WORLDWIDE INFLUENZA CENTRE

WHO CC for Reference & Research on Influenza

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Report prepared for the WHO annual consultation on the composition of influenza vaccine for the Southern Hemisphere 2022

13th – 23rd September 2021

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Laboratories involved in Global Influenza Surveillance

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Influenza Epidemiology in the WHO European Region

The epidemiological section of this report was prepared using data reported to The European Surveillance System (TESSy) and presented in Flu News Europe (http://www.flunewseurope.org) the joint ECDC-WHO Europe weekly influenza update, with the assistance of members of the Influenza and Other Respiratory Pathogens Group at the WHO European Office and the ECDC Influenza Surveillance Group:

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WHO Vaccine Recommendation Meeting for the 2022 Southern Hemisphere influenza season

WHO CC, London – Final Report for the meeting: 13-23 September 2021

Epidemiology

Influenza activity in the WHO European Region, October 2020 – August 2021

Note

The novel coronavirus disease 2019 (**COVID-19**) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**), continues to adversely affect healthcare presentations and testing capacities of some countries, territories and areas in the Region. Consequently the analysis presented here, based on data reported to The European Surveillance System (TESSy), should be interpreted with care.

Summary

In the Region as a whole, for surveillance data based on sentinel and non-sentinel sources over weeks 40/2020-32/2021 compared to the same period of the 2019-2020 season, there was a 14.5% increase in the number of clinical specimens tested for influenza but a 99.4% reduction in the number of specimens testing positive for an influenza virus (**Table E1**). With the caveat relating to the low number of detections in 2020-2021 compared to 2019-2020, the ratio of type A:type B has dropped from 2.7:1 to 1.2:1, while the ratio of A subtypes remained the same (0.8:1), with A(H1N1)pdm09 viruses dominating over A(H3N2), and B/Victoria-lineage viruses continued to greatly outnumber those of the B/Yamagata-lineage.

Timing and spread

Over the 2020-2021 season, weeks 40/2020 to 20/2021 representing the period in most seasons when influenza detections can be above baseline (inter-seasonal) levels and reporting to TESSy is conducted on a weekly basis, influenza activity in the WHO European Region remained at baseline levels. A threshold of 10% of tested ILI or ARI specimens from sentinel primary care sites testing positive for influenza viruses has been taken to indicate the start of the influenza season in the Region in previous years. The weekly proportion of specimens testing positive for influenza did not exceed 2% this season (**Figure E1-A/B**). Weekly reporting on the intensity of influenza activity, based on ILI and/or ARI activity, was conducted by 54 countries, territories and areas. Only 11 of these reported activity above baseline, with only two (Ukraine and Kyrgyzstan) having reported medium activity in some weeks. (Note, at least one virus detection per week is required to adhere to the definition for an intensity level above baseline but not all countries, territories or areas reporting intensity above baseline have reported detections) (**Figure E2**).

Distribution of viruses

For the period of weeks 40/2020 to 20/2021 where at least 10 detections were reported in a subregion, the proportions of types A and B viruses were similar in western Europe and northern Europe, but a higher proportion of type A virus detections was reported in eastern

Europe (71%) whereas a higher proportion of type B viruses were detected in southern Europe (62%) (**Table E2-A**).

Combined sentinel and non-sentinel data for type A viruses in the Region showed a higher proportion of A(H1N1)pdm09 viruses (65%) than A(H3N2) viruses (35%), with A(H1N1)pdm09 viruses predominantly being reported in eastern (74%) and northern Europe (67%: **Table E2-A**). Only 16 of the type B viruses reported were ascribed to a lineage and 13 of these were B/Victoria. The subtype distribution proportions for influenza type A viruses detected, from non-sentinel sources, were relatively consistent for most weeks in the season (**Figure E1-C**).

When the analysis was restricted to sentinel source data only for the period weeks 40/2020 to 32/2021, the regional distribution of influenza by type and subtype differed: of the viruses detected (n=47), the majority were type A (62%) and, of these, a higher proportion of A(H1N1)pdm09 viruses was reported (62%). Of the total detections 57% were from eastern Europe (**Table E2-B**). Of influenza type B virus detections from sentinel source data, only two were ascribed to a lineage and both were B/Victoria. A dominant virus (sub)type (comprising 60% or more of at least 10 influenza virus detections) could be assigned by Ukraine only, where A(H1N1)pdm09 was dominant (**Figure E3**).

Influenza virus characterisation

Of 1,008 influenza virus detections between week 40/2020 and 32/2021, genetic characterisation of only 15 viruses was reported to TESSy. Of these, eight viruses had collection dates after week 5/2021.

Of the eight influenza A(H3) viruses characterised six were attributed to the subgroup 3C.2a1b + T131K-A, represented by A/Slovenia/1637/2020, one was attributed to the subgroup 3C.2a1b+T131K-B represented by A/Bretagne/1323/2020, and one was attributed to the subgroup 3C.2a1b + T135K-A, represented by A/Denmark/3264/2019. Five of these viruses had collection dates after week 5/2021: four belonged to the subgroup 3C.2a1b + T131K-A and one to the subgroup 3C.2a1b+T131K-B.

Two A(H1)pdm09 viruses were characterised. One was attributed to the group 6B.1A5A + 187A represented by A/Guangdong-Maonan/SWL1536/2019 and one to the group 6B.1A5A represented by A/Norway/3433/2018 (N156K). Neither A(H1)pdm09 virus had a collection date after week 5/2021.

Five B/Victoria-lineage viruses were characterised, all of which belonged to the clade1A del162-164 group, represented by B/Washington/02/2019. Three of these viruses had collection dates after week 5/2021.

No antigenic characterisation data were reported.

Neuraminidase inhibitor susceptibility

Neuraminidase inhibitor susceptibility was assessed for 13 influenza viruses (8 A(H3) and 5 B/Victoria-lineage) with collection dates between week 40/2020 and 20/2021. Of these, 5A(H3) and 3 B/Victoria viruses had collection dates after week 5/2021. None of the

neuraminidase genes of these 13 viruses carried mutations that encode amino acid substitutions known to be associated with reduced susceptibility to neuraminidase inhibitors. Normal inhibition by oseltamivir and zanamivir was confirmed for three of the B/Victoria-lineage viruses by phenotypic assays.

Hospitalised cases

Between weeks 40/2020 and 20/2021, a total of 14 hospitalised laboratory-confirmed influenza cases were reported to TESSy. Of these, 12 cases were admitted to intensive care units (ICUs) in the United Kingdom (England) (n=9, 75%), Ukraine (n=2, 17%) and Sweden (n=1, 8%). The remaining cases were reported from other hospital wards in Ukraine (n=2). Among the 12 cases admitted to ICUs, 11 were infected with type A viruses (all A(H1N1)pdm09) and one with a type B virus (not ascribed to a lineage). Only three cases had a recorded age, falling within different age groups: one 5-14 years, one 15-64 years and one in the 65 years or older range (**Figure E4**).

A total of 16 countries, territories and areas (Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Serbia, Spain, Turkmenistan, Ukraine, Uzbekistan and Kosovo*) with surveillance systems for severe acute respiratory infection (SARI) reported a total of 74,424 cases for the season. In most countries majorities of cases were in adults aged 30 years and older but in Armenia, Kazakhstan, Kyrgyzstan, Spain, Turkmenistan and Uzbekistan, most SARI cases were among children aged less than 5 years (**Table E3**). Only Azerbaijan, Armenia and Ukraine reported at least one sample that tested positive for influenza to date. Only Azerbaijan reported a sample that was type B of the Victoria-lineage; all other samples positive for influenza virus were type A. Of 10 subtyped influenza type A viruses, three were A(H1N1)pdm09 and seven were A(H3N2). Information on distributions of influenza types and subtypes or lineages by age group are not available for these data.

Mortality data

Pooled analyses of all-cause excess and influenza-attributable mortality from 29 European countries or sub-national regions participating in the EuroMOMO network (Austria, Belgium, Cyprus, Berlin (Germany), Denmark, England (United Kingdom (UK)), Estonia, Finland, France, Germany, Greece, Hesse (Germany), Hungary, Ireland, Israel, Italy, Luxemburg, Malta, the Netherlands, Northern Ireland (UK), Norway, Portugal, Scotland (UK), Slovenia, Spain, Sweden, Switzerland, Ukraine and Wales (UK)) showed a substantial increased excess all-cause mortality overall for the participating European countries. This excess mortality was driven by a substantial excess in a few countries. The increased excess all-cause mortality was seen among persons aged 15 years and older and coincided with periods of increased SARS-CoV- 2 circulation.

* In accordance with. United Nations Security Council. Resolution 1244 (1999).

Table E1. 2020-21 Influenza Season in the WHO European Region: weeks 40/2020-32/2021[a]

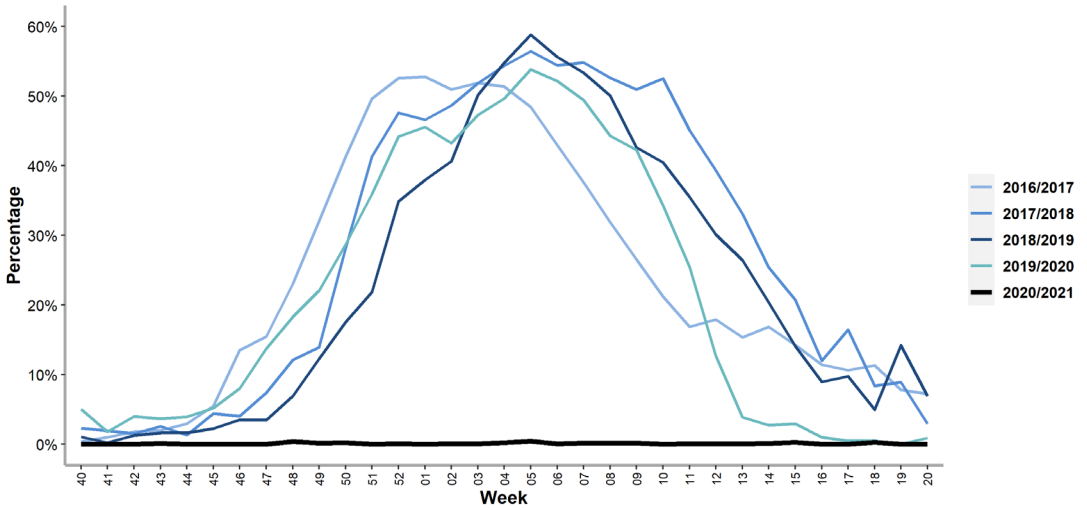
Virus type/subtype/lineage	Cumulative number of detections for weeks 40/2020-32/2021			Totals*		Cumulative number of detections for weeks 40/2019-34/2020			Totals*	
	Sentinel sources	Non-sentinel sources	Totals	%	Ratios	Sentinel sources	Non-sentinel sources	Totals	%	Ratios
Influenza A	**29**	**513**	**542**	**53.8**	**1.2:1**	**11302**	**108953**	**120255**	**72.9**	**2.7:1**
A(H1N1)pdm09	13	69	82	56.9		6126	20303	26429	56.0	
A(H3N2)	8	54	62	43.1	0.8:1	4174	16593	20767	44.0	0.8:1
A not subtyped	8	390	398			1002	72057	73059		
Influenza B	**18**	**448**	**466**	**46.2**		**6325**	**38313**	**44638**	**27.1**	
Victoria lineage	2	11	13	92.9	13:1	2449	2030	4479	98.1	50.3:1
Yamagata lineage	0	1	1	7.1		23	66	89	1.9	
Lineage not ascribed	16	436	452			3853	36217	40070		
Total detections	**47**	**961**	**1,008**			**17,627**	**147,266**	**164,892**		
Total tested	**48,181**	**>1, 043,991**	**>1,092,172**			**52,576**	**>901,628**	**>954,204**		

[a] Numbers taken from Flu News Europe to week 32/2021 and week 34/2020 reports

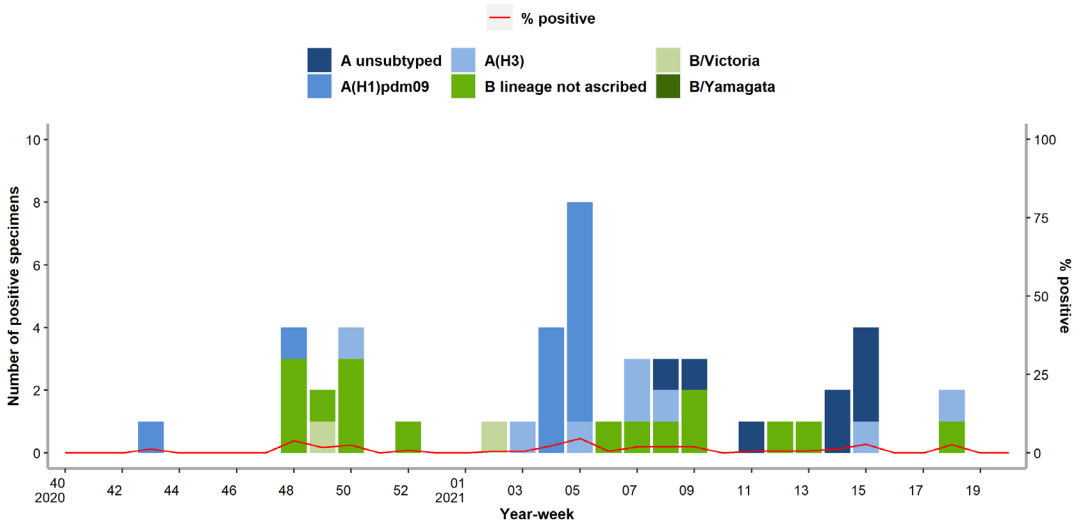
*** Percentages are shown for total detections (types A & B [in bold type], and for viruses ascribed to influenza A subtype and influenza B lineage). Ratios are given for type A:B [in bold type], A(H3N2):A(H1N1)pdm09 and Victoria:Yamagata lineages.**

Figure E1. Seasonal influenza activity in the WHO European Region: weeks 40/2020-20/2021

