-01-04	MDCK2/SIAT1	40	40	40	40	<	40	320	<	40	<
A/La Rochelle/85/2019	3C.3a	2019-01-05	MDCK2/SIAT1	40	40	40	40	<	80	320	<	40	<
A/Lyon/95/2019	3C.3a	2019-01-09	MDCK2/SIAT1	40	40	40	40	<	80	320	<	40	<
A/Lyon-EHPAD/108/2019	3C.2a1b	2019-01-09	MDCK2/SIAT1	40	40	80	40	80	80	<	<	80	160

Vaccine SH 2018 NH 2018-19

Vaccine SH 2019

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) [1] < = <40; ND = Not Done

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									
													NEW	NEW
					A/Stock 6/14	A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/La Rioja 2202/18	A/Swit 8060/17	A/Eng 538/18	A/Norway 3275/18	A/Kansas 14/17	A/Kansas 14/17
		Passage history			SIAT	MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	SIAT	Egg	Egg
		Ferret number			F14/14[*1]	St J F60/17[*1]	F01/18[*1]	F46/17*[1]	F26/18[*1]	F27/18[*1]	F31/18[*1]	F03/19[*1]	F11/19[*1]	F12/19[*1]
		Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.3a	3C.3a
REFERENCE VIRUSES														
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	160	160	160	160	320	160	160	160	160
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	160	160	160	80	320	160	320	160	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	640	160	80	640	160	320	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	80	160	80	640	320	160	80	80	40	40
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	80	160	1280	640	160	1280	80	80	40	80
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	80	80	80	80	40	80	640	40	320	320
A/Kansas/14/2017		3C.3a	2017-12-14	E7/E2	40	<	40	40	<	<	320	<	1280	1280
TEST VIRUSES														
A/Belgium/G0023/2019		3C.3a	2019-01-03	SIAT1	160	80	80	80	40	80	640	40	320	320
A/Belgium/S0275/2019		3C.3a	2019-01-15	SIAT1	160	80	80	80	40	80	640	40	320	320
A/Niedersachsen/81/2019		3C.3a	2019-01-25	C1/MDCK1	160	80	80	80	40	80	640	40	320	320
A/Nordrhein-Westfalen/53/2019		3C.3a	2019-02-11	C1/MDCK1	160	80	80	80	40	80	640	40	160	160
A/Bayern/53/2019		3C.3a	2019-02-11	C1/MDCK1	160	80	80	80	40	80	640	40	320	320
A/Berlin/28/2019		3C.3a	2019-02-11	C1/MDCK1	160	80	80	80	40	80	640	40	320	320
A/Nordrhein-Westfalen/60/2019		3C.3a	2019-02-18	C1/MDCK1	160	80	80	80	40	80	640	40	320	320
A/Bremen/12/2019		3C.3a	2019-02-18	C1/MDCK1	160	80	80	160	80	80	640	80	320	320
A/Hessen/34/2019		3C.3a	2019-02-18	C1/MDCK1	160	80	80	160	80	160	640	80	320	320
A/Berlin/37/2019		3C.3a	2019-02-21	C1/MDCK1	80	80	80	80	40	80	640	40	320	320
A/Baden-Wurttemberg/87/2019		3C.3a	2019-02-25	C1/MDCK1	160	80	80	80	40	80	640	40	320	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; ND = Not Done

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera A/Stock 6/14 SIAT F14/14*1 3C.3a	A/HK 5738/14 MDCK St J 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/Swit 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	A/Kansas 14/17 Egg F11/19*1 3C.3a
REFERENCE VIRUSES													
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	160	80	160	80	160	160	80	160
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	160	160	160	160	160	320	160	160	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	640	320	80	640	160	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	40	80	40	640	320	160	80	40	40
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	40	160	1280	640	160	1280	80	80	80
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	80	40	40	80	40	80	640	<	320
A/Kansas/14/2017		3C.3a	2017-12-14	E7/E2	<	<	<	80	<	<	320	<	1280
TEST VIRUSES													
A/Valladolid/560/2018		3C.3a	2018-12-27	SIAT1/SIAT1	40	40	40	80	40	80	640	<	160
A/Valladolid/2/2019		3C.3a	2019-01-02	SIAT1/SIAT1	40	40	40	80	40	80	640	<	320
A/Avila/3/2019		3C.3a	2019-01-03	SIAT1/SIAT1	40	40	40	80	40	80	640	<	320
A/Valladolid/5/2019			2019-01-04	SIAT1/SIAT1	40	40	40	80	40	80	640	<	320
A/Valladolid/9/2019		3C.3a	2019-01-08	SIAT1/SIAT1	80	40	80	80	40	80	640	40	320
A/Valladolid/13/2019		3C.3a	2019-01-09	SIAT1/SIAT1	40	<	40	80	40	40	640	<	160
A/Soria/11/2019		3C.2a1b	2019-01-09	SIAT1/SIAT1	80	40	40	80	320	80	40	160	80
A/Avila/15/2019		3C.3a	2019-01-10	SIAT1/SIAT1	80	40	40	80	40	80	640	<	160
A/Palencia/20/2019		3C.3a	2019-01-12	SIAT1/SIAT1	80	40	40	80	40	80	640	40	160
A/Valladolid/18/2019		3C.3a	2019-01-12	SIAT1/SIAT1	80	40	40	80	80	80	640	<	320
A/Valladolid/17/2019		3C.3a	2019-01-12	SIAT1/SIAT1	40	<	40	80	40	40	320	<	160
A/Valladolid/27/2019			2019-01-14	SIAT1/SIAT1	80	40	40	80	40	40	640	<	160
A/Valladolid/26/2019		3C.3a	2019-01-14	SIAT1/SIAT1	80	80	40	80	80	80	640	<	320
A/Valladolid/25/2019		3C.3a	2019-01-14	SIAT1/SIAT1	80	80	40	80	80	80	640	<	320
A/Valladolid/24/2019		3C.3a	2019-01-14	SIAT1/SIAT1	40	<	40	80	<	40	320	<	160
								Vaccine SH 2018 NH 2018-19		Vaccine SH 2019			Vaccine NH 2019-20
Sequences in phylogenetic trees													

*Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used) [1] < = <40; ND = Not Done

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

Viruses	Other information	Passage history / Ferret number / Genetic group	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	A/Kansas 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]	F11/19[*1]	CDC F2019-083[*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	320	160	160	160	160	80	80
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	160	80	640	160	160	160	80
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	160	40	640	320	160	80	80	<	<
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	320	1280	640	160	1280	80	80	40	40
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	40	<	<	<	<	320	<	160	80
A/Kansas/14/2017		3C.3a	2017-12-14	E7/E2	<	<	40	<	<	160	<	640	80
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	40	40	40	<	40	320	<	160	80
TEST VIRUSES													
A/Melilla/3115/2018		3C.2a1b	2018-12-18	SIAT1/SIAT1	<	<	80	<	<	320	<	640	40
A/Extremadura/283/2019		3C.3a	2019-01-06	SIAT1	80	40	40	<	40	320	<	160	160
A/Castilla La Mancha/242/2019		3C.3a	2019-01-17	SIAT1	80	40	40	40	40	320	<	160	160
A/Castilla La Mancha/337/2019		3C.3a	2019-01-21	SIAT1	80	40	40	<	40	320	<	160	80
A/Malta/53539/2019		3C.3a	2019-01-23	SIAT1	40	<	40	<	40	320	<	160	80
A/Greece/357/2019		3C.2a1b	2019-02-04	SIAT1	80	<	<	160	40	<	80	40	40
A/Latvia/02-013062/2019		3C.2a1b	2019-02-04	MDCK2/SIAT1	40	<	40	160	<	<	80	<	<
A/Latvia/02-033614/2019		3C.3a	2019-02-12	MDCK2/SIAT1	40	40	40	<	40	320	<	80	80
A/Latvia/02-053853/2019		3C.2a1b	2019-02-18	MDCK2/SIAT2	80	40	80	320	80	40	160	40	<
A/Latvia/02-073849/2019		3C.2a1b	2019-02-25	MDCKx/SIAT1	40	<	<	80	<	<	40	<	<
A/Latvia/02-073821/2019		3C.2a1b	2019-02-25	MDCK1/SIAT1	40	<	<	80	<	<	40	<	<
A/Latvia/03-012433/2019		3C.3a	2019-03-04	MDCKx/SIAT1	40	<	40	<	40	320	<	160	80
A/Greece/1451/19/2019		3C.3a	2019-03-04	SIAT1	40	<	40	<	<	320	<	80	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; ND = Not Done

