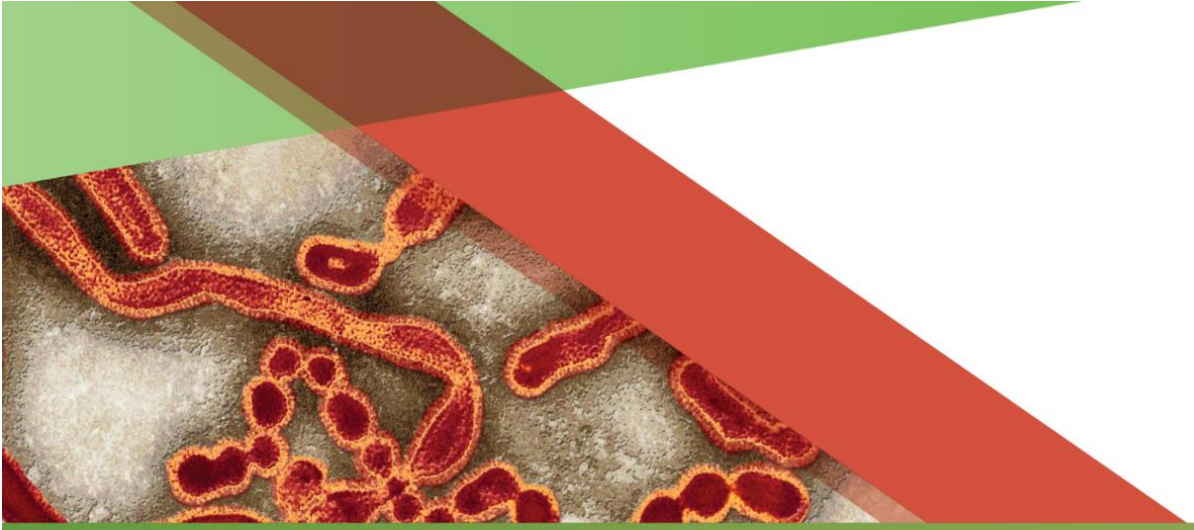

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, April 2020

Summary

This is the sixth report for the 2019–20 influenza season. As of week 18/2020, 162 345 influenza detections across the WHO European Region had been reported; 73% type A viruses, with A(H1N1)pdm09 prevailing over A(H3N2), and 27% type B viruses, with 4 418 (98%) of 4 505 ascribed to a lineage being B/Victoria.

Since the March 2020 characterisation report[1], no shipments of influenza-positive specimens from EU/EEA countries have been received at the London WHO CC, the Francis Crick Worldwide Influenza Centre (WIC). In total, 1 076 virus specimens, with collection dates after 31 August 2019, have been received.

Since the last report, no A(H1N1)pdm09 test viruses from EU/EEA countries were characterised antigenically but previous analyses have shown the great majority of test viruses to be well recognised by antisera raised against the 2019–20 vaccine virus, A/Brisbane/02/2018. Those viruses showing poor reactivity generally carried amino acid substitutions (notably N156K) in the HA1 150-loop region. The 267 EU/EEA test viruses with collection dates from week 40/2019 genetically characterised at the WIC have fallen within subclades of clade 6B.1A: 237 6B.1A5A, 20 6B.1A5B, 1 6B.1A6 and 9 6B.1A7.

Since the last report, no A(H3N2) viruses have been characterised antigenically, but previous analyses have shown clade 3C.3a-specific recognition by antisera raised against egg-propagated A/Kansas/14/2017, the current vaccine virus. Globally there have been approximately equal proportions of clade 3C.3a and subgroups 3C.2a1b+T131K and 3C.2a1b+T135K viruses detected. However, based on sequences available in GISAID from viruses detected since 1 February 2020, subgroups 3c.2a1b+T135KA/B are prevalent in the USA while those of clade 3C.3a and subgroup 3C.2a1b+T131K dominate in Europe. In total, 351 viruses from EU/EEA countries have been characterised genetically at the WIC: 183 clade 3C.3a, 111 3C.2a1b+T131K, 42 3C.2a1b+T135K-A and 15 3C.2a1b+T135K-B.

No B/Victoria-lineage viruses were characterised antigenically in this reporting period. Viruses detected in EU/EEA countries during February and March 2020, based on sequences available in GISAID, have all fallen in the 1A(Δ3)B subgroup. Viruses in this subgroup have been antigenically similar to B/Washington/02/2019, the vaccine virus for the 2020–2021 northern hemisphere influenza season. In total, 209 EU/EEA viruses have been characterised genetically at the WIC: 196 subgroup 1A(Δ3)B and 13 subclade 1A(Δ2).

[1] European Centre for Disease Prevention and Control. Influenza virus characterisation, summary Europe, March 2020. Stockholm: ECDC; 2020. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/influenza-virus-characterisation-march-2020.pdf

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No B/Yamagata-lineage viruses were characterised antigenically in this reporting period. All seven EU/EEA viruses characterised genetically at the WIC since week 40/2019, as for all recently circulating B/Yamagata-lineage viruses, belong to genetic clade 3 and contain at least two HA amino acid substitutions (HA1 L172Q and M251V) compared to B/Phuket/3073/2013, the antigenic effects of which have been minimal as assessed in earlier reports.

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 2019–20 season (weeks 40/2019–18/2020), with a total of 162 345 detections over this period. Since week 13/2020, reported in the March 2020 characterisation report, the proportion of type A viruses has continued to decrease (from 73.4% to 73.2%), with a concomitant rise in the proportion of type B viruses (from 26.6% to 26.8%). Of the type B viruses ascribed to a lineage (n = 4 505) B/Victoria-lineage viruses (n = 4 418) have continued to predominate over B/Yamagata-lineage viruses (n = 87) by a large margin, while for type A viruses subtyped (n = 46 851) there has been a continued increase in the proportion of A(H1N1)pdm09 viruses (55.7% to 55.9%) and reduction in the proportion of A(H3N2) viruses (44.3% to 44.1%). Overall, there have been 43 602 (21%) less influenza detections reported than in 2018–19, but this is probably due to the increasing number of countries that either stopped influenza surveillance or stopped reporting (or reported sporadically) to TESSy from week 5/2020 due to responses to COVID–19 which WHO declared a pandemic on 11 March 2020 (week 11/2020). With this caveat, the ratio of type A to type B detections is dramatically reduced compared with the 2018–19 season (86:1 to 2.7:1), and while proportions of influenza A subtypes are similar, B/Victoria-lineage viruses have predominated among the type B viruses compared to near equivalence with B/Yamagata-lineage viruses in the 2018–19 season.

Table 1. Influenza virus detections in the WHO European Region from the start of reporting for the 2019–20 season (weeks 40/2019–18/2020)[a]

	Cumulative number of detections			Totals*		Totals for 2018-19 season*		
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Number	%	Ratios
Influenza A	**11257**	**107644**	**118901**	**73.2**	**2.7:1**	**203564**	**98.8**	**86:1**
A(H1N1)pdm09	6101	20111	26212	55.9		44179	57.2	
A(H3N2)	4163	16476	20639	44.1	0.79:1	33117	42.8	0.7:1
A not subtyped	993	71057	72050			126271		
Influenza B	**6262**	**37182**	**43444**	**26.8**		**2380**	**1.2**	
Victoria lineage	2388	2030	4418	98.1		79	47.9	
Yamagata lineage	21	66	87	1.9	0.02:1	86	52.1	1.1:1
Lineage not ascribed	3853	35086	38939			2215		
Total detections (total tested)	**17519 (50630)**	**144826 (>784737)**	**162345 (>835367)**			**205947 (>849439)**		

[a] **Numbers taken from Flu News Europe week 18/2020**

*** 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 40/2019, 44 shipments of specimens (virus isolates and/or clinical specimens) have been received at the Crick Worldwide Influenza Centre (WIC), from 26 EU/EEA countries, but none of these were received in April 2020. The packages contained 1 076 virus-related samples with collection dates after 31 August 2019 and were made up of 772 type A viruses, with 325 and 439 subtyped as A(H1N1)pdm09 and A(H3N2), respectively, and 304 type B viruses, with 247 and 14 ascribed to B/Victoria and B/Yamagata lineages, respectively (Table 2). Genetic and antigenic characterisation data generated at the WIC for viruses with collection dates after 31 August 2019 until 31 January 2020, up to 21 February 2020, formed the basis of the February 2020 virus characterisation report and were presented at the WHO influenza vaccine composition meeting in February 2020 when recommendations were made for the northern hemisphere 2020–21 season. Recommendations for the current 2019–20 northern hemisphere and the subsequent 2020 southern hemisphere and 2020–21 northern hemisphere seasons, have been published [1, 2, 3].

