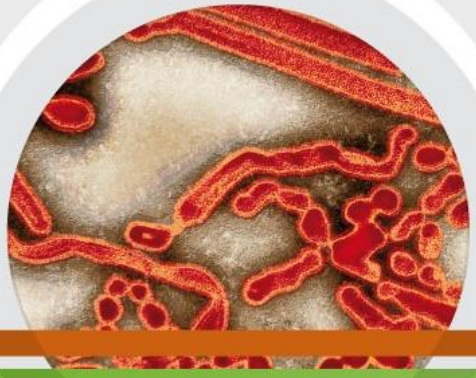

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, February 2019

Summary

This is the fourth report for the 2018–19 influenza season. As of week 8/2019, 147 766 influenza detections across the WHO European Region had been reported. Detections were 99.2% type A viruses, with A(H1N1)pdm09 prevailing over A(H3N2), and 0.8% type B viruses, with 63 (70%) of 90 ascribed to a lineage being B/Yamagata-lineage.

Since the December 2018 characterisation report[1], a further 16 EU/EEA countries have shared influenza-positive specimens with the London WHO CC, the Francis Crick Worldwide Influenza Centre (WIC). A total of 899 virus specimens, with collection dates after 31 August 2018, have been received.

203/204 (99.5%) A(H1N1)pdm09 test viruses characterised antigenically showed good reactivity with antiserum raised against the 2018–2019 vaccine virus, A/Michigan/45/2015 (clade 6B.1), as did the single A(H1N2) reassortant virus. The 210 test viruses with collection dates from week 40/2018 genetically characterised at the WIC have all fallen in a 6B.1 subclade, designated 6B.1A, defined by HA1 amino acid substitutions of S74R, S164T and I295V. The majority of recently circulating viruses also have HA1 S183P substitution, often with additional substitutions in HA1 and/or HA2.

Since the last report only 33 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 177 viruses with collection dates from week 40/2018 genetically characterised at the WIC, 159 were clade 3C.2a (with 14 3C.2a2, six 3C.2a3, five 3C.2a4 and 134 3C.2a1b), and 18 were clade 3C.3a.

All B/Victoria-lineage viruses with recent collection dates 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. Of the five viruses characterised antigenically, two reacted well with antisera raised against the current vaccine virus, B/Colorado/06/2017, which belongs to a subclade defined by deletions of two (Δ162-163, 1A(Δ2)) amino acids in HA1. The other three reacted well with an antiserum raised against a virus of African origin with deletion of three (Δ162-164, 1A(Δ3)) amino acids in HA1. HI analyses with panels

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, December 2018. Stockholm: ECDC; 2018. Available from: https://www.ecdc.europa.eu/sites/portal/files/documents/ECDC%20Influenza%20Characterisation%20Report%20Dec%202018.pdf

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of post-infection ferret antisera have shown these virus groups to be antigenically distinguishable. Δ162-163 viruses spread globally, in low numbers, during previous seasons while Δ162-164 viruses of the African subgroup have been detected outside West Africa in the course of the present season. Of six viruses characterised genetically, two have been Δ162-163 and three Δ162-164 of the African subgroup.

All B/Yamagata-lineage viruses with recent collection dates, including the seven characterised here, 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. HI analyses with post-infection ferret antisera raised against B/Phuket/3073/2013 have shown such viruses, including the seven characterised here, to be antigenically similar to the 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 40/2018–8/2019). Since week 1/2019, the cumulative number of detections has increased from 18 049 to 147 766, with type A (99.2%) predominating over type B (0.8%) 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 = 56076) and the type B viruses ascribed to a lineage (n = 90), A(H1N1)pdm09 (n = 35009) have continued to prevail over A(H3N2) (n = 21067) viruses and 63 of 90 B viruses have been B/Yamagata-lineage; these relative proportions have increased in favour of A(H3N2) and B/Yamagata-lineage viruses compared to the summary in the December 2018 characterisation report[1]. Overall, the ratio of type A to type B detections is dramatically increased compared with the 2017–18 season (0.8:1 to 124:1), and of the influenza A viruses that have been subtyped, an increase in the proportion of A(H1N1)pdm09 has been seen (62.4% 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 40/2018–8/2019)

	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	**16794**	**129790**	**146584**	**99.2**	**124:1**	**106003**	**44.1**	**0.8:1**
A(H1N1)pdm09	7454	27555	35009	62.4		23121	50.6	
A(H3N2)	5358	15709	21067	37.6	0.6:1	22568	49.4	1:1
A not subtyped	3982	86526	90508			60314		
Influenza B	**156**	**1026**	**1182**	**0.8**		**134618**	**55.9**	
Victoria lineage	8	19	27	30.0		301	1.9	
Yamagata lineage	44	19	63	70.0	2.3:1	15701	98.1	52.2:1
Lineage not ascribed	104	988	1092			118616		
Total detections (total tested)	**16950 (41191)**	**130816 (535831)**	**147766 (577022)**			**240621 (903182)**		

*** Percentages are shown for total detections (types A & B [in bold type], and for viruses ascribed to influenza A subtype and influenza B lineage). Ratios are given for type A:B [in bold type], A(H3N2):A(H1N1)pdm09 and Yamagata:Victoria lineages.**

Since week 40/2018, 42 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 899 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, 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		H1N1pdm09		H3N2			B		B Victoria lineage		B Yamagata lineage	
		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]	Number received	Number propagated[1]
2018														
SEPTEMBER														
France	7					6	3	3					1	1
Spain	1			1	1									
Sweden	1			1	in process									
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	in process						1	in process
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	7	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	in process	2	in process							
Bulgaria	1			1	0									
Croatia	1			1	in process									
Czech Republic	1			1	1									
Denmark	12			8	8	3	0	3			1	1		
Estonia	3			3	in process									
Finland	4			2	2	2	0	2						
France	17			10	10	7	in process							
Germany	8			4	in process	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	in process	12	1	10						
Portugal	1												1	0
Spain	8			2	in process	6	in process							
Sweden	1			1	in process									
United Kingdom	14			6	in process	6	2	1			1	0	1	1
DECEMBER														
Austria	1					1	0	1						
Belgium	6			2	in process	4	in process							
Bulgaria	9			5	in process	4	0	4						
Croatia	8			6	in process	2	0	1						
Cyprus	3			3	1									
Denmark	7			5	5	2	0	2						
Estonia	18	1	0	16	in process	1	0							
France	33			17	in process	14	in process				1	1	1	in process
Germany	11			5	in process	6	0	6						
Greece	11			8	in process	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	in process							
Norway	15			6	in process	7	in process				2	in process		
Poland	1			1	0									
Portugal	18			8	8	9	0	9					1	1
Romania	12			2	in process	10	1	9						
Slovenia	3			1	1						2	2		
Spain	28			15	in process	13	in process							
Sweden	11			7	in process	4	3	1						
United Kingdom	8			5	in process	3	1							
2019														
JANUARY														
Belgium	47			8	in process	39	in process							
Bulgaria	8			7	5	1	0	1						
Croatia	2												2	1
Cyprus	17			17	in process									
France	26			11	in process	15	in process							
Germany	32			15	in process	17	in process							
Greece	27			19	in process	8	in process							
Hungary	2					2	2							
Italy	4			3	3	1	0	1						
Lithuania	1			1	1									
Luxembourg	25			10	in process	14	in process						1	1
Malta	42			24	in process	18	in process							
Netherlands	12			8	8	4	2	2						
Norway	19			10	in process	7	in process						2	in process
Poland	6			6	3									
Portugal	5			1	1	4	3	1						
Romania	13			11	in process	2	1	1						
Slovenia	11			8	8	3	0	3						
Spain	73			30	in process	43	in process							
United Kingdom	38	3	0	31	in process	4	in process							
FEBRUARY														
Germany	3			2	in process	1	0	1						
Greece	7			5	in process	2	in process							
Malta	8			5	in process	3	in process							
29 Countries	899	6	0	474	126	396	35	106	0	0	7	4	16	8
					52.7%		44.0%					0.8%		1.8%
					97.4%							2.6%		

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

1 virus is H1N2

As of 2019-03-04

Influenza A(H1N1)pdm09 virus analyses

Tables 3-1 to 3-7 show the results of haemagglutination inhibition (HI) assays of A(H1N1)pdm09 viruses, against a panel of post-infection ferret antisera, carried out since the December 2018 characterisation report. 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 is shown in Table 3-8 and a summary for viruses sorted by genetic group is shown in Table 3-9.

The vast majority of A(H1N1)pdm09 test viruses, 203 of 204 (99.5%), were antigenically indistinguishable from the egg-propagated vaccine virus for the northern hemisphere 2018–19 influenza season, A/Michigan/45/2015 [2], as assessed with post-infection ferret antisera, being recognised at titres within twofold of the titre of the antiserum with the homologous virus (Table 3-8). The virus that was recognised poorly, A/Cyprus/F886/2018 (Table 3-5), carried three unusual **HA1** amino acid substitutions of **K130N**, **N156K** and **K211R**.

Antisera raised against eight reference viruses (A/Bayern/69/2009, A/Astrakhan/1/2011, A/Hong Kong/5659/2012, A/Slovenia/2903/2015, A/Paris/1447/2017, A/Switzerland/3330/2017, A/Norway/3433/2018 and A/Ireland/84630/2018) recognised ≥85% 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 3-8). The antiserum raised against A/Switzerland/2656/2017 recognised 95% of test viruses at titres within fourfold of the titre of the antiserum with the homologous virus and 74% within twofold. The antisera raised against egg-propagated A/California/7/2009 and cell culture-propagated A/Lviv/N6/2009 recognised 72% and 14%, respectively, of test viruses at titres within twofold of the homologous titres, and 88% and 56%, respectively, 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**. The seasonal A(H1N2) reassortant virus recovered in Sweden, A/Ystad/1/2018 (Table 3-4), reacted at titres equivalent to or better than the respective homologous titres with all antisera in the panel, with the exception of that raised against A/Lviv/N6/2009.

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 have remained antigenically similar to A/Michigan/45/2015 as shown in the December 2018 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 sequenced at the Francis Crick Institute, with collection dates since the start of the 2018–19 influenza season, and other representative viruses. 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 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 3-9 shows that test viruses from EU/EEA countries in subclade 6B.1A and viruses in each of the genetic groups 183P-1, -2, -4, -5, -6 and -7 show similar patterns of recognition by the panel of post-infection ferret antisera. Generally, test viruses showed good reactivity, ≥80% reacting within twofold of respective homologous titres, with all but two of the antisera (those raised against A/California/7/2009 and A/Lviv/N6/2009). Nevertheless, 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	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
				A/Mich 45/15 Egg NIB F42/16^{-1}	A/Cal 7/09 Egg F07/16^{-1}	A/Bayern 69/09 MDCK F09/15^{-1}	A/Lviv N6/09 MDCK F14/13^{-1}	A/Astrak 1/11 MDCK F22/13^{-1}	A/HK 5659/12 MDCK F17/15^{-1}	A/Slov 2903/15 Egg F02/16^{-1}	A/Paris 1447/17 MDCK F03/18^{-2}	A/Swit 2656/17 Egg F20/18^{-1}	A/Swit 3330/17 Egg F23/18^{-1}
Passage history														
Ferret number														
Genetic group				6B.1				5	6A	6B.1	6B.1A	6B.1A	6B.1A5	
REFERENCE VIRUSES														
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	320	320	640	640	1280	2560	640	320	
A/California/7/2009	clone 38-32		2009-04-09	E3/E5	1280	640	640	640	1280	1280	2560	1280	640	
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	320	160	<	<	40	160	40	40	
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	1280	640	40	80	160	640	320	160	
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK7	640	640	320	320	640	640	2560	320	320	
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	160	80	160	640	640	640	160	160	
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	320	640	640	1280	2560	640	320	
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	160	320	640	1280	2560	640	320	
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	640	320	320	640	640	1280	2560	640	320	
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	160	160	320	320	1280	320	320	
TEST VIRUSES														
A/England/595/2018		6B.1A	2018-10-20	SIAT1/MDCK1	320	320	80	320	320	320	640	320	160	
A/Caen/2372/2018		6B.1A	2018-10-24	MDCK1/MDCK1	640	320	160	320	320	1280	2560	640	320	
A/England/603/2018		6B.1A	2018-11-05	MDCK1/MDCK1	640	320	160	320	640	1280	1280	640	320	
A/England/607/2018		6B.1A	2018-11-14	SIAT1/MDCK1	320	320	80	320	320	640	1280	640	160	
A/England/606/2018		6B.1A	2018-11-14	MDCK1/MDCK1	640	320	160	320	640	1280	1280	640	320	
A/Iceland/24352/2018		6B.1A	2018-11-27	MDCK1	640	320	80	160	320	640	1280	640	160	
A/Iceland/24861/2018		6B.1A	2018-12-03	MDCK1	320	320	80	160	320	640	1280	320	320	
A/Iceland/25090/2018		6B.1A	2018-12-06	MDCK1	640	320	160	320	640	1280	2560	640	320	
A/Estonia/118411/2018		6B.1A	2018-12-28	SIAT1	640	320	160	320	640	1280	2560	640	320	
A/Estonia/118399/2018		6B.1A	2018-12-28	SIAT1	640	640	160	320	640	1280	2560	1280	320	
A/Estonia/118387/2018		6B.1A	2018-12-28	SIAT1	640	320	160	160	320	1280	2560	640	320	
A/Paris/2313/2018		6B.1A5	2018-10-04	MDCK1/MDCK1	640	320	160	160	320	640	1280	320	160	
A/England/608/2018		6B.1A5	2018-11-13	SIAT1/MDCK1	320	320	160	160	320	640	1280	320	320	
A/Czech Republic/2018/2018		6B.1A5	2018-11-14	MDCK3/MDCK1	640	160	320	160	320	640	1280	320	320	
A/Baden-Wurttemberg/162/2018		6B.1A5	2018-11-20	C1/MDCK1	640	320	160	160	640	640	1280	320	320	
A/Thuringen/61/2018		6B.1A5	2018-11-21	C1/MDCK1	320	320	160	320	320	640	1280	320	320	
A/Norway/3594-2/2018		6B.1A5	2018-11-23	Px/MDCK1	320	160	160	160	320	640	1280	160	160	
A/Iceland/111/2018		6B.1A5	2018-11-27	MDCK1/MDCK1	320	160	80	80	320	640	640	160	160	
A/Picardie/2488/2018		6B.1A5	2018-11-27	MDCK1/MDCK1	320	160	80	160	160	320	640	160	160	
A/Austria/1108922/2018		6B.1A5	2018-11-29	SIAT1/MDCK1	1280	320	320	320	640	1280	2560	640	320	
A/Norway/3750/2018		6B.1A5	2018-11-30	MDCK1	640	320	320	320	640	1280	2560	640	320	
A/Iceland/24775/2018		6B.1A5	2018-12-01	MDCK1	640	640	320	320	640	1280	2560	640	320	
A/Norway/3681/2018		6B.1A5	2018-12-04	MDCK1	320	320	160	160	320	640	1280	320	320	
A/Norway/3743/2018		6B.1A5	2018-12-05	MDCK1	640	160	160	160	320	640	1280	160	160	
A/Estonia/118397/2018		6B.1A5	2018-12-28	SIAT1	320	160	160	160	160	640	1280	160	160	
A/Latvia/10-064408/2018		6B.1A7	2018-10-23	MDCK2/MDCK1	320	160	160	160	320	640	1280	320	160	
A/Mecklenburg-Vorpommern/4/2018		6B.1A7	2018-11-01	C1/MDCK1	640	320	160	320	640	1280	2560	640	320	
A/Paris/2406/2018		6B.1A7	2018-11-09	MDCK3/MDCK1	320	160	80	160	320	640	1280	320	160	
A/England/605/2018		6B.1A7	2018-11-12	SIAT1/MDCK1	640	320	320	320	640	1280	2560	640	320	
A/Picardie/2549/2018		6B.1A7	2018-12-04	MDCK1/MDCK1	640	320	320	320	640	1280	2560	640	640	
A/Latvia/12-013993/2018		6B.1A7	2018-12-04	MDCK1/MDCK1	640	320	160	320	640	1280	2560	640	320	
A/Latvia/12-014030/2018		6B.1A7	2018-12-05	MDCK1/MDCK1	640	320	160	320	640	1280	2560	640	320	
A/Latvia/12-013970/2018		6B.1A7	2018-12-05	MDCK1/MDCK1	640	320	160	320	640	1280	1280	640	320	
A/Latvia/12-027178/2018		6B.1A7	2018-12-11	MDCKx/MDCK1	320	160	80	160	160	640	1280	320	160	
A/Czech Republic/1927/2018		6B.1A1	2018-10-13	MDCK4/MDCK1	640	320	160	160	640	1280	2560	320	160	
A/Czech Republic/1928/2018		6B.1A1	2018-10-15	MDCK4/MDCK1	640	160	160	160	320	640	1280	320	160	
A/Iceland/23365/2018	A261S	6B.1A1	2018-11-13	MDCK1	320	80	80	80	160	320	640	160	80	
A/Dijon/2407/2018		6B.1A2	2018-11-07	MDCK1/MDCK1	640	640	320	320	640	1280	2560	640	320	
A/Latvia/12-024461/2018		6B.1A6	2018-12-10	MDCKx/MDCK1	320	160	160	80	160	320	640	160	160	