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
							NEW				NEW			
				A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/Singapore 0019/16	A/La Rioja 2202/18	A/Switz 8060/17	A/Eng 538/18	A/Eng 538/18	A/Norway 3275/18	A/Kansas 14/17
	Passage history			MDCK	SIAT	Egg 10^{-4}	Egg 10^{-4}	SIAT	Egg	SIAT	SIAT	SIAT	Egg
	Ferret number			St Judes F60/17[-1]	F01/18[*1]	F46/17[*1]	F13/19[*1]	F26/18[*1]	F27/18[*1]	F31/18[*1]	F14/19[*1]	F03/19[*1]	F11/19[*1]
	Genetic group			3C.2a	3C.2a2	3C.2a1	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.3a	3C.2a1b	3C.3a
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	160	80	160	160	160	160	160	80	160	160
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	640	320	320	80	640	160	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	80	40	320	320	160	160	40	40	40	<
A/Switzerland/8060/2017 clone 57	3C.2a2	2017-12-12	E7/E1	160	640	320	320	80	1280	80	40	40	<
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	<	<	40	40	<	<	320	640	<	160
A/Kansas/14/2017	3C.3a	2017-12-14	E7/E2	<	<	40	40	<	<	320	160	<	640
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	<	40	80	<	40	320	640	<	160
TEST VIRUSES													
A/Hessen/42/2019		2019-02-27	C1/SIAT1	40	40	40	40	<	40	320	640	<	80
A/Rheinland-Pfalz/34/2019		2019-03-01	C1/SIAT1	80	40	40	40	160	40	<	<	160	40
A/Berlin/48/2019		2019-03-04	C1/SIAT1	80	40	40	40	<	40	320	640	<	80
A/Baden-Wurttemberg/132/2019		2019-03-06	C1/SIAT1	80	40	40	80	160	80	<	<	160	40
A/Saarland/15/2019		2019-03-11	C2/SIAT1	<	<	<	40	<	<	320	320	<	80
A/Bremen/17/2019		2019-03-11	C1/SIAT1	40	<	40	80	<	40	320	320	<	80
A/Nordrhein-Westfalen/82/2019		2019-03-11	C1/SIAT1	40	40	40	40	<	40	320	640	<	80
A/Nordrhein-Westfalen/97/2019		2019-03-14	C1/SIAT1	40	40	40	40	<	40	320	320	<	80
A/Nordrhein-Westfalen/89/2019		2019-03-15	C1/SIAT1	80	40	80	80	<	80	320	640	<	160
A/Hessen/56/2019		2019-03-20	C1/SIAT1	160	40	40	40	160	40	<	<	160	40
A/Niedersachsen/151/2019		2019-03-25	C1/SIAT1	40	<	40	40	<	40	320	320	<	80
A/Bremen/20/2019		2019-03-25	C1/SIAT1	40	<	40	40	<	40	320	320	<	80
A/Nordrhein-Westfalen/101/2019		2019-03-25	C1/SIAT1	40	40	40	40	<	40	320	320	<	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; ND = Not Done

Sequences in phylogenetic trees

Table 4-6. Antigenic analysis of A(H3N2) viruses by HI – Summary all test viruses

Viruses	Other information	Haemagglutination inhibition titre												
		Post-infection ferret antisera												
		A/Stock	A/HK	A/Bretagne	A/Singapore	A/La Rioja	A/Swit	A/Eng	A/Neth	A/Neth	A/Norway	A/Kansas	A/Kansas
		6/14	5738/14	1413/17	0019/16	2202/18	8060/17	538/18	10260/18	10260/18	3275/18	14/17	14/17
	Passage history	SIAT	MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	Egg	SIAT	SIAT	Egg	SIAT
	Ferret number	F14/14[-1]	St J F60/17[-1]	F01/18[-1]	F46/17[-1]	F26/18[-1]	F27/18[-1]	F31/18[-1]	F02/19[-1]	F07/19[-1]	F03/19[-1]	F11/19[-1]	CDC F2019-083[-1]
	Genetic group	3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.2a1b	3C.2a1b	3C.3a	3C.3a
REFERENCE VIRUSES													
A/Stockholm/6/2014	3C.3a	160	160	80	160	80	160	160	<	40	80	160	ND
A/Hong Kong/5738/2014	3C.2a	160	160	160	160	80	160	160	40	80	160	160	80
A/Bretagne/1413/2017	3C.2a2	160	320	1280	320	160	1280	320	40	80	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	<	80	40	640	160	160	80	40	40	40	40	<
A/Switzerland/8060/2017 clone 57	3C.2a2	<	160	640	320	80	640	80	40	80	40	80	40
A/England/538/2018	3C.3a	40	<	40	40	40	40	320	<	40	<	320	80
A/Netherlands/10260/2018	3C.2a1b	<	160	80	80	320	80	80	1280	320	160	ND	ND
A/Kansas/14/2017	3C.3a	<	<	<	80	<	<	320	ND	ND	<	1280	80
A/Kansas/14/2017	3C.3a	ND	40	40	40	<	40	320	ND	ND	<	160	80
TEST VIRUSES													
Number of viruses tested*		39	65	65	65	65*	65	65	13	13*	65*	52	13
No with titre reduction ≥2-fold		15	27			12		50		2	10	1	9
%		*38.5*	*41.5*			*18.5*		*76.9*		*15.4*	*15.4*	*2.0*	*69.2*
No with titre reduction =4-fold		16	33		5		4	1				23	4
%		*41.0*	*50.8*		*7.7*		*6.2*	*1.6*				*44.2*	*30.8*
No with titre reduction ≥8-fold		8	5	65	60		61	14	13			28	
%		*20.5*	*7.7*	*100*	*92.3*		*93.8*	*21.5*	*100*			*53.8*	
					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