The lack of sample receipts at the WIC in April is undoubtedly related to within-country responses to the COVID–19 pandemic. The following message was sent by e-mail, after the Easter break, to WHO-recognised national influenza centres and other laboratories that share influenza-positive samples with the WIC for detailed virus characterisation:

> Responses to the COVID–19 pandemic have affected us all, in terms of our working practices, and the way in which seasonal influenza is being monitored in our various countries. We recognise that you, like all members of the WHO GISRS, will be especially busy in your response to the current emergency. Although workloads will be hugely increased, we would encourage you to ship influenza-positive samples to us for analysis in time for the September 2020 WHO vaccine consultation meeting (VCM) to provide data important for the development of recommendations for the composition of influenza vaccines for the southern hemisphere 2021.
>
> We (WIC) will prioritise sequencing of the samples received to monitor for the emergence of any new variants and then focus on characterising isolates of emerging genetic groups. If you (NICs and other laboratories) cannot carry out virus isolation due to pressure of work at this very busy time, feel free to share clinical specimens (with rtRTPCR Ct values of ≤30 to give us the greatest likelihood of generating good gene sequence data and making virus isolates) with us for analysis. If shipping on dry ice becomes an issue, clinical specimens could be placed in lysis buffer allowing RNA extraction to be conducted at the WIC – this, of course, would preclude the isolation of virus in cell culture or eggs for full characterisation and use as reference viruses or potential vaccine candidates.

Shipping might be more difficult than usual because of the reduced number of international flights taking place, but the WHO Shipping Fund Project (https://www.who.int/influenza/gisrs_laboratory/logistic_activities/en/) is still operating and will assist with arrangements and funding. We continue to have few problems with dispatch of shipments (dry-ice packages) from our centre (WIC). Please note that to inform the September 2020 southern hemisphere influenza VCM we focus on samples with collection dates from 1 February 2020 on, and more than one shipment from a country is encouraged to ensure that we capture any 'end-of-season' samples from countries in the northern hemisphere.

Table 2. Summary of clinical samples and virus isolates*, with collection dates from 1 September 2019, contained in packages received from EU/EEA Member States since week 40/2019

MONTH / Country	TOTAL RECEIVED Seasonal viruses	A Number received	A Number propagated[1]	H1N1pdm09 Number received	H1N1pdm09 Number propagated[1]	H3N2 Number received	H3N2 Number propagated[2]		B Number received	B Number propagated[1]	B Victoria lineage Number received	B Victoria lineage Number propagated[1]	B Yamagata lineage Number received	B Yamagata lineage Number propagated[1]
SEPTEMBER														
Czech Republic	1					1	1							
Finland	1					1	1							
France	6			1	1	3	2	1			2	2		
Norway	7			1	1	4	1	3			2	2		
Romania	1					1	0	1						
Sweden	3			2	2	1	1							
United Kingdom	4			2	2	2	in process							
OCTOBER														
Denmark	3			2	2	1	1							
Finland	2			1	1	1	1							
France	5			3	3						2	2		
Germany	6			2	2	4	in process							
Greece	1					1	1							
Iceland	9					8	4	4			1	1		
Ireland	11			1	1	9	1	1					1	0
Latvia	3			1	1						2	2		
Lithuania	1										1	1		
Netherlands	3			1	1	2	0	2						
Norway	28			5	4	19	3	15			3	2	1	0
Poland	1	1	0											
Portugal	7			2	2	2	in process		3	in process				
Spain	5			3	3						2	2		
Sweden	3					2	2				1	1		
United Kingdom	29			5	2	21	11	6			3	0		
NOVEMBER														
Austria	4			2	2	1	0	1					1	1
Belgium	3			2	2	1	1							
Croatia	3			2	2						1	1		
Czech Republic	2					2	2							
Denmark	16			7	7	6	3	3			3	3		
Finland	1			1	1									
France	16			8	8	4	3	1			2	2	2	2
Germany	8			5	5	3	0	3						
Greece	1					1	0							
Iceland	3					2	0	2			1	1		
Ireland	49			18	12	22	7	5	2	0	7	6		
Italy	7			2	2	3	1	2			2	2		
Latvia	10			2	2	3	3				5	5		
Lithuania	2			2	2									
Netherlands	3			2	2	1	1							
Norway	22			6	5	9	3	4			4	4	3	1
Poland	1	1	0											
Portugal	102	1	0	13	in process	3	in process		26	in process	59	in process		
Slovenia	1			1	1									
Spain	6			2	2	2	2		1	0	1	1		
Sweden	8			5	5	1	0	1			2	2		
United Kingdom	62			9	4	52	14	2			1	in process		
DECEMBER														
Austria	18			5	5	9	7	2			4	4		
Belgium	18			5	3	9	8	0			4	3		
Bulgaria	2			1	0	1	1							
Croatia	6			4	1	1	0	1			1	0		
Cyprus	2					1	in process		1	in process				
Czech Republic	2					2	1	1						
Estonia	1			1	1									
France	36			14	1	7	3	4			15	14		
Germany	13			6	6	6	4	2			1	1		
Greece	6			4	in process	2	in process							
Iceland	5			2	2	2	0	1			1	1		
Italy	12			2	2	6	2	4			4	4		
Latvia	1					1	0	1						
Lithuania	20	1	0	6	6	12	9	3			1	1		
Netherlands	10			1	1	9	7	2						
Norway	15			8	in process	1	in process				1	in process	5	2
Poland	5	2	0	1	0	2	1	0						
Portugal	20			2	2	3	2	1			15	15		
Romania	8										8	8		
Slovenia	9			5	5	3	3				1	1		
Spain	30			12	12	6	0	6			12	12		
United Kingdom	13			3	3	9	9				1	1		
2020														
JANUARY														
Austria	2	1	in process						1	in process				
Bulgaria	28			15	in process	11	in process				2	0		
Cyprus	26			4	in process	21	in process				1	in process		
Czech Republic	5			2	2	3	3							
Estonia	14			7	4	3	1	1			4	4		
France	1										1	1		
Germany	24			6	6	9	8	1			8	8	1	1
Greece	45			22	in process	20	in process		2	0	1	1		
Italy	3			1	1	1	1				1	1		
Lithuania	2					2	1	1						
Norway	17			1	0	11	in process				5	in process		
Poland	4	1	0	2	1	1	1							
Romania	15			4	3	7	in process		1	0	3	3		
Slovenia	10			6	in process	3	in process				1	1		
Spain	18			13	12				1	0	4	4		
United Kingdom	31			15	in process	10	in process		3	in process	3	in process		
FEBRUARY												in process		
Bulgaria	26			5	in process	12	in process				9			
Cyprus	21			3	in process	13	in process				5	in process		
Germany	7			5	5	2	2							
Slovenia	30			10	in process	14	in process		2	in process	4	in process		
MARCH														
Bulgaria	9			1	in process	1	in process				7	in process		
Slovenia	16					4	in process				12	in process		
	1076	8	0	325	176	439	144	88	43	0	247	130	14	7
26 Countries			0.74%		30.2%		40.8%			4.0%		23.0%		1.3%
					71.7%							28.3%		

*** Note: Where clinical sample and a virus isolate from the same patient were received, this is counted as one in the Total Received and following columns.**

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

Includes clinical samples in lysis-mix from Northern Ireland and Scotland and RNA extracts from Greece and Portugal for which genetic characterisation only can be performed. In addition, some clinical samples from Bulgaria, Estonia, Greece, Ireland, Poland and Portugal were not cultured as either sequencing from the clinical sample failed or sequences generated were identical to those from other clinical samples.

As of 2020-05-01

Influenza A(H1N1)pdm09 virus analyses

While no A(H1N1)pdm09 viruses from EU/EEA countries were characterised antigenically since the March 2020 report, Table 3 shows HI results repeated from the March report but with genetic group information updated. Test viruses are sorted by date of collection and genetic group/subgroup.

14/18 (78%) A(H1N1)pdm09 test viruses were antigenically indistinguishable from the A/Michigan/45/2015 northern hemisphere 2018–19 influenza season vaccine virus [4], being recognised at titres within twofold of the titre of the post-infection ferret antiserum with the homologous virus. Somewhat poorer recognition was observed with the ferret antiserum raised against egg-propagated A/Brisbane/02/2018, the northern hemisphere 2019–20 influenza season vaccine virus [1], and A/Switzerland/3330/2017 (genetic subgroup 6B.1A5B) with 12/18 (67%) and 14/18 (78%) being recognised at titres within twofold and fourfold, respectively. Antisera raised against an egg-propagated subgroup 6B.1A5A virus with **HA1 D187A** and **Q189E** substitutions, A/Guangong-Maonan/SWL1536/2019 (vaccine recommendation for the northern hemisphere 2020–2021 influenza season), gave a higher homologous titre and recognised test viruses slightly less well: 10/18 (56%) within twofold but 14/18 (78%) with fourfold of the homologous titre. The four test viruses showing low reactivity with antisera raised against all three vaccine viruses all carried **HA1 N156K** amino acid substitution (Table 3), often having additional substitutions with a phylogenetic group being formed by those that carried additional substitutions of **K130N** and **L161I** in genetic subgroup **6B.1A5A** (Figures 1a and 1b).