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

Sequences in phylogenetic trees — Vaccine

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre										
				Post-infection ferret antisera										
			Passage history	A/Mich 45/15 Egg NIB	A/Cal 7/09 Egg	A/Bayern 69/09 MDCK	A/Lviv N6/09 MDCK	A/Astrak 1/11 MDCK	A/HK 5659/12 MDCK	A/Slov 2903/15 Egg	A/Paris 1447/17 MDCK	A/Swit 2656/17 Egg	A/Swit 3330/17 Egg
			Ferret number	F42/16-1	F07/16-1	F09/15-1	F14/13-1	F22/13-1	F17/15-1	F02/16-1	F03/18-2	F20/18-1	F23/18-1
			Genetic group	6B.1				5	6A	6B.1	6B.1A	6B.1A	6B.1A5
REFERENCE VIRUSES													
A/Michigan/45/2015		6B.1	E3/E3	320	320	320	320	320	320	640	1280	320	320
A/California/7/2009	clone 38-32	2015-09-07	E3/E3	320	320	320	640	320	640	640	1280	640	320
A/Bayern/69/2009	G155E	2009-04-09	MDCK5/MDCK1	<	<	320	160	<	<	40	160	40	<
A/Lviv/N6/2009	G155E, D222G	2009-07-01	MDCK4/SIAT1/MDCK3	40	40	640	320	160	40	80	320	160	80
A/Astrakhan/1/2011	5	2009-10-27	MDCK1/MDCK7	320	320	640	320	160	320	640	1280	320	320
A/Hong Kong/5659/2012	6A	2011-02-28	MDCK4/MDCK2	320	160	160	160	160	320	640	1280	160	160
A/Slovenia/2903/2015	6B.1	2012-05-21	E4/E2	320	320	160	160	320	320	640	1280	320	320
A/Paris/1447/2017	6B.1A	2015-10-26	MDCK1/MDCK3	160	160	160	80	160	160	640	1280	160	160
A/Switzerland/2656/2017	6B.1A	2017-10-20	E5/E2	640	640	640	320	640	640	1280	2560	1280	640
A/Switzerland/3330/2017	6B.1A5	2017-12-21	E6/E2	320	160	160	160	160	160	640	1280	320	640
TEST VIRUSES													
A/Estonia/118321/2018		2018-12-20	MDCK1	640	320	320	160	160	320	1280	1280	640	320
A/Estonia/118316/2018		2018-12-20	MDCK1	160	80	80	40	80	80	320	640	160	80
A/Estonia/118371/2018		2018-12-27	MDCK2	320	<	160	80	80	80	320	640	160	160
A/Bulgaria/028/2019		2019-01-07	MDCK1	320	320	160	80	160	320	640	1280	320	320
A/Bulgaria/041/2019		2019-01-08	MDCK1	640	320	320	160	160	320	1280	2560	640	320
A/Lyon/CHU-R18.112.40/2018		2018-11-15	MDCK2/MDCK1	320	160	160	80	80	160	640	1280	160	160
A/Lyon/2119/2018		2018-11-22	MDCK2/MDCK1	640	160	320	160	160	320	640	1280	320	320
A/Ireland/84720/2018	D187X(D/N), S190X(S/R)	2018-11-29	MDCK2/MDCK1	160	40	80	40	40	160	320	640	80	80
A/Clermont-Ferrand/2180/2018		2018-12-03	MDCK2/MDCK1	160	80	80	80	80	160	320	640	80	80
A/Ireland/85958/2018		2018-12-04	MDCK2/MDCK1	640	160	320	320	320	320	1280	2560	640	320
A/Ireland/85950/2018		2018-12-04	MDCK2/MDCK1	640	160	320	160	320	320	1280	1280	320	640
A/Lithuania/MB36587/2018		2018-12-17	MDCK1/MDCK1	640	320	320	320	320	640	1280	2560	640	640
A/Estonia/118306/2018		2018-12-19	MDCK1	640	320	320	160	160	320	640	1280	320	320
A/Estonia/118323/2018		2018-12-20	MDCK1	640	160	160	160	160	160	640	1280	160	160
A/Estonia/118355/2018		2018-12-21	MDCK1	1280	320	640	320	320	640	2560	2560	640	640
A/Bulgaria/043/2019		2019-01-08	MDCK1	320	160	160	160	80	160	640	640	320	160
A/Ireland/84816/2018		2018-11-29	MDCK1/MDCK1	640	160	320	160	160	320	640	1280	320	160
A/Denmark/1848/2018		2018-12-03	MDCK3/MDCK1	320	160	160	80	80	160	640	1280	320	320
A/Denmark/1839/2018		2018-12-03	MDCK3/MDCK1	320	80	160	160	80	160	640	1280	320	320
A/Denmark/1849/2018		2018-12-05	MDCK3/MDCK1	320	80	80	40	80	160	320	640	160	160
A/Denmark/1850/2018		2018-12-06	MDCK3/MDCK1	320	40	160	80	80	160	640	640	320	160
A/Poitiers/2104/2018		2018-11-13	MDCK3/MDCK1	320	80	160	40	80	160	320	1280	160	80
A/Bulgaria/023/2019		2019-01-07	MDCK1	320	160	160	80	160	160	640	1280	320	160
A/Macon/2132/2018		2018-11-27	MDCK2/MDCK1	320	160	160	80	160	160	640	1280	320	160
A/Ireland/84630/2018		2018-11-28	MDCK2/MDCK1	640	320	320	160	320	320	1280	2560	320	320
A/Saint-Etienne/2167/2018		2018-11-28	MDCK2/MDCK1	320	160	160	80	160	160	640	1280	320	320
A/Denmark/1832/2018		2018-11-29	MDCK3/MDCK1	320	<	160	160	80	160	640	1280	320	160
A/Denmark/1841/2018	S106X(S/N), F111X(F/I)	2018-12-03	MDCK3/MDCK1	160	<	80	80	80	80	320	640	160	80

Vaccine

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

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera										
					A/Mich 45/15	A/Cal 7/09	A/Bayern 69/09	A/Lviv N6/09	A/Astrak 1/11	A/HK 5659/12	A/Slov 2903/15	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	NEW A/Norway 3433/18
		Passage history			Egg	Egg	MDCK	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK
		Ferret number			NIB F42/16*1	F07/16*1	F09/15*1	F14/13*1	F22/13*1	F17/15*1	F02/16*1	F03/18*2	F20/18*1	F23/18*1	F04/19*1
		Genetic group			6B.1				5	6A	6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	320	320	160	160	160	320	640	640	640	160	640
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	320	320	320	160	320	320	640	640	320	160	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	<	320	160	<	<	40	160	<	40	160
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	40	80	640	640	40	80	160	640	160	160	640
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK7	160	160	320	320	160	160	320	1280	320	160	1280
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	320	160	80	160	320	640	640	320	160	1280
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	160	320	160	160	160	160	640	640	640	160	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	320	160	160	80	80	160	640	1280	320	160	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E1	640	640	320	320	320	320	1280	2560	640	320	2560
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	160	160	160	160	160	160	320	640	320	320	1280
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK2	320	160	160	80	160	160	640	1280	320	160	1280
TEST VIRUSES															
A/Poland/261/2019		6B.1A	2019-01-02	MDCK2	160	160	160	40	80	160	640	640	320	160	640
A/Bulgaria/032/2019		6B.1A	2019-01-04	MDCK2	160	160	80	40	80	160	320	320	160	160	640
A/Finland/971/2018		6B.1A5	2018-10-31	MDCK1/MDCK1	1280	640	640	320	320	640	1280	2560	1280	640	2560
A/Finland/976/2018		6B.1A5	2018-11-15	MDCK1/MDCK1	320	80	160	160	80	160	640	1280	320	160	1280
A/Finland/977/2018		6B.1A5	2018-11-28	MDCK1/MDCK1	320	160	160	160	160	320	640	640	320	160	2560
A/Linkoping/70/2018		6B.1A5	2018-12-20	MDCK0/MDCK1	160	160	160	80	80	160	320	640	160	160	1280
A/Linkoping/69/2018		6B.1A5	2018-12-21	MDCK0/MDCK1	160	80	80	40	40	80	320	640	160	160	1280
A/Parma/182/2018		6B.1A5	2018-12-24	MDCK1/MDCK1	640	160	160	160	160	320	640	1280	640	160	2560
A/Uppsala/5/2018		6B.1A5	2018-12-25	MDCK0/MDCK1	640	320	320	160	320	320	640	1280	640	320	2560
A/Bretagne/2731/2018		6B.1A5	2018-12-26	MDCK1/MDCK1	640	640	640	320	320	320	1280	1280	640	320	5120
A/Dijon/2783/2018		6B.1A5	2019-01-03	MDCK1/MDCK1	320	80	80	80	80	80	320	640	160	160	1280
A/Nordrhein-Westfalen/1/2019		6B.1A5	2019-01-04	P1/MDCK1	320	160	160	160	160	320	640	1280	320	320	2560
A/Slovenia/69/2019		6B.1A5	2019-01-07	SIATx/MDCK1	320	160	160	80	80	160	640	1280	320	160	1280
A/Bucuresti/239582/2019		6B.1A5	2019-01-07	SIAT1/MDCK1	320	160	160	80	80	160	320	640	160	160	1280
A/Parma/6/2019		6B.1A5	2019-01-07	MDCK1/MDCK1	640	320	320	320	320	320	640	1280	640	320	2560
A/Bremen/1/2019		6B.1A5	2019-01-07	P1/MDCK1	320	160	160	80	80	160	640	640	160	160	1280
A/Arges/239662/2019		6B.1A5	2019-01-08	SIAT1/MDCK1	320	160	160	160	80	160	640	1280	320	160	2560
A/Bucuresti/239743/2019		6B.1A5	2019-01-10	SIAT1/MDCK1	320	160	160	160	160	160	640	1280	320	320	2560
A/Ireland/86125/2018		6B.1A7	2018-12-05	MDCK2/MDCK2	320	160	160	160	160	160	640	1280	320	160	1280
A/Eskilstuna/6/2018		6B.1A7	2018-12-17	MDCK0/MDCK1	160	160	80	40	80	160	320	320	160	80	640
A/Lithuania/MB37407/2018		6B.1A7	2018-12-22	MDCK1	320	320	160	80	80	160	640	1280	320	160	1280
A/Lorraine/2699/2018		6B.1A7	2018-12-26	MDCK1/MDCK1	640	320	160	80	160	320	1280	1280	640	320	2560
A/Picardie/2725/2018		6B.1A7	2018-12-27	MDCK1/MDCK1	640	320	320	160	320	640	1280	2560	1280	640	2560
A/Lorraine/2721/2018		6B.1A7	2018-12-27	MDCK1/MDCK1	320	160	160	40	80	160	640	640	320	160	1280
A/Franche-Comte/021/2019		6B.1A7	2019-01-02	MDCK1/MDCK1	160	160	80	40	80	80	320	640	160	80	640
A/Bayern/1/2019		6B.1A7	2019-01-03	P1/MDCK1	320	160	80	80	80	160	320	1280	160	160	1280
A/Lithuania/MB357/2019		6B.1A7	2019-01-03	MDCK1	320	160	160	80	160	160	640	1280	320	160	2560
A/Parma/2/2019		6B.1A7	2019-01-04	MDCK1/MDCK1	320	160	160	80	80	160	320	640	160	160	1280
A/Bucuresti/239595/2019		6B.1A7	2019-01-07	SIAT1/MDCK1	320	160	160	80	80	160	640	1280	160	160	1280
A/Slovenia/107/2019		6B.1A7	2019-01-08	SIATx/MDCK1	640	320	320	160	160	320	1280	2560	640	320	2560
A/Slovenia/92/2019		6B.1A7	2019-01-08	MDCKx/MDCK1	320	160	160	80	160	160	640	1280	320	160	1280
A/Slovenia/131/2019		6B.1A7	2019-01-09	SIATx/MDCK1	1280	640	320	320	320	320	1280	2560	640	320	2560
A/Slovenia/125/2019		6B.1A7	2019-01-09	SIATx/MDCK1	640	640	320	160	160	320	1280	2560	640	320	2560
A/Parma/7/2019		6B.1A7	2019-01-09	MDCK1/MDCK1	160	80	80	40	40	80	320	640	160	80	640
A/Lithuania/MB7/2018		6B.1A6	2018-12-31	MDCK1	160	80	80	40	40	80	160	640	160	80	640
A/Poland/50/2019		6B.1A6	2019-01-07	MDCK1	640	320	320	320	320	640	1280	2560	640	640	2560
A/Slovenia/54/2019		6B.1A6	2019-01-07	MDCKx/MDCK1	160	80	80	40	80	80	320	320	160	80	640
A/Poland/57/2019		6B.1A6	2019-01-08	MDCK1	1280	640	320	320	640	640	2560	2560	1280	640	2560