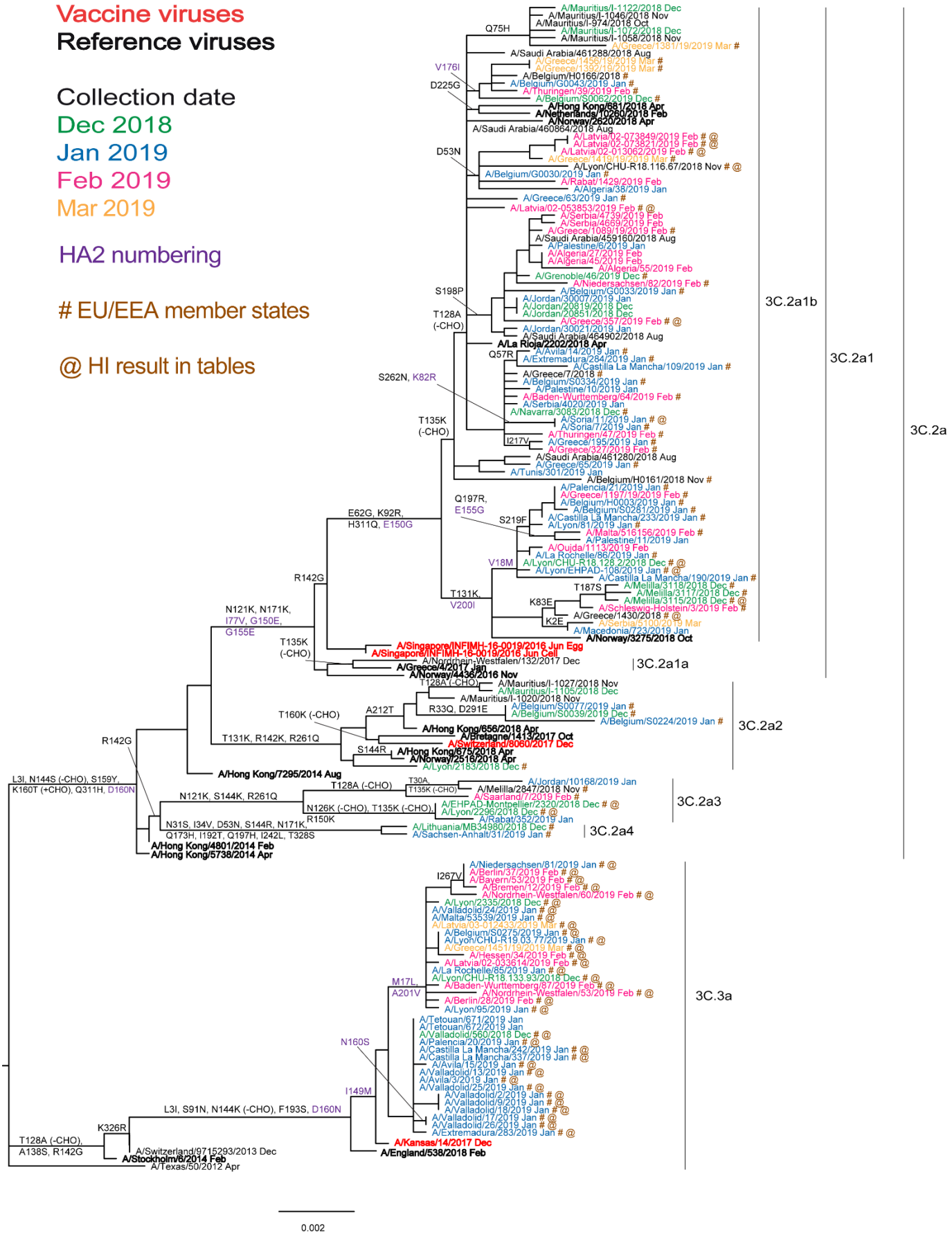
Reference virus results are taken from individual tables as examples. Summaries for each antiserum are based on fold-reductions observed on the days that HI assays were performed.

Table 4-7. Antigenic analysis of A(H3N2) viruses by HI – Summary by test virus genetic group

Viruses	Other information	Haemagglutination inhibition titre												
		Post-infection ferret antisera												
	Passage history	A/Stock 6/14 SIAT	A/HK 5738/14 MDCK	A/Bretagne 1413/17 SIAT	A/Singapore 0019/16 Egg 10^{-4}	A/La Rioja 2202/18 SIAT	A/Swit 8060/17 Egg	A/Eng 538/18 SIAT	A/Neth 10260/18 Egg	A/Neth 10260/18 SIAT	A/Norway 3275/18 SIAT	A/Kansas 14/17 Egg	A/Kansas 14/17 SIAT
	Ferret number	F14/14[*1]	St J F60/17[*1]	F01/18[*1]	F46/17[*1]	F26/18[*1]	F27/18[*1]	F31/18[*1]	F02/19[*1]	F07/19[*1]	F03/19[*1]	F11/19[*1]	CDC F2019-083[*1]
	Genetic group	3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.2a1b	3C.2a1b	3C.3a	3C.3a
TEST VIRUSES													
Total number tested		35	48	48	48	48*	48	48	11	11*	48*	37	13
Number tested	3C.2a1b	5	11	11	11	11	11	11	4	4	11	7	6
No with titre reduction ≤2-fold		1	3			5		1		1	6	1	2
%		*20.0*	*27.3*			*45.5*		*9.1*		*25.0*	*54.5*	*14.3*	*33.3*
No with titre reduction =4-fold		3	7				1						4
%		*60.0*	*63.6*				*9.1*						*66.7*
No with titre reduction ≥8-fold		1	1	11	11		10	10	4			6	
%		*20.0*	*9.1*	*100*	*100*		*90.9*	*90.9*	*100*			*85.7*	
Number tested	3C.3a	28	35	35	35	35	35	35	5	5	35	30	7
No with titre reduction ≤2-fold		11	16					35					7
%		*39.3*	*45.7*					*100*					*100*
No with titre reduction =4-fold		11	16		2							20	
%		*39.3*	*45.7*		*5.7*							*66.7*	
No with titre reduction ≥8-fold		6	3	35	33		35		5			10	
%		*21.4*	*9*	*100*	*94.3*		*100*		*100*			*33.3*	
Number tested	3C.2a3	2	2	2	2	2	2	2	2	2	2		
No with titre reduction ≤2-fold		2	2			2		2		1			
No with titre reduction =4-fold					2		2						
No with titre reduction ≥8-fold				2					2				
		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