A. Percentage of sentinel specimens testing positive for influenza by week and season, 2016/17 to 2020/21



B. Sentinel specimens testing positive for influenza by week, (sub)type and percentage positive, 2020/21 season



C. Non-sentinel specimens testing positive for influenza by week and sub(type), 2020/21 season

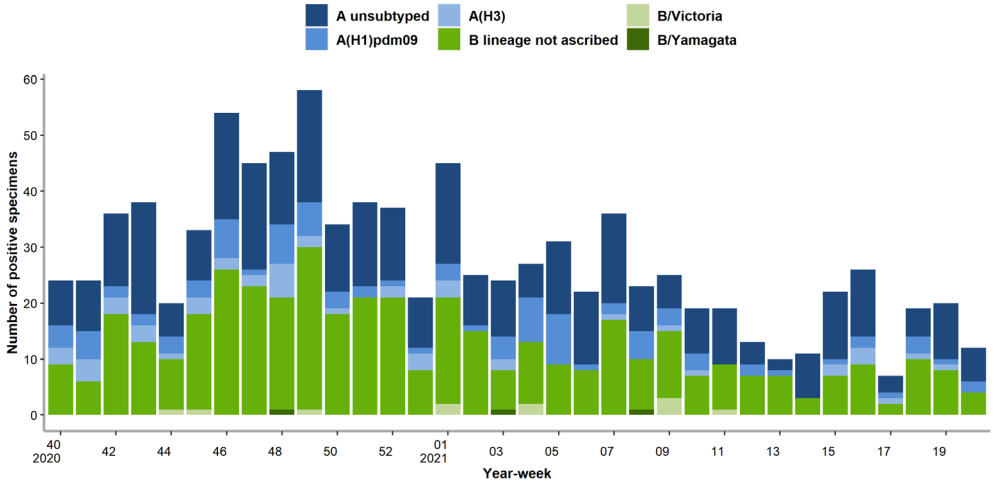
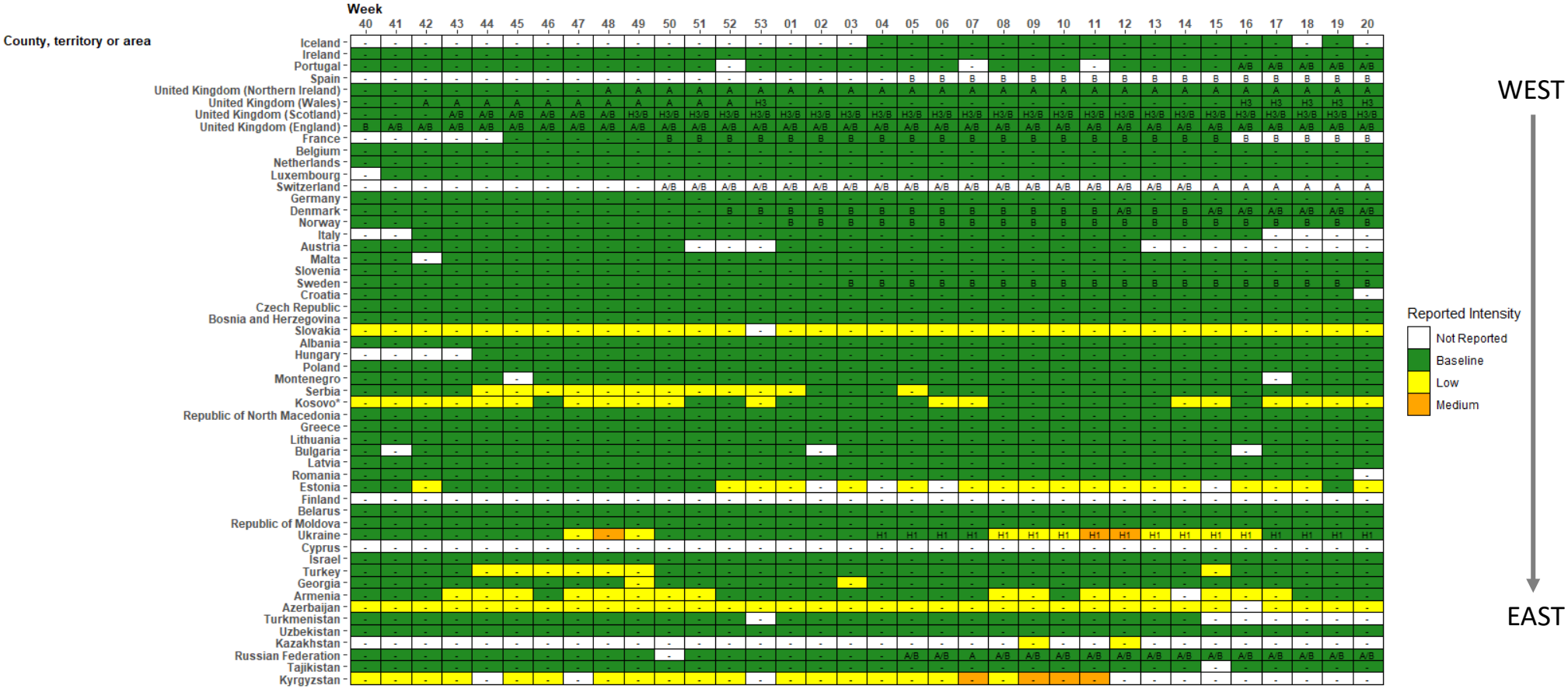


Figure E2. Intensity of influenza activity and dominant virus (sub)type in the WHO European Region by week and country, territory or area, 2020/21 season

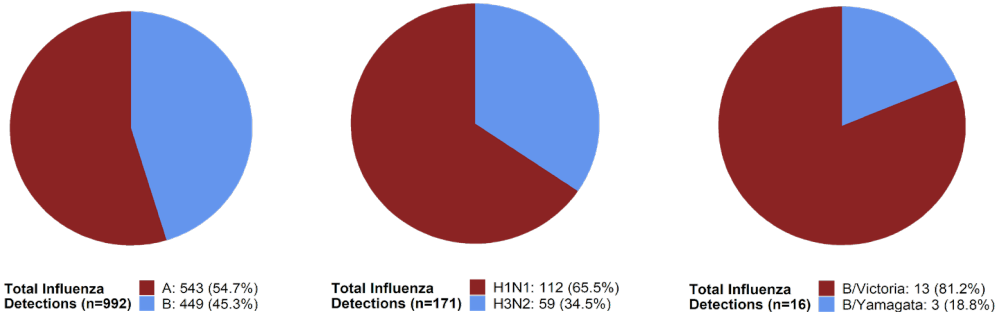


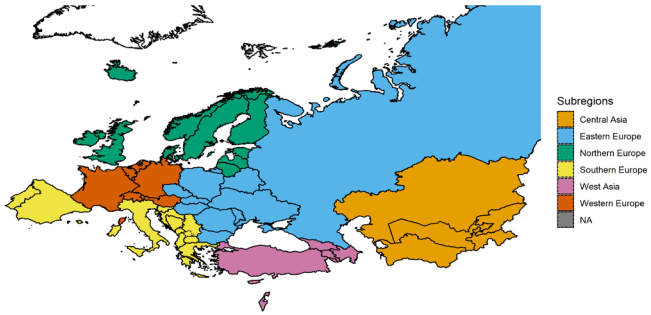
* In accordance with. United Nations Security Council. Resolution 1244 (1999).

Baseline intensity influenza activity is the level at which clinical influenza activity remains throughout the summer.
Dominant virus (sub)type is defined as at least 60% of sentinel detections.

Table E2. Distribution of Influenza Detections in the WHO European Region[1], 2020/21 season

Laboratory confirmed influenza from sentinel and non-sentinel sources by type and subtype/lineage





A. Laboratory confirmed influenza from sentinel and non-sentinel sources by geographic sub-region and influenza type and subtype/lineage

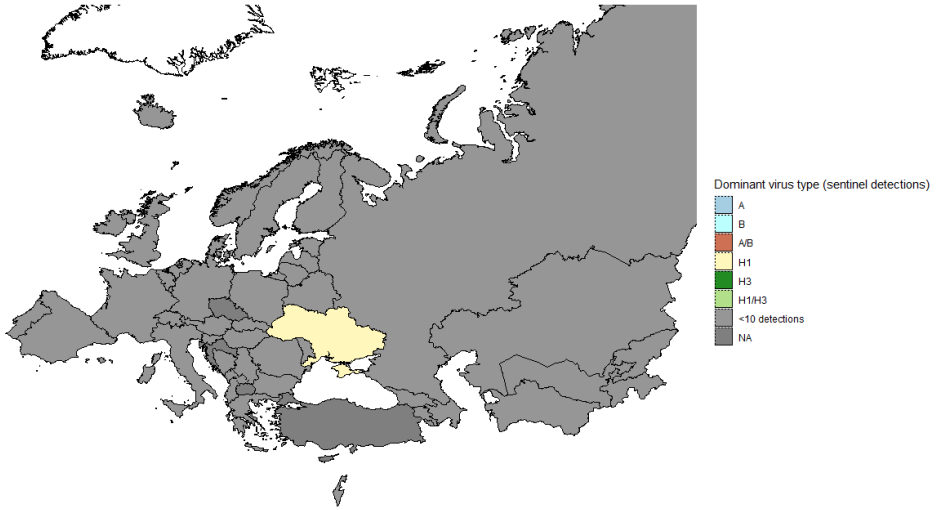
Influenza type and subtype/lineage	Southern Europe	Western Europe	Eastern Europe	Northern Europe	West Asia	Central Asia	WHO European Region
Influenza A	**10 (38%)**	**38 (47%)**	**68 (71%)**	**423 (55%)**	**4 (57%)**	**0 (0%)**	**543 (55%)**
Influenza A subtyped	5	5	38	119	4	0	171
A(H1N1)pdm09	3 (-)	1 (-)	28 (74%)	80 (67%)	0 (-)	-	112 (65%)
A(H3N2)	2 (-)	4 (-)	10 (26%)	39 (33%)	4 (-)	-	59 (35%)
Influenza B	**16 (62%)**	**43 (53%)**	**28 (29%)**	**353 (45%)**	**3 (43%)**	**4 (100%)**	**447 (45%)**
Influenza B lineage determined	0	5	1	8	0	0	14
B/Yamagata-lineage	-	0 (-)	1 (-)	0 (-)	-	-	1 (7%)
B/Victoria-lineage	-	5 (-)	0 (-)	8 (-)	-	-	13 (93%)
Total	**26**	**81**	**96**	**706**	**6**	**4**	**992**

[1] WHO European Region Member States grouped into sub-regions according to United Nations geographic composition. Available from: http://unstats.un.org/UNSD/METHODS/M49/M49REGIN.HTM

B. Laboratory confirmed influenza from sentinel sources by geographic sub-region and influenza type and subtype/lineage

	Southern Europe	Western Europe	Eastern Europe	Northern Europe	West Asia	Central Asia	WHO European Region
Influenza A	**0 (0%)**	**1 (17%)**	**23 (85%)**	**1 (20%)**	**4 (57%)**	**0 (0%)**	**29 (62%)**
Influenza A subtyped	0	1	15	2	4	0	21
A(H1N1)pdm09	-	0 (-)	13 (87%)	1 (-)	0	-	13 (62%)
A(H3N2)	-	1 (-)	2 (13%)	1 (-)	4 (-)	-	8 (38%)
Influenza B	**2 (100%)**	**5 (83%)**	**4 (15%)**	**4 (80%)**	**3 (43%)**	**0 (0%)**	**18 (38%)**
Influenza B lineage determined	2	2	0	0	0	0	2
B/Yamagata-lineage	-	0 (-)	-	-	-	-	0 (-)
B/Victoria-lineage	-	2 (-)	-	-	-	-	2 (-)
Total	**2**	**6**	**27**	**5**	**7**	**0**	**47**

Figure E3. Influenza circulation[2] in the WHO European Region by (sub)type and Country, territory or area, 2020/21 season.



[2] Dominance of (sub)type is based on at least 60% of detections and co-dominance is based on between 40% and 60% of detections. Calculations are only considered valid if at least 10 viruses were detected.

Figure E4. Distribution of virus (sub)type in laboratory-confirmed hospitalised cases in intensive care units by age group in the WHO European Region, 2020/21 season

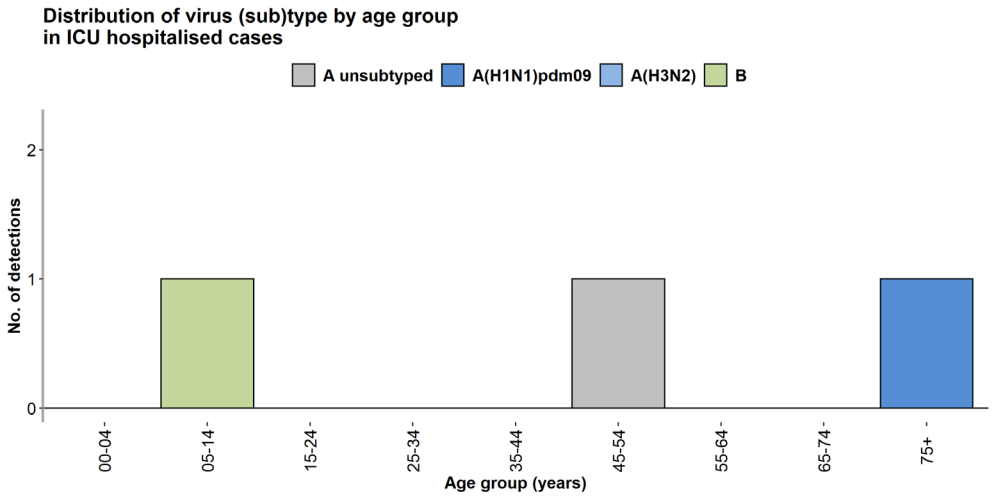


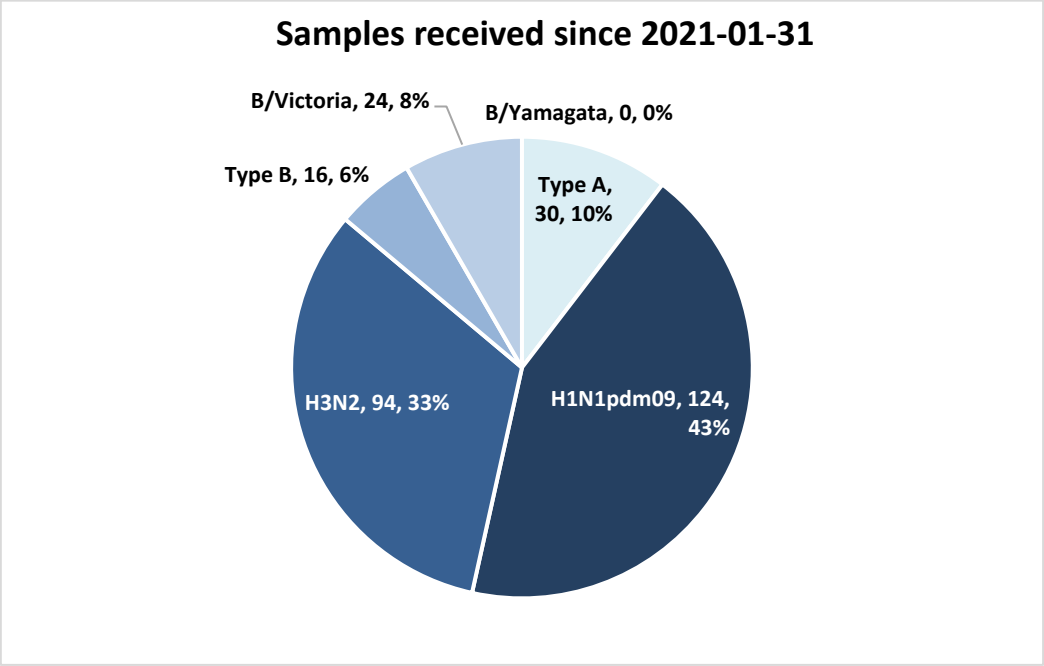
Table E3. Percentage distribution of severe acute respiratory infection (SARI) cases by age group and country, territory or area, and influenza positives, 2020/21 season

Country, territory or area	SARI cases with age data	Percentage (%) of total cases					Positive detections (%)
		0<5 years	5<15 years	15<30 years	30<65 years	>=65 years	
Albania	7,705	2	1	3	45	50	0 (0%)
Armenia	1,802	59	18	5	10	8	19 (2%)
Azerbaijan	93	18	17	19	22	24	1 (100%)
Belarus	11,106	3	1	19	42	36	0 (0%)
Bosnia and Herzegovina	71	4	3	18	49	25	0 (0%)
Georgia	3,083	16	10	14	37	23	0 (0%)
Kazakhstan	9,482	58	13	6	14	9	0 (0%)
Kyrgyzstan	2,113	64	4	3	18	11	0 (0%)
Republic of Moldova	3,118	34	13	4	28	21	0 (0%)
Russian Federation	3,554	23	10	12	31	24	0 (0%)
Serbia	437	6	4	2	38	51	0 (0%)
Spain	953	80	20	0	0	0	- (-%)
Turkmenistan	2,373	56	20	0	0	24	0 (0%)
Ukraine	5,413	1	1	3	58	37	4 (0%)
Uzbekistan	144	47	13	14	19	6	0 (0%)
Kosovo[b]	19	16	0	0	21	63	0 (0%)
Totals	51,466	25	7	8	32	27	24

[b] In accordance with. United Nations Security Council. Resolution 1244 (1999).