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

Vaccine

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera										
					A/Mich 45/15 Egg NIB F42/16[*1] 6B.1	A/Cal 7/09 Egg F07/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/Lviv N6/09 MDCK F14/13[*1]	A/Astrak 1/11 MDCK F22/13[*1] 5	A/HK 5659/12 MDCK F17/15[*1] 6A	A/Slov 2903/15 Egg F02/16[*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
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	640	320	640	640	1280	2560	1280	320	1280
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	320	320	320	320	320	320	640	1280	640	160	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	<	320	160	<	<	80	160	<	40	320
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	80	1280	1280	80	80	320	640	320	160	1280
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK7	320	320	640	640	320	320	640	2560	640	320	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	320	320	320	160	320	320	640	1280	320	320	1280
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	320	640	320	320	320	320	1280	1280	640	320	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	320	320	160	80	160	160	640	1280	320	160	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	640	640	320	320	320	320	1280	2560	640	640	2560
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	320	320	320	320	320	640	1280	640	640	2560
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK2	320	160	320	160	320	320	640	1280	320	320	2560
TEST VIRUSES															
A/Hungary/7/2019		6B.1A	2018-12-17	Cx/SIAT1	1280	640	640	320	640	640	1280	2560	1280	640	2560
A/Croatia/5354/2018		6B.1A5	2018-12-04	MDCKx/MDCK1	1280	1280	640	640	640	640	2560	5120	1280	640	5120
A/Hungary/6/2019		6B.1A5	2018-12-19	Cx/MDCK1	320	320	320	160	160	320	1280	1280	320	320	2560
A/Greece/2/2019		6B.1A5	2019-01-02	MDCK1/MDCK1	1280	640	1280	640	1280	1280	2560	5120	1280	640	5120
A/Greece/5/2019		6B.1A5	2019-01-03	MDCK1/MDCK1	640	160	320	160	320	320	640	1280	320	320	2560
A/Luxembourg/2482/2019		6B.1A5	2019-01-14	MDCK1	640	160	320	320	320	320	1280	2560	640	320	2560
A/Luxembourg/2180/2019		6B.1A5	2019-01-14	MDCK1	640	320	640	320	320	640	1280	2560	640	640	5120
A/Luxembourg/2489/2019		6B.1A5	2019-01-15	MDCK1	640	320	320	320	320	320	1280	1280	640	320	2560
A/Valladolid/38/2019		6B.1A5	2019-01-16	MDCK1/MDCK1	640	320	320	320	320	320	1280	2560	640	320	2560
A/Croatia/5358/2018		6B.1A7	2018-12-04	MDCKx/MDCK1	1280	1280	640	320	640	640	1280	5120	1280	640	5120
A/Croatia/5562/2018		6B.1A7	2018-12-14	MDCKx/MDCK2	640	320	320	160	320	320	640	1280	640	320	2560
A/Portugal/84/2018		6B.1A7	2018-12-19	SIAT1/MDCK1	1280	640	640	320	640	640	1280	2560	1280	640	5120
A/Portugal/125/2018		6B.1A7	2018-12-24	SIAT1/MDCK1	1280	640	640	160	640	640	1280	2560	1280	640	5120
A/Portugal/90/2018		6B.1A7	2018-12-27	SIAT1/MDCK1	1280	640	320	320	320	640	2560	2560	640	640	2560
A/Portugal/150/2019		6B.1A7	2019-01-08	SIAT1/MDCK1	640	640	640	320	320	640	1280	2560	640	320	2560
A/Valladolid/37/2019		6B.1A7	2019-01-15	MDCK1/MDCK1	1280	640	640	320	640	640	1280	2560	640	640	2560
A/Cyprus/FA17/2019		6B.1A7	2019-01-15	MDCK1	640	320	320	160	320	320	1280	2560	640	320	2560
A/Valladolid/40/2019		6B.1A7	2019-01-16	MDCK1/MDCK1	1280	640	640	320	640	640	2560	2560	1280	320	5120
A/Valladolid/39/2019		6B.1A7	2019-01-16	MDCK1/MDCK1	640	320	320	160	320	320	640	2560	640	320	2560
A/Luxembourg/3119/2019		6B.1A7	2019-01-17	MDCK1	1280	640	640	320	640	640	2560	2560	1280	640	2560
A/Cyprus/F107/2019		6B.1A2	2019-01-14	MDCK1	320	320	320	160	320	320	640	1280	640	320	2560
A/Cyprus/F105/2019		6B.1A2	2019-01-14	MDCK1	320	320	320	160	320	320	640	2560	640	320	2560
A/Netherlands/02307/2018		6B.1A6	2018-11-06	SIAT1/MDCK1	1280	640	320	320	320	640	2560	2560	1280	640	2560
A/Hungary/1/2019		6B.1A6	2018-12-13	Cx/MDCK1	640	320	320	320	320	640	1280	2560	640	320	2560
A/Netherlands/10612/2018		6B.1A6	2018-12-21	MDCK-MIX2/MDCK1	1280	640	320	320	640	640	2560	2560	640	640	5120
A/Ystad/1/2018	H1N2	6B.1A6	2018-12-26	MDCK0/MDCK1	640	640	640	160	640	640	1280	2560	1280	640	2560
A/Hungary/20/2019		6B.1A4	2018-12-17	Cx/MDCK1	320	160	160	160	160	320	640	1280	320	160	2560
A/Netherlands/10605/2018			2018-11-30	MDCK-MIX2/MDCK1	640	160	320	160	320	320	1280	1280	320	320	2560
A/Netherlands/10611/2018			2018-12-19	MDCK-MIX2/MDCK1	640	320	320	320	320	640	1280	2560	640	320	2560

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

1 < = <40; 2 < = <80

Vaccine

Sequences in phylogenetic trees

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				A/Mich 45/15 Egg NIB F42/16[*1] 6B.1	A/Cal 7/09 Egg F07/16[*1]	A/Bayern 69/09 MDCK F09/15[*1]	A/L viv N6/09 MDCK F13/18[*1]	A/Astrak 1/11 MDCK F22/13[*1] 5	A/HK 5659/12 MDCK F17/15[*1] 6A	A/Slov 2903/15 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
	Passage history														
	Ferret number														
	Genetic group														
REFERENCE VIRUSES															
A/Michigan/45/2015	6B.1	2015-09-07	E3/E3	640	640	320	320	320	640	1280	2560	1280	320	1280	
A/California/7/2009	clone 38-32	2009-04-09	E3/E3	320	640	320	320	320	320	640	1280	640	320	1280	
A/Bayern/69/2009	G155E	2009-07-01	MDCK5/MDCK1	40	<	320	320	<	<	40	320	<	40	320	
A/Lviv/N6/2009	G155E, D222G	2009-10-27	MDCK4/SIAT1/MDCK3	80	80	1280	1280	80	80	160	640	320	320	1280	
A/Astrakhan/1/2011	5	2011-02-28	MDCK1/MDCK7	640	640	640	640	320	640	1280	2560	640	640	2560	
A/Hong Kong/5659/2012	6A	2012-05-21	MDCK4/MDCK2	320	160	160	80	160	320	320	640	320	160	1280	
A/Slovenia/2903/2015	6B.1	2015-10-26	E4/E2	640	640	320	320	640	640	1280	2560	1280	640	2560	
A/Paris/1447/2017	clone 37	2017-10-20	MDCK1/MDCK3	640	320	320	80	320	320	1280	2560	640	320	2560	
A/Switzerland/2656/2017	6B.1A	2017-12-21	E5/E3	640	640	640	320	640	640	1280	2560	1280	640	2560	
A/Switzerland/3330/2017	clone 35	2017-12-20	E6/E2	320	640	320	160	320	320	640	2560	1280	640	2560	
A/Norway/3433/2018	6B.1A5	2018-10-30	MDCK3	640	160	160	80	160	160	640	1280	640	320	2560	
TEST VIRUSES															
A/Norway/4114/2018	6B.1A	2018-12-18	MDCK1/MDCK1	1280	1280	1280	320	640	640	2560	5120	2560	1280	5120	
A/Belgium/H0159/2018	6B.1A5	2018-11-02	C1/MDCK1	640	640	640	160	320	320	1280	2560	1280	640	2560	
A/Palermo/325/2018	6B.1A5	2018-11-08	MDCK3/MDCK1	640	640	320	160	320	640	1280	2560	1280	640	2560	
A/Denmark/1823/2018	6B.1A5	2018-11-15	MDCK3/MDCK1	320	160	160	160	160	160	640	1280	320	320	1280	
A/Denmark/1818/2018	6B.1A5	2018-11-22	MDCK3/MDCK1	1280	320	320	160	160	320	1280	2560	640	640	2560	
A/Belgium/G0621/2018	6B.1A5	2018-11-26	C1/MDCK1	640	320	640	320	320	640	1280	2560	640	640	2560	
A/Belgium/S2849/2018	6B.1A5	2018-12-01	C1/MDCK1	640	320	640	320	320	640	1280	2560	640	640	2560	
A/Paris/2627/2018	6B.1A5	2018-12-18	MDCK1/MDCK1	1280	640	640	160	640	640	1280	1280	1280	640	2560	
A/Paris/2693/2018	6B.1A5	2018-12-24	MDCK1/MDCK1	640	320	640	320	320	640	1280	1280	1280	640	2560	
A/Norway/70/2019	6B.1A5	2019-01-08	MDCK1/MDCK1	1280	320	640	320	320	320	1280	2560	640	640	5120	
A/Netherlands/10007/2019	6B.1A5	2019-01-15	MDCK-MIX2/MDCK1	640	160	320	160	160	320	640	1280	640	320	2560	
A/Netherlands/10008/2019	6B.1A5	2019-01-16	MDCK-MIX2/MDCK1	640	320	320	160	160	320	640	2560	640	640	5120	
A/Norway/272/2019	6B.1A5	2019-01-17	MDCK1	1280	640	640	320	640	640	1280	2560	1280	640	5120	
A/Norway/254/2019	6B.1A5	2019-01-17	MDCK1	1280	640	640	320	320	320	1280	2560	1280	640	5120	
A/Netherlands/10010/2019	6B.1A5	2019-01-17	MDCK-MIX1/MDCK1	640	160	320	160	320	320	640	2560	640	640	2560	
A/Denmark/1807/2018	6B.1A7	2018-11-14	MDCK2/MDCK1	320	80	80	<	80	80	320	1280	320	160	640	
A/Palermo/326/2018	6B.1A7	2018-11-16	MDCK3/MDCK1	640	640	320	160	320	640	1280	2560	1280	640	2560	
A/Denmark/1819/2018	6B.1A7	2018-11-23	SIAT1/MDCK3/MDCK1	640	320	320	80	160	320	640	1280	640	320	2560	
A/Denmark/1820/2018	6B.1A7	2018-11-26	SIAT1/MDCK3/MDCK1	320	80	160	40	160	160	640	1280	320	320	1280	
A/Alsace/2651/2018	6B.1A7	2018-12-19	MDCK1/MDCK1	1280	640	640	320	640	640	2560	2560	2560	1280	5120	
A/Belgium/H0004/2019	6B.1A7	2019-01-16	MDCK1	640	640	640	80	320	640	1280	5120	1280	640	5120	
A/Netherlands/10012/2019	6B.1A7	2019-01-17	MDCK-MIX1/MDCK1	1280	640	640	320	640	640	2560	5120	1280	640	5120	
A/Croatia/5357/2018	6B.1A1	2018-12-04	MDCKx/MDCK3	640	80	320	80	160	160	640	1280	640	320	1280	
A/Cyprus/F886/2018	6B.1A2	2018-12-31	MDCK2	40	<	160	80	<	<	<	40	<	<	160	
A/Denmark/1815/2018	6B.1A6	2018-11-21	MDCK3/MDCK1	640	80	320	160	160	160	640	2560	640	640	2560	
A/Denmark/1831/2018	6B.1A6	2018-11-28	MDCK3/MDCK1	320	40	320	80	160	160	640	1280	320	320	1280	
A/Pays de Loire/2779/2018	6B.1A6	2018-12-12	MDCK1/MDCK1	640	320	160	80	160	320	640	1280	640	320	2560	