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



Influenza B virus analyses

Influenza B viruses represented only 2.9% of the samples received with collection dates after 31 August 2018 and were received from NICs in 11 countries: Croatia, Denmark, France, Greece, Iceland, Ireland, Luxembourg, Norway, Portugal, Slovenia and the United Kingdom (Table 1). Of the small number received 18 were B/Yamagata-lineage and nine were B/Victoria-lineage.

Influenza B/Victoria-lineage

No B/Victoria lineage viruses from EU/EEA countries have been tested by HI since the March 2019 characterisation report.
A relatively small number (689 in total of which 593 were full length, as of 8 May 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 28 (19 full length) from countries in Europe. All recent viruses, those with collection dates from 15 January to 8 May 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 geographically dispersed group seen in Europe, the Americas, Asia, and Oceania 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 **K52N** and **E198G** (within the **197-199** glycosylation site) or **G133R**. The great majority of recently collected viruses fall equally among these two deletion groups with the vast majority of viruses having been collected in the USA and Asia, with only three from Europe. The three viruses detected in EU/EEA countries all fall in the 1A(Δ3) West African subgroup (Figure 3).

It was noted in the September 2018 characterisation report [14], 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, 3] and 2019 southern hemisphere [4] seasons.

The vast majority of viruses have been collected in the USA and Asia, with only three from Europe.

Influenza B/Yamagata-lineage

HI results for the two B/Yamagata-lineage viruses characterised since the March 2019 report are shown in Table 5, sorted by date of collection. The antiserum raised against egg-propagated B/Phuket/3073/2013, recommended for inclusion in quadrivalent vaccines for the 2018–2019 and 2019–20 [1, 2, 3] northern hemisphere and the 2019 [4] southern hemisphere seasons, recognised both test viruses at titres within twofold of the titre of the antiserum with the homologous virus. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 recognised both test viruses poorly, at titres eightfold reduced compared to the homologous titre. Antisera raised against two other egg-propagated clade 3 viruses, B/Wisconsin/1/2010 (a former vaccine virus) and B/Stockholm/12/2011, recognised both test viruses at titres within twofold of the respective homologous titres, as was the case for antisera raised against two recently circulating clade 3 cell culture-propagated viruses, B/Mauritius/1791/2017 and B/Mauritius/I-762/2018.

Antisera raised against a cell culture-propagated clade 2 virus, B/Estonia/55669/2011, recognised both test viruses at titres within fourfold of the homologous titre, while antisera raised against cell culture- and egg-propagated cultivars of a previous clade 2 vaccine virus, B/Massachusetts/02/2012, gave similar reactivity profiles recognising one each of the two test viruses at titres within fourfold (B/Greece/1244/2019) and eightfold (B/Greece/1037/2019) of the respective homologous titres.

A smaller number (549 in total of which 499 were full length, as of 8 May) of B/Yamagata-lineage HA sequences for viruses collected from 1 September 2018 have been deposited in the GISAID EpiFlu database; the great majority of these have been from China and the USA, with only 34 (24 full length) from countries in Europe. Both test viruses carried an HA gene in genetic clade 3 (Table 5), the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade, as is the case for all viruses collected in the 2017–2018 season and since. Figure 4 shows a phylogenetic analysis of the HA genes of recently circulating B/Yamagata-lineage viruses, those with collection dates from 1 January to 8 May 2019 that have data deposited in GISAID, with just six being from EU/EEA countries. HA sequences of all viruses with collection dates after 31 August 2018 deposited in the EpiFlu database of GISAID, including those from European countries, fall 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, 3] northern hemisphere and the 2019 [4] southern hemisphere seasons.