Antisera raised against three cell culture-propagated viruses (A/Paris/1447/2017 [6B.1A], A/Norway/3433/2018 [6B.1A5A] and A/Ireland/84630/2018 [6B.1A6]) recognised between 61–83% of test viruses at titres within fourfold of the respective homologous titres. The antiserum raised against cell culture-propagated A/Denmark/3280/2019 (subgroup 6B.1A5A), a virus encoding **HA1** amino substitution **N156K**, recognised only 3/18 (17%) test viruses, all of which also carried **N156K** substitution, at titres within both twofold and fourfold of the homologous titre. The fourth test virus with this substitution, A/Sachsen/3/2020, showed an eightfold reduced titre and carried additional **HA1** substitutions of **P137S** and **A195E**.

The first A(H1N1)pdm09 HA phylogeny is repeated from the March 2020 report and was generated based on sequences deposited in GISAID for recently circulating viruses with collection dates from 1 February 2020, as of 31 March 2020 (Figure 1a). The second is again based on viruses with collection dates from 1 February 2020, but with sequences deposited in GISAID during April 2020 (Figure 1b). All recently circulating viruses fell into clade 6B.1A, defined by the amino acid substitutions **S74R**, **S84N**, **S162N** (introducing a potential N-linked glycosylation site), **S164T** (which alters the glycosylation motif at residues 162 to 164), **I216T** and **I295V** in **HA1**. Within clade 6B.1A, clusters of viruses (genetic groups) encoding a range of **HA** amino acid substitutions have emerged, with most recently circulating viruses carrying the substitution **S183P** in **HA1**, although this is not retained in all genetic groups. Figures 1a and 1b are annotated with **HA1 S183P** substitution groups assigned for the February 2019 WHO Vaccine Consultation Meeting (6B.1A/183P-1 to -7, abbreviated to 6B.1A1 to 6B.1A7); the recommended vaccine viruses for the northern hemisphere 2019–2020 and 2020–2021 influenza seasons are shown in red [1, 3]. The seven subclades are defined by the following HA amino acid substitutions:

1. Subclade **6B.1A1** viruses, represented by the current vaccine virus **A/Brisbane/02/2018**, carry an HA gene mutation encoding **HA1 S183P** amino acid substitution;
2. Subclade **6B.1A2** viruses, represented by **A/Denmark/2728/2019**, carry HA gene mutations encoding **HA1 S183P** and **L233I** with **HA2 V193A** amino acid substitutions - a subgroup within this subclade has emerged with additional **HA1** amino acid substitutions of **N129D, K130N, P137S, N156K** and **K211R** (e.g. **A/Hong Kong/110/2019**);
3. Subclade **6B.1A3** viruses, represented by **A/Norway/3737/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions;
4. Subclade **6B.1A4** represented by **A/Hungary/20/2018** carries HA gene mutations encoding **HA1 N129D, A144E** and **S183P** amino acid substitutions;
5. Subclade **6B.1A5** viruses carry HA gene mutations encoding **HA1 S183P** and **N260D** amino acid substitutions and splits into two subgroups designated **6B.1A5A** represented by **A/Norway/3433/2018** with additional **HA1** amino acid substitutions of **N129D** and **T185A**, and **6B.1A5B** represented by **A/Switzerland/3330/2017** with additional amino acid substitutions of **HA1 E235D** and **HA2 V193A**;
6. Subclade **6B.1A6** viruses, represented by **A/Ireland/84630/2018**, carry HA gene mutations encoding **HA1 T120A** and **S183P** amino acid substitutions, like subclade **6B.1A3** viruses, but fall within a separate phylogenetic branch which is closer to subclade **6B.1A5** viruses;
7. Subclade **6B.1A7** viruses, represented by **A/Slovenia/1489/2019**, carry HA gene mutations encoding **HA1 K302T** and **HA2 I77M, N169S** and **E179D** amino acid substitutions sometimes with additional **HA1** substitutions of **E68D, S121N** and **L161I** (e.g. **A/Moscow/193/2019**). Note: a subgroup of this subclade has emerged with **P183S** (reversion)**, T185I, I240V** and **I286L** substitutions in **HA1** (e.g. **A/Estonia/120012/2019**).

The majority of recently circulating viruses have fallen in subgroup **6B.1A5A**, which contains a number of virus clusters, two of which have been detected in significant numbers, one defined by **HA1 D187A** and **Q189E** substitutions, and the other by **HA2 V193A** substitution. Significant numbers of viruses in subgroup **6B.1A5B** (with additional **HA1** substitutions of **K130N**, **K160M**, **T216K** and **H296N**) have also been detected. However, as indicated in the March report, based on sequences deposited in GISAID for viruses detected in February and March 2020, the vast majority fell

in subgroup 6B.1A5A, with an approximately equal split between two genetic clusters defined by **HA1** amino acid substitutions of either **D187A** and **Q189E** or **K130N**, **N156K**, **L161V** and **V250A**, with a minority falling in a cluster defined by **R205K** substitution and small numbers falling in subclade **6B.1A7** and subgroup **6B.1A5B** (Figure 1a). This pattern was seen for viruses detected in the USA and EU/EEA countries (France, Netherlands, Spain and Sweden). An updated phylogeny, based on sequences deposited in April for viruses detected since the beginning of February, is shown in Figure 1b. This phylogeny is again made up largely with sequences from viruses detected in February, with more from March and none from April, and gives a profile very similar to that of Figure 1a. The majority of most recently deposited sequences were from viruses detected in the Russian Federation and the USA, together with 39 from EU/EEA countries (Bulgaria, Cyprus, Germany, Netherlands, Slovenia and Sweden).

The great majority of viruses in the various subgroups characterised to date have remained antigenically similar to the northern hemisphere 2019–2020 vaccine virus, A/Brisbane/02/2018, as assessed with post-infection ferret antisera and shown in earlier characterisation reports; this is also the case for the relatively small number of viruses tested with antisera raised against A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like viruses (with **HA1 D187A** and **Q189E** amino acid substitutions) that were recommended for use in the northern hemisphere 2020–2021 influenza season [3].

Table 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 fereret antisera								
					A/Mich 45/15 Egg F31/16[-1] 6B.1	A/Paris 1447/17 MDCK F03/18[+2] 6B.1A	A/Bris 02/18 Egg F09/19[-1] 6B.1A1	A/Norway 3433/18 MDCK F04/19[-1] 6B.1A5A	A/Denmark 3280/19 MDCK F08/20[-1] 6B.1A5A	CNIC-1909 A/G-MSWL1536/19 Egg CNIC F1014/19 6B.1A5A	A/Swit 3330/17 Egg F23/18[-1] 6B.1A5B	A/Ire 84630/18 MDCK F08/19[-1] 6B.1A6
REFERENCE VIRUSES												
A/Michigan/45/2015		6B.1	2015-09-07	E3/E3	640	160	640	1280	<	640	640	640
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	1280	2560	1280	2560	<	640	1280	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E1	1280	2560	640	2560	<	640	640	1280
A/Norway/3433/2018		6B.1A5A	2018-10-30	MDCK3	320	640	320	1280	<	320	320	320
A/Denmark/3280/2019	N156K	6B.1A5A	2019-11-10	MDCK4/MDCK3	40	40	40	160	640	40	40	<
CNIC-1909 (A/Guangong-Maonan/SWL1536/2019)	D187A, Q189E	6B.1A5A	2019-06-17	E2/E8/E1	2560	2560	1280	2560	80	1280	1280	2560
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	640	1280	640	1280	<	320	640	640
A/Ireland/84630/2018		6B.1A6	2018-11-28	MDCK1/MDCK3	1280	2560	1280	2560	<	640	1280	2560
TEST VIRUSES												
A/Norway/2906/2019		6B.1A7	2019-12-16	MDCK1/MDCK1	1280	2560	1280	2560	<	640	640	1280
A/Norway/2886/2019		6B.1A7	2019-12-18	MDCK1	640	2560	1280	2560	<	640	640	1280
A/Norway/3118/2019		6B.1A7	2019-12-29	MDCK1	640	1280	640	2560	<	640	320	640
A/Lithuania/MB39709/2019		6B.1A5A	2019-11-20	MDCK2/MDCK1	320	640	320	640	<	320	320	640
A/Lithuania/MB39710/2019		6B.1A5A	2019-11-27	MDCK2/MDCK1	320	640	160	640	<	320	160	320
A/Lithuania/MB39704/2019		6B.1A5A	2019-12-01	MDCK2/MDCK1	640	640	320	1280	<	640	320	640
A/Lithuania/MB40148/2019		6B.1A5A	2019-12-04	MDCK2/MDCK1	320	640	160	640	<	320	160	320
A/Norway/2970/2019	K130N, N156K, L161I, V250A	6B.1A5A	2019-12-24	MDCK1/MDCK2	<	<	<	80	640	<	<	<
A/Norway/2969/2019		6B.1A5A	2019-12-24	MDCK1	640	1280	640	1280	<	640	320	640
A/Hessen/2/2020		6B.1A5A	2020-01-13	C1/MDCK1	640	1280	640	2560	40	640	640	640
A/Sachsen/3/2020	P137S, N156K, A195E	6B.1A5A	2020-01-14	C1/MDCK1	80	160	40	640	80	40	80	40
A/Baden-Wurttemberg/11/2020		6B.1A5A	2020-01-20	C1/MDCK1	640	640	320	1280	<	640	320	640
A/Rheinland-Pfalz/12/2020		6B.1A5A	2020-01-30	C1/MDCK1	640	640	320	1280	<	320	320	320
A/Thuringen/17/2020	V47A, R113S, K130N, H138R, N156K, L161I, K209M, V250A	6B.1A5A	2020-02-01	C1/MDCK1	<	<	<	40	320	<	<	<
A/Berlin/28/2020	K130N, N156K, L161I, V250A	6B.1A5A	2020-02-01	C1/MDCK1	40	<	40	160	1280	40	40	<
A/Bremen/5/2020		6B.1A5A	2020-02-04	C1/MDCK1	1280	2560	640	2560	<	1280	640	1280
A/Baden-Wurttemberg/73/2020		6B.1A5A	2020-02-11	C1/MDCK1	640	640	320	1280	<	640	320	640
A/Mecklenburg-Vorpommern/3/2020		6B.1A5A	2020-02-11	C1/MDCK1	1280	1280	640	2560	<	1280	640	1280
					Vaccine NH 2018-19 SH 2019		Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21		