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

Vaccine

Sequences in phylogenetic trees

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

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
					A/Mich 45/15 Egg NIB 6B.1	A/Cal 7/09 Egg $F07/16^{-1}$	A/Bayern 69/09 MDCK $F09/15^{-1}$	A/Lviv N6/09 MDCK $F13/18^{-1}$	A/Astrak 1/11 MDCK $F22/13^{-1}$ 5	A/HK 5659/12 MDCK $F17/15^{-1}$ IIB 6A	A/Slov 2903/15 Egg $F48/16^{-1}$ 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
REFERENCE VIRUSES															
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	320	320	640	320	1280	1280	640	320	1280
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	640	320	320	320	320	320	640	1280	640	160	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	<	<	320	320	<	<	<	320	40	40	320
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	80	1280	1280	80	80	160	640	160	160	1280
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK7	640	320	640	640	640	320	1280	2560	640	320	2560
A/Hong Kong/5659/2012		6A	2012-05-21	MDCK4/MDCK2	640	320	160	160	320	320	640	1280	320	320	1280
A/Slovenia/2903/2015	clone 37	6B.1	2015-10-26	E4/E2	640	320	320	320	320	320	640	1280	640	320	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	320	160	320	320	640	2560	640	320	2560
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	640	320	640	640	320	320	1280	1280	1280	320	2560
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	320	160	160	160	160	160	320	1280	320	320	1280
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	640	160	160	80	160	160	640	1280	320	160	1280
TEST VIRUSES															
A/Saint-Etienne/1883/2018			2018-08-31	MDCK3/MDCK1	640	320	320	80	320	320	1280	1280	640	320	2560
A/Marseille/1989/2018			2018-10-05	MDCK2/MDCK1	1280	320	320	160	320	320	1280	2560	640	320	2560
A/Ireland/70370/2018			2018-10-07	MDCK2/MDCK1	640	160	160	160	160	160	640	1280	320	160	1280
A/Ireland/78012/2018			2018-11-05	MDCK1/MDCK1	320	160	160	<	160	160	640	1280	320	160	1280
A/Ireland/78268/2018			2018-11-06	MDCK1/MDCK1	640	160	160	320	160	320	640	1280	320	320	2560
A/Lyon/2065/2018			2018-11-08	MDCK3/MDCK1	320	80	320	320	160	160	640	1280	320	320	2560
A/Ireland/80216/2018			2018-11-12	MDCK1/MDCK1	640	320	320	160	320	320	640	1280	640	320	1280
A/Ireland/79897/2018			2018-11-12	MDCK1/MDCK1	640	160	160	80	160	160	640	2560	640	160	2560
A/Lyon/2088/2018			2018-11-12	MDCK2/MDCK1	1280	320	640	320	320	320	1280	2560	640	640	2560
A/Ireland/81752/2018			2018-11-20	MDCK2/MDCK1	640	320	320	320	320	640	1280	2560	640	640	2560
A/Netherlands/10615/2018			2018-12-28	MDCK-MIX2/MDCK1	640	320	320	320	320	320	1280	2560	640	320	2560
A/Netherlands/10614/2018			2018-12-28	MDCK-MIX2/MDCK1	640	320	320	160	320	320	640	2560	640	320	2560
A/Netherlands/10000/2019			2019-01-02	MDCK-MIX2/MDCK1	640	160	160	320	160	160	640	1280	320	160	2560
A/Netherlands/10001/2019			2019-01-07	MDCK-MIX2/MDCK1	640	320	320	160	320	160	1280	2560	640	320	2560
A/Netherlands/10003/2019			2019-01-10	MDCK-MIX2/MDCK1	640	320	320	320	320	320	640	2560	640	320	2560
A/Netherlands/10004/2019			2019-01-11	MDCK-MIX2/MDCK1	640	640	640	640	640	640	1280	2560	640	640	2560

Vaccine

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

Table 3-7. 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											NEW
					A/Mich 45/15 Egg NIB F42/16-1 6B.1	A/Cal 7/09 Egg F07/16-1	A/Bayern 69/09 MDCK F09/15-1	A/Lviv N6/09 MDCK F13/18-1	A/Astrak 1/11 MDCK F22/13-1 5	A/HK 5659/12 MDCK F17/15-1 6A	A/Slov 2903/15 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/Ireland 84630/18 MDCK F08/19-1 6B.1A6
REFERENCE VIRUSES																
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	640	640	320	640	640	1280	2560	1280	320	2560	1280
A/California/7/2009	clone 38-32		2009-04-09	E3/E3	640	640	640	320	640	640	1280	2560	1280	320	2560	1280
A/Bayern/69/2009	G155E		2009-07-01	MDCK5/MDCK1	40	<	320	320	<	<	<	320	40	40	320	40
A/Lviv/N6/2009	G155E, D222G		2009-10-27	MDCK4/SIAT1/MDCK3	80	80	1280	1280	80	160	160	1280	320	160	1280	320
A/Astrakhan/1/2011		5	2011-02-28	MDCK1/MDCK7	640	640	640	640	640	640	640	2560	640	320	2560	1280
A/Hong Kong/5659/2012	clone 37	6A	2012-05-21	MDCK4/MDCK2	640	320	320	160	320	640	1280	2560	640	320	2560	1280
A/Slovenia/2903/2015		6B.1	2015-10-26	E4/E2	640	640	320	320	640	640	1280	2560	1280	320	2560	1280
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	320	160	320	320	1280	2560	1280	640	2560	1280
A/Switzerland/2656/2017		6B.1A	2017-12-21	E5/E3	640	640	320	320	640	640	1280	2560	1280	640	2560	1280
A/Switzerland/3330/2017	clone 35	6B.1A5	2017-12-20	E6/E2	640	320	320	160	320	320	640	1280	640	640	1280	1280
A/Norway/3433/2018		6B.1A5	2018-10-30	MDCK3	320	160	160	80	160	320	640	1280	320	320	2560	640
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK2	640	320	320	160	320	320	640	2560	640	320	2560	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	1280	640	640	640	1280	2560	5120	2560	640	5120	2560
TEST VIRUSES																
A/Baden-Wurttemberg/161/2018			2018-08-16	C1/MDCK1	1280	640	640	320	640	1280	2560	5120	1280	640	5120	2560
A/Valladolid/559/2018			2018-09-24	MDCK1/MDCK1	640	320	160	80	160	320	640	1280	640	320	2560	1280
A/Slovenia/2615/2018			2018-10-15	MDCKx/MDCK1	1280	1280	640	320	640	1280	2560	5120	2560	1280	5120	2560
A/Lisboa/26/2018			2018-10-25	MDCK3/MDCK1	1280	640	640	160	640	320	1280	5120	1280	640	5120	2560
A/Lisboa/25/2018			2018-10-25	MDCK1/MDCK1	640	160	320	160	320	160	640	2560	640	320	2560	1280
A/Ireland/83112/2018			2018-11-22	MDCK2	1280	640	640	320	640	640	2560	5120	1280	640	2560	2560
A/Ireland/82546/2018			2018-11-22	MDCK2	1280	640	640	320	640	640	2560	5120	1280	640	5120	2560
A/Lisboa/29/2018			2018-12-06	MDCK1/MDCK1	1280	320	640	160	640	320	1280	2560	1280	640	2560	1280
A/Lisboa/27/2018			2018-12-08	MDCK1/MDCK1	640	320	320	160	320	160	1280	5120	640	320	2560	1280
A/Lisboa/28/2018			2018-12-10	MDCK2/MDCK1	640	320	160	80	320	160	640	2560	640	320	2560	1280
A/Lisboa/30/2018			2018-12-14	MDCK2/MDCK1	640	320	320	160	320	320	1280	2560	640	320	2560	1280
A/Slovenia/3088/2018			2018-12-26	SIATx/MDCK1	1280	640	640	320	640	640	2560	5120	2560	640	2560	2560
A/Burgos/561/2018			2018-12-28	MDCK1/MDCK1	2560	1280	1280	640	640	1280	2560	5120	2560	1280	5120	5120
A/Portugal/119/2018			2018-12-29	MDCK1	640	320	320	160	320	320	1280	2560	640	320	2560	1280
A/Valladolid/1/2019			2019-01-02	MDCK1/MDCK1	1280	640	640	320	640	1280	2560	5120	2560	1280	5120	5120
A/Slovenia/82/2019			2019-01-03	MDCKx/MDCK1	640	320	320	160	320	320	640	2560	640	320	2560	1280
A/Slovenia/80/2019			2019-01-03	SIATx/MDCK1	640	320	320	160	320	640	640	1280	640	320	2560	1280
A/Valladolid/8/2019			2019-01-08	MDCK1/MDCK1	1280	640	640	320	640	640	1280	5120	1280	640	5120	2560
A/Burgos/6/2019			2019-01-08	MDCK1/MDCK1	1280	640	640	160	320	640	1280	5120	1280	640	5120	2560
A/Valladolid/10/2019			2019-01-09	MDCK1/MDCK1	640	320	320	160	320	320	1280	2560	1280	640	2560	1280
A/Valladolid/16/2019			2019-01-11	MDCK1/MDCK1	1280	640	640	320	640	640	2560	5120	2560	1280	5120	5120
A/Palencia/19/2019			2019-01-12	MDCK1/MDCK1	640	320	320	160	320	320	1280	2560	1280	640	2560	2560
A/Valladolid/22/2019			2019-01-13	MDCK1/MDCK1	1280	640	320	160	640	320	1280	5120	1280	640	5120	2560
A/Burgos/35/2019			2019-01-15	MDCK1/MDCK1	640	320	320	160	640	320	1280	2560	1280	640	2560	2560
A/Avila/33/2019			2019-01-15	MDCK1/MDCK1	640	320	320	320	640	320	1280	2560	640	320	2560	1280
A/Valladolid/29/2019			2019-01-15	MDCK1/MDCK1	1280	640	640	320	640	640	2560	5120	1280	640	5120	2560
A/Valladolid/28/2019			2019-01-15	MDCK1/MDCK1	1280	640	640	320	640	320	1280	2560	1280	640	2560	2560
A/Schleswig-Holstein/3/2018				C2/MDCK1	640	320	320	160	320	320	1280	2560	640	320	2560	1280

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

Sequences in phylogenetic trees

Vaccine

Table 3-8. Antigenic analysis of A(H1N1)pdm09 viruses by HI – Summary all test viruses

Viruses	Other information	Haemagglutination inhibition titre												
		Post-infection ferret antisera												
		A/Mich 45/15	A/Cal 7/09	A/Bayern 69/09	A/Lviv N6/09	A/Astrak 1/11	A/HK 5659/12	A/Slov 2903/15	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18	A/Ireland 84630/18
	Passage history	Egg	Egg	MDCK	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK
		NIB						NIB					
	Ferret number	F42/16*1	F07/16*1	F09/15*1	F13/18*1	F22/13*1	F17/15*1	F48/16*1	F03/18*2	F20/18*1	F23/18*1	F04/19*1	F08/19*1
	Genetic group	6B.1				5	6A	6B.1	6B.1A	6B.1A	6B.1A5	6B.1A5	6B.1A6
REFERENCE VIRUSES													
A/Michigan/45/2015		640	640	640	320	640	640	1280	2560	1280	320	2560	1280
A/California/7/2009	clone 38-32	640	640	640	320	640	640	1280	2560	1280	320	2560	1280
A/Bayern/69/2009	G155E	40	<	320	320	<	<	40	320	40	40	320	40
A/Lviv/N6/2009	G155E, D222G	80	80	1280	1280	80	160	160	1280	320	160	1280	320
A/Astrakhan/1/2011	5	640	640	640	640	640	640	640	2560	640	320	2560	1280
A/Hong Kong/5659/2012	6A	640	320	320	160	320	640	1280	2560	640	320	2560	1280
A/Slovenia/2903/2015	6B.1	640	640	320	320	640	640	1280	2560	1280	320	2560	1280
A/Paris/1447/2017	6B.1A	640	320	320	160	320	320	1280	2560	1280	640	2560	1280
A/Switzerland/2656/2017	6B.1A	640	640	320	320	640	640	1280	2560	1280	640	2560	1280
A/Switzerland/3330/2017	6B.1A5	640	320	320	160	320	320	640	1280	640	640	1280	1280
A/Norway/3433/2018	6B.1A5	320	160	160	80	160	320	640	1280	320	320	2560	640
A/Ireland/84630/2018	6B.1A6	640	320	320	160	320	320	640	2560	640	320	2560	1280
A/Brisbane/02/2018	6B.1A1	1280	1280	640	640	640	1280	2560	5120	2560	640	5120	2560
TEST VIRUSES													
Number of viruses tested*		205	205	205	205	205	205	205	205	205	205	138	28
No with titre reduction ≤2-fold		204	147	189	29	189	186	198	195	151	181	136	28
%		*99.5*	*71.7*	*92.2*	*14.1*	*92.2*	*90.7*	*96.6*	*95.1*	*73.7*	*88.3*	*98.6*	*100.0*
No with titre reduction =4-fold			34	16	85	15	18	6	9	44	18	1	
%			*16.6*	*7.8*	*41.5*	*7.3*	*8.8*	*2.9*	*4.4*	*21.5*	*8.8*	*0.7*	
No with titre reduction ≥8-fold		1	24		91	1	1	1	1	10	6	1	
%		*0.5*	*11.7*		*44.4*	*0.5*	*0.5*	*0.5*	*0.5*	*4.8*	*2.9*	*0.7*	