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

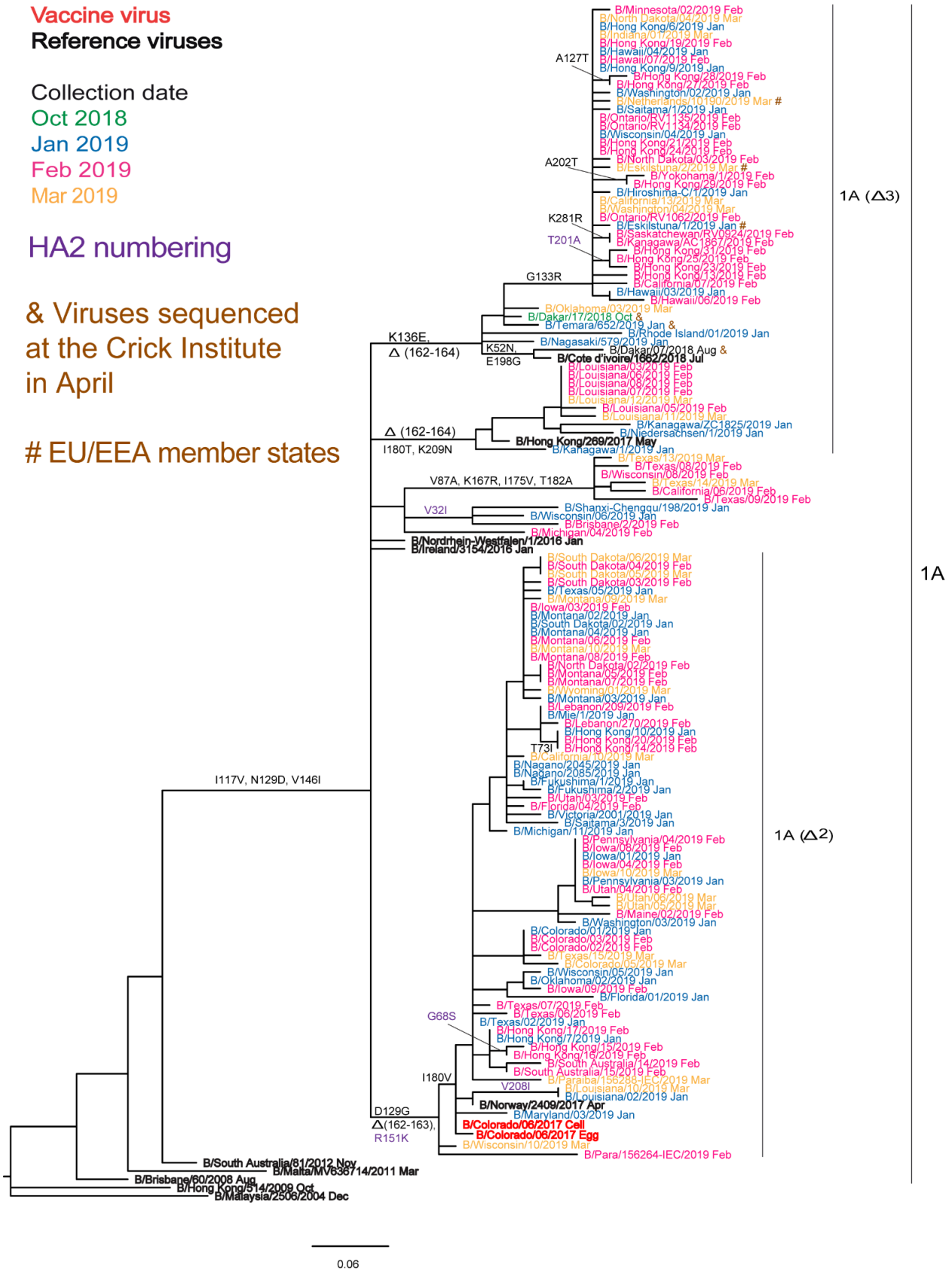


Table 5. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

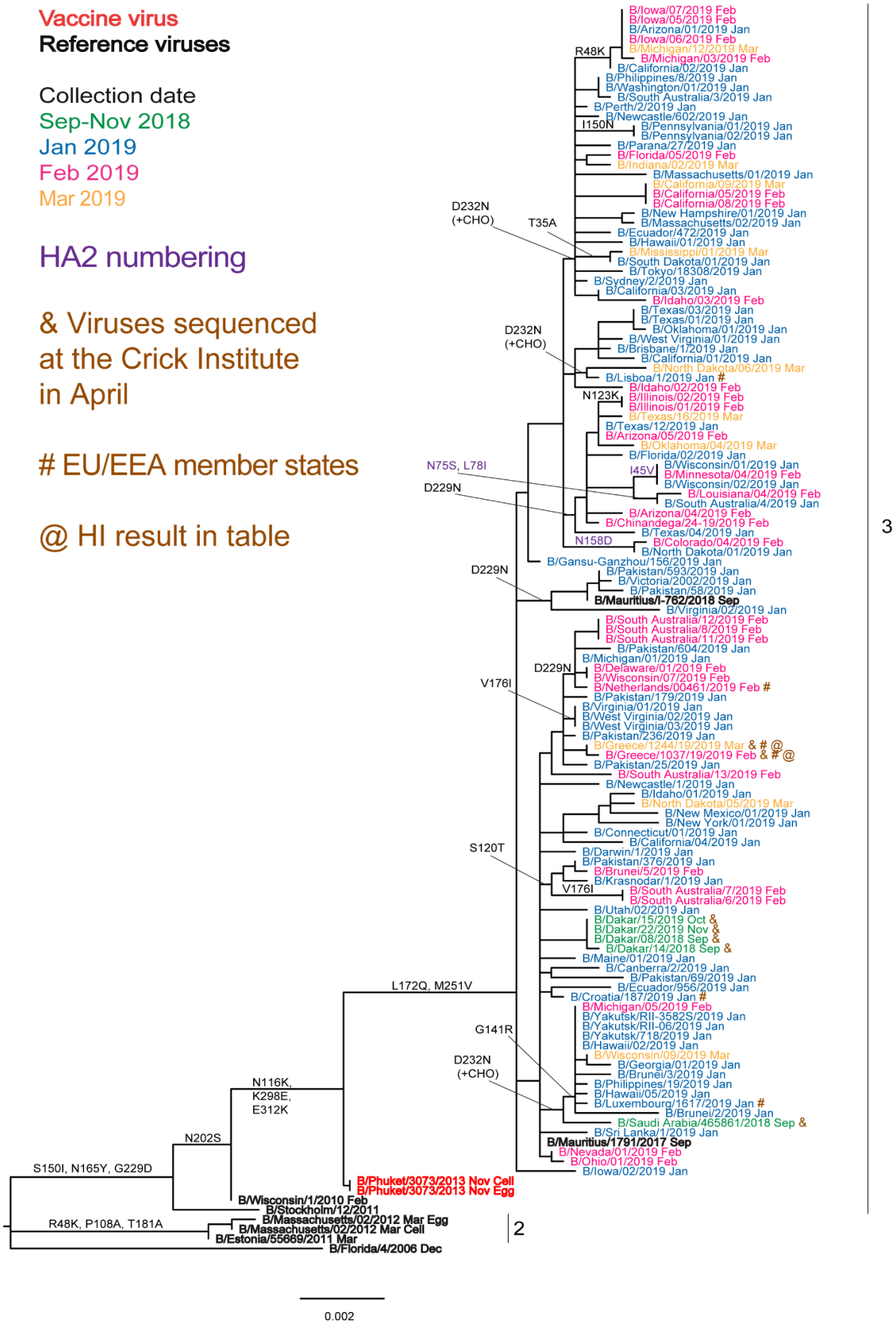
Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					B/Phuket 3073/13	B/Estonia 55669/11	B/Mass 02/12	B/Mass 02/12	B/Wis 1/10	B/Stock 12/11	B/Phuket 3073/13	B/Phuket 3073/13	B/Maur 1791/17	B/Maur I-762/18
		Passage history			Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	MDCK	MDCK
		Ferret number			SH614[*1,4]	F39/17[*2]	F10/16[*2]	F06/17[*2]	F36/15[*2]	F05/17[*2]	F27/15[*2]	F25/17[*2]	F04/18[*2]	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	80	160	20	20	<	40	<	80
B/Massachusetts/02/2012		2	2012-03-13	MDCK1/C2/MDCK4	2560	160	160	320	80	80	20	160	40	320
B/Massachusetts/02/2012		2	2012-03-13	E3/E4	640	20	20	320	20	40	<	80	<	20
B/Wisconsin/1/2010		3	2010-02-20	E3/E2	1280	<	10	160	40	80	<	160	10	40
B/Stockholm/12/2011		3	2011-03-28	E4/E1	640	<	10	80	20	40	<	80	<	40
B/Phuket/3073/2013		3	2013-11-21	MDCK2/MDCK3	2560	160	320	320	80	160	80	320	80	640
B/Phuket/3073/2013		3	2013-11-21	E4/E3	640	<	10	80	20	40	<	80	10	40
B/Mauritius/1791/2017		3	2017-09-20	MDCK1/MDCK4	1280	10	20	80	20	40	10	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/Greece/1037/19/2019		3	2019-02-20	MDCK1	1280	20	20	40	20	40	10	40	20	80