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

1 < = <40; 2 < = <80; ND =Not Done

Figure 1a. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID, March 2020)

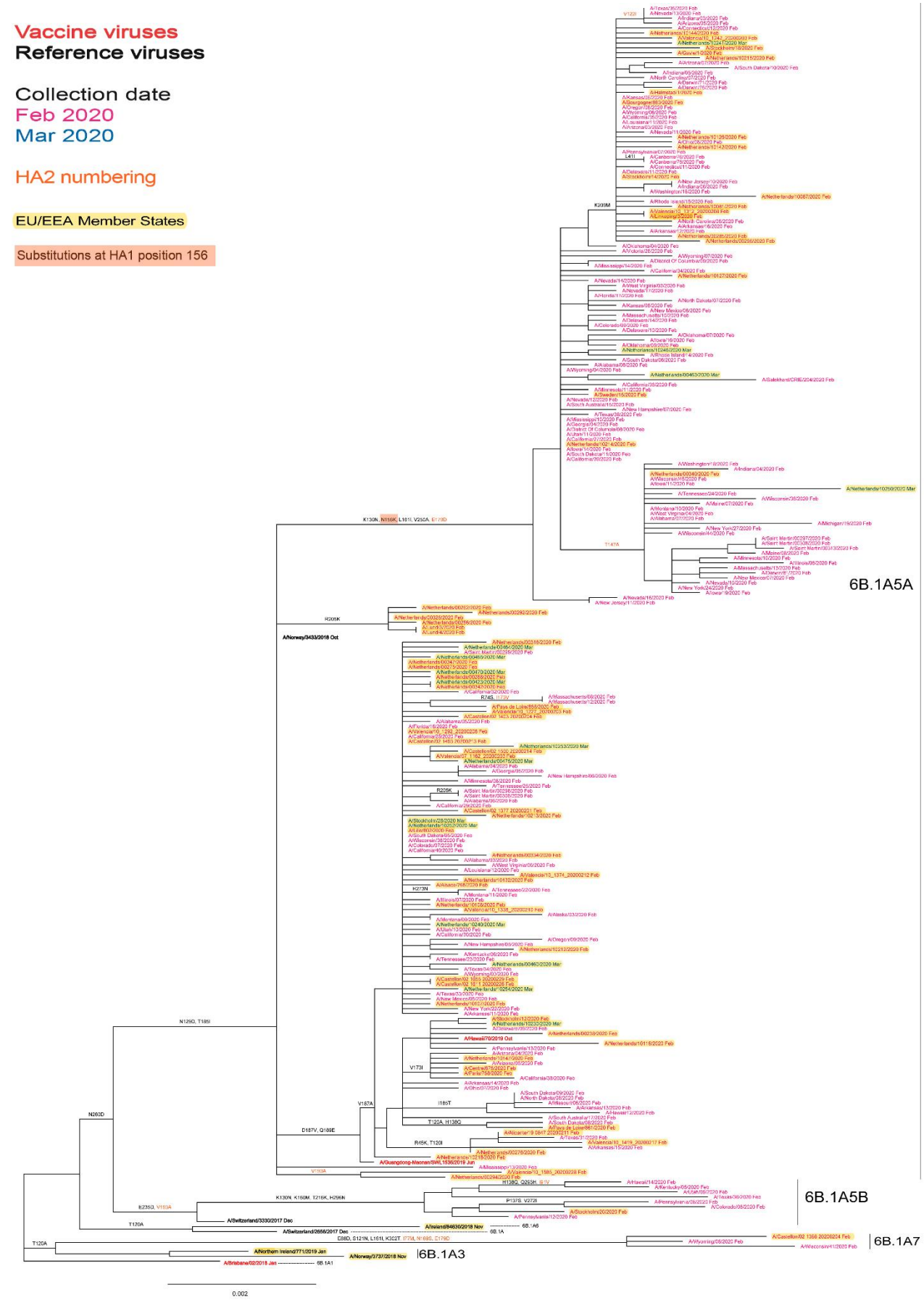


Figure 1b. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes (GISAID, April 2020)

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.

No A(H3N2) viruses from EU/EEA countries were characterised antigenically since the March 2020 report, but Table 3 shows HI results repeated from the March report but with genetic group information updated. Test viruses are sorted by date of collection and genetic group/subgroup.

Test viruses were poorly recognised by antiserum raised against the egg-propagated subgroup 3C.2a1b+T131K virus A/South Australia/34/2019, the vaccine virus for the southern hemisphere 2020 season, only two being recognised at titres within fourfold of the homologous titre [2]. Similarly, antisera raised against two cell culture-propagated subgroup 3C.2a1b viruses, A/La Rioja/2202/2018 (3C.2a1b+T135K-A) and A/Norway/3275/2018 (3C.2a1b+T131K), for which no homologous titres are given due to the inability of these cell culture-propagated reference viruses to agglutinate RBCs, recognised only three (15%) and four (20%) test viruses, respectively, at titres of ≥160. Test viruses reacted better with antiserum raised against the northern hemisphere 2018–19 vaccine virus [4], egg-propagated A/Singapore/INFOMH-16-0019/2016 (3C.2a1), with seven (35%) and 19 (95%) test viruses being recognised at titres within twofold and fourfold of the homologous titre, respectively.

Antisera raised against two cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, recognised 15 (75%) and 17 (85%) test viruses at titres within twofold, respectively, with both antisera recognising 90% of test viruses within fourfold of homologous titres. However, the antiserum raised egg-propagated NYMC X-327 (A/Kansas/14/2017), the vaccine virus for the northern hemisphere 2019–2020 season [1], recognised only 16 (80%) test viruses at titres within fourfold of the homologous titre. Antiserum raised against cell culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised all but one (95%) test viruses at titres within fourfold of the homologous titre. Antiserum raised against a tissue culture-propagated subgroup 3C.2a1b+T135K-B virus, A/Hong Kong/2669/2019, recognised five (91%) test viruses in subgroups 3C.2a1b+T135K-A/B at titres within twofold of the homologous titre, but antiserum raised against the egg-propagated cultivar of A/Hong Kong/2671/2019 gave poor recognition of the great majority of test viruses with only one (5%) reacting within fourfold of the homologous titre.

Overall, the HI data show poor recognition of test viruses by post-infection ferret antisera raised against two of four egg-propagated vaccine/reference viruses. The HA genes of the 20 test viruses fell in three clusters, 15 in clade 3C.3a, four in subgroup 3C.2a1b+T135K-A and one in subgroup 3C.2a1b+T135K-B (Table 4), so the HI data indicates: (i) poor cross-reactivity of antisera raised against subclade 3C.2a2 viruses, (ii) significant clade specificity of the antisera raised against cell culture-propagated clade 3C.3a viruses, A/England/538/2018 and A/Kansas/14/2017, and (iii), of the six antisera raised against cell culture-propagated viruses, the one raised against A/Hong Kong/5738/2014 (clade 3C.2a) gives the broadest cross-clade/subclade reactivity.