Vaccine

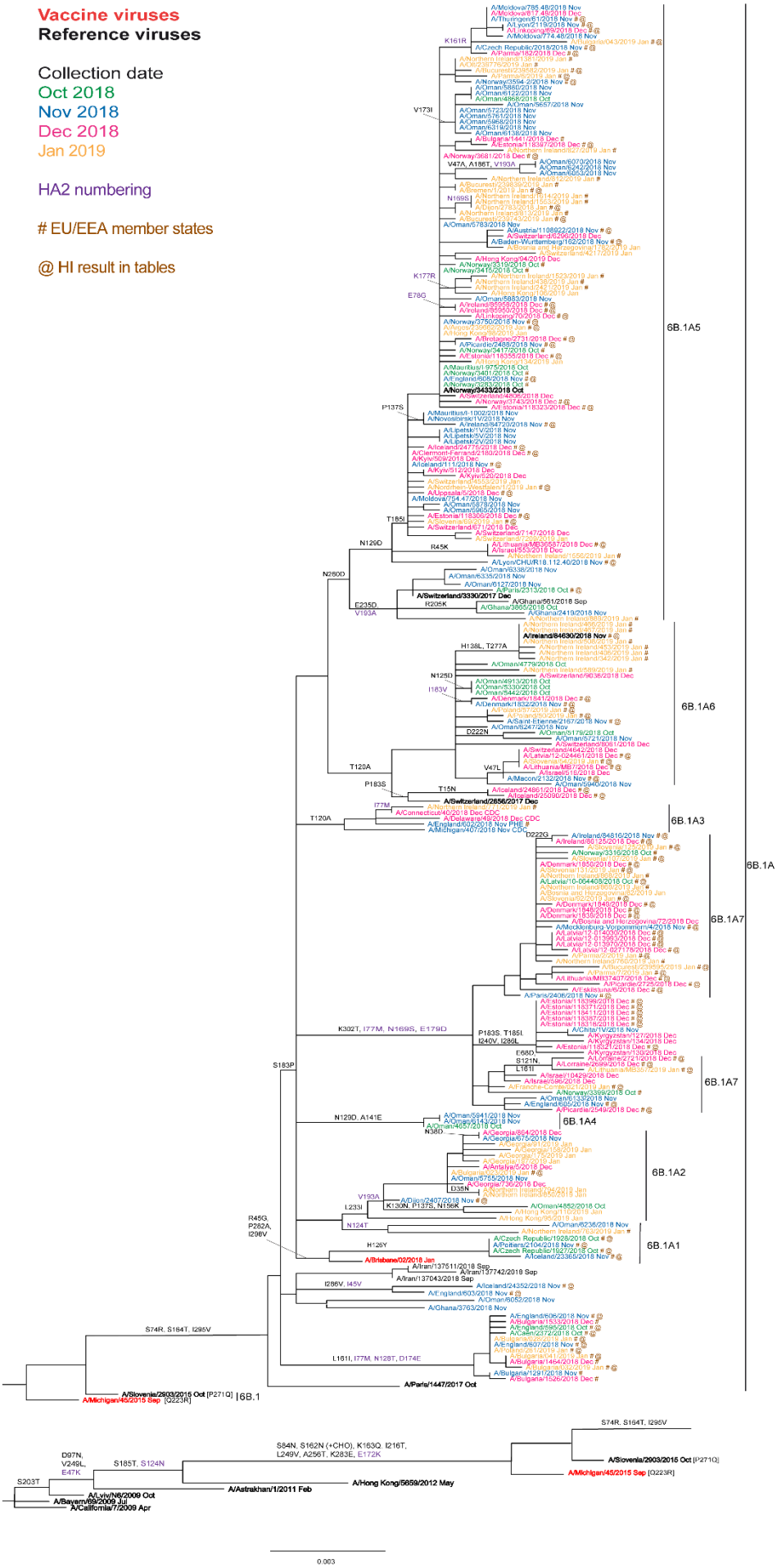
* Of those with available HA sequence, all were clade 6B.1A

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 3-9. 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/Cal 7/09	A/Bayern 69/09	A/Lviv N6/09	A/Astrak 1/11	A/HK 5659/12	A/Slov 2903/15	A/Paris 1447/17	A/Swit 2656/17	A/Swit 3330/17	A/Norway 3433/18
	Passage history	Egg	Egg	MDCK	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Egg	MDCK
	Ferret number	NIB F42/16[*1]	F07/16[*1]	F09/15[*1]	F14/13[*1]	F22/13[*1]	F17/15[*1]	F02/16[*1]	F03/18[*2]	F20/18[*1]	F23/18[*1]	F04/19[*1]
	Genetic group	6B.1	6B.1			5 6A	6B.1	6B.1A	6B.1A	6B.1A	6B.1A5	6B.1A5
TEST VIRUSES												
Total number tested		159	159	159	159	159	159	159	159	159	159	81
Number tested	6B.1A	20	20	20	20	20	20	20	20	20	20	4
No with titre reduction ≤2-fold		20	9	18	2	20	18	19	17	16	18	4
%		100.0	45.0	90.0	10.0	100.0	90.0	95.0	85.0	80.0	90.0	100.0
No with titre reduction =4-fold			10	2	11		2	1	3	2	1	
%			50.0	10.0	55.0		10.0	5.0	15.0	10.0	5.0	
No with titre reduction ≥8-fold			1		7					2	1	
%			5.0		35.0					10.0	5.0	
Number tested	6B.1A1	5	5	5	5	5	5	5	5	5	5	
No with titre reduction ≤2-fold		5		4		4	4	4	4	3	3	
%		100.0		80.0		80.0	80.0	80.0	80.0	60.0	60.0	
No with titre reduction =4-fold			2	1		1	1	1	1	1	1	
%			40.0	20.0		20.0	20.0	20.0	20.0	20.0	20.0	
No with titre reduction ≥8-fold			3		5					1	1	
%			60.0		100.0					20.0	20.0	
Number tested	6B.1A2	5	5	5	5	5	5	5	5	5	5	3
No with titre reduction ≤2-fold		4	4	5		4	4	4	4	3	3	2
%		80.0	80.0	100.0		80.0	80.0	80.0	80.0	60.0	60.0	66.7
No with titre reduction =4-fold					2					1	1	
%					40.0					20.0	20.0	
No with titre reduction ≥8-fold		1	1		3	1	1	1	1	1	1	1
%		20.0	20.0		60.0	20.0	20.0	20.0	20.0	20.0	20.0	33.3
Number tested	6B.1A4	1	1	1	1	1	1	1	1	1	1	1
No with titre reduction ≤2-fold		1	1	1		1	1	1	1	1		1
%		100.0	100.0	100.0		100.0	100.0	100.0	100.0	100.0		100.0
No with titre reduction =4-fold											1	
%											100.0	
No with titre reduction ≥8-fold					1							
%					100.0							
Number tested	6B.1A5	63	63	63	63	63	63	63	63	63	63	28
No with titre reduction ≤2-fold		63	42	59	16	60	59	62	61	44	58	28
%		100.0	66.7	93.7	25.4	95.2	93.7	98.4	96.8	69.8	92.0	100.0
No with titre reduction =4-fold			13	4	28	3	4	1	2	15	3	
%			20.6	6.3	44.4	4.8	6.3	1.6	3.2	23.9	4.8	
No with titre reduction ≥8-fold			8		19					4	2	
%			12.7		30.2					6.3	3.2	
Number tested	6B.1A6	17	17	17	17	17	17	17	17	17	17	11
No with titre reduction ≤2-fold		17	10	14	4	15	13	15	15	8	12	11
%		100.0	58.9	82.4	23.5	88.2	76.5	88.2	88.2	47.1	70.7	100.0
No with titre reduction =4-fold			3	3	6	2	4	2	2	8	4	
%			17.6	17.6	35.4	11.8	23.5	11.8	11.8	47.1	23.5	
No with titre reduction ≥8-fold			4		7					1	1	
%			23.5		41.1					5.8	5.8	
Number tested	6B.1A7	48	48	48	48	48	48	48	48	48	48	34
No with titre reduction ≤2-fold		48	37	42	5	46	44	47	47	35	41	33
%		100.0	77.1	87.5	10.4	95.8	91.7	97.9	97.9	72.9	85.4	97.1
No with titre reduction =4-fold			5	6	19	2	4	1	1	12	7	1
%			10.4	12.5	39.6	4.2	8.3	2.1	2.1	25.0	14.6	2.9
No with titre reduction ≥8-fold			6		24					1		
%			12.5		50.0					2.1		
	Vaccine											

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 December 2018 report of the viruses recovered, based on positive neuraminidase activity, only 33 retained sufficient HA activity to allow antigenic analysis by HI (Tables 4-3 and 4-6). Of the 33 test viruses, only three were recognised at titres 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 five cell culture-propagated subclade 3C.2a1 viruses for which no homologous titres are given, due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, that reacted with the majority of reference viruses at titres of ≥160. Those raised against A/Norway/4436/2016, A/Greece/4/2017 (both subgroup 3C.2a1a viruses), A/Norway/3275/2018, A/Netherlands/10260/2018 and A/La Rioja/2202/2018 (three subgroup 3C.2a1b viruses) recognised, respectively, 3/4 (75%), 0/4 (0%), 8/27 (30%), 5/18 (28%) and 13/33 (39%) test viruses at titres of ≥160. An antiserum raised against egg-propagated A/Netherlands/10260/2018 recognised test viruses poorly, all 27 yielded titres at least thirty-twofold reduced compared to the homologous titre.

Antisera raised against subclade 3C.2a2 viruses generally recognised the test viruses poorly. Those raised against cell culture-propagated viruses, A/Bretagne/1413/2017 and A/Hong Kong/656/2018, recognised 2/27 (7%) and 0/4 (0%) viruses, respectively, at titres within fourfold of the homologous titres, with all others having titres at least eightfold reduced. Antisera raised against egg-propagated A/Switzerland/8060/2017, the vaccine virus recommended for use in the 2019 southern hemisphere season, recognised only 1/33 (3%) test viruses at a titre within fourfold of the homologous titre.

Antiserum raised against a cell culture-propagated clade 3C.2a virus, A/Hong Kong/5738/2014, recognised all 33 test viruses at titres within fourfold of the homologous titre and 12 (36%) within twofold. Antisera raised against cell culture-propagated cultivars of A/Stockholm/6/2014 and A/England/538/2018, clade 3C.3a viruses, recognised 23 (70%) and 8/29 (28%) test viruses, respectively, at titres within fourfold of the titres of the antisera with their homologous viruses, and 15 (45%) and 5/29 (17%) within twofold.

A summary of the HI data presented in Tables 4-1 to 4-6 is presented in Table 4-7 and for those test viruses with known HA sequences at the time this report was prepared this is broken down by virus clade/subclade in Table 4-8. The latter shows (i) the poor recognition of test viruses by post-infection ferret antisera raised against egg-propagated vaccine/reference viruses, (ii) the 3C.2a2 subclade specificity of antisera raised against clade 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 December 2018 report are now available and the genetic clades are shown in updated Tables (4-1 and 4-2) 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 numbers of detections in January 2019 have increased in some WHO European Region countries (e.g. France, Israel, Netherlands and Spain) (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

[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

- 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 January 2019 (Figure 2). Notably, a significant number of the subgroup 3C.2a1b viruses have fallen in a recently emerged cluster defined by substitutions **T131K** and **K135T** (a reversion resulting in re-establishment of the **133-135** glycosylation sequon) in **HA1** with **V200I** in **HA2**. Further, as indicated above, numbers of clade 3C.3a virus detections have been increasing in recent weeks in a number of countries/regions.

The location of A/Singapore/INFIMH-16-0019/2016 (3C.2a1), the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2018–2019 influenza season [2], is indicated in Figure 2, as is A/Switzerland/8060/2017 (3C.2a2) the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2019 [3].

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/Stock 6/14	A/HK 5738/14	A/Bretagne 1413/17	A/Nor 4436/16	A/Greece 4/17	A/Singapore 0019/16	A/HK 656/18	A/La Rioja 2202/18	A/Switz 8060/17
		Passage history			SIAT	MDCK	SIAT	SIAT	SIAT	Egg 10^{-4}	SIAT	SIAT	Egg
		Ferret number			F14/14[*1]	F30/14[*1]	F01/18[*1]	F03/17[*1]	F27/17[*1]	F41/17[*1]	F25/18[*1]	F26/18[*1]	F27/18[*1]
		Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1a	3C.2a1	3C.2a2	3C.2a1b	3C.2a2
REFERENCE VIRUSES													
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	160	160	320	320	320	160	160	320
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	160	160	320	320	320	320	160	320
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	1280	320	320	320	1280	160	1280
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	<	40	40	160	160	640	40	160	80
A/Hong Kong/656/2018		3C.2a2	2018-04-07	MDCK1/SIAT3	160	160	640	320	320	320	1280	80	640
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	40	160	2560	320	160	640	2560	160	2560
TEST VIRUSES													
A/Latvia/11-019324/2018		3C.2a2	2018-11-07	MDCK2/SIAT1	160	160	640	320	160	160	640	80	640
A/Clermont-Ferrand/2062/2018		3C.2a3	2018-11-07	MDCK3/SIAT1	160	160	80	320	320	160	80	160	160
A/Iceland/108/2018		3C.2a1b	2018-11-13	MDCK1/SIAT1	40	40	<	80	160	80	<	160	40
A/Austria/1102969/2018		3C.2a1b	2018-11-16	SIAT1/SIAT1	160	80	40	320	320	160	40	320	80
A/Lyon/2106/2018		3C.2a1b	2018-11-20	MDCK3/SIAT1	160	80	80	160	160	160	40	320	80
A/Paris/2511/2018		3C.3a	2018-11-29	MDCK1/SIAT1	80	80	80	320	160	160	80	40	160
A/Latvia/12-005233/2018		3C.2a2	2018-12-03	MDCK1/SIAT1	160	160	640	320	320	160	640	160	320
A/Paris/2538/2018		3C.3a	2018-12-04	MDCK1/SIAT1	80	80	80	320	160	160	160	40	80
A/Paris/2544/2018		3C.3a	2018-12-04	MDCK1/SIAT1	80	80	80	320	160	160	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

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								
					A/Stock 6/14	A/HK 5738/14	A/Bretagne 1413/17	A/Nor 4436/16	A/Greece 4/17	A/Singapore 0019/16	A/HK 656/18	A/La Rioja 2202/18	A/Switz 8060/17
		Passage history			SIAT	MDCK	SIAT	SIAT	SIAT	Egg 10^{-4}	SIAT	SIAT	Egg
		Ferret number			F14/14[*1]	F30/14[*1]	F01/18[*1]	F03/17[*1]	F27/17[*1]	F15/18[*1]	F25/18[*1]	F26/18[*1]	F27/18[*1]
		Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1a	3C.2a1	3C.2a2	3C.2a1b	3C.2a2
REFERENCE VIRUSES													
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	160	160	320	160	160	160	160	160
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	160	160	320	160	160	160	160	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	640	320	160	160	640	160	640
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	<	40	40	80	80	160	40	160	80
A/Hong Kong/656/2018		3C.2a2	2018-04-07	MDCK1/SIAT3	320	320	640	320	320	320	1280	160	640
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	40	160	1280	160	160	160	1280	160	1280
TEST VIRUSES													
A/Saint-Etienne/1912/2018		3C.2a1b	2018-09-07	MDCK2/SIAT1	80	40	40	160	80	40	<	320	40
A/Poitiers/1978/2018		3C.2a1b	2018-10-08	MDCK2 /SIAT1	40	40	<	80	80	40	<	160	40
A/Poitiers/1976/2018		3C.2a1b	2018-10-09	MDCK3/SIAT1	40	40	<	80	80	<	<	160	40
A/Poitiers/2003/2018		3C.2a1b	2018-10-20	MDCK2/SIAT1	40	80	40	80	80	40	160	320	40
A/Lorraine/2365/2018		3C.2a1b	2018-10-22	MDCK2/SIAT2	<	40	<	40	80	<	<	80	<
A/Iceland/101/2018		3C.2a1b	2018-11-01	MDCK1/SIAT1	<	40	<	40	40	40	<	80	<
A/Iceland/100/2018		3C.2a1b	2018-11-01	MDCK1/SIAT1	40	80	<	40	80	40	160	160	40
A/Iceland/102/2018		3C.2a1b	2018-11-02	MDCK1/SIAT1	40	40	<	40	40	80	<	160	<
A/Iceland/103/2018		3C.2a1b	2018-11-03	MDCK1/SIAT1	40	40	<	80	80	80	<	160	<
A/Iceland/104/2018			2018-11-05	MDCK1/SIAT1	<	40	<	40	80	80	<	160	<
A/Iceland/107/2018		3C.2a1b	2018-11-09	MDCK1/SIAT2	40	40	<	80	80	40	<	160	<
A/Norway/3668/2018		3C.2a1b	2018-11-29	SIAT1	80	80	80	80	160	160	40	320	80
A/Norway/3735/2018		3C.2a1b	2018-12-03	SIAT1	160	80	320	320	160	160	80	320	160
A/Paris/2572/2018		3C.3a	2018-12-06	SIAT1	80	40	<	160	40	80	80	40	80
										Vaccine SH 2018 NH 2018-19			Vaccine SH 2019