B/Greece/1244/19/2019		3	2019-03-01	MDCK1	1280	20	40	80	20	40	10	80	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 18/2019, 3772 viruses had been characterised genetically and ascribed to a genetic clade:

- 1 800 A(H1N1)pdm09 were subclade 6B.1, represented by the vaccine virus A/Michigan/45/2015, with a further 3 attributed to a subgroup not listed.
- 1 917 were A(H3N2) viruses, with 1272 being subgroup 3C.2a1b represented by A/Alsace/1746/2018, 68 being subclade 3C.2a2 represented by A/Switzerland/8060/2017, 33 being subclade 3C.2a3 represented by A/Cote d'Ivoire/544/2016, 466 being clade 3C.3a represented by A/England/538/2018, 57 being subclade 3C.2a1 represented by A/Singapore/16-0019/2016, 5 being clade 3C.2a represented by A/Hong Kong/4801/2014, 9 being subgroup 3C.2a1a represented by A/Greece/4/2017 and 7 were attributed to a subgroup not listed in current TESSy reporting categories.
- 27 were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013.
- 25 were B/Victoria-lineage viruses, with 5 being clade 1A represented by B/Brisbane/60/2008, 5 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 18/2019, 1495 A(H1N1)pdm09, 1004 A(H3N2) and 29 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 (confirmed phenotypically for 3), and 1 type B virus showed evidence of reduced inhibition by oseltamivir and zanamivir.