Viruses in clade 3C.2a have been dominant since the 2014–15 influenza season, and subgroup 3C.2a1b viruses predominated over the course of the 2018–19 season, but the HA gene sequences of viruses in both clades 3C.2a and 3C.3a continue to diverge. Notably, clade 3C.3a viruses have evolved to carry **HA1** amino acid substitutions of **L3I, S91N**, **N144K** (loss of a N-linked glycosylation motif at residues 144-146), **F193S** and **K326R**, and **D160N** in **HA2**, compared with cell culture-propagated A/Stockholm/6/2014, and levels of detection since January 2019 had increased in a number of WHO European Region countries and North America. Greater variation has been observed among clade 3C.2a viruses, resulting in the designation of new subclades/subgroups. Amino acid substitutions that define these subclades/subgroups are:

- 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** (a former vaccine virus)
- Subgroup **3C.2a1a**: Those in subclade **3C.2a1** plus **T135K** in **HA1**, resulting in the loss of a potential glycosylation site, and **G150E** in **HA2**, e.g. **A/Greece/4/2017**
- Subgroup **3C.2a1b**: Those in subclade **3C.2a1** plus **E62G, R142G** and **H311Q** in **HA1**, often with additional amino acid substitutions – notably **HA1 T131K** and **HA2 V200I**, the **3C.2a1b+T131K** cluster (e.g. **A/South Australia/34/2019**) or **HA1 T135K** (resulting in the loss of a potential glycosylation site) commonly with **T128A** (resulting in the loss of a potential glycosylation site), the **3C.2a1b+T135K-A** cluster (e.g. **A/La Rioja/2202/2018**) or a recently emerged, antigenically distinct group with **HA1 T135K, T128A, S137F, A138S** and **F193S**, the **3C.2a1b+T135K-B** cluster (e.g. **A/Hong Kong/2675/2019**)

[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: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf

- Clade **3C.3a**: represented by **A/Switzerland/9715293/2013** (see above), but recently a resurgence of clade **3C.3a** viruses, carrying additional substitutions of **S91N, N144K** (resulting in the loss of a potential glycosylation site)**, and F193S** in **HA1** and **D160N** in **HA2**, e.g. **A/England/538/2018** and **A/Kansas/14/2017**, the A(H3N2) vaccine virus for the 2019–20 influenza season.

An HA phylogeny was generated for the March report based on sequences deposited in GISAID for recently circulating viruses with collection dates from 1 February 2020, as of 31 March 2020, the great majority of which were from Europe and the USA (Figure 2a). Globally, viruses in the **3C.2a1b** subgroup had circulated recently in the greatest numbers, with a majority falling in the **3C.2a1b+T131K** cluster. Diversification of subgroup **3C.2a1b** viruses with **HA1 T135K** substitution had occurred, notably with significant geographic spread of viruses in the antigenically distinct **3C.2a1b+T135K-B** cluster, a factor that influenced the selection of an A/Hong Kong/2671/2019-like virus as the A(H3N2) component of vaccines for the 2020–2021 northern hemisphere influenza season [3]. The geographic distribution of clade 3C.3a viruses was more restricted with the great majority of recently detected viruses being reported from the European Region, notably by countries in the western part of the Region (France, Germany, Netherlands [the greatest number], Spain and Sweden) and the USA (Figure 2a). While viruses of subgroups 3C.2a1b+T135KA/B represented the majority of detections in the USA, clade 3C.3a and subgroup 3C.2a1b+T131K viruses were dominant in Europe. An updated phylogeny, based on sequences deposited in April for viruses detected since the beginning of February, is shown in Figure 2b. This phylogeny is again made up largely with sequences from viruses detected in February, with more from March and none from April, and gives a profile very similar to that of Figure 2a. An apparent decrease in the proportion of viruses in the **3C.2a1b+T131K** cluster, compared to that in the March report, is due to the Netherlands having deposited a large number of sequences from viruses falling in this cluster before preparation of the March report. Sequences from viruses detected in six EU/EEA countries (Bulgaria, Cyprus, Germany, Netherlands, Slovenia and Sweden) were deposited in GISAID in approximately equivalent numbers during April.

The locations of A/Kansas/14/2017 (3C.3a), the A(H3N2) virus recommended for inclusion in vaccines for the northern hemisphere 2019–20 influenza season [1], and A/South Australia/34/2019 (3C.2a1b+T131K), the A(H3N2) virus recommended for inclusion in vaccines for the southern hemisphere 2020 influenza season [2], are indicated in Figures 2a and 2b in red. The location on the A/Hong Kong/2671/2019 (**3C.2a1b+T135K-B**) virus and its cell culture-equivalent A/Hong Kong/45/2019, recently recommended for egg- and cell culture-generated vaccines to be used in the 2020–2021 northern hemisphere season [3], are also indicated.

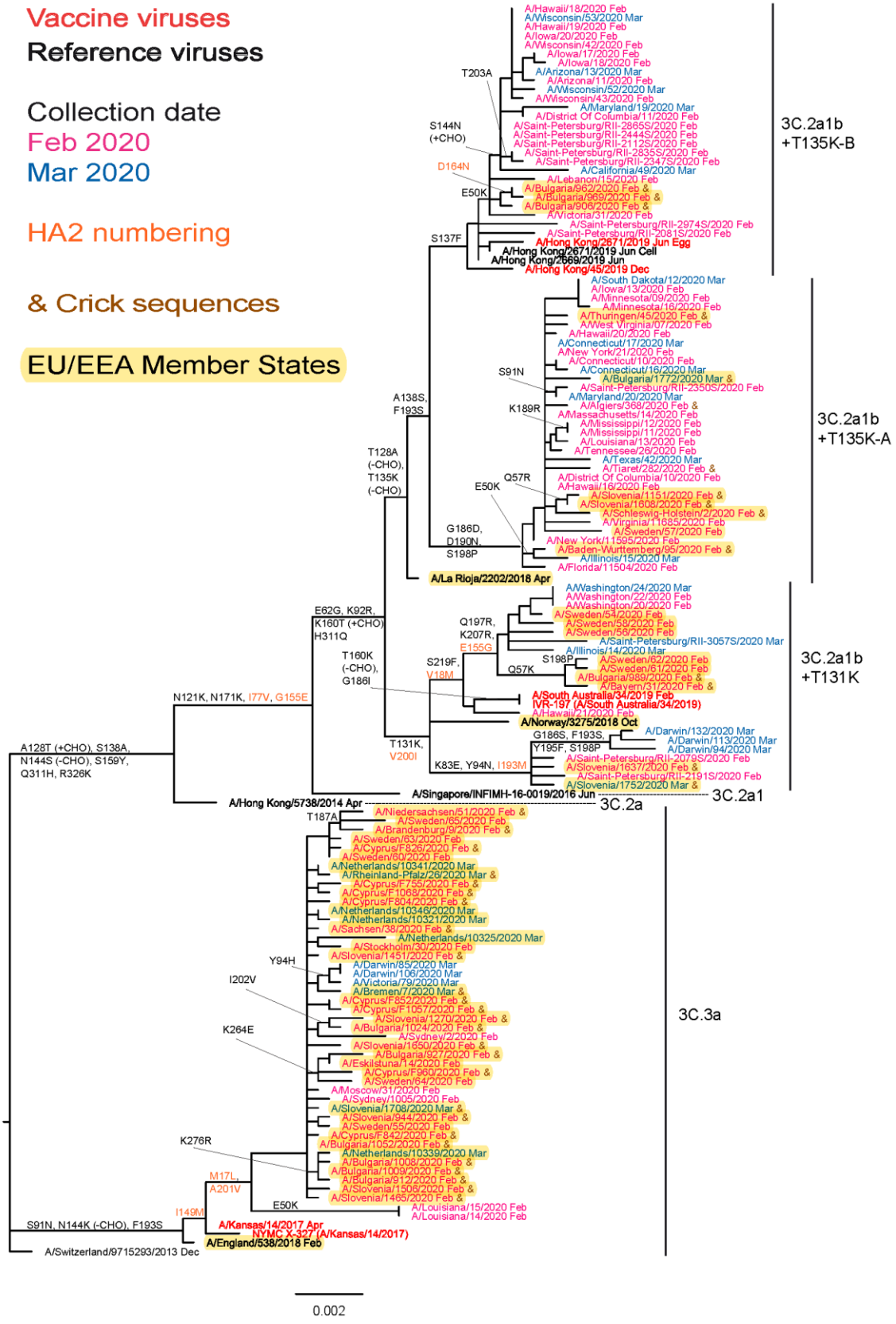
Table 4. Antigenic analysis of A(H3N2) viruses by HI