Influenza specimens received at the Francis Crick Institute.

Seasonal influenza virus samples with collection dates after 2021-01-31, totalling only 123, were received from seven countries in Europe, Africa and the Middle East. Additional samples, with collection dates prior to 2021-02-01, had been shipped from four additional countries. Overall, Influenza A viruses represented 86% of the samples, (81% when viruses with collection dates post January were considered), of which A(H1N1)pdm09 viruses outnumbered A(H3N2) viruses at a ratio of >1.3:1 overall, but A(H3N2) viruses outnumbered A(H1N1)pdm09 viruses at a ratio of 2:1 for viruses collected after January. Influenza B viruses represented 14% of the samples received overall, 19% post-January. All influenza B viruses ascribed to a lineage were B/Victoria (**Table 1**). Receipts are summarised in the pie charts below.



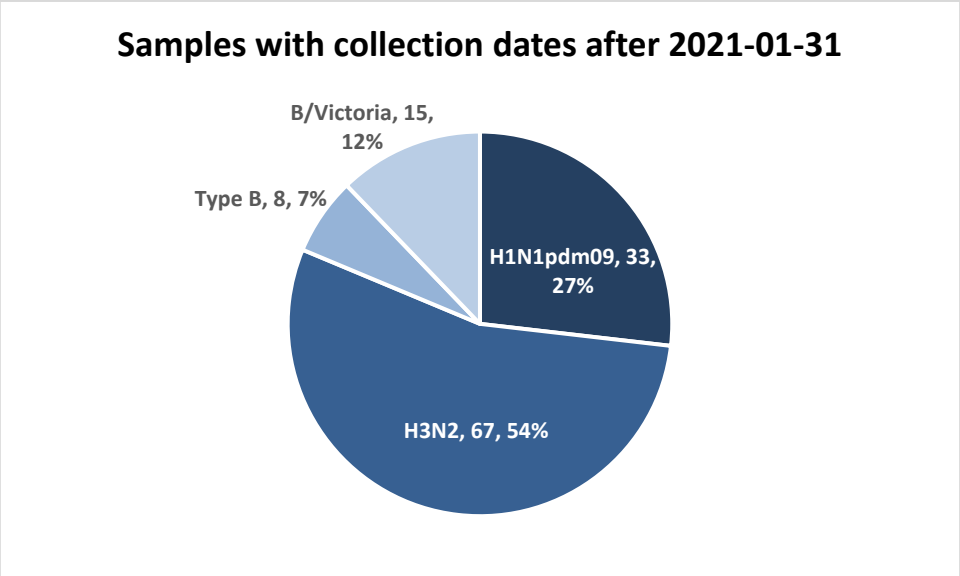


Table 2 shows the recovery/isolation rates from the small number of samples received with collection dates after 2021-01-31, as of 2021-09-10. For samples sent as clinical specimens that were taken for culture virus recoveries of 54% for influenza A(H1N1pdm09) viruses and 100% were achieved for both influenza A(H3N2) and B/Victoria-lineage viruses, respectively. Recoveries of samples sent as viruses were 100% for both influenza A subtypes and the B/Victoria-lineage. All A(H3N2) viruses (n = 24) retained sufficient agglutination of guinea pig red blood cells (all propagated viruses yielded HA titres of ≥4 in the presence of 20nM oseltamivir) to allow assessment by HI assay with use of 4 HA units/well. No viruses of the B/Yamagata-lineage were received.

Table 3 summarises the reactivity of A(H1N1)pdm09, A(H3N2) and B/Victoria-lineage viruses, collected since 2021-01-31, with post-infection ferret antisera raised against vaccine viruses or reference viruses in HI assays. For A(H3N2) viruses, the reactivity of test viruses in plaque reduction neutralisation assays (PRNA) is also summarised. Numbers and percentages of viruses showing ≤2-, 4- and ≥8-fold reductions in titres relative to the titres of the antisera with their respective homologous reference/vaccine viruses are shown.

For A(H1N1)pdm09 test viruses the HI titres obtained with antisera raised against the egg-propagated vaccine viruses A/Brisbane/02/2018, A/Guangdong-Maonan/SWL1536/2019 and A/Victoria/2570/2019, and against the cell culture-propagated cultivar of A/Denmark/3280/2019 (A/Victoria/2570/2019-like) were compared to the respective homologous titres.

For A(H3N2) test viruses the HI titres of antisera raised against egg-propagated vaccine viruses A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1), A/Hong Kong/2671/2019 (3C.2a1b+T135K-B subgroup), A/Cambodia/e0826360/2020 (3C.2a1b+T131K-A subgroup) and egg-propagated X-327, derived from egg-propagated A/Kansas/14/2017 (clade 3C.3a), and the cell culture-propagated cultivars of A/Hong Kong/2671/2019, and cell culture-propagated A/Hong Kong/2671/2019 (3C.2a1b +T135K-B subgroup) were compared to the titres of the antisera with their homologous viruses.

For the A(H3N2) test viruses assessed by PRNA the 50% neutralising titres of antisera raised against cell culture-propagated cultivars of A/Hong Kong/2671/2019 (3C.2a1b+T135K-B subgroup), A/Cambodia/925256/2020 (3C.2a1b+T131K-A subgroup), A/Bangladesh/4005/2020 (3C.2a1b+T131K-A subgroup) and egg-propagated cultivars of A/Cambodia/e0826360/2020 (3C.2a1b+T131K-A; vaccine virus for the northern hemisphere 2021-2022 influenza season), A/Bangladesh/2004/2020 (3C.2a1b+T131K-A subgroup) and NIB-127B (A/Darwin/6/2021; 3C.2a1b+T131K-A subgroup) were compared to the titres of the antisera with their homologous viruses.

For Influenza B viruses of the B/Victoria-lineage the HI titres of test viruses with antisera raised against both cell culture- and egg-propagated cultivars of the vaccine virus B/Washington/02/2019 (subclade 1A(△3)B) and B/Austria/1359417/2021 (subclade 1A(△3)B – 150K group with additional HA1 substitutions A127T, P144L and K203R) were compared to the titres of the antisera with their homologous viruses.

Note: During the course of the consultation, virus genetic clade/group nomenclature for seasonal influenza viruses was reviewed by the WHO Collaborating Centres. This report was written using the previous nomenclature, but the main HA phylogenies (Figures 1, 7, 12 and 17) were updated to show the new nomenclature in **bold red type**.

Table 1. Summary of clinical samples and virus isolates received, in shipments since the February 2021 VCM, by country*

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]	H3N2	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]
2019														
DECEMBER														
Egypt	3			1	0	2	1	0						
2020														
JANUARY														
Cameroon	3					3	0	0						
Egypt	7			7	1									
FEBRUARY														
Cameroon	9			1	0	7	0	0	1	0				
MARCH														
Cameroon	1			1	0									
OCTOBER														
Cameroon	2					2	0	0						
Saudi Arabia	1										1	1		
NOVEMBER														
Cameroon	6					6	0	0						
Saudi Arabia	9								7	0	2	1		
DECEMBER														
Cameroon	2					2	1	0						
Saudi Arabia	3										3	3		
2021														
JANUARY														
Norway	1			1	1									
Saudi Arabia	1										1	1		
Sweden	4					2	2				2	0		
Togo	113	30	0	80	5	3	0	0						
FEBRUARY														
Norway	1			1	1									
Sweden	1					1	1							
March														
Sweden	4					1	1				3	3		
April														
Ghana	3			3	in process									
Norway	1					1	1							
Qatar	3								2	in process	1	in process		
Sweden	2					2	2							
May														
Ghana	4			4	in process									
Qatar	8								3	in process	5	in process		
June														
France	2			2	2									
Ghana	7			7	in process									
Qatar	4								3	in process	1	in process		
July														
France	4			2	2	1	1				1	1		
Ghana	16			11	in process	5	in process							
Qatar	9					6	in process				3	in process		
August														
Netherlands	1					1	in process							
Norway	2					2	in process							
Qatar	50			3	in process	46	in process				1	in process		
Russia	1					1	in process							
11 Countries	288	30	0	124	12	94	10	0	16	0	24	10	0	0
Samples Feb on	Seasonal count	10.4%		43.1%		32.6%			5.6%		8.3%		0.0%	
7 Countries	123 (Feb on)	86.1%									13.9%			

*** 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 (H3N2 only)
Ct value high - not cultured or Failed sequence – not cultured
Viruses normally considered for a southern hemispere VCM are shown below the red line
Samples from Abidjan

As of 2021-09-10

Table 2. Isolation rates for specimens collected after 2021-01-31

	Clinical sample			Virus isolate		
	Number processed	Number propagated[1]	Percent recovered	Number processed	Number propagated[1]	Percent recovered
H1	13	7	54%	6	6	100%
H3	18	18	100%	6	6	100%
B Victoria	6	6	100%	4	4	100%
B Yamagata						

1. Propagated to sufficient HA titre to perform HI assay

As of 2021-09-10

Table 3. Summary of isolates with collection dates after 2021-01-31 showing reduction in reactivity with antisera raised against reference viruses in HI & plaque-reduction neutralisation assays (PRNA)

Virus type/subtype	Number tested	≤2-fold[a]	4-fold[a]	≥8-fold[a]
H1[1a]	13	8 (62%)	3 (23%)	2 (15%)
H1[1b]	13	13 (100%)	0	0
H1[1c]	13	0	0	13 (100%)
H1[1d]	13	0	0	13 (100%)
H3[2a]	24	0	3 (13%)	21 (87%)
H3[2b]	24	0	0	24 (100%)
H3[2c]	24	1 (4%)	3 (13%)	20 (83%)
H3[2d]	24	0	1 (4%)	23 (96%)
H3[2e]	24	0	0	24 (100%)
H3[3a]	28	0	6 (21%)	22 (79%)
H3[3b]	28	7 (25%)	7 (25%)	14 (50%)
H3[3c]	28	5 (18%)	4 (14%)	19 (68%)
H3[3d]	28	10 (36%)	6 (21%)	12 (43%)
H3[3e]	28	2 (7%)	2 (7%)	24 (86%)
H3[3f]	27	13 (48%)	4 (15%)	10 (37%)
B/Victoria[4a]	10	10 (100%)	0	0
B/Victoria[4b]	10	9 (90%)	1 (10%)	0
B/Victoria[4c]	10	0	0	10 (100%)
B/Victoria[4d]	10	0	0	10 (100%)

a. Reduction in titre, compared to the homologous titre with post-infection ferret antisera indicated below:
b. Reduction in titre, compared to the homologous titre based on actual computer read values from a digitized image for PRNA:

1a. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus A/Brisbane/02/2018 (genetic subgroup 6B.1A1)
1b. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus A/Guangdong-Maonan/SWL1536/2019 (genetic subgroup 6B.1A5A+187V/A)
1c. Compared to homologous titres for ferret antiserum raised against cell culture-propagated A/Denmark/3280/2019 (genetic subgroup 6B.1A5A+156K)
1d. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus A/Victoria//2570/2019 (genetic subgroup 6B.1A5A+156K)

2a. Compared to homologous titres for ferret antiserum raised against egg-propagated A/Singapore/INFIMH-16-0019/2016 (genetic subclade 3C.2a1)
2b. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus A/Hong Kong/2671/2019 (genetic subgroup 3C.2a1b + T135K-B)
2c. Compared to homologous titres for ferret antiserum raised against cell culture-propagated A/Hong Kong/2671/2019 (genetic subgroup 3C.2a1b + T135K-B)
2d. Compared to homologous titres for ferret antiserum raised against egg-propagated A/Cambodia/e0826360/2020 (genetic subgroup 3C.2a1b+T131K-A)
2e. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus NYMC X-327, derived from A/Kansas/14/2017 (genetic clade 3C.3a)

3a. Compared to homologous titres for ferret antiserum raised against cell culture-propagated A/Hong Kong/2671/2019 (genetic subgroup 3C.2a1b + T135K-B)
3b. Compared to homologous titres for ferret antiserum raised against cell culture-propagated A/Cambodia/925256/2020 (genetic subgroup 3C.2a1b+T131K-A)
3c. Compared to homologous titres for ferret antiserum raised against egg-propagated A/Cambodia/e0826360/2020 (genetic subgroup 3C.2a1b+T131K-A)
3d. Compared to homologous titres for ferret antiserum raised against cell culture-propagated A/Bangladesh/4005/2020 (genetic subgroup 3C.2a1b+T131K-A)
3e. Compared to homologous titres for ferret antiserum raised against egg-propagated A/Bangladesh/2004/2020 (genetic subgroup 3C.2a1b+T131K-A)
3f. Compared to homologous titres for ferret antiserum raised against egg-propagated NIB-127B (A/Darwin/6/2021) (genetic subgroup 3C.2a1b+T131K-A)

4a. Compared to homologous titres for ferret antiserum raised against cell culture-propagated B/Austria/1359417/2021 - Clade 1A(Δ3)B N150K gp + A127T, P144L, K203R
4b. Compared to homologous titres for ferret antiserum raised against egg-propagated B/Austria/1359417/2021 - Clade 1A(Δ3)B N150K gp + A127T, P144L, K203R
4c. Compared to homologous titres for ferret antiserum raised against cell culture-propagated B/Washingto/02/2019 - Clade 1A(Δ3)B
4d. Compared to homologous titres for ferret antiserum raised against egg-propagated vaccine virus B/Washingto/02/2019 - Clade 1A(Δ3)B

As of 2021-09-15

H1N1pdm09

Influenza A(H1N1)pdm09 viruses with collection dates after 2021-01-31 were received from NICs in four countries in three WHO Regions: African (Ghana and Cote d'Ivoire [via France]), Eastern Mediterranean (Qatar) and European (Norway) (**Table 1**). **Table 4** summarises antigenic (HI) results for the recognition of the viruses, propagated at the time of preparing this report, by antisera raised against egg-propagated A/Brisbane/02/2018, a previous vaccine virus, egg-propagated A/Guangdong-Maonan/SWL1536/2019 (the recommended vaccine virus for the Northern Hemisphere 2020-2021 influenza season), egg-propagated A/Victoria/2570/2019 (the vaccine virus for the Southern Hemisphere 2021 and the Northern Hemisphere 2021/2022 seasons) and against A/Denmark/3280/2019, a cell culture-propagated virus similar to A/Victoria/2570/2019.