At the WIC for this season, 623 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 331 A(H1N1)pdm09, 272 A(H3N2), 7 B/Victoria-lineage and 13 B/Yamagata-lineage. All but one virus showed normal inhibition by the two neuraminidase inhibitors. B/Norway/3241/2018 (Victoria-lineage) showed reduced inhibition by the inhibitors and the NA gene encoded D197N amino acid substitution.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [5] reported that the China Health and Family Planning Commission notified the WHO of three cases of human infection with influenza A(H7N9). A description of the characteristics of H7N9 viruses can be found on the WHO website [6]. Increased numbers of cases 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 [7]. WHO posted an analysis of information on A(H7N9) viruses on 10 February 2017 [8]; a summary and assessment of influenza viruses at the human-animal interface on 9 April 2019 contains a report of one new case of human infection detected in March 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 but for one report of an outbreak in domesticated birds in Liaoning Province [9]. The previous human case was detected early in February 2018 [10]. 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 [11].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 9 April 2019, indicating that various A(H5Nx) subtypes continue to be detected in birds in Africa, Europe and Asia; no new human cases were detected since the last update published on 12 February 2019 [9]. By 9 April 2019, no cases of human infection by A(H5N1) viruses had been reported to WHO in 2018–19 [12]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [13]. 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 [11].

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 7 May 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 EpiFlu database of GISAID. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from the EpiFlu database of GISAID 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.

References

1. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2019–2020 northern hemisphere influenza season. https://www.who.int/influenza/vaccines/virus/recommendations/201902_recommendation.pdf
2. World Health Organization. Addendum to the recommended composition of influenza virus vaccines for use in the 2019–2020 northern hemisphere influenza season. https://www.who.int/influenza/vaccines/virus/recommendations/201902_recommendation_addendum.pdf
3. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2018–2019 northern hemisphere influenza season. Wkly Epidemiol Rec. 2018 Mar 23;93(12):133-152. http://apps.who.int/iris/bitstream/handle/10665/260550/WER9312.pdf
4. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2019 southern hemisphere influenza season. Wkly Epidemiol Rec. 2018 Oct 19;93(42):553-576. http://apps.who.int/iris/bitstream/handle/10665/275475/WER9342.pdf
5. World Health Organization. Emergencies preparedness, response – Human infection with influenza A(H7N9) virus in China. 1 April 2013 [internet]. Geneva: WHO; 2013 [accessed 8 May 2019]. Available from: http://www.who.int/csr/don/2013_04_01/en/index.html
6. World Health Organization. Influenza – Avian influenza A(H7N9) virus [internet]. Geneva: WHO; 2017 [accessed 8 May 2019]. Available from: http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/
7. World Health Organization. Emergencies preparedness, response – Human infection with avian influenza A(H7N9) virus – China [internet]. Geneva: WHO; 2017 [accessed 8 May 2019]. Available from: http://www.who.int/csr/don/26-october-2017-ah7n9-china/en/
8. World Health Organization. Analysis of recent scientific information on avian influenza A(H7N9) virus. 10 February 2017 [internet]. Geneva: WHO, 2017 [accessed 8 May 2019]. Available from: http://www.who.int/influenza/human_animal_interface/avian_influenza/riskassessment_AH7N9_201702/en
9. World Health Organization. Influenza at the human-animal interface. Summary and assessment, 13 February to 9 April 2019 [internet]. Geneva: WHO, 2019 [accessed 8 May 2019]. Available from: https://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_09_04_2019.pdf
10. World Health Organization. Influenza at the human–animal interface. Summary and assessment, 26 January to 2 March 2018 [internet]. Geneva: WHO; 2018 [accessed 8 May 2019]. Available from: http://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_02_03_2018.pdf
11. European Centre for Disease Prevention and Control, European Food Safety Authority, European Union Reference Laboratory for Avian influenza. Avian influenza overview, November 2018 – February 2019. Parma and Stockholm: EFSA, ECDC; 2019 [accessed 8 May 2019]. Available from: https://ecdc.europa.eu/en/publications-data/surveillance-report-avian-influenza-overview-november-2018-february-2019
12. World Health Organization. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003–2019. Geneva: WHO; 2019 [accessed 8 May 2019]. Available from: https://www.who.int/influenza/human_animal_interface/2019_04_09_tableH5N1.pdf
13. European Centre for Disease Prevention and Control. Outbreak of highly pathogenic avian influenza A(H5N8) in Europe – 18 November 2016. Stockholm: ECDC; 2016 [accessed 8 May 2019]. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/risk-assessment-avian-influenza-H5N8-europe.pdf
14. 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