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
				A/HK	A/Singapore	A/Norway	A/Sth Aus	A/La Rioja	A/HK	A/HK	A/Eng	NYMC X-327	A/Kansas
				5738/14	0019/16	3275/18	34/19	2202/18	2671/19	2669/19	538/18	A/Kansas/14	14/17
				MDCK	Egg 10^{-4}	SIAT	Egg	SIAT	Egg	SIAT	SIAT	Egg	SIAT
	Passage history			St Judes	F13/19^{-1}	F03/19^{-1}	F45/19^{-1}	F26/18^{-1}	F44/19^{-1}	F04/20^{-1}	F31/18^{-1}	F16/19^{-1}	F17/19^{-1}
	Ferret number			F60/17^{-1}									
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T131K	3C.2a1b+T131K	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK3/SIAT2	160	160	160	160	80	<	40	160	160	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E2	160	320	40	40	160	80	80	40	40	<
A/South Australia/34/2019	3C.2a1b+T131K	2019-02-06	E6/E1	160	320	640	640	40	160	<	40	40	40
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E2	40	160	<	40	40	640	160	160	320	80
A/Hong Kong/2669/2019	3C.2a1b+T135K-B	2019-06-18	MDCK1/SIAT5	160	160	320	160	160	160	320	160	80	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT4	40	40	<	<	<	40	<	640	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	<	<	<	<	<	160	<	320	640	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	80	<	<	<	40	<	640	160	320
TEST VIRUSES													
A/Athens.GRI1848/2019	3C.2a1b+T135K-A	2019-10-02	SIAT1	80	160	320	80	160	80	160	160	80	80
A/Lithuania/MB40701/2019	3C.2a1b+T135K-A	2019-12-07	SIAT1/SIAT2	40	80	80	<	80	<	160	40	<	<
A/Baden-Wurttemberg/17/2020	3C.2a1b+T135K-A	2020-01-21	C2/SIAT2	80	160	160	40	160	80	160	160	80	160
A/Schleswig-Holstein/2/2020	3C.2a1b+T135K-A	2020-02-03	C1/SIAT1	160	320	160	160	160	80	160	160	160	160
A/Ireland/91453/2019	3C.2a1b+T135K-B	2019-11-17	SIAT1	40	80	80	<	<	80	160	40	<	40
A/Ireland/85561/2019	3C.3a	2019-10-24	SIAT2	40	80	<	<	<	<	<	320	160	320
A/Ireland/88070/2019	3C.3a	2019-11-02	SIAT2	40	80	<	<	<	<	<	320	160	320
A/Ireland/89141/2019	3C.3a	2019-11-06	SIAT2	40	80	40	40	40	40	<	640	320	320
A/Ireland/91781/2019	3C.3a	2019-11-17	SIAT2	40	80	<	<	<	<	<	320	160	320
A/Belgium/G0506/2019	3C.3a	2019-11-28	SIAT2	80	160	40	40	40	40	<	640	320	640
A/Belgium/G0514/2019	3C.3a	2019-12-10	SIAT1	40	80	<	<	<	40	<	640	320	320
A/Belgium/G0528/2019	3C.3a	2019-12-19	SIAT1	80	160	<	40	40	40	<	640	160	320
A/Belgium/G0542/2019	3C.3a	2019-12-23	SIAT1	40	160	<	40	40	40	<	640	320	640
A/Bulgaria/1575/2019	3C.3a	2019-12-23	SIAT1	40	80	<	<	<	40	<	640	160	320
A/Bayern/2/2020	3C.3a	2020-01-13	C1/SIAT1	40	80	<	<	<	40	<	640	160	320
A/Athens.GRI84/2020	3C.3a	2020-01-14	SIAT1	160	320	640	320	40	160	40	640	320	320
A/Sachsen/5/2020	3C.3a	2020-01-21	C1/SIAT1	<	<	<	<	<	<	<	320	160	160
A/Berlin/21/2020	3C.3a	2020-01-28	C1/SIAT1	40	80	<	<	<	<	<	320	160	320
A/Thuringen/11/2020	3C.3a	2020-01-30	C1/SIAT1	40	80	<	<	<	<	<	320	160	160
A/Niedersachsen/51/2020	3C.3a	2020-02-11	C1/SIAT1	40	80	<	<	<	<	<	320	160	160
					Vaccine NH 2018-19		Vaccine SH 2020		Vaccine NH 2020-21			Vaccine NH 2019-20	

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

Figure 2a. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID, March 2020)

Figure 2b. Phylogenetic comparison of influenza A(H3N2) HA genes (GISAID, April 2020)



Influenza B virus analyses

A total of 304 influenza type B viruses with collection dates after 31 August 2019 have been received at the WIC (Table 2). Of these, 261 were sent with pre-assignment to a lineage: 247 B/Victoria and 14 B/Yamagata.

Influenza B/Victoria-lineage

No B/Victoria-lineage viruses from EU/EEA countries were characterised antigenically since the March report.

All recently circulating B/Victoria-lineage viruses have fallen in genetic **clade 1A**, represented by **B/Brisbane/60/2008** a former vaccine virus, but with additional **HA1** amino acid substitutions of **I117V, N129D** and **V146I** (e.g. **B/Ireland/3154/2016**). Viruses retaining full-length HAs have remained antigenically similar to B/Brisbane/60/2008. However, three genetic groups (described below with amino acid substitutions/deletions relative to B/Brisbane/60/2008 indicated) containing deletions of HA gene codons have emerged and the viruses in these groups are antigenically distinct from B/Brisbane/60/2008 and each other (as noted in the September 2018 characterisation report[4] and earlier ones), such that four antigenically distinguishable groups had been circulating:

- A group with double deletion of **HA1** residues **162** and **163** (**subclade △162-163** or **1A(△2)**) with amino acid substitutions of **D129G** and **I180V**, and **HA2 R151K** that spread worldwide and is represented by the current vaccine virus, **B/Colorado/06/2017**;
- A group with triple deletion of **HA1** residues **162** to **164** (**subclade △162-164A** or **1A(△3)A**), first detected in Asia, with amino acid substitutions of **I180T** and **K209N** that showed limited spread worldwide and is represented by **B/Hong Kong/269/2017**;
- A group with triple deletion of **HA1** residues **162** to **164** (**subclade △162-164B** or **1A(△3)B**), first detected in Africa, with amino acid substitution **K136E** often with **G133R** that showed geographic spread in recent months and is represented by the recently recommended vaccine virus **B/Washington/02/2019**.

An HA phylogeny was generated for the March report based on sequences deposited in GISAID for recently circulating viruses with collection dates from 1 February 2020, as of 31 March 2020 (Figure 3a). Over the six months to the end of March, viruses in **subclade 1A(△3)B** dominated, with the great majority having **HA1 K136E,** often with **G133R** substitution, and a number of virus clusters have emerged defined by specific amino acid substitutions, e.g. **HA1 N126K, E128K** or **N150K** with **G184E**, **N197D** (loss of a glycosylation site) and **R279K**, and relatively few **subclade 1A(△2)** viruses had been detected. Submission of sequences from recently circulating B/Victoria lineage viruses (February and March 2020) had been dominated by the USA, but those from 24 viruses detected in EU/EEA countries (France, Netherlands, Spain and Sweden) all fell within **subclade 1A(△3)B** , notably in two clusters defined by **HA1 N126K** or **N233K** (loss of a glycosylation site) (Figure 3a). An updated phylogeny, based on sequences deposited in April for viruses detected since the beginning of February, is shown in Figure 3b. This phylogeny is made up largely with sequences from viruses detected in the Russian Federation, the USA, and 57 viruses from EU/EEA countries (Bulgaria, Cyprus, Germany, Netherlands, Slovenia and Sweden) for which viral sequence analysis was conducted during February and March, and gives a profile very similar to that of Figure 3a. A notable difference is a cluster of viruses defined by **HA1 D129N** amino acid substitution (a reversion) which splits into three subclusters defined by additional substitutions. Viruses from this cluster have not been characterised antigenically at the WIC.

Following the spread of **1A(Δ2)** viruses a representative, B/Colorado/06/2017, was recommended for use in trivalent influenza vaccines for the 2018–19 and 2019–20 northern hemisphere [4, 1] and 2019 southern hemisphere [5] seasons. Recent predominance of **1A(Δ3)B** viruses led to recommendation of a representative (B/Washington/02/2019) for use in trivalent influenza vaccines for the 2020 southern hemisphere and northern hemisphere 2020–2021 seasons [2, 3].

Influenza B/Yamagata-lineage

No B/Yamagata-lineage viruses from EU/EEA countries were characterised either antigenically or genetically at the WIC since the March report.

The HA phylogeny (Figure 4) was updated from the March report to contain the six sequences submitted to GISAID in April, for viruses with collection dates from 1 January 2020. All six viruses were detected in the USA, one in January and five in February. The HA genes continue to fall in genetic **clade 3**, the B/Wisconsin/1/2010–B/Phuket/3073/2013 clade, within a subgroup defined by **HA1 L172Q** and **M251V** amino acid substitutions compared to B/Phuket/3073/2013. Some sub-clustering of sequences from recently collected viruses, defined by specific amino acid substitutions (e.g. **HA1 N164K, K211R, D229N** or **D232N** [introducing a potential N-linked glycosylation site] sometimes with **R48K**), has occurred. As noted in previous characterisation reports for 2018, 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, 2019–2020 and 2020–2021 [4, 1, 3] northern hemisphere and the 2019 and 2020 [5, 2] southern hemisphere seasons.