HI analysis

Tables 5-2 to 5-5 show the results of HI analysis of samples analysed after the February VCM. Viruses below the red line in **Tables 5-3**, **5-4** and **5-5** had collection dates after 2021-01-31, and represented only ~40% of the total of 31 viruses analysed. **Table 5-1** shows HI results from some viruses shared by CDC, **Table 5-4** includes a virus shared by NIID, and **Table 5-5** one shared by VIDRL.

Antisera raised against the vaccine virus egg-propagated A/Victoria/2570/2019 or against cell culture-propagated A/Denmark/3280/2019, recognised one of the viruses sent by CDC at a titre within 4-fold of the homologous titres of the antisera, all other viruses were recognised poorly by these antisera. The antisera raised against the egg-propagated and cell culture-propagated cultivars of A/Guangdong-Maonan/SWL1536/2019 and other related reference viruses (A/Paris/1447/2017, A/Brisbane/02/2018, A/Ireland/87733/2019, A/Switzerland/3330/2017) recognised two thirds (68%) to three quarters (77%) of the test viruses at titres within 4-fold of the homologous titres of the antisera, and half (48%) to three quarters (77%) of viruses at titres within 2-fold of the homologous titres of the antisera. Six viruses, all from Madagascar, collected in early 2020, were recognised poorly by these antisera, as they were by antisera raised against egg-propagated A/Victoria/2570/2019 and cell culture-propagated A/Denmark/3280/2019. An antiserum raised against one of these viruses, A/Toamasina/00806/2020, was used in **Tables 5-4** and **5-5.** Fourteen test viruses, thirteen from West Africa and one from VIDRL, were analysed by this antiserum and eight (57%) were recognised at titres within 4-fold of the homologous titres but none within 2-fold.

Genetic analysis

All test viruses, for which HA gene sequences were known, fell into subclade 6B.1A which is defined by the amino acid substitutions **S74R**, **S164T** (altering a glycosylation motif introduced at residues 162-164 in clade 6B.1 viruses) and **I295V** in **HA1,** compared with the clade 6B.1 prototype virus, A/Michigan/45/2019. The vast majority of A(H1N1)pdm09-positive clinical specimens and viruses analysed had HA genes in group 6B.1A5A, although A/Norway/4776/2021 had an HA gene in subclade 6B.1A7.

Figure 1 shows a phylogenetic tree for HA genes of A(H1N1)pdm09 viruses sequenced at the Francis Crick Institute and other representative viruses, with

collection dates from 2021-02-01, as deposited in GISAID at the time of preparing this report.

Within subclade 6B.1A genetic groups of viruses encoding a range of **HA1** amino acid substitutions have emerged. All test viruses carried the **S183P** amino acid substitution in **HA1** and the major groups in circulation recently are:

- 6B.1A5A, defined by **N129D**, **T185I** and **N260D** substitutions in **HA1**, with two major genetic subgroups.

- 6B.1A5A + 187V/A: the HA genes of viruses in this subgroup encode **D187A** and **Q189E** substitutions in **HA1**, and many viruses, notably from West Africa, encode the additional **HA1** substitutions **I166T**, **A186T** with some also encoding **V193A in HA2**;

- 6B.1A5A + 156K: the HA genes of most viruses in this subgroup encode **HA**s with **K130N**, **N156K**, **L161I** and **V250A** substitutions in **HA1** and **E179D** substitution in **HA2**. A recently emerged subgroup form India also encode **K54Q**, **A186T, Q189E** and **E224A** in **HA1**. Within this subgroup some viruses have HA genes that encode **R259K** and **K308R** in **HA1**, some of which also encode **N43S** in **HA2**.

An amino acid sequence alignment of the HAs for representative A(H1N1)pdm09 viruses is shown in **Figure 2**; the vaccine viruses are shown in red, reference viruses are coloured blue, glycosylation motifs are highlighted, the genetic group/subgroup is shown in green and the HA1/HA2 proteolytic-processing site is highlighted.

Figure 3a shows H1pdm09-HA structures with the positions of amino acid substitutions that differentiate virus genetic groups indicated. Those differentiating subclade 6B.1A viruses (**S74R**, **S164T** and **I295V** in **HA1**) from clade 6B.1 viruses are indicated in red. Those that define group 6B.1A5A viruses (**N129D, S183P, T185I** and **N260D** in **HA1**) are indicated in blue and within this group the substitutions **D187A** and **Q197E**, defining the predominant genetic subgroup in recent months, are indicated in purple. Locations of the substitutions **I166T** and **A186T**, seen in some of the viruses from West Africa, are highlighted in teal. **Figure 3b** again shows **HA1** substitutions defining subclade 6B.1A and group 6B.1A5A viruses, with those in **HA1** (**K130N**, **N156K**, **L161I** and **V250A**) that define an antigenically distinct genetic subgroup within group 6B.1A5A shown in green, and the substitutions predominant in viruses of this N156K subgroup from India, **K54Q**, **A186T, Q189E** and **E224A** in **HA1,** are shown in teal.

Figure 4 shows a phylogenetic tree for the NA genes of representative A(H1N1)pdm09 viruses sequenced at the Francis Crick Institute and other representative viruses, as for **Figure 1**. The vast majority encoded the amino acid substitutions **Q51K, F74S, I389K**, **D416N** and **T452I** compared with the NA of A/Brisbane/02/2018. There are two distinct genetic subgroups. Viruses in one subgroup, from West Africa, also encode **S52N**, resulting in the loss of a glycosylation site in the stalk domain. Another subgroup has NAs with the substitutions **M19T**, **Y66F**, and **N222K**; viruses in this subgroup from India and West Africa encode **V453M** and **T16A** substitutions, respectively.

Figure 5 shows a NA amino acid alignment for the same representative set of A(H1N1)pdm09 viruses as used in **Figure 2**.

Antiviral analysis

Susceptibility to the neuraminidase inhibitors (NAIs) oseltamivir and zanamivir was assessed phenotypically and by full NA gene sequencing, for 21 A(H1N1)pdm09 viruses detected and received within the course of the 2020-2021 influenza season (**Table 11**). All showed normal inhibition (NI: no reduced susceptibility) by both antivirals.

All of the 24 A(H1N1)pdm09 full-length PA gene sequences generated at the Crick, from individual viruses detected in the course of the 2020-2021 influenza season, encoded isoleucine at position 38 (I38) and showed no evidence of other substitutions associated with reduced susceptibility to baloxavir marboxil.

Conclusion

The majority of viruses with collection dates after 31 January 2021 were from West Africa. These viruses were genetically similar to the former vaccine virus A/Guangdong-Maonan/SWL1536/2019 and were recognised well by antisera raised against A/Guangdong-Maonan/SWL1536/2019. Viruses genetically similar to the vaccine virus A/Victoria/2570/2019 were not received in recent months. All viruses showed normal inhibition by oseltamivir and zanamivir and none showed amino acid substitutions indicative of reduced susceptibility to baloxavir marboxil.

Table 4. Summary of influenza A(H1N1)pdm09 viruses collected after 2021-01-31, analysed by HI

MONTH	H1N1pdm09												
			Post infection ferret antisera raised against										
			Clade 6B.1A1 virus			Clade 6B.1A5A+187V/A virus			Clade 6B.1A5A+N156K virus			Clade 6B.1A5A+156K virus		
Country	Number received	Number propagated[1,2]	≤2 fold[3]	4 fold[3]	≥8 fold[3]	≤2 fold[4]	4 fold[4]	≥8 fold[4]	≤2 fold[5]	4 fold[5]	≥8 fold[5]	≤2 fold[6]	4 fold[6]	≥8 fold[6]
2021														
FEBRUARY														
Norway	1	1	1			1					1			1
MARCH														
APRIL														
Ghana	3	2	2			2					2			2
MAY														
Ghana	4	0												
JUNE														
France	2	2	1		1	2					2			2
Ghana	7	0												
JULY														
France	2	2	2			2					2			2
Ghana	11	6	2	3	1	6					6			6
AUGUST														
Qatar	3	0												
4 Countries	33	13	8	3	2	13	0	0	0	0	13	0	0	13
			61.5%	23.1%	15.4%	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%

1 Numbers shown in red indicate that not all of the specimens received had been propagated at the time this report was prepared
2 Propagated to sufficient titre to perform HI assay
3 Reduction in HI titre with post-infection ferret antiserum raised against A/Brisbane/02/2018 (egg-propagated vaccine virus)
4 Reduction in HI titre with post-infection ferret antiserum raised against A/Guangdong-Maonan/SWL1536/2019 (egg-propagated vaccine virus)
5 Reduction in HI titre with post-infection ferret antiserum raised against A/Denmark/3280/2019 (cell-propagated virus)
6 Reduction in HI titre with post-infection ferret antiserum raised against A/Victoria/2570/2019 (egg-propagated vaccine virus)

As of 2021-09-10

Table 5-1. Antigenic analyses of influenza A(H1N1)pdm09 viruses (2021-02-24)

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection fereret antisera							
					A/Paris/1447/17 MDCK F03/18[*3] 6B.1A	A/Brisbane/02/18 Egg F09/19[*2] 6B.1A1	A/Ireland/87733/19 Egg St Jude's F18/20[*1] 6B.1A5A	A/G-MDCK/SWL1536/19 Egg F12/20[*1] 6B.1A5A	A/G-MDCK/SWL1536/19 MDCK F09/20[*1] 6B.1A5A	A/Denmark/3280/19 MDCK F08/20[*1] 6B.1A5A	A/Victoria/2570/19 Egg F26/20[*1] 6B.1A5A	A/Switzerland/3330/17 Egg F23/18*[1] 6B.1A5B
REFERENCE VIRUSES												
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	2560	640	640	2560	1280	40	<	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E2	5120	1280	1280	2560	2560	40	80	1280
A/Ireland/87733/2019	D187A, Q189E	6B.1A5A+187V/A	2019-11-03	E4	2560	640	1280	2560	2560	<	80	640
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	E3/E1	2560	640	1280	2560	2560	<	80	1280
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	C2/MDCK1	2560	640	1280	2560	2560	<	80	640
A/Denmark/3280/2019	N156K	6B.1A5A+156K	2019-11-10	MDCK4/MDCK5	<	<	40	40	<	2560	2560	80
A/Victoria/2570/2019	N156K	6B.1A5A+156K	2018-11-22	E4/E	320	80	80	160	160	2560	2560	80
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	2560	640	640	640	1280	40	40	1280
TEST VIRUSES												
A/Maryland/42/2019		6B.1A5B	2019-11-29	C1/SIAT1/MDCK1	2560	640	640	1280	1280	80	160	640
A/Louisiana/01/2020		6B.1A7	2020-01-04	SIAT2/MDCK1	5120	1280	1280	2560	2560	<	<	1280
A/Arkansas/08/2020		6B.1A5A+156K	2020-01-25	C1/SIAT1/MDCK1	<	<	<	<	<	640	640	40
						Vaccine NH 2019-20 SH 2020		Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 5-2. Antigenic analyses of influenza A(H1N1)pdm09 viruses (2021-04-27)

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection fereret antisera							
					A/Paris 1447/17 MDCK	A/Bris 02/18 Egg	A/Ire 87733/19 Egg	A/G-M SWL1536/19 Egg	A/G-M SWL1536/19 MDCK	A/Denmark 3280/19 MDCK	A/Vict 2570/19 Egg	A/Swit 3330/17 Egg
		Ferret number			F03/18[*2]	F09/19[*1]	St Jude's F18/20[*1]	F12/20[*1]	F09/20[*1]	F08/20[*1]	F26/20[*1]	F23/18*[1]
		Genetic group			6B.1A	6B.1A1	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5B
REFERENCE VIRUSES												
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	5120	640	640	1280	1280	<	40	1280
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E2	5120	1280	1280	2560	2560	40	160	1280
A/Ireland/87733/2019	D187A, Q189E	6B.1A5A+187V/A	2019-11-03	E4	2560	1280	1280	2560	2560	40	160	1280
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	E3/E2	2560	640	640	1280	1280	<	80	640
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	C2/MDCK1	2560	640	640	1280	1280	<	80	640
A/Denmark/3280/2019	N156K	6B.1A5A+156K	2019-11-10	MDCK4/MDCK5	80	40	40	80	80	1280	2560	80
A/Victoria/2570/2019	N156K	6B.1A5A+156K	2018-11-22	E4/E2	160	40	40	80	80	1280	1280	40
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	2560	640	640	1280	1280	<	40	1280
TEST VIRUSES												
A/Egypt/333/2020		6B.1A5A	2020-01-06	MDCK2	2560	640	640	1280	1280	<	80	640
A/Toamasina/00806/2020		6B.1A5A	2020-02-17	MDCK1	160	40	40	40	160	<	<	80
A/Togo/34/2021		6B.1A5A+187V/A	2021-01-22	MDCK1	1280	640	640	1280	1280	40	80	640
A/Togo/44/2021		6B.1A5A+187V/A	2021-01-22	MDCK1	1280	320	640	1280	1280	40	80	640
A/Togo/45/2021		6B.1A5A+187V/A	2021-01-22	MDCK1	1280	320	640	1280	1280	<	40	640
						Vaccine NH 2019-20 SH 2020		Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 5-3. Antigenic analyses of influenza A(H1N1)pdm09 viruses (2021-06-03)

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection fereret antisera							
					A/Paris 1447/17 MDCK	A/Bris 02/18 Egg	A/Ire 87733/19 Egg	A/G-M SWL1536/19 Egg	A/G-M SWL1536/19 MDCK	A/Denmark 3280/19 MDCK	A/Vict 2570/19 Egg	A/Swit 3330/17 Egg
		Ferret number			F03/18*2	F09/19*1	St Jude's F18/20*1	F12/20*1	F09/20*1	F08/20*1	F26/20*1	F23/18*1
		Genetic group			6B.1A	6B.1A1	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5B
REFERENCE VIRUSES												
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	2560	640	640	1280	640	<	<	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E2	2560	640	1280	2560	1280	40	80	1280
A/Ireland/87733/2019	D187A, Q189E	6B.1A5A+187V/A	2019-11-03	E4	1280	640	640	2560	1280	40	80	640
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	E3/E2	1280	320	640	1280	1280	<	40	320
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	C2/MDCK1	2560	640	1280	2560	2560	40	80	640
A/Denmark/3280/2019	N156K	6B.1A5A+156K	2019-11-10	MDCK4/MDCK5	160	<	80	<	160	>5120	>5120	160
A/Victoria/2570/2019	N156K	6B.1A5A+156K	2018-11-22	E4/E2	80	<	80	80	80	1280	1280	40
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	1280	640	320	1280	640	<	40	640
TEST VIRUSES												
A/Toamasina/00138/2020		6B.1A5A	2020-01-07	MDCK1	160	<	40	<	160	<	<	80
A/Toamasina/00293/2020		6B.1A5A	2020-01-21	MDCK2	320	<	40	80	160	<	<	80
A/Toamasina/00357/2020		6B.1A5A	2020-01-29	MDCK1	640	160	160	160	320	<	<	160
A/Mahajanga/00563/2020		6B.1A5A	2020-02-05	MDCK2	160	<	40	<	160	<	<	80
A/Mahajanga/00562/2020		6B.1A5A	2020-02-11	MDCK1	320	80	80	80	160	<	<	160
A/Togo/64/2021		6B.1A5A+187V/A	2021-01-15	MDCK1	2560	640	1280	2560	2560	40	40	1280
A/Togo/35/2021		6B.1A5A+187V/A	2021-01-22	MDCK1	2560	1280	1280	2560	2560	40	80	640
A/Norway/2967/2021		6B.1A7	2021-01-30	MDCK2	>5120	2560	1280	2560	2560	80	40	1280
A/Norway/4776/2021		6B.1A7	2021-02-24	MDCK1	2560	1280	640	2560	1280	<	40	1280
						Vaccine NH 2019-20 SH 2020		Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 5-4. Antigenic analyses of influenza A(H1N1)pdm09 viruses (2021-08-18)