* 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/Stock 6/14 SIAT	A/HK 5738/14 MDCK	A/Bretagne 1413/17 SIAT	A/Nor 4436/16 SIAT	A/Greece 4/17 SIAT	A/Singapore 0019/16 Egg 10^{-4}	A/HK 656/18 SIAT	A/La Rioja 2202/18 SIAT	A/Switz 8060/17 Egg
	Ferret number			F14/14[*1]	F30/14[*1]	F01/18[*1]	F03/17[*1]	F27/17[*1]	F46/17[*1]	F25/18[*1]	F26/18[*1]	F27/18[*1]
	Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1a	3C.2a1	3C.2a2	3C.2a1b	3C.2a2
REFERENCE VIRUSES												
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	320	80	80	320	160	320	80	80	160
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	320	160	160	320	160	640	160	160	320
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	160	160	1280	320	160	160	640	80	640
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	<	40	40	80	40	640	40	160	80
A/Hong Kong/656/2018	3C.2a2	2018-04-07	MDCK1/SIAT3	160	320	640	320	160	320	1280	160	640
A/Switzerland/8060/2017 clone 57	3C.2a2	2017-12-12	E7/E1	<	160	1280	160	80	640	1280	80	1280
TEST VIRUSES												
A/Trollhattan/3/2018	3C.2a1b	2018-12-01	MDCK0/SIAT1	40	40	40	80	80	80	40	160	40
A/Paris/2671/2018	3C.3a	2018-12-17	MDCK1/SIAT1	80	40	40	160	40	80	40	<	40
A/Bretagne/026/2019	3C.3a	2019-01-02	MDCK1/SIAT1	80	80	40	160	80	80	40	40	80
A/Paris/029/2019	3C.3a	2019-01-03	MDCK1/SIAT1	80	80	40	160	40	80	80	40	80
									Vaccine SH 2018 NH 2018-19			Vaccine SH 2019

* 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	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]	A/HK 5738/14 MDCK F30/14[*1]	A/Singapore 0019/16 Egg 10-4 F46/17*1	A/La Rioja 2202/18 SIAT F26/18[*1]	A/Switz 8060/17 Egg F27/18[*1]	A/Eng 538/18 SIAT F31/18[*1]	NEW A/Neth 10260/18 Egg F02/19[*1]	NEW A/Nor 3275/18 SIAT F03/19[*1]
		Genetic group			3C.3a	3C.2a	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.2a1b
REFERENCE VIRUSES												
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	40	160	80	160	320	<	80
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	80	320	160	320	320	40	320
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	40	40	640	160	80	80	40	40
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	40	80	640	160	1280	160	40	80
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT1	80	ND	ND	ND	40	1280	ND	ND
A/Netherlands/10260/2018		3C.2a1b	2018-02-15	E5	40	40	160	320	80	80	2560	160
TEST VIRUSES												
A/Sundsvall/2/2018		3C.3a	2018-12-01	MDCK0/SIAT1	40	<	<	<	<	320	ND	ND
A/Sundsvall/1/2018		3C.3a	2018-12-03	MDCK0/SIAT1	40	<	<	<	<	320	ND	ND
A/Portugal/139/2019		3C.2a3	2019-01-04	MDCK1/SIAT1	160	<	80	80	80	160	<	80
A/Portugal/151/2019		3C.2a1b	2019-01-06	SIAT1/SIAT1	160	80	160	320	80	160	<	320
A/Portugal/146/2019		3C.2a1b	2019-01-07	MDCK1/SIAT1	80	40	40	160	40	40	<	160
A/Burgos/31/2019		3C.3a	2019-01-15	SIAT1/SIAT1	160	<	80	40	80	640	<	<

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

Vaccine SH 2018 NH 2018-19

Vaccine SH 2019

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								
					A/Stock 6/14	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/Neth 10260/18	A/Nor 3275/18
		Passage history			SIAT	MDCK	SIAT	Egg 10^{-4}	SIAT	Egg	SIAT	Egg	SIAT
		Ferret number			F14/14[*1]	F30/14[*1]	F01/18[*1]	F46/17[*1]	F26/18[*1]	F27/18[*1]	F31/18[*1]	F02/19[*1]	F03/19[*1]
		Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.2a1b
REFERENCE VIRUSES													
A/Stockholm/6/2014		3C.3a	2014-02-06	SIAT1/SIAT3	320	40	80	320	80	160	320	<	80
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT1	160	80	160	320	160	160	160	40	160
A/Bretagne/1413/2017		3C.2a2	2017-10-09	MDCK1/SIAT4	160	40	640	320	80	640	160	40	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	40	<	40	640	160	80	80	<	40
A/Switzerland/8060/2017	clone 57	3C.2a2	2017-12-12	E7/E1	80	80	2560	1280	160	1280	160	40	160
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	80	<	40	80	40	80	1280	<	40
A/Netherlands/10260/2018		3C.2a1b	2018-02-15	E5	40	<	80	160	320	160	80	1280	160
TEST VIRUSES													
A/Hungary/5/2019		3C.2a1b	2018-12-19	Cx/SIAT1	160	<	<	80	160	<	40	<	160
A/Hungary/28/2019		3C.2a1b	2019-01-03	Cx/SIAT1	80	<	<	80	80	<	40	<	80
A/Hungary/26/2019		3C.2a1b	2019-01-07	Cx/SIAT1	160	40	40	80	320	80	80	40	80
A/Netherlands/10002/2019		3C.3a	2019-01-07	MDCK-MIX2/SIAT1	80	<	40	40	<	<	640	<	<
A/Netherlands/10006/2019		3C.3a	2019-01-14	MDCK-MIX2/SIAT1	40	<	40	40	<	<	640	<	<
								Vaccine SH 2018 NH 2018-19		Vaccine SH 2019			

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

Sequences in phylogenetic trees

Table 4-6. 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/Switz 8060/17	A/Eng 538/18	A/Neth 10260/18	A/Neth 10260/18	A/Neth 10260/18	A/Nor 3275/18
	Ferret number			SIAT $F14/14^{-1}$	MDCK $F30/14^{-1}$	SIAT $F01/18^{-1}$	Egg 10^{-4} $F46/17^{-1}$	SIAT $F26/18^{-1}$	Egg $F27/18^{-1}$	SIAT $F31/18^{-1}$	Egg $F02/19^{-1}$	SIAT $F07/19^{-1}$	SIAT $F03/19^{-1}$	SIAT
	Genetic group			3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a1b	3C.2a2	3C.3a	3C.2a1b	3C.2a1b	3C.2a1b	3C.2a1b
REFERENCE VIRUSES														
A/Stockholm/6/2014	3C.3a	2014-02-06	SIAT1/SIAT3	160	40	80	160	80	160	160	<	40		80
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	80	160	160	80	160	160	<	80		160
A/Bretagne/1413/2017	3C.2a2	2017-10-09	MDCK1/SIAT4	80	<	640	160	80	640	80	<	80		160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	<	<	40	640	80	80	40	<	40		<
A/Switzerland/8060/2017	3C.2a2 clone 57	2017-12-12	E7/E1	<	40	1280	320	80	1280	80	40	80		40
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	<	40	80	<	40	640	<	80		<
A/Netherlands/10260/2018	3C.2a1b	2018-02-15	E5/E1	40	<	80	80	320	80	80	1280	320		160
TEST VIRUSES														
A/Parma/177/2018		2018-11-20	SIAT2/SIAT2	160	80	40	160	320	160	80	<	320		160
A/Parma/180/2018		2018-11-21	SIAT1/SIAT2	80	40	<	80	80	40	40	<	160		80
A/Parma/179/2018		2018-11-22	SIAT1/SIAT1	160	40	<	80	160	40	40	<	160		80
A/Parma/174/2018		2018-11-22	SIAT1/SIAT1	160	40	<	40	160	40	40	<	160		80
A/England/630/2018		2018-11-23	SIAT1/SIAT1	80	40	160	80	80	160	40	<	80		160
A/Palermo/327/2018		2018-11-28	SIAT3/SIAT1	160	40	640	160	160	640	160	<	80		160
A/England/646/2018		2018-11-28	SIAT2/SIAT1	<	<	<	<	80	<	<	<	80		80
A/Constanta/239165/2018		2018-12-07	SIAT1/SIAT2	<	<	<	<	80	<	<	<	40		40
A/England/754/2018		2018-12-13	MDCK1/SIAT1	<	<	<	<	<	40	80	<	<		<
A/Nord Pas de Calais/2726/2018		2018-12-26	SIAT1	80	<	<	40	80	80	40	<	40		40
A/Bourgogne/074/2019		2019-01-02	SIAT1	40	<	40	<	<	<	320	<	40		<
A/Centre/013/2019		2019-01-02	SIAT1	160	<	<	80	160	<	<	<	160		40
A/Pays de Loire/040/2019		2019-01-04	SIAT1	80	<	80	40	160	80	40	<	80		160
A/Haute Normandie/085/2019		2019-01-07	SIAT1	<	<	<	<	<	<	320	<	40		<
A/Nord Pas de Calais/054/2019		2019-01-07	SIAT1	40	<	<	80	160	40	40	<	80		80
A/England/3/2019		2019-01-07	MDCK1/SIAT1	<	<	<	40	<	40	80	<	<		<
A/Paris/105/2019		2019-01-08	SIAT1	<	<	<	<	80	<	<	<	80		40
A/Iasi/239836/2019		2019-01-09	SIAT1	80	40	80	80	160	80	40	<	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 4-7. Antigenic analysis of A(H3N2) viruses by HI – Summary all test viruses

Viruses	Other information	Haemagglutination inhibition titre													
		Post-infection ferret antisera													
		A/Stock 6/14	A/HK 5738/14	A/Bretagne 1413/17	A/Singapore 0019/16	A/Switz 8060/17	A/Eng 538/18	A/Neth 10260/18	A/HK 656/18	A/Neth 10260/18	A/Nor 4436/16	A/Greece 4/17	A/La Rioja 2202/18	A/Nor 3275/18
Passage history		SIAT	MDCK	SIAT	Egg 10^{-4}	Egg	SIAT	Egg	SIAT	SIAT	SIAT	SIAT	SIAT	SIAT
Ferret number		F14/14-1	F30/14-1	F01/18-1	F46/17-1	F27/18-1	F31/18-1	F02/19-1	F25/18-1	F07/19-1	F03/17-1	F27/17-1	F26/18-1	F03/19-1
Genetic group		3C.3a	3C.2a	3C.2a2	3C.2a1	3C.2a2	3C.3a	3C.2a1b	3C.2a2	3C.2a1b	3C.2a1	3C.2a1a	3C.2a1b	3C.2a1b
REFERENCE VIRUSES														
A/Stockholm/6/2014	3C.3a	160	40	80	160	160	160	<	160	40	320	320	80	80
A/Hong Kong/5738/2014	3C.2a	160	80	160	160	160	160	<	320	80	320	320	80	160
A/Bretagne/1413/2017	3C.2a2	80	<	640	160	640	80	<	1280	80	320	320	80	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	<	<	40	640	80	40	<	40	40	160	160	80	<
A/Switzerland/8060/2017	clone 57 3C.2a2	<	40	1280	320	1280	80	40	2560	80	320	160	80	40
A/England/538/2018	3C.3a	40	<	40	80	40	640	<	ND	80	ND	ND	<	<
A/Netherlands/10260/2018	3C.2a1b	40	<	80	80	80	80	1280	ND	320	ND	ND	320	160
A/Hong Kong/656/2018	3C.2a2	160	160	640	320	640	ND	ND	1280	ND	320	320	80	ND
TEST VIRUSES														
Number of viruses tested*		56	56	50	56	56	29	27	27	18*	27*	27*	56*	27*
No with titre reduction ≤2-fold		21	24	4	6	1	5		2	5	14	11	29	8
%		*37.5*	*42.9*	*8.0*	*10.7*	*1.8*	*17.2*		*7.4*	*27.8*	*51.9*	*40.7*	*51.8*	*29.6*
No with titre reduction =4-fold		14	32	1	17	1	3							
%		*25.0*	*57.1*	*2.0*	*30.4*	*1.8*	*10.4*							
No with titre reduction ≥8-fold		21		45	33	54	21	27	25					
%		*37.5*		*90.0*	*58.9*	*96.4*	*72.4*	*100.0*	*92.6*					

	Vaccine SH 2018 NH 2018-19	Vaccine SH 2019

* 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.