[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

Figure 3a. Phylogenetic comparison of influenza B/Victoria-lineage HA genes (GISAID, March 2020)

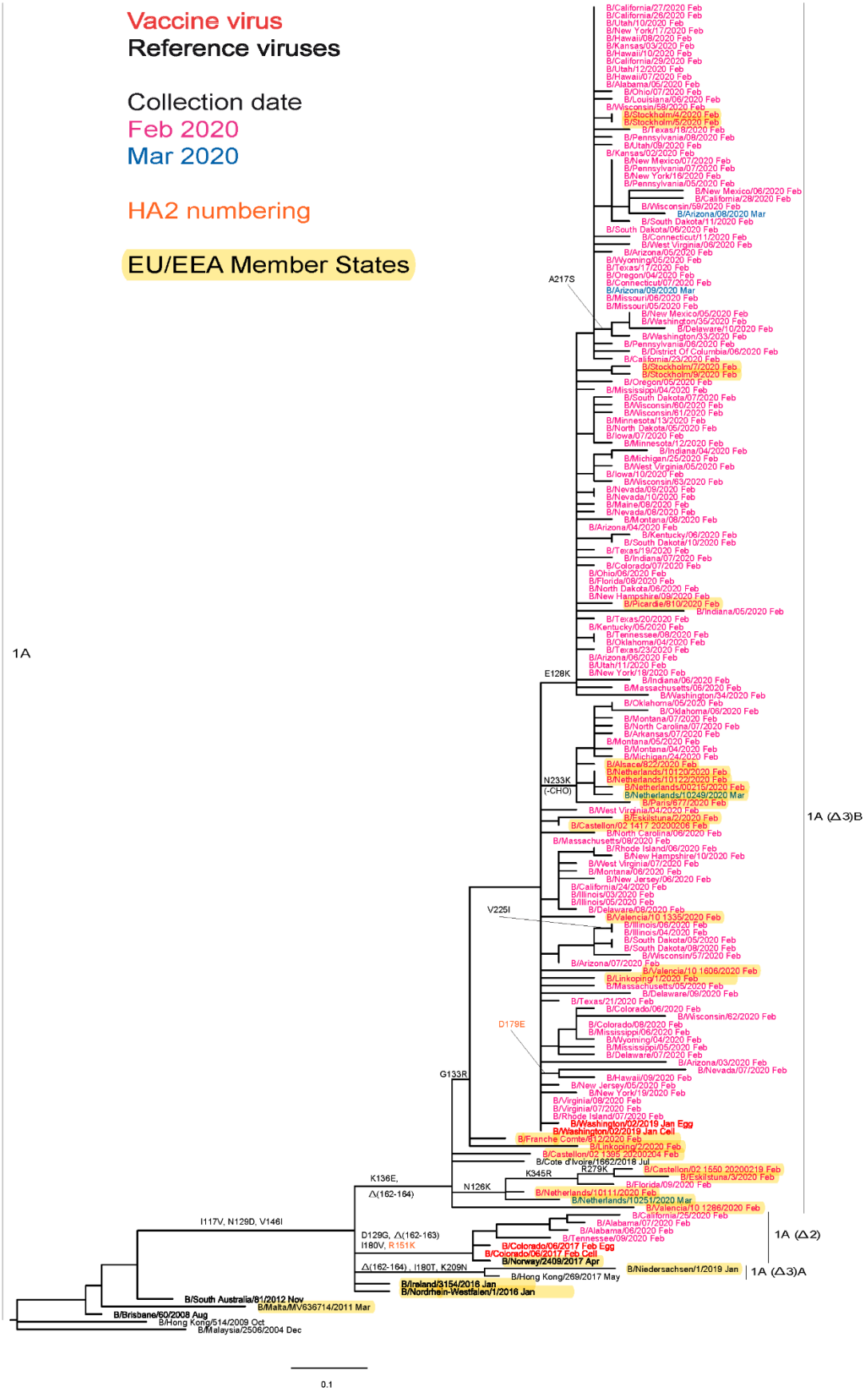


Figure 3b. Phylogenetic comparison of influenza B/Victoria-lineage HA genes (GISAID, April 2020)

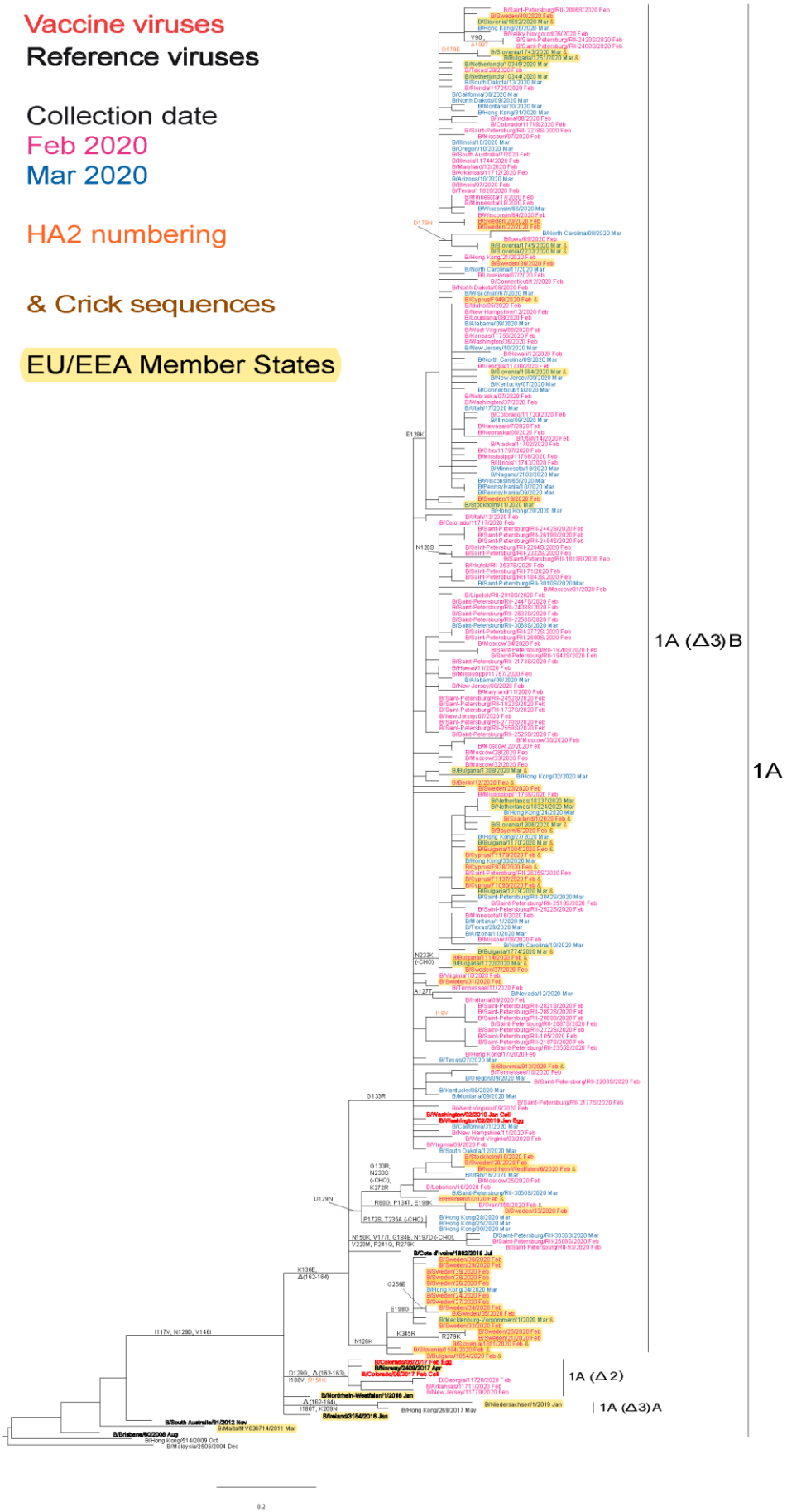
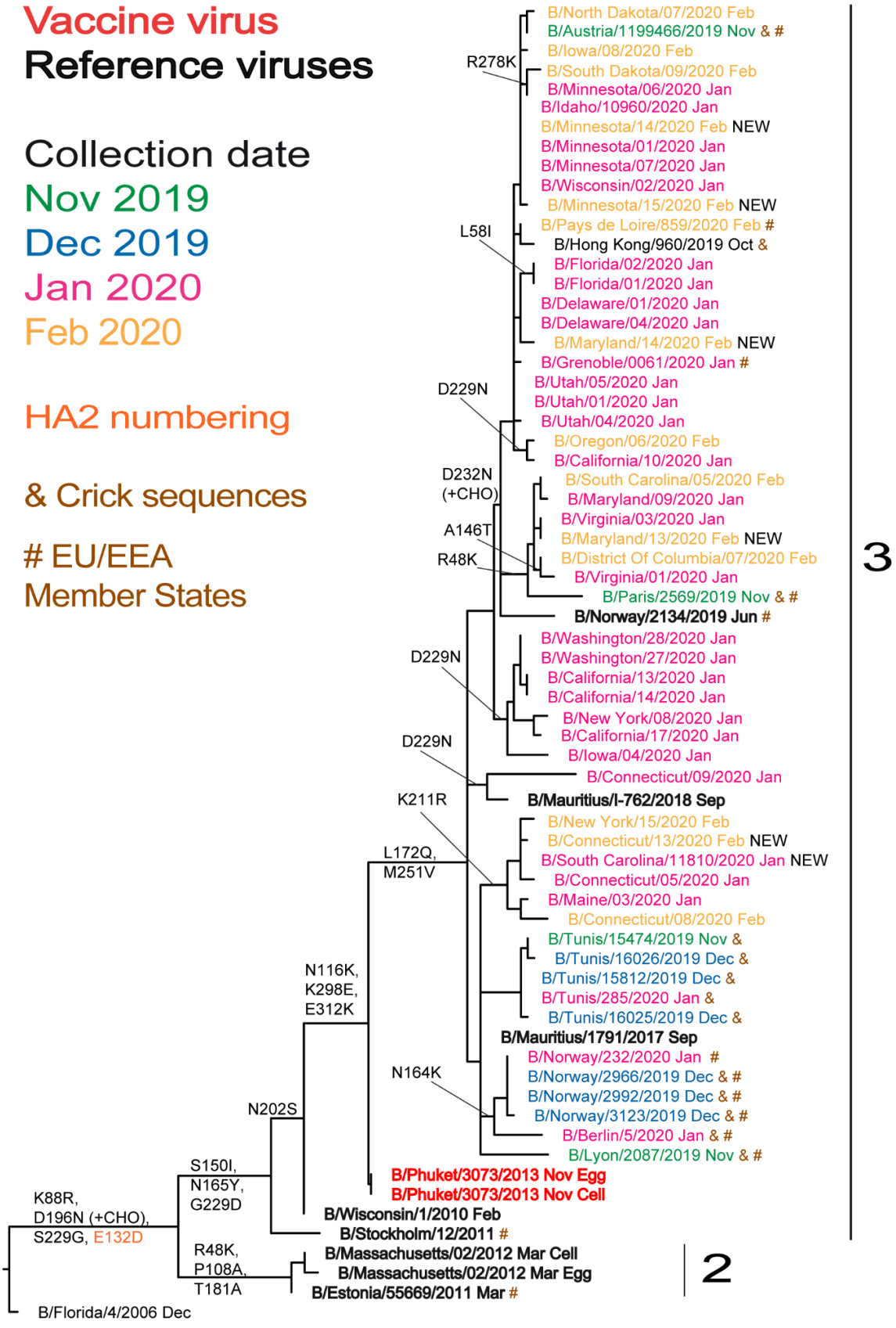