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre								
					Post-infection fereret antisera								
		Passage history			A/Paris 1447/17 MDCK	A/Bris 02/18 Egg	A/Ire 87733/19 Egg	A/G-M SWL1536/19 Egg	A/G-M SWL1536/19 MDCK	A/Denmark 3280/19 MDCK	A/Vict 2570/19 Egg	A/Toamas 00806/20 MDCK	A/Swit 3330/17 Egg
		Ferret number			F03/18[*2]	F09/19[*1]	St Jude's F18/20[*1]	F12/20[*1]	F09/20[*1]	F08/20[*1]	F26/20[*1]	F32/21*[1]	F23/18*[1]
		Genetic group			6B.1A	6B.1A1	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5B
REFERENCE VIRUSES													
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	2560	640	640	1280	640	<	<	160	640
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E2	2560	1280	1280	2560	1280	40	80	160	1280
A/Ireland/87733/2019	D187A, Q189E	6B.1A5A+187V/A	2019-11-03	E4	1280	640	1280	2560	1280	40	80	160	640
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	E3/E2	1280	320	640	1280	1280	<	40	160	320
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	C2/MDCK1	2560	640	1280	2560	2560	40	80	320	640
A/Denmark/3280/2019	N156K	6B.1A5A+156K	2019-11-10	MDCK4/MDCK5	160	<	80	<	160	1280	1280	80	160
A/Victoria/2570/2019	N156K	6B.1A5A+156K	2018-11-22	E4/E2	80	<	80	80	80	1280	1280	80	40
A/Toamasina/00806/2020	G155R, A285S	6B.1A5A	2020-02-17	MDCK3	160	80	80	80	320	<	40	640	160
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	1280	640	320	1280	640	<	40	160	1280
TEST VIRUSES													
A/Nagasaki/8/2020		6B.1A5A+187V/A	2020-10-27	hCK2/MDCK1	640	160	320	640	640	<	<	80	320
A/Abidjan/428/2021		6B.1A5A+187V/A	2021-06-14	MDCK2/MDCK1	640	160	320	640	640	<	<	80	160
A/Abidjan/458/2021		6B.1A5A+187V/A	2021-06-29	MDCK2/MDCK1	1280	640	640	1280	1280	<	40	160	640
A/Abidjan/455/2021		6B.1A5A+187V/A	2021-07-02	MDCK3/MDCK1	1280	640	640	1280	1280	<	40	160	640
A/Abidjan/457/2021		6B.1A5A+187V/A	2021-07-03	MDCK2/MDCK1	1280	640	640	1280	1280	<	40	160	640
						Vaccine NH 2019-20 SH 2020		Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22		

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80; ND =Not Done

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 5-5. Antigenic analyses of influenza A(H1N1)pdm09 viruses (2021-09-08)

Viruses	Other information	Passage history	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection fereret antisera								
							NEW						
					A/Paris 1447/17	A/Bris 02/18	A/Toamas 00806/20	A/Ire 87733/19	A/G-M SWL1536/19	A/G-M SWL1536/19	A/Denmark 3280/19	A/Vict 2570/19	A/Swit 3330/17
		Passage history			MDCK	Egg	MDCK	Egg	Egg	MDCK	MDCK	Egg	Egg
		Ferret number			F03/18*2	F09/19*1	F32/21*1	St Jude's F18/20*1	F12/20*1	F09/20*1	F08/20*1	F26/20*1	F23/18*1
		Genetic group			6B.1A	6B.1A1	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5A	6B.1A5B
REFERENCE VIRUSES													
A/Paris/1447/2017		6B.1A	2017-10-20	MDCK1/MDCK3	640	320	80	320	1280	640	<	<	320
A/Brisbane/02/2018		6B.1A1	2018-01-04	E3/E2	1280	1280	160	1280	2560	2560	40	160	1280
A/Toamasina/00806/2020		6B.1A5A	2020-02-17	MDCK3	160	80	640	80	160	160	<	40	160
A/Ireland/87733/2019	D187A, Q189E	6B.1A5A+187V/A	2019-11-03	E4	1280	640	160	1280	2560	2560	40	160	1280
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	E3/E2	640	320	80	320	1280	640	<	80	320
A/Guangdong-Maonan/SWL1536/2019	D187A, Q189E	6B.1A5A+187V/A	2019-06-17	C2/MDCK1	640	640	160	640	1280	1280	<	80	640
A/Denmark/3280/2019	N156K	6B.1A5A+156K	2019-11-10	MDCK4/MDCK5	40	<	80	40	40	160	640	1280	80
A/Victoria/2570/2019	N156K	6B.1A5A+156K	2018-11-22	E4/E2	40	40	80	80	80	160	1280	1280	320
A/Switzerland/3330/2017	clone 35	6B.1A5B	2017-12-20	E6/E2	640	320	80	320	1280	320	<	40	640
TEST VIRUSES													
A/Victoria/2454/2019	D122E	6B.1A5A+187V/A	2019-08-28	E4	160	160	40	160	640	320	<	40	160
A/Ghana/64/2021	I166T, A186T	6B.1A5A+187V/A	2021-04-26	MDCKx/MDCK1	640	640	160	640	1280	1280	<	80	640
A/Ghana/755/2021		6B.1A5A+187V/A	2021-04-27	MDCKx/MDCK1	1280	640	160	640	2560	1280	<	80	640
A/Ghana/167/2021		6B.1A5A+187V/A	2021-07-01	MDCK1	640	320	80	640	1280	1280	<	80	320
A/Ghana/1348/2021	I166T, A186T	6B.1A5A+187V/A	2021-07-05	MDCK1	640	640	160	640	2560	1280	<	80	640
A/Ghana/182/2021	I166T, A186T	6B.1A5A+187V/A	2021-07-06	MDCK1	320	160	80	320	1280	640	<	40	320
A/Ghana/1581/2021		6B.1A5A+187V/A	2021-07-19	MDCK1	320	320	80	320	640	640	<	40	320
A/Ghana/231/2021		6B.1A5A+187V/A	2021-07-21	MDCK1	640	320	160	320	1280	640	<	80	320
A/Ghana/1894/2021	I166T, A186T	6B.1A5A+187V/A	2021-07-21	MDCK1	640	640	160	640	1280	1280	<	80	640
						Vaccine NH 2019-20 SH 2020			Vaccine NH 2020-21			Vaccine SH 2021 NH 2021-22	

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used)
1 < = <40; 2 < = <80; ND =Not Done

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Figure 1. Phylogenetic comparison of A(H1N1)pdm09 HA genes

Vaccine viruses

Reference viruses

Collection date

Aug 2021

Jul 2021

Jun 2021

May 2021

Apr 2021

Mar 2021

Feb 2021

HA2 numbering

recent Crick sequences

$ proposed serology antigens

Substitutions at HA1 position 156

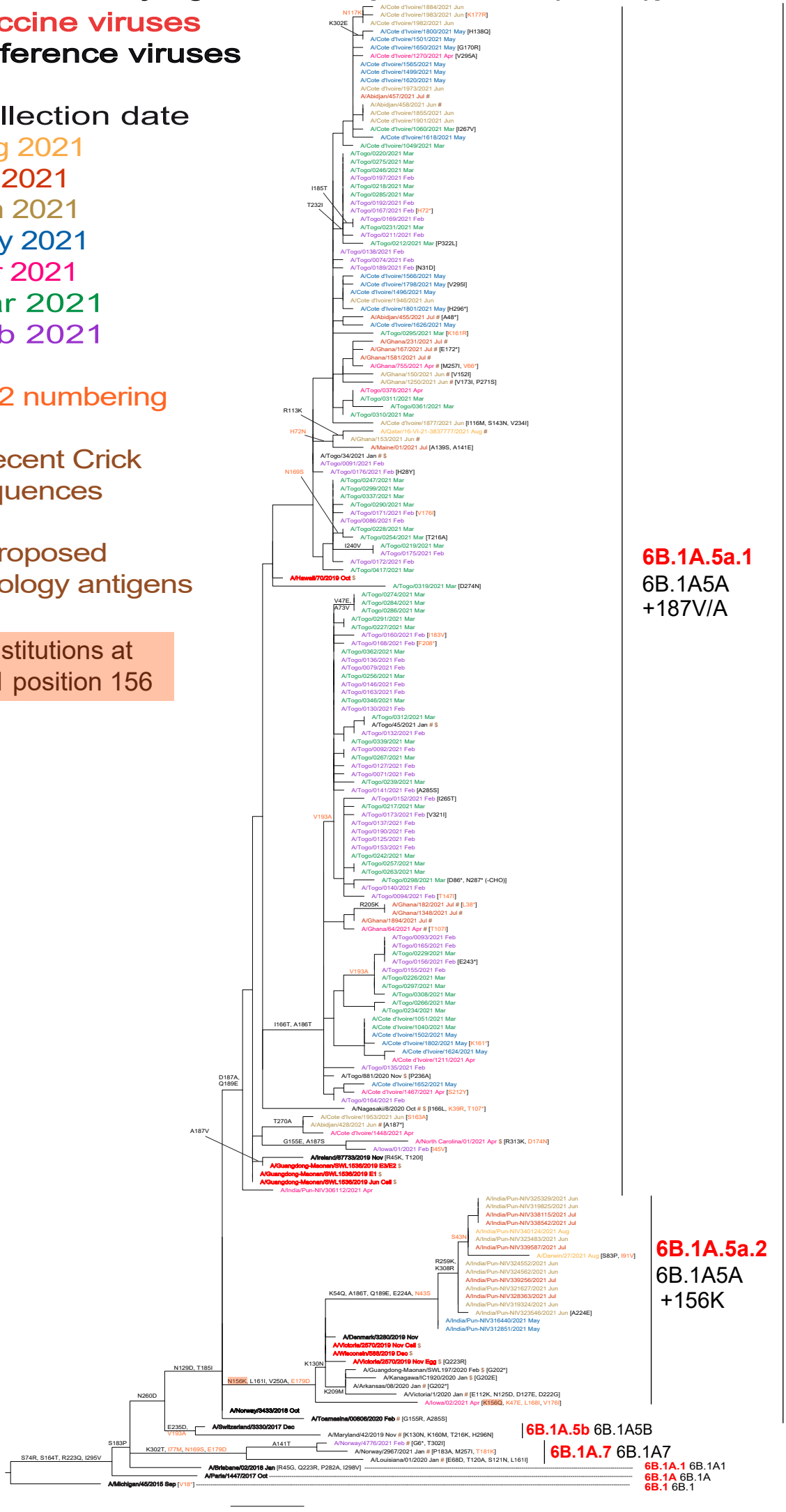
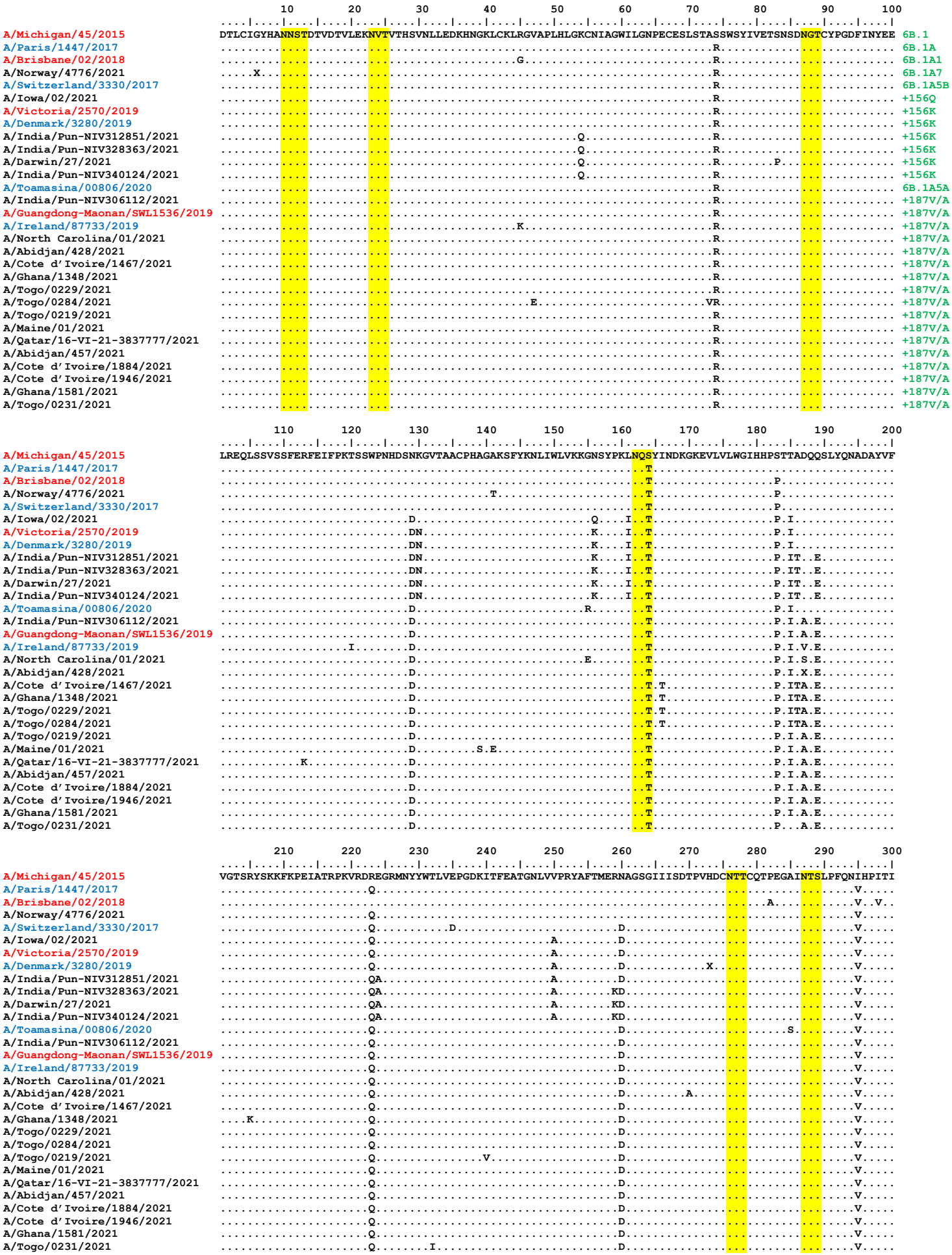
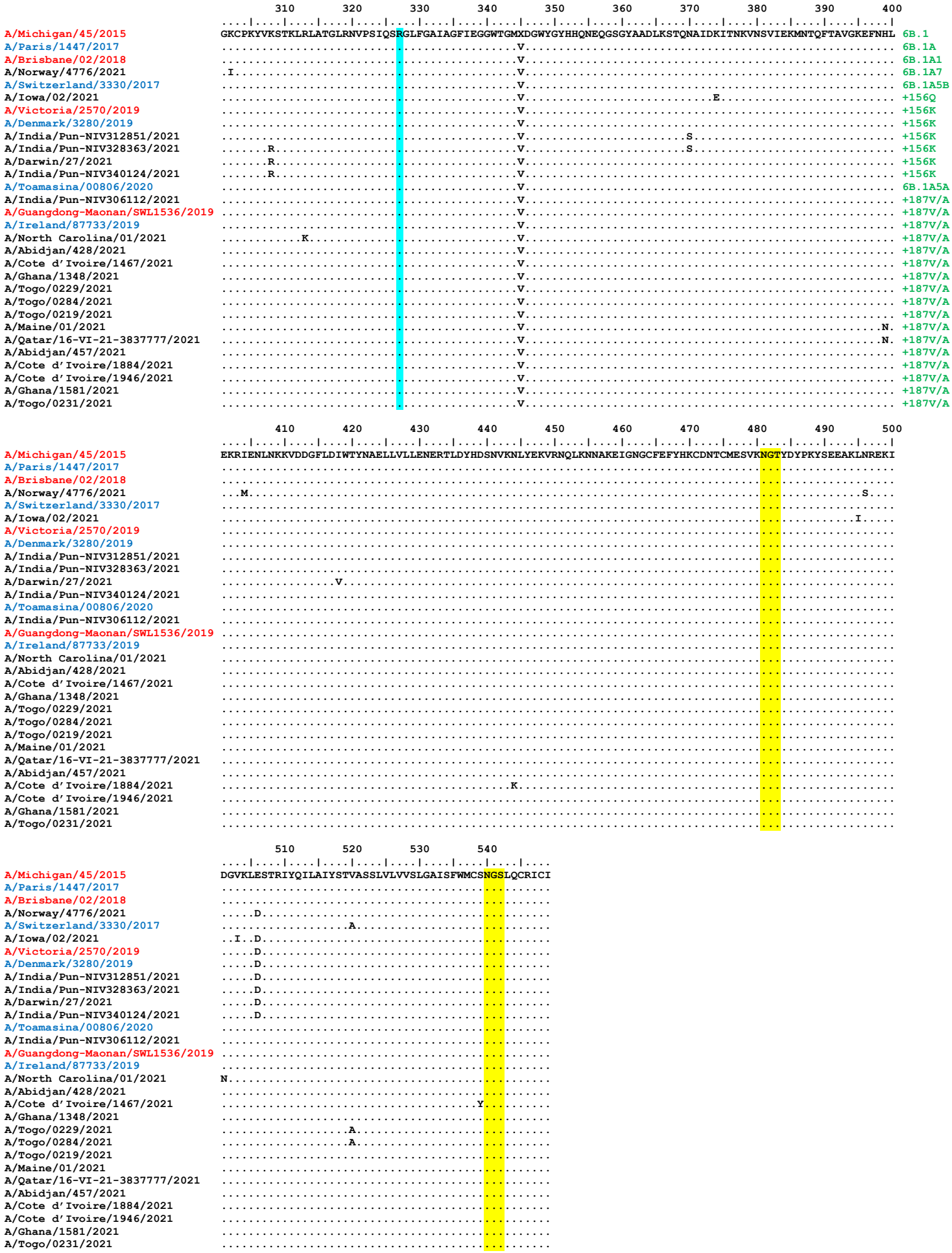