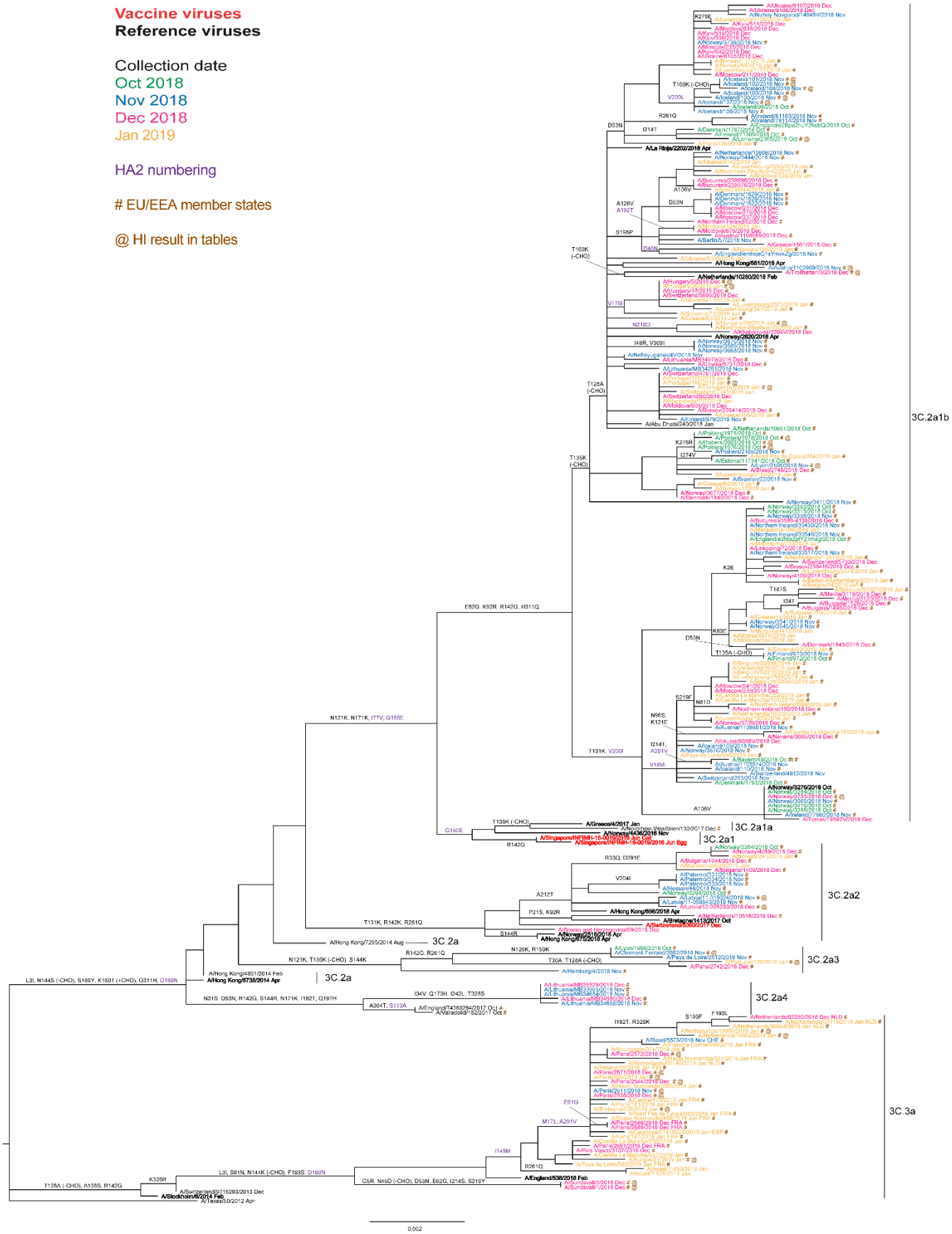
Table 4-8. Antigenic analysis of A(H3N2) viruses by HI – Summary by test virus genetic group

Viruses	Other information	Haemagglutination inhibition titre																					
		Post-infection ferret antisera																					
		A/Stock 6/14		A/Eng 538/18		A/HK 5738/14		A/Bretagne 1413/17		A/HK 656/18		A/Switz 8060/17		A/Singapore 0019/16		A/Nor 4436/16		A/Greece 4/17		A/Neth 10260/18		A/La Rioja 2202/18	
	Passage history	SIAT		SIAT		MDCK		SIAT		SIAT		Egg		Egg 10^{-4}		SIAT		SIAT		Egg		SIAT	
	Ferret number	F14/14[*1]		F31/18[*1]		F30/14[*1]		F01/18[*1]		F25/18[*1]		F27/18[*1]		F46/17[*1]		F03/17[*1]		F27/17[*1]		F02/19[*1]		F26/18[*1]	
	Genetic group	3C.3a		3C.3a		3C.2a		3C.2a2		3C.2a2		3C.2a2		3C.2a1		3C.2a1		3C.2a1a		3C.2a1b		3C.2a1b	
TEST VIRUSES																							
Total number tested			37		11		37		31		26		37		37		26*		26*		9		37*
Number tested	3C.2a2	2		0		2		2		2		2		2		2		2		0		2	
No with titre reduction ≤2-fold		2				2		2		2		1				2		2				1	
%		*100.0*				*100.0*		*100.0*		*100.0*		*50.0*				*100.0*		*100.0*				*50.0*	
No with titre reduction =4-fold														2									
%														*100.0*									
No with titre reduction ≥8-fold												1											
%												*50.0*											
Number tested	3C.2a3	2		1		2		1		1		2		2		1		1		1		2	
No with titre reduction ≤2-fold		2				1										1		1				1	
%		*100.0*				*50.0*										*100.0*		*100.0*				*50.0*	
No with titre reduction =4-fold						1								1									
%						*50.0*								*50.0*									
No with titre reduction ≥8-fold			1					1		1		2		1						1			
%			*100.0*					*100.0*		*100.0*		*100.0*		*50.0*						*100.0*			
Number tested	3C.2a1b	21		5		21		19		16		21		21		16		16		5		21	
No with titre reduction ≤2-fold		6				9		1						4		4		5				18	
%		*28.6*				*42.9*		*5.3*						*19.0*		*25.0*		*31.3*				*85.7*	
No with titre reduction =4-fold		4				12								9									
%		*19.0*				*57.1*								*42.9*									
No with titre reduction ≥8-fold		11		5				18		16		21		8						5			
%		*52.4*		*100.0*				*94.7*		*100.0*		*100.0*		*38.1*						*100.0*			
Number tested	3C.3a	12		5		12		9		7		12		12		7		7		3		12	
No with titre reduction ≤2-fold		1		3		5								1		7		3					
%		*8.3*		*60.0*		*41.7*								*8.3*		*100.0*		*42.9*					
No with titre reduction =4-fold		8		2		7								3									
%		*66.7*		*40.0*		*58.3*								*25.0*									
No with titre reduction ≥8-fold		3						9		7		12		8						3			
%		*25.0*						*100.0*		*100.0*		*100.0*		*66.7*						*100.0*			

Vaccine SH 2019	Vaccine SH 2018 NH 2018-19

* 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 2.6% of the samples received with collection dates after 31 August 2018 and were received from NICs in 10: Croatia, Denmark, France, Iceland, Ireland, Luxembourg, Norway, Portugal, Slovenia and the United Kingdom (Table 1). Of the small number received 16 were B/Yamagata-lineage and seven were B/Victoria-lineage.

Influenza B/Victoria-lineage

HI results for the five test viruses propagated to date are shown in Table 5, sorted by date of collection. The HA genetic group of the test viruses is indicated and those included in phylogenetic trees are highlighted. All but one (B/Denmark/3938/2018) of the test viruses reacted poorly with sheep hyperimmune serum raised against egg-propagated B/Brisbane/60/2008 (clade 1A), and all reacted poorly with post-infection ferret antisera raised against clades 1A and 1B reference viruses. Two reactivity patterns were observed with other post-infection ferret antisera. Two viruses reacted with antisera raised against viruses carrying a two amino acid deletion in HA1 [1A(Δ2)] viruses (cell culture-propagated B/Norway/2409/2017 and B/Colorado/06/2017, and egg-propagated B/Colorado/06/2017). Three viruses reacted with an antiserum raised against a virus of African origin carrying a three amino acid deletion in HA [1A(Δ3)] (cell culture-propagated B/Cote d'Ivoire/1662/2018) and showed low reactivity with the antiserum raised against cell culture-propagated B/Colorado/06/2017. HA gene sequencing supported these antigenic profiles in terms of genetic subclade identified.

A relatively small number 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 six from EU countries (Denmark 1, France 1, Slovenia 2 and Sweden 2; Figure 3). All recently collected viruses continue to have HA genes that fall in the B/Brisbane/60/2008 clade (clade 1A; Figure 3), with virtually all falling in a subclade defined by **HA1** amino acid substitutions **I117V**, **N129D** and **V146I** within clade 1A. Two new groups within this subclade have deletions in the HA gene. A major group seen in Europe, the Americas, Asia, and Oceania have HA genes encoding an HA with deletion of residues **K162** and **N163** of **HA1** (1A(Δ2) in Figure 3). These viruses have additional substitutions of **D129G** and **I180V** in **HA1**, and **R151K** in **HA2**, with a recent cluster in China also carrying **N178S** in **HA2**. This group of viruses is more prevalent than the subclade viruses that show no deletions. Of the low numbers of B/Victoria-lineage viruses detected recently, those with HA genes encoding a deletion of three **HA1** amino acids, **K162**, **N163** and **D164** (1A(Δ3) in Figure 3), are predominant; 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** or **E198K** (within the **197-199** glycosylation site) or **G133R**. Viruses in the latter subgroup have been detected recently in China, and viruses from France, Slovenia and Sweden fell in this subgroup. It was noted in the September 2018 characterisation report[4], and earlier ones, that the clade 1A viruses without deletions, the 1A(Δ2) group and the 1A(Δ3) subgroups are antigenically distinct from one another. Following the emergence and spread of viruses in the 1A(Δ2) group a representative, B/Colorado/06/2017, has been recommended for use in trivalent influenza vaccines for the 2018–19 and 2019–20 northern hemisphere [1,2] and 2019 southern hemisphere [3] seasons.

Influenza B/Yamagata-lineage

HI results for the seven B/Yamagata-lineage viruses characterised since the December 2018 report are shown in Table 6, 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] northern hemisphere and the 2019 [3] southern hemisphere seasons, recognised the 5/7 (71%) test virus at a titre within twofold of the titre of the antiserum with the homologous virus, and six within fourfold. An antiserum raised against the cell culture-propagated cultivar of B/Phuket/3073/2013 recognised the test viruses less well, 1/7 (14%) at a titre within twofold of the homologous titre of the antiserum, and 4 within fourfold. Antisera raised against two other egg-propagated clade 3 viruses, B/Wisconsin/1/2010 (a former vaccine virus) and B/Stockholm/12/2011, recognised all seven and 3/7 (43%) test virus, respectively, at titres within twofold of the homologous titres. An antiserum raised against a recently circulating clade 3 cell culture-propagated virus, B/Mauritius/1791/2017, recognised 6/7 (86%) test viruses at titres higher than, or within twofold of, the titre with the homologous virus.

Antisera raised against cell culture-propagated clade 2 viruses, B/Estonia/55669/2011 and B/Massachusetts/02/2012, each recognised 5/7(71%) test virus at titres within twofold of the homologous titres, while that raised against egg-propagated B/Massachusetts/02/2012 recognised only 1/7 (14%) test viruses at a titre within twofold of the homologous titre.

[4] 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

All test viruses carried an HA gene in genetic clade 3 (Table 6). Figure 4 shows a phylogenetic analysis of the HA genes of representative B/Yamagata-lineage viruses, including recently circulating ones. Worldwide, all HA genes from viruses collected in the 2017–2018 season and since have fallen in clade 3, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade. All viruses with collection dates after 31 August 2018, including those from EU/EEA countries, as deposited in the GISAID EpiFlu database, 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] northern hemisphere and the 2019 [3] southern hemisphere seasons.

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

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre													
				Post-infection ferret antisera													
				B/Bris 60/08 Egg Sh 539, 540, 543, 544, 570, 571, 574[1,3]	B/Bris 60/08 Egg F44/17[-4]	B/Malta 636714/11 Egg F29/13[-1]	B/Sth Aus 81/12 Egg F25/16[-4]	B/HK 514/09 MDCK NIB F47/16[-2]	B/Ireland 3154/16 MDCK F15/16[-2]	B/Nord-West 1/16 MDCK F16/16[-2]	B/Nor 2409/17 MDCK F40/17[-2]	B/Colorado 06/17 MDCK F09/18[-1,5]	B/Colorado 06/17 Egg F10/18[-4,5]	B/Clv 1662/18 MDCK F37/18[-1]	B/HK 269/17 Egg F50/17[-1]
	Passage history			Egg	Egg	Egg	Egg	MDCK	MDCK	MDCK	MDCK	MDCK	Egg	MDCK	Egg
	Ferret number			539, 540, 543, 544, 570, 571, 574[1,3]	F44/17[-4]	F29/13[-1]	F25/16[-4]	NIB F47/16[-2]	F15/16[-2]	F16/16[-2]	F40/17[-2]	F09/18[-1,5]	F10/18[-4,5]	F37/18[-1]	F50/17[-1]
	Genetic group			1A	1A	1A	1A	1B	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)	1A(Δ3)
REFERENCE VIRUSES															
B/Brisbane/60/2008	1A	2008-08-04	E4/E4	2560	320	320	640	320	40	40	<	20	80	<	10
B/Malta/636714/2011	1A	2011-03-07	E4/E1	2560	320	640	640	320	80	40	<	40	80	<	20
B/South Australia/81/2012	1A	2012-11-28	E4/E2	2560	320	160	640	320	40	40	<	20	40	<	10
B/Hong Kong/514/2009	1B	2009-10-11	MDCK1/MDCK2	2560	40	<	40	320	80	80	<	20	<	<	<
B/Ireland/3154/2016	1A	2016-01-14	MDCK1/MDCK4	2560	10	<	10	80	160	80	<	<	<	<	<
B/Nordrhein-Westfalen/1/2016	1A	2016-01-04	C2/MDCK2	2560	10	<	10	80	80	80	<	<	<	<	<
B/Norway/2409/2017	1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	<	<	<	<	<	<	80	40	40	<	<
B/Colorado/06/2017	1A(Δ2)	2017-02-05	MDCK1/MDCK2	160	<	<	<	<	<	<	40	40	10	<	<
B/Colorado/06/2017	1A(Δ2)	2017-02-05	E5/E2	1280	160	40	80	20	<	<	40	80	160	<	10
B/Cote D'Ivoire/1662/2018	1A(Δ3)	2018-07-25	P0/MDCK3	160	<	<	<	<	<	<	<	20	<	40	<
B/Hong Kong/269/2017	1A(Δ3)	2017-05-24	E5	1280	ND	ND	ND	ND	ND	ND	ND	ND	ND	80	160
TEST VIRUSES															
B/Norway/3241/2018	1A(Δ2)	2018-08-21	MDCK1/MDCK1	160	<	<	<	<	<	<	40	40	<	<	<
B/Denmark/39938/2018	1A(Δ2)	2018-11-29	MDCK2/MDCK1	1280	40	<	40	10	<	<	40	80	40	<	<
B/Slovenia/3020/2018	1A(Δ3)	2018-12-18	SIATx/MDCK1	<	<	<	<	<	<	<	<	10	<	40	<
B/Paris/2659/2018	1A(Δ3)	2018-12-20	MDCK1/MDCK1	40	<	<	<	<	<	<	<	10	<	40	<
B/Slovenia/3103/2018	1A(Δ3)	2018-12-30	SIATx/MDCK1	40	<	<	<	<	<	<	<	10	<	40	<
					Vaccine[#]								Vaccine[$]		