Figure 4. Phylogenetic comparison of influenza B/Yamagata-lineage HA genes (GISAID, April 2020)



Summaries of data submitted to TESSy

Genetic characterisation

For the 2019–20 season, as of week 18/2020, 2 687 viruses had been characterised genetically and ascribed to a genetic clade:

- 962 were A(H1N1)pdm09 viruses, with 925 being subclade 6B.1A5 (884 subgroup 6B.1A5A represented by A/Norway/3433/2018 and 41 subgroup 6B.1A5B represented by A/Switzerland/3330/2018), 19 being subgroup 6B.1A7 represented by A/Slovenia/1489/2019, 11 being subgroup 6B.1A1 represented by A/Brisbane/02/2018 and seven attributed to a known group not listed in the 2019–20 reporting categories
- 1 032 were A(H3N2) viruses, with 332 being subgroup 3C.2a1b+T131K represented by A/South Australia/34/2019, 554 being clade 3C.3a represented by A/Kansas/14/2017, 81 being subgroup 3C.2a1b+T135K-B represented by A/Hong Kong/2675/2019, 64 being subgroup 3C.2a1b+T135K-A represented by A/La Rioja/2202/2018 and one attributed to a known group not listed in the 2019–20 reporting categories
- 26 were B/Yamagata-lineage clade 3 represented by the vaccine virus B/Phuket/3073/2013 with a further two attributed to a known group not listed in the 2019–20 reporting categories
- 665 were B/Victoria-lineage viruses, with 601 being subclade 1A(Δ3)B represented by B/Washington/02/2019, 19 being subclade 1A(Δ2) represented by the vaccine virus B/Colorado/06/2017, five being subclade 1A(Δ3)A represented by B/Hong Kong/269/2017 and 40 attributed to a known group not listed in the 2019–20 reporting categories.

Antiviral susceptibility

Up to week 18/2020, a total of 1 681 viruses (710 A(H1N1)pdm09, 598 A(H3N2) and 373 type B) collected in the course of the 2019–20 season had been tested for susceptibility to neuraminidase inhibitors, oseltamivir and zanamivir. Three A(H1N1)pdm09 viruses carried amino acid substitution H275Y in NA, with one of them also having H295S substitution, both of which are indicative of highly reduced inhibition (HRI) by oseltamivir. One A(H3N2) virus showed HRI by oseltamivir with reduced inhibition (RI) by zanamivir and carried NA R292K amino acid substitution.

At the WIC this season, 535 viruses from EU/EEA countries have been assessed phenotypically against oseltamivir and zanamivir: 185 A(H1N1)pdm09, 198 A(H3N2), 145 B/Victoria-lineage and seven B/Yamagata-lineage. Two A(H1N1)pdm09 viruses (A/Denmark/3295/2019 and A/Denmark/3311/2019) showed HRI by zanamivir associated with NA Q136K amino acid substitution, one A(H3N2) virus (A/Limoges/2326/2019) showed RI by zanamivir associated with NA T148I substitution (resulting in the loss of a potential N-linked glycosylation motif) and one B/Victoria-lineage virus (B/Estonia/125782/2020) showed RI by zanamivir.

Influenza A(H7N9) virus

On 1 April 2013, the World Health Organization (WHO) Global Alert and Response [6] 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 [7]. 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 [8]. WHO posted an analysis of information on A(H7N9) viruses on 10 February 2017 [9], and ECDC published a rapid risk assessment on the implications of A(H7N9) for public health on 3 July 2017 [10]. Current risk assessments are included in the WHO monthly summary and assessment of influenza at human-animal interface (accessed 11 May 2020). The assessment published on 8 May 2020 indicates that there have been no publicly available reports from animal health authorities in China or other countries on influenza A(H7N9) virus detections in animals in recent months [11]. The most recent human case was detected in mid-March 2019 [12]. 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 31 March 2020 and can be found on the ECDC website [13].

Influenza A(H5) virus

The most recent monthly risk assessment of influenza at the human–animal interface was published by WHO on 8 May 2020, while no new human cases were reported, according to reports received by the World Organisation for Animal Health (OIE), various influenza A(H5) subtypes continue to be detected in birds in Africa, Europe and Asia [11]. No new human cases of A(H5N1) infection have been detected since the case in Nepal in March 2019, the first human case of A(H5N1) infection reported to WHO since 2017; there have been, however, reports of A(H5N1) infection in domestic birds since February 2019 [14]. On 18 November 2016, ECDC published a rapid risk assessment related to outbreaks of highly pathogenic avian influenza H5N8 viruses in Europe [15]. As described above, the EU Reference Laboratory for Avian Influenza, in collaboration with ECDC and the European Food Safety Authority, published on 31 March 2020 the latest overview of avian influenza, which can be found on the ECDC website [13].

Influenza A(H9N2) virus

Since the last update on 28 February 2020, two new laboratory-confirmed human cases of influenza A(H9N2) virus infections in China, both in children with mild disease symptoms and exposure to poultry, were reported [11]: one in Guangdong province (30 March 2020, disease onset 22 March) and one in Hunan province (1 May 2020, disease onset 20 April). Avian influenza A(H9N2) viruses are enzootic in poultry in Asia and increasingly reported in poultry in Africa.

WHO CC reports

A description of results generated by the London WHO CC at the WIC and used at the most recent WHO vaccine composition meeting (held in Geneva, Switzerland 24–28 February 2020), and previous ones, can be found at https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports.

Note on the figures

The phylogenetic trees were constructed using RAxML, drawn using FigTree and annotated using Adobe Illustrator. The bars indicate the proportion of nucleotide changes between sequences. Reference strains are viruses to which post-infection ferret antisera have been raised. The colours indicate the month of sample collection. Isolates from WHO NICs in EU/EEA countries are highlighted in yellow or 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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