Figure 2. HA protein alignment for A(H1N1)pdm09 viruses

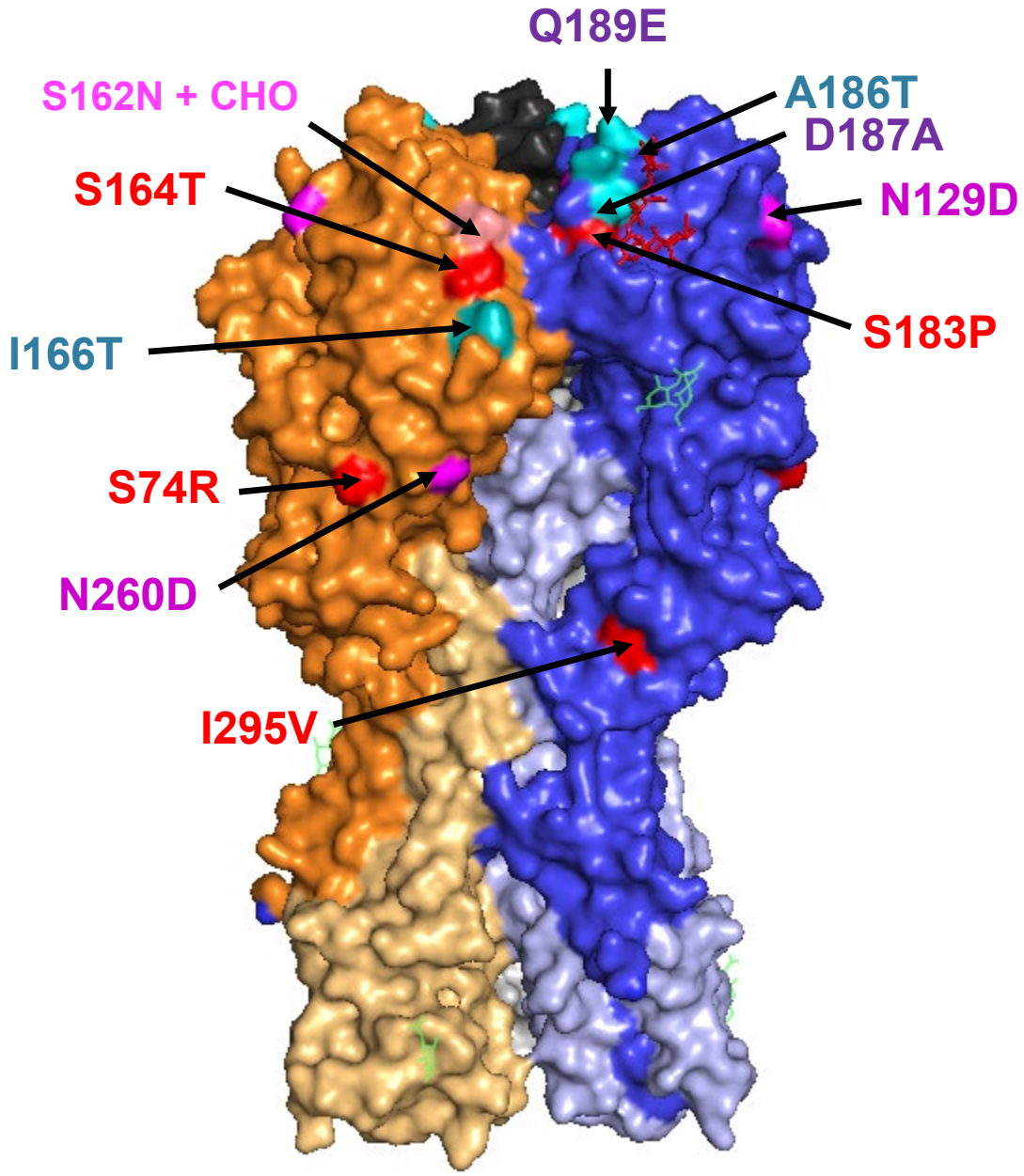
Vaccine virus: Reference virus: 6B Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site





Vaccine virus: Reference virus: 6B Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site

Figure 3a. HA amino acid substitutions defining H1N1pdm09 subgroup 6B.1A5A viruses



Signature HA1 substitutions defining:

Subclade 6B.1A

Subgroup 6B.1A5A 187/189 cluster viruses (A/Guangdong-Maonan/SWL1536/2019-like), West African viruses

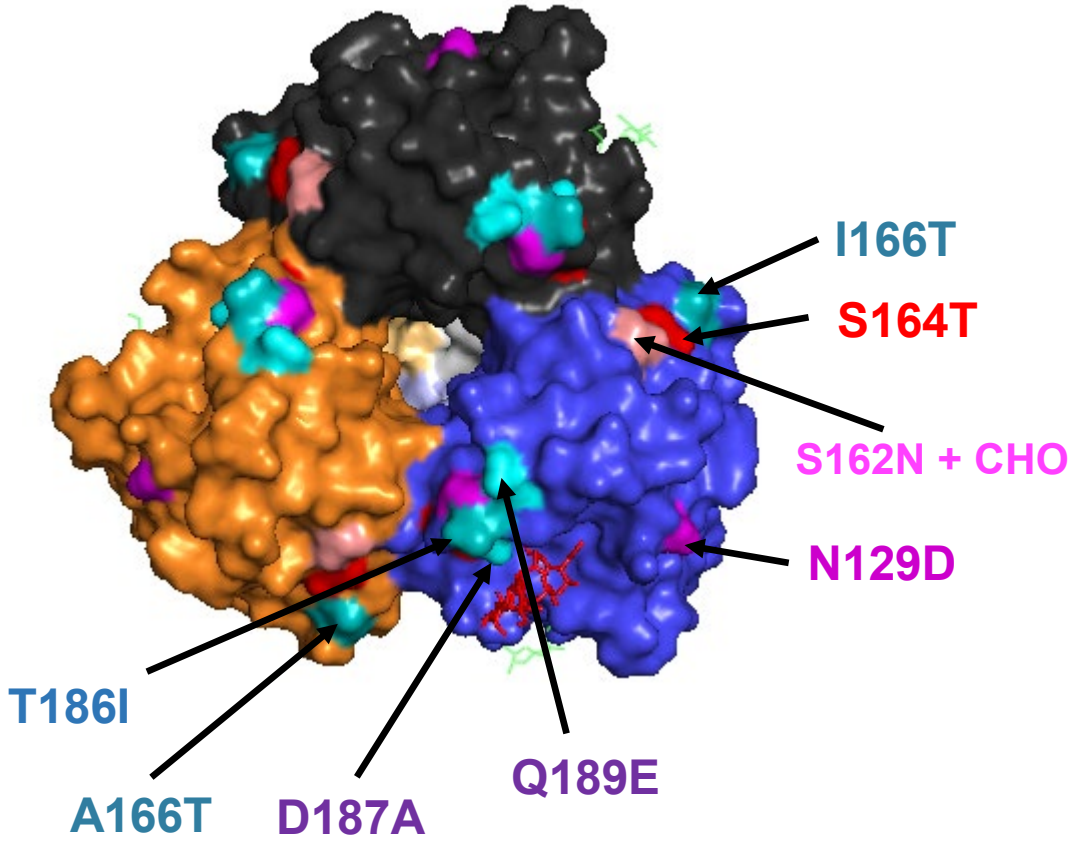
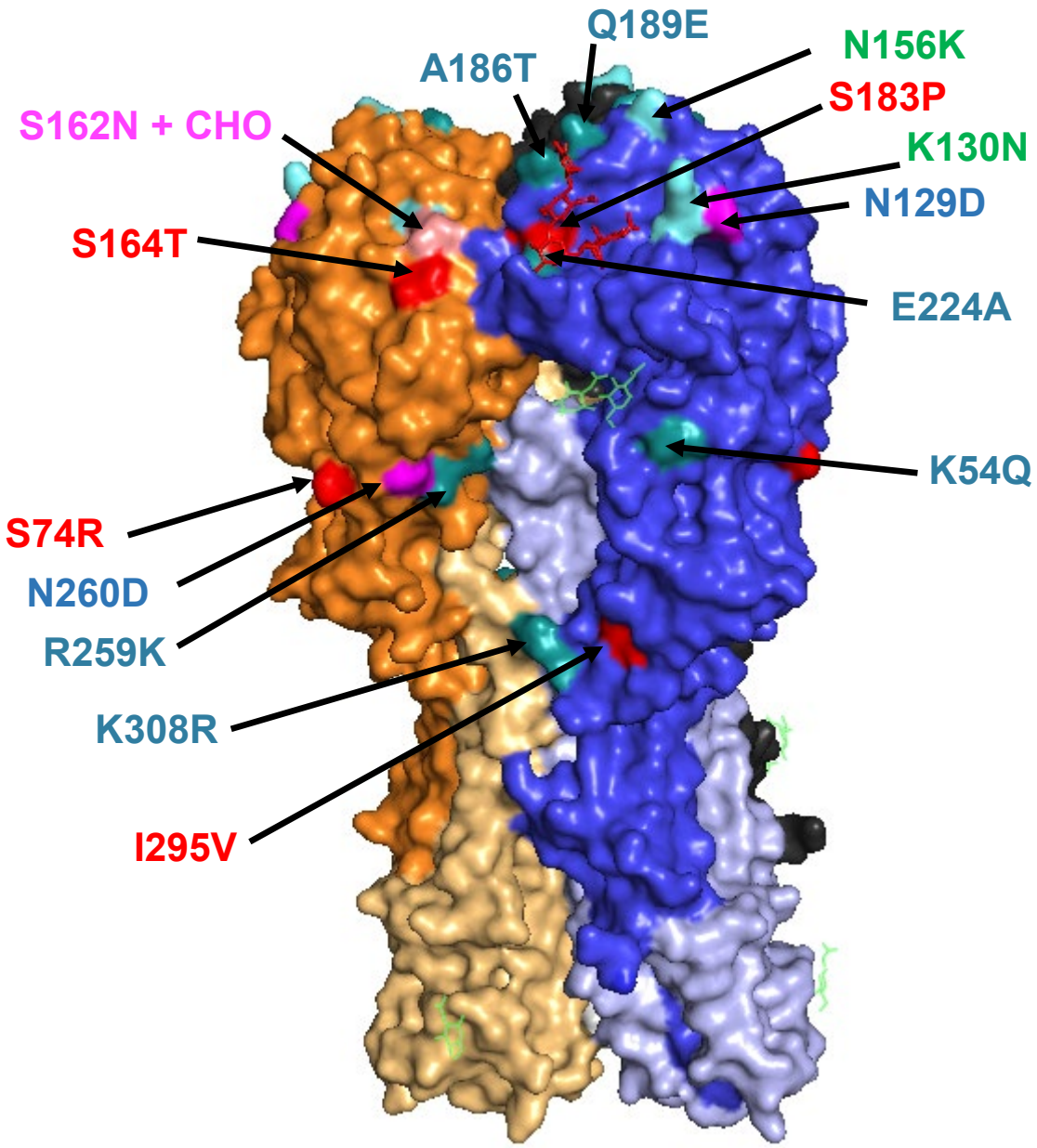