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20; 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 and SH 2019
Sequences in phylogenetic trees

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

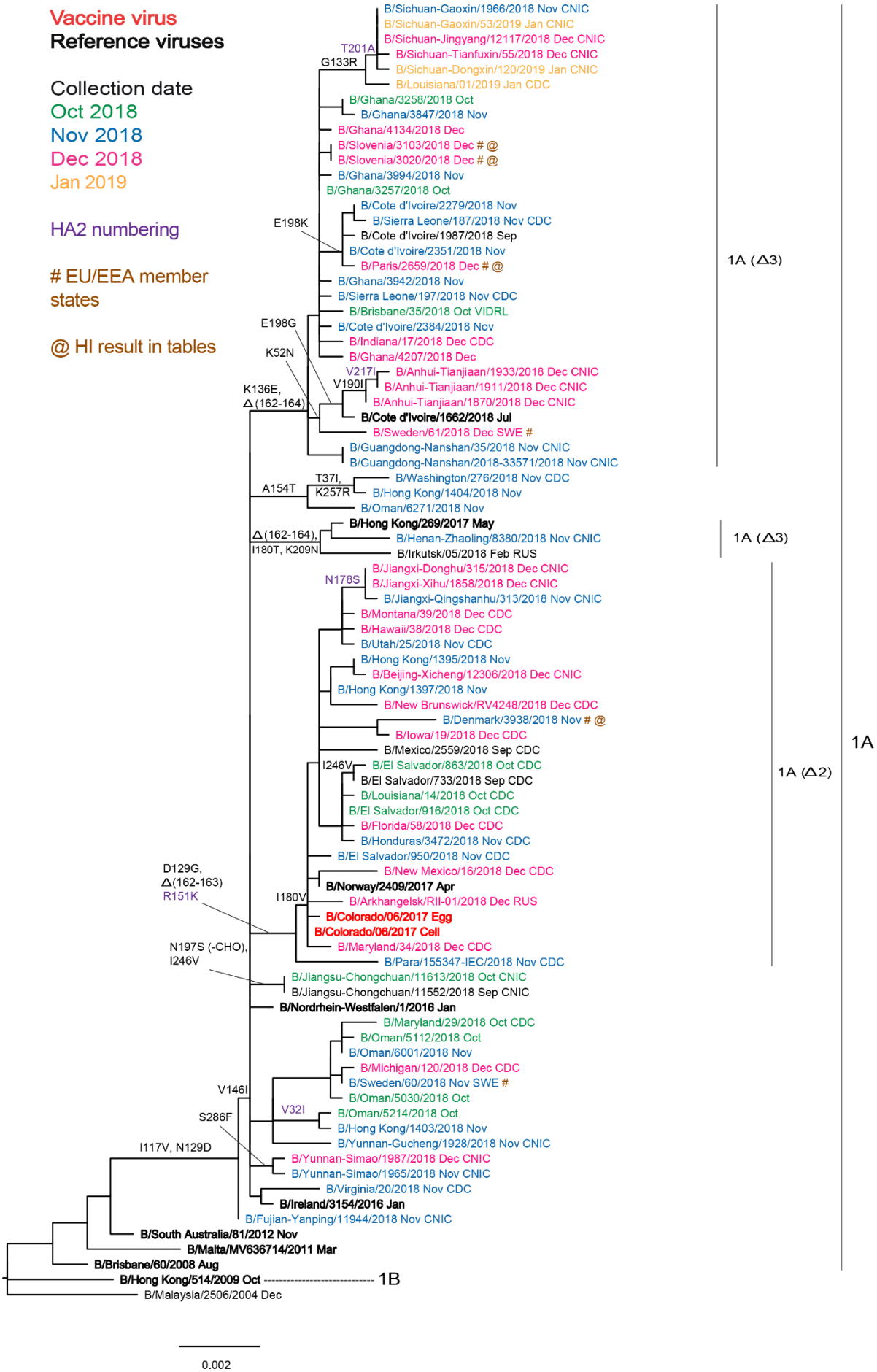
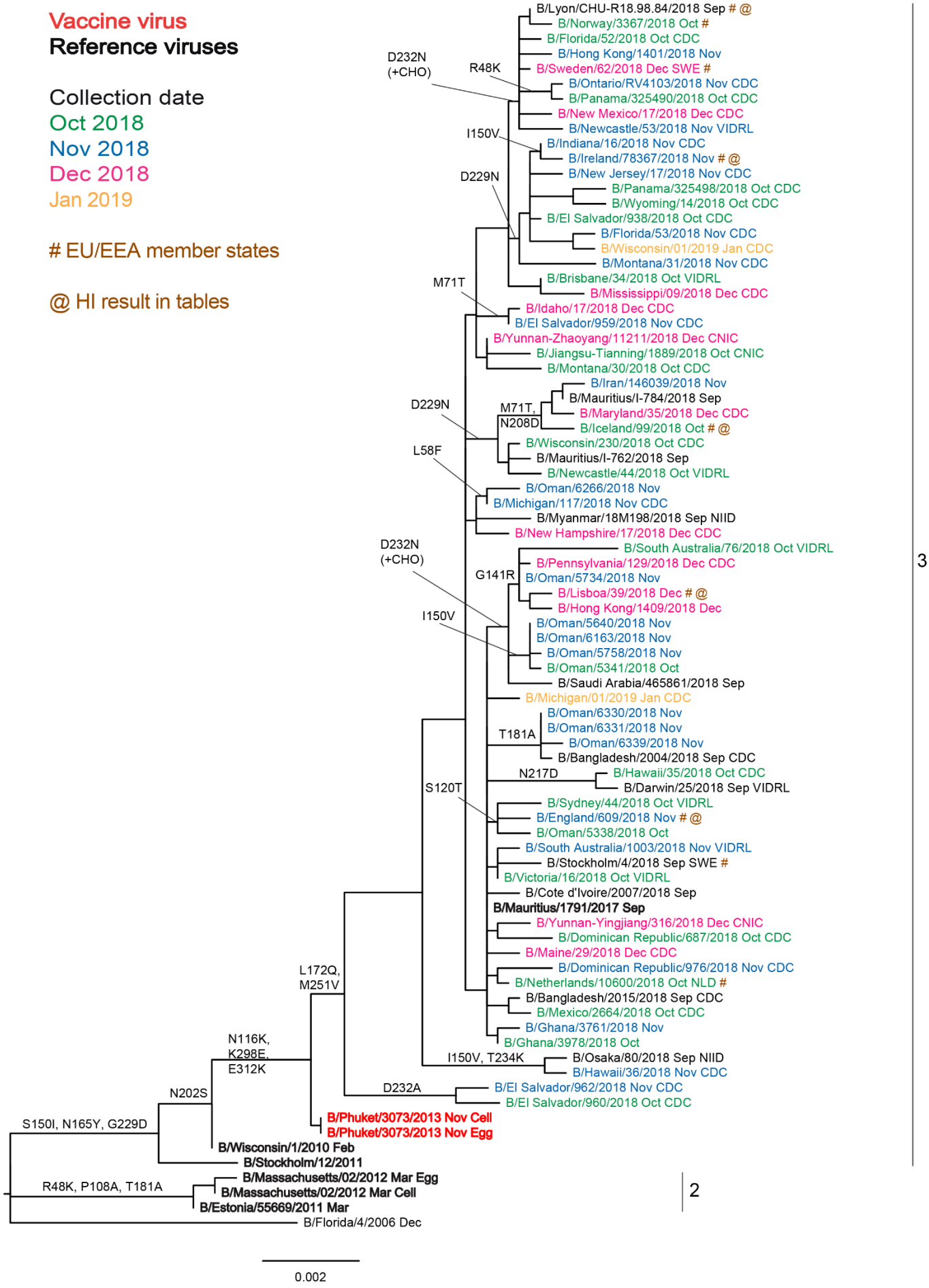


Table 6. Antigenic analysis of influenza B/Yamagata-lineage viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
	Passage history			B/Phuket	B/Estonia	B/Mass	B/Mass	B/Wis	B/Stock	B/Phuket	B/Phuket	B/Maur
				3073/13	55669/11	02/12	02/12	1/10	12/11	3073/13	3073/13	1791/17
				Egg	MDCK	MDCK	Egg	Egg	Egg	MDCK	Egg	MDCK
	Ferret number			SH614[*1,3]	F40/18[*1]	F10/16[*2]	F06/17[*1]	F36/15[*2]	F05/17[*2]	F27/15[*2]	F25/17[*2]	F04/18[*2]
	Genetic Group			3	2	2	2	3	3	3	3	3
REFERENCE VIRUSES												
B/Estonia/55669/2011	2	2011-03-14	MDCK2/MDCK3	640	160	40	<	20	20	20	40	<
B/Massachusetts/02/2012	2	2012-03-13	MDCK1/C2/MDCK3	1280	160	80	320	80	80	40	320	20
B/Massachusetts/02/2012	2	2012-03-13	E3/E4	640	40	20	160	40	80	10	160	<
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	2560	80	20	160	80	160	20	320	40
B/Stockholm/12/2011	3	2011-03-28	E4/E1	1280	20	10	80	40	160	20	160	<
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK3	2560	640	160	160	160	160	320	320	160
B/Phuket/3073/2013	3	2013-11-21	E4/E3	1280	40	40	80	40	80	20	160	20
B/Mauritius/1791/2017	3	2017-09-20	MDCK1/MDCK4	2560	<	40	<	20	40	40	80	40
TEST VIRUSES												
B/Lyon/CHU-R18.98.84/2018	3	2018-09-26	MDCK2/MDCK1	2560	80	40	<	40	40	80	80	80
B/Iceland/99/2018	3	2018-10-28	MDCK1/MDCK1	5120	640	640	160	320	320	320	320	320
B/Ireland/78367/2018	3	2018-11-06	MDCK1/MDCK1	2560	80	40	<	40	40	80	80	40
B/England/609/2018	3	2018-11-15	MDCK1/MDCK1	2560	80	80	<	40	80	80	160	160
B/Lisboa/39/2018	3	2018-12-12	SIAT1/MDCK1	640	40	<	20	20	20	<	20	<
B/Croatia/187/2019	3	2019-01-04	MDCK1	1280	80	40	40	20	80	10	80	40
B/Luxembourg/1617/2019	3	2019-01-10	MDCK1	640	40	<	20	20	20	<	40	20
											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 and SH 2019
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 8/2019, 1793 viruses had been characterised genetically and ascribed to a genetic clade:

- 1041 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;
- 716 were A(H3N2) viruses, with 469 being subgroup 3C.2a1b represented by A/Alsace/1746/2018, 41 being subclade 3C.2a2 represented by A/Switzerland/8060/2017, 16 being subclade 3C.2a3 represented by A/Cote d'Ivoire/544/2016, 111 being clade 3C.3a represented by A/England/538/2018 (this represents a 15-fold increase in the proportion of 3C.3a viruses compared to the same period in the 2017–18 season), 46 being subclade 3C.2a1 represented by A/Singapore/16-0019/2016, 4 being clade 3C.2a represented by A/Hong Kong/4801/2014, 3 were attributed to a subgroup not listed in current TESSy reporting categories and 26 were not attributed to a clade;
- 19 were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013;
- 14 were B/Victoria-lineage viruses, with 2 being clade 1A represented by B/Brisbane/60/2008, 4 being subclade 1A.Δ2 with a two amino acid deletion in HA represented by the vaccine virus B/Colorado/06/2017, 7 being subclade 1A.Δ3 with a three amino acid deletion in HA represented by B/Hong Kong/269/2017 and 1 was not attributed to a clade.

Antiviral susceptibility

For viruses collected in the course of the 2018–19 season, as of week 8/2019, 796 A(H1N1)pdm09, 387 A(H3N2) and 17 type B have been tested for susceptibility to neuraminidase inhibitors. Six A(H1N1)pdm09 viruses carried NA H275Y amino acid substitution indicative of highly reduced inhibition (confirmed phenotypically for 2), 1 A(H3N2) virus showed reduced inhibition (RI) by oseltamivir only and 1 type B virus showed evidence of RI by the zanamivir only.

At the WIC for this season 413 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 216 A(H1N1)pdm09, 184 A(H3N2), 7 B/Victoria-lineage and 6 B/Yamagata-lineage. All but one virus showed normal inhibition (NI) by the two neuraminidase inhibitors. B/Norway/3241/2018 (Victoria-lineage) showed reduced inhibition (RI) 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 [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 12 February 2019 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], with the latest human case having occurred early in February 2018 [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 27 September 2018 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 12 February 2019, indicating that various A(H5Nx) subtypes continue to be detected in birds in Africa, Europe and Asia, notably A(H5N6) viruses; no new human cases were detected since the last update published on 21 January 2019 [8]. By 12 February 2019, no cases of human infection by A(H5N1) viruses had been reported to WHO in 2018–19 [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 27 September 2018 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 WHO vaccine composition meetings held in 1) WHO Geneva, 19–21 February 2018, and 2) CDC Atlanta, 24–26 September 2018, can be found at:

https://www.crick.ac.uk/sites/default/files/2018-07/crick_feb2018_report_for_the_web.pdf [accessed 5 Mar 2019]

and

https://www.crick.ac.uk/sites/default/files/2018-10/September%202018%20interim%20report_opt.pdf [accessed 5 Mar 2019]

Note on the figures

The phylogenetic trees were constructed using RAxML, drawn using FigTree and annotated using Adobe Illustrator. The bars indicate the proportion of nucleotide changes between sequences. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the month of sample collection. Isolates from WHO NICs in EU/EEA countries are marked (#). Sequences for most viruses from non-EU/EEA countries were recovered from the GISAID EpiFlu database. We gratefully acknowledge the authors, originating and submitting laboratories of the sequences from the GISAID EpiFlu database, which were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website), along with all laboratories who submitted sequences directly to WHO CC London.

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