Figure 3b. HA amino acid substitutions defining H1N1pdm09 subgroup 6B.1A5A viruses

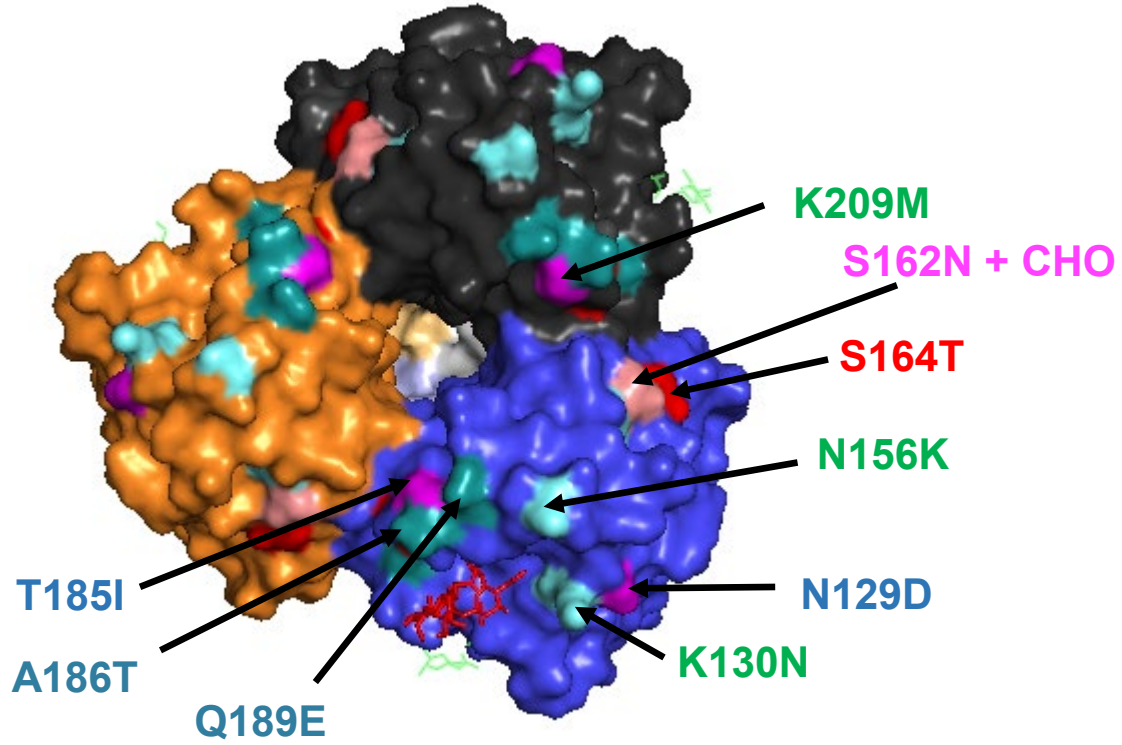


Signature HA1 substitutions defining:

Subclade 6B.1A

Subgroup 6B.1A5A

130/156 cluster viruses (A/Victoria/2570/2019-like), Indian subcluster



L161I, V250A and E179D (HA2) are not shown

Figure 4. Phylogenetic comparison of A(H1N1)pdm09 NA genes

Vaccine viruses

Reference viruses

Collection date

Aug 2021

Jul 2021

Jun 2021

May 2021

Apr 2021

Mar 2021

Feb 2021

recent Crick sequences

$ proposed serology antigens

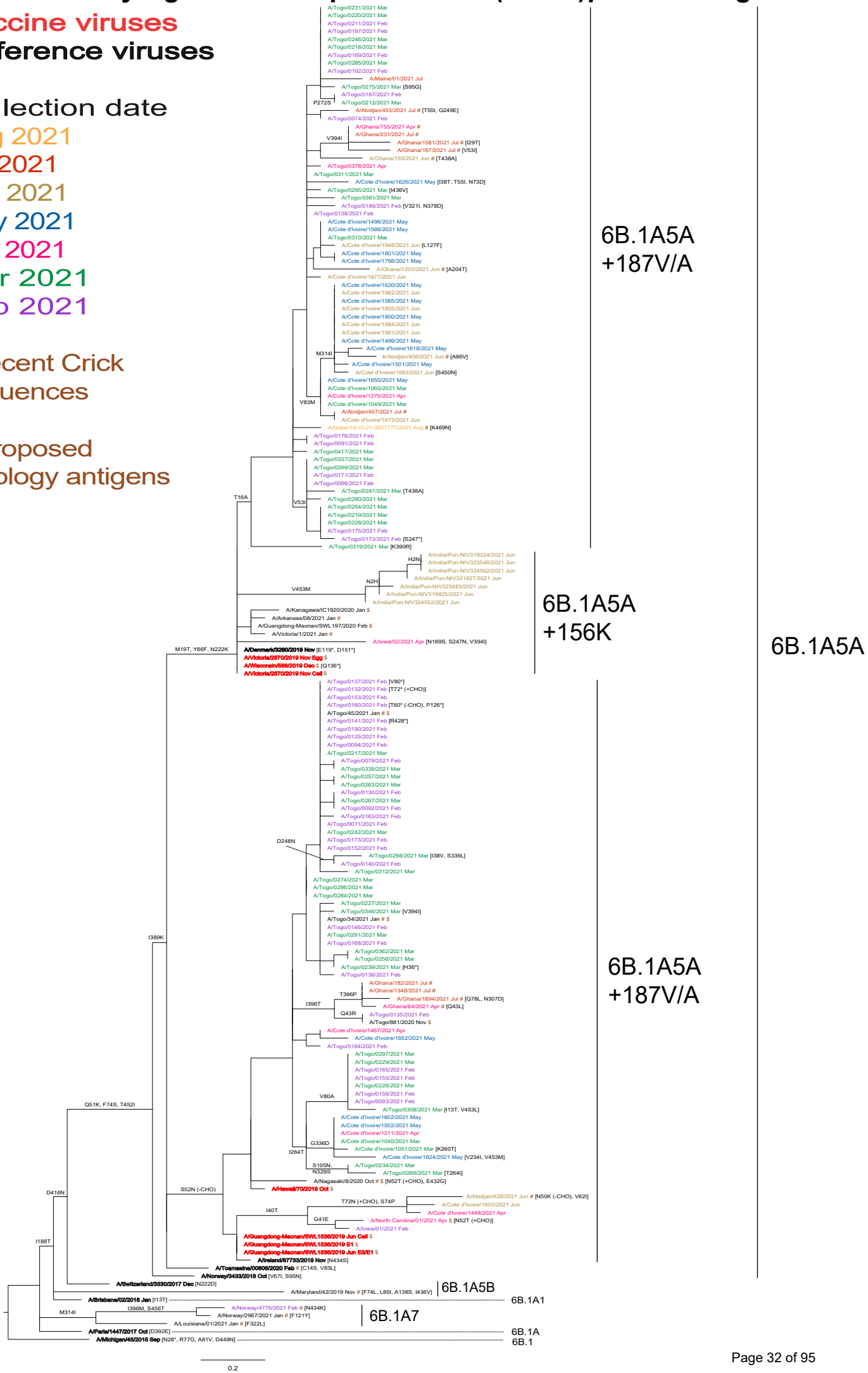
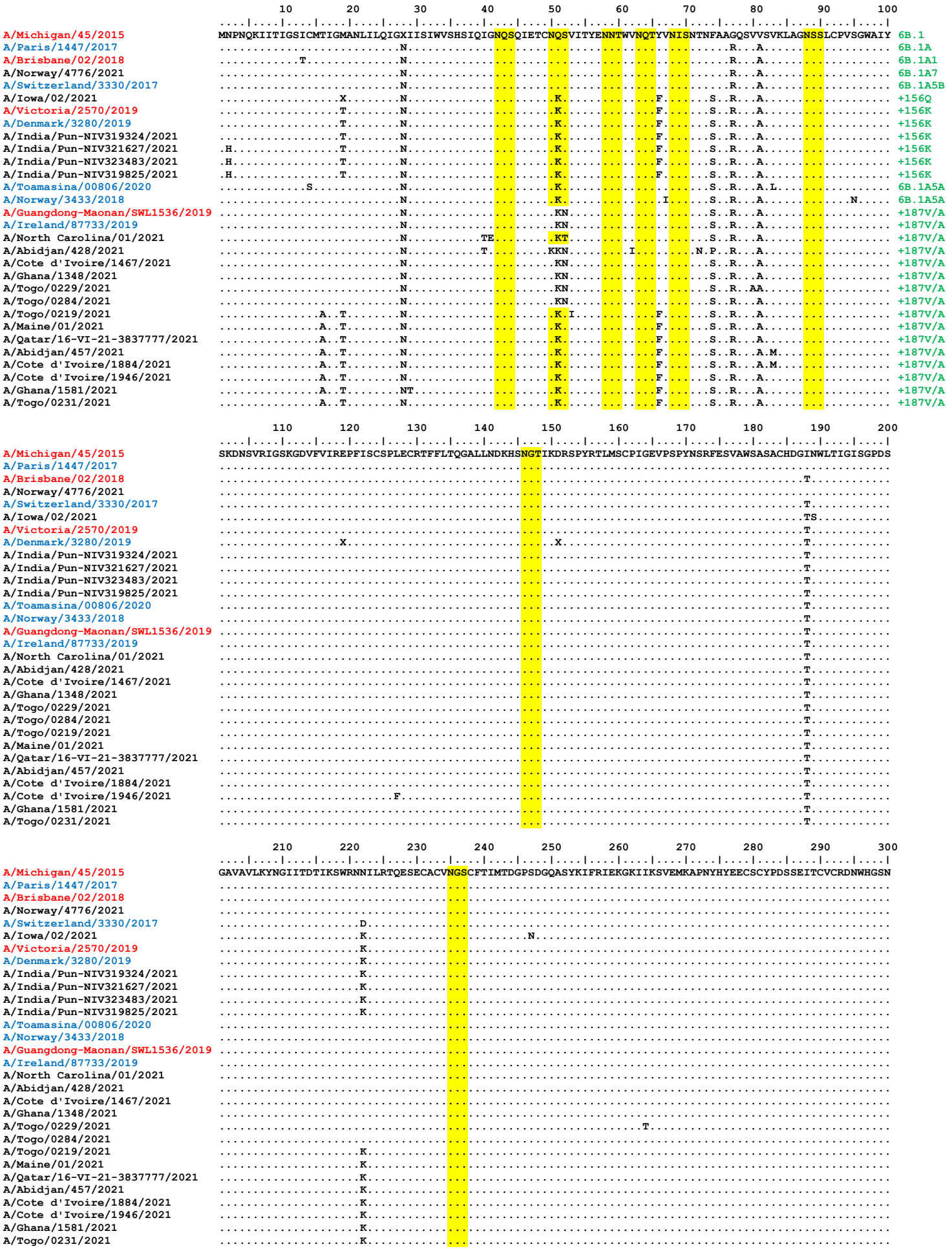
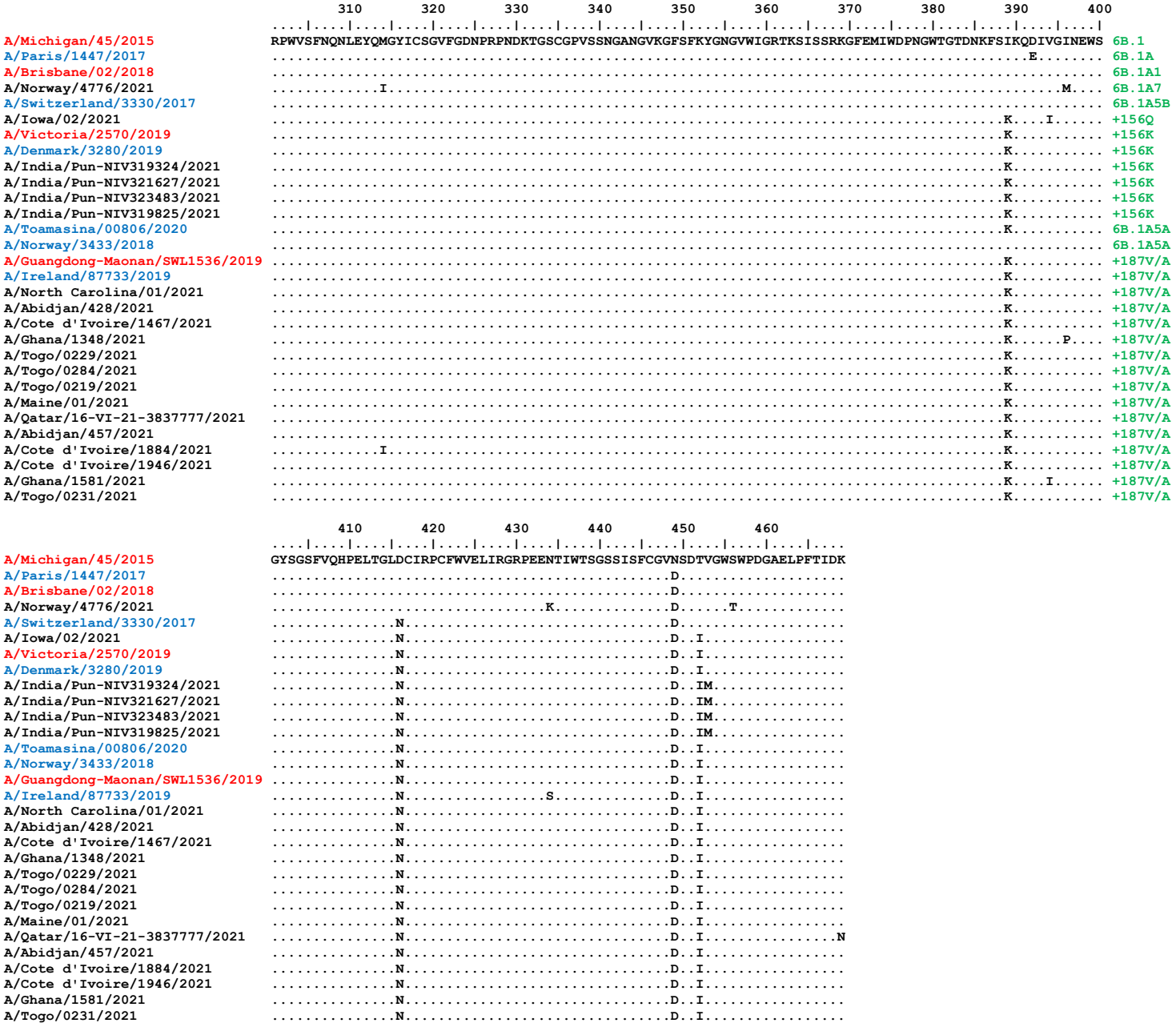


Figure 5. NA protein alignment for A(H1N1)pdm09 viruses

Vaccine virus: Reference virus: 6B Genetic group: Potential N-linked glycosylation site





Vaccine virus: Reference virus: 6B Genetic group: Potential N-linked glycosylation site

Influenza A(H3N2) virus analyses.

Influenza A(H3N2) viruses collected since 2021-01-31 were received from NICs in seven countries or administrative regions in three WHO Regions: African (Ghana and Cote d'Ivoire [via France]), Eastern Mediterranean (Qatar), and European (the Netherlands, Norway, Russia and Sweden) (**Table 1**).

Influenza A(H3N2) viruses have been difficult to characterise antigenically by HI assay due to either the variable agglutination of red blood cells (RBCs) from guinea pigs, turkeys and humans or the loss of the ability of viruses to agglutinate any of these RBCs. However, since the February VCM HI analysis was able to be done on 37 viruses propagated in cell culture that agglutinated guinea pig RBCs (**Tables 7-1 to 7-10**) with 28 having collection dates after 2021-01-31. Virus neutralisation by plaque reduction neutralisation assay (PRNA) was done on 28 test viruses of which 23 were propagated in cell culture (**Tables 8-1 to 8-5**). Twenty of these viruses had collection dates after 2021-01-31, all of which were propagated in cell culture.

HI analyses.

A total of 42 viruses, 27 with collection dates after 2021-01-31, were analysed by HI assay and summaries of the HI results are shown in **Tables 3** and **6**. Individual HI results are shown in **Tables 7-1** to **7-10**. Test viruses in each table are sorted by date of collection and genetic clade/subclade/group/subgroup for those viruses that were sequenced, with those below the red horizontal lines in the tables being viruses with collection dates after 2021-01-31 (**Tables 7-5 to 7-10**). The viruses sequenced and analysed by HI fell into clade 3C.2a subgroups 3C.2a1b+131K-A (n = 32, 23 collected after 2021-01-31), 3C.2a1b+135K-A (n = 9, four collected after 2021-01-31) and 3C.2a1b+135K-B (one collected in December 2019).

A summary of the HI results for viruses collected since 2021-01-31 with antisera raised against the egg-propagated cultivars of A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1), A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B), A/Cambodia/e08626360/2020 (subgroup 3C.2a1b+T131K-A) and A/Kansas/14/2017 (NYMC X-327, clade 3C.3a), previously recommended vaccine viruses, and the cell culture-propagated cultivar of A/Hong Kong/2671/2019 is shown in **Table 6.**

Viruses in subgroup 3C.2a1b+T131K-A (n = 32 with 23 collected after 2021-01-31) all fell in the 'Bangladesh-like' cluster characterised by **HA1** amino acid substitutions **Y159N**, **T160I** (resulting in loss of a glycosylation site), **L164Q**, **G186D** and **D190N**:

- antisera raised against the cell culture-propagated clade 3C.3a viruses A/Kansas/14/2017 and A/England/538/2018 recognised 30% and 85%, respectively, of viruses in subgroup T131K-A at titres within 4-fold of the homologous titres, 15% and 58% within 2-fold.
- the antiserum raised against cell culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised only 15% of the subgroup T131K-A viruses at titres within 4-fold of the homologous titre of the antiserum, only one within 2-fold;

- the antiserum raised against cell culture-propagated A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B) recognised 12% of the subgroup T131K-A test viruses at titres within 4-fold of the homologous titre, none within 2-fold;
- an antiserum raised against A/Denmark/3264/2019 (subgroup 3C.2a1b+T135K-A) recognised 85% of the subgroup T131K-A test viruses at titres within 4-fold of the homologous virus, 66% within 2-fold
- an antiserum raised against cell culture-propagated A/Bangladesh/4005/2020 (subgroup 3C.2a1b+T131K-A) recognised 93% of the subgroup T131K-A test viruses at titres within 4-fold of the homologous virus, 79% within 2-fold;
- an antiserum raised against cell culture-propagated A/Stockholm/5/2021 (subgroup 3C.2a1b+T131K-A) recognised all of the T131K-A test viruses at titres within 2-fold of the homologous virus;
- an antiserum raised against cell culture-propagated A/Cambodia/925256/2020 (subgroup 3C.2a1b+T131K-A) could be used in **Tables 7-1** and **7-2**, but subsequently HA titre was lost, and recognised three of the five test viruses in the T131K-A subgroup at titres within 4-fold of the homologous titres, one within 2-fold;
- antisera raised against the egg-propagated reference viruses and vaccine viruses recognised the subgroup T131K-A viruses poorly in general: the antiserum raised against A/Singapore/INFIMH-16-0019/2016 recognised six of the 32 test viruses at titres within 4-fold of the homologous titre; those raised against the egg-propagated cultivars of A/Hong Kong/2671/2019, A/Cambodia/e0826360/2020, and X-327 (derived from A/Kansas/14/2017) recognised none, two and two, respectively, out of 32 subgroup T131K-A test viruses at titres within 4-fold of the corresponding homologous titres.

Viruses in subgroup 3C.2a1b+T135K-A (n = 9, only four of which were collected after 2021-01-31), had the **HA1** amino acid substitutions **A138S**, **G186D**, **D190N**, **F193S** and **S198P**:

- antisera raised against the cell culture-propagated clade 3C.3a viruses A/Kansas/14/2017 and A/England/538/2018 recognised 22% of test viruses in subgroup T135K-A at titres within 4-fold of the homologous titres;
- the antiserum raised against cell culture-propagated A/Hong Kong/5738/2014 (clade 3C.2a) recognised five of the nine subgroup T135K-A viruses at titres within 4-fold of the homologous titres of the antiserum, but none within 2-fold;
- the antiserum raised against the cell culture-propagated cultivar of A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B) recognised eight of the nine (89%) subgroup T135K-A test viruses at titres within 4-fold of the homologous titre, but only three (33%) within 2-fold;
- eight of the nine (89%) test viruses in subgroup T135K-A were recognised by the antiserum raised against cell culture-propagated A/Denmark/3264/2019 (subgroup 3C.2a1b+T135K-A) at titres within 4-fold of the homologous titre, four within 2-fold;
- all four of the test viruses in subgroup T135K-A were recognised by the antiserum raised against cell culture-propagated A/Finland/183/2020 (subgroup 3C.2a1b+T131K-A) at titres within 4-fold of the homologous titre, one within 2-fold;
- an antiserum raised against cell culture-propagated A/Bangladesh/4005/2020 (subgroup 3C.2a1b+T131K-A) recognised three of the nine (33%) subgroup T135K-

A test viruses at titres within 4-fold of the homologous titre, but only one (11%) within 2-fold;

- an antiserum raised against A/Cambodia/925256/2020 (subgroup 3C.2a1b+T131K-A), used in **Tables 7-1** and **7-2**, recognised all four tested subgroup T135K-A viruses at titres within 4-fold of the homologous titres, three within 2-fold;
- antisera raised against the egg-propagated reference viruses and vaccine viruses recognised the subgroup T135K-A viruses poorly in general: however, the antiserum raised against A/Singapore/INFIMH-16-0019/2016 recognised eight of the nine test viruses at titres within 4-fold of the homologous titre; those raised against the egg-propagated cultivars of A/Hong Kong/2671/2019, A/Cambodia/e0826360/2020, and X-327 (derived from A/Kansas/14/2017) recognised none, one and three, respectively out of nine subgroup T135K-A test viruses at titres within 4-fold of the corresponding homologous titres.

Virus Neutralisation results

Results of virus neutralisation, assessed by PRNA, are shown in **Tables 8-1 to 8-5**. A total of 28 viruses were analysed of which 20 had collection dates after 2021-01-31. Nineteen viruses analysed (68%) were in subgroup 3C.2a1b+T131K-A, eight (29%) were in subgroup 3C.2a1b+T135K-A and a single virus (A/Nepal/20FL1005/2020 from NIID) was in subgroup 3C.2a1b+T135K-B. Five were egg isolates. A phylogenetic tree of the HA gene of the viruses analysed by PRNA is shown in **Figure 6.**

Viruses in subgroup 3C.2a1b+T131K-A (n = 19):

- an antiserum raised against cell culture-propagated A/Kansas/14/2007 (clade 3C.3a) recognised seven of the 19 (37%) subgroup T131K-A test viruses at titres within 4-fold of the homologous titre, three (16%) within 2-fold;
- an antiserum raised against cell culture-propagated A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B) recognised three of the 19 (16%) subgroup T131K-A test viruses at titres within 4-fold of the homologous titre of the antiserum, two (11%) within 2-fold;
- an antiserum raised against cell culture-propagated A/Denmark/3264/2019, (subgroup 3C.2a1b+T135K-A) recognised seven of the 19 (37%) subgroup T131K-A test viruses at titres within 4-fold of the homologous titre of the antiserum, three (16%) within 2-fold;
- an antiserum raised against a founder group 3C.2a1b+T131K virus, cell culture-propagated A/Norway/3275/2018, prior to the emergence of the -A and -B subgroups and splitting of subgroup T131K-A into Cambodia and Bangladesh clusters of viruses, recognised none of the test viruses in subgroup T131K-A at titres within 4-fold of the homologous titre of the antiserum;
- an antiserum raised against cell culture-propagated A/Cambodia/925256/2020 (subgroup 3C.2a1b+T131K-A) recognised eight of the 19 (42%) subgroup T131K-A test viruses at titres within 4-fold of the homologous titre of the antiserum, five (26%) within 2-fold;
- an antiserum raised against cell culture-propagated A/Bangladesh/4005/2020 (subgroup 3C.2a1b+T131K-A) recognised eleven of the 19 (58%) subgroup T131K-

A test viruses at titres within 4-fold of the homologous titre of the antiserum, 10 (53%) within 2-fold;

- antisera raised against cell culture-propagated viruses, A/Cambodia/925256/2020 and A/Bangladesh/4005/2020, that were tested against cell culture-propagated subgroup T131K-A viruses recognised eight of 14 (57%) and four of 14 (29%), respectively, at titres within 4-fold of the homologous titres, six of 14 (43%) and three of 14 (21%) at titres within 2-fold. Those with **HA1** amino acid substitution **H156S** were recognised less well by the antiserum raised against A/Bangladesh/4005/2020 (**Table 8-2**).

Viruses in subgroup 3C.2a1b+T135K-A (n = 8):

- an antiserum raised against cell culture-propagated A/Kansas/14/2007 (clade 3C.3a) recognised none of the eight subgroup T135K-A test viruses at titres within 4-fold of the homologous titre;
- an antiserum raised against cell culture-propagated A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B) recognised two of the eight (25%) subgroup T135K-A test viruses at titres within 4-fold of the homologous titre of the antiserum, none within 2-fold;
- an antiserum raised against cell culture-propagated A/Denmark/3264/2019, (subgroup 3C.2a1b+T135K-A) recognised three of the eight (38%) subgroup T135K-A test viruses at titres within 2-fold of the homologous titre of the antiserum;
- an antiserum raised against a founder group 3C.2a1b+T131K virus, cell culture-propagated A/Norway/3275/2018, prior to the emergence of the -A and -B subgroups and splitting of subgroup T131K-A into Cambodia and Bangladesh clusters of viruses, recognised none of the test viruses in subgroup T135K-A at titres within 4-fold of the homologous titre of the antiserum;
- an antiserum raised against cell culture-propagated A/Cambodia/925256/2020 (subgroup 3C.2a1b+T131K-A) recognised seven of the eight (88%) subgroup T135K-A test viruses at titres within 4-fold of the homologous titre of the antiserum, three (38%) within 2-fold;
- an antiserum raised against cell culture-propagated A/Bangladesh/4005/2020 (subgroup 3C.2a1b+T131K-A) recognised none of the eight subgroup T135K-A test viruses at titres within 4-fold of the homologous titre of the antiserum.

Antisera raised against egg-propagated vaccine/reference/reassortant viruses, A/Cambodia/e0826360/2020, A/Bangladesh/2004/2020, NIB-127B from A/Darwin/6/2021 and NIB-126A from A/Darwin/9/2021 were used in PRNA.

The antisera raised against these egg-propagated viruses recognised the test viruses poorly in general compared with the homologous titres of the antisera.

- None of the cell culture-propagated subgroup T135K-A test viruses were recognised at titres within 4-fold of the homologous titres of the antisera;

- the antiserum raised against egg-propagated A/Cambodia/e0826360/2020 recognised a single subgroup T131K-A test virus (A/Stockholm/1/2021) propagated in cell culture at a titre within 4-fold of the homologous titre;
- the antiserum raised against egg-propagated A/Bangladesh/2004/2020 recognised none of cell culture-propagated test viruses at titres within 4-fold of the homologous titre of the antiserum;
- the antiserum raised against NIB-126A (derived from A/Darwin/9/2021) also recognised none of the cell culture-propagated test viruses at titres within 4-fold of the homologous titre of the antiserum;
- however, the antiserum raised against NIB-127B (derived from A/Darwin/6/2021) recognised nine of the test viruses at titres within 4-fold of the homologous titre of the antiserum, three within 2-fold. Note that the absolute titres with the test viruses recognised by antiserum raised against NIB-127B were generally similar to those seen with the antisera raised against NIB-126A, egg-propagated A/Bangladesh/2004/2020, and higher than those for the antiserum raised against A/Cambodia/e0826360/2020.

There are two sets of heat maps shown adjacent to the phylogenetic tree in **Figure 6.** These summarise the VN results and the HI results for the same viruses, where available, and a selection from the panel of reference antisera used in the HI assay. The heat map for the VN results illustrates the better recognition of test viruses by antisera raised against viruses within the same clade/subclade/group/subgroup/cluster. The generally poor recognition of test viruses by antisera raised against egg-propagated reference viruses can also be seen.

Genetic analyses.

Phylogenetic analysis of the HA genes of representative recently circulating A(H3N2) viruses analysed at the Francis Crick Institute and elsewhere (as available in GISAID with collection dates after 2021-01-31) is shown in **Figure 7**. The HA genes of the huge majority fell within clade 3C.2a, primarily subgroups 3C.2a1b+T131K-A and 3C.2a1b+T135K-A, with the T131K-A subgroup predominating.

Major HA clades/subclades

- Clade **3C.3a** viruses differ from older clade **3C.3a** viruses with substitutions **S91N**, **N144K** (with the loss of a glycosylation site, -CHO) and **F193S** in HA1; most also had the substitutions **M17L**, **I149M** and **A209V** in **HA2**.
- Clade **3C.2a** viruses have a series of amino acid substitutions differentiating them from clade 3C.3a viruses: **A128T** (+CHO), **S138A**, **N144S** (-CHO), **S159Y**, **K160T** (+CHO), **Q311H** and **R326K** in **HA1**;
- Subclade **3C.2a1** viruses have additional substitutions **N121K** and **N171K** in **HA1** and **I77V** and **G155E** in **HA2** and subclade **3C.2a1b** viruses have the substitutions **E62G, K92R** and **H311Q** in **HA1.** There are four groups/subgroups.

- Group **3C.2a1b+T131K** viruses have HAs with the substitutions **T131K** in **HA1** and **V200I** in **HA2**. Within this group two main genetic subgroups have emerged;
  - viruses in the **+T131K-A** subgroup have HA genes encoding amino acid substitutions **K83E** and **Y94N** in **HA1** and **I193M** in **HA2** and the large majority also carry **HA1** substitutions **F193S** and **Y195F**. Within this subgroup two clusters have emerged. Viruses in the larger cluster (Bangladesh-like) seen most recently in viruses from India, the Middle East, Russia and other parts of the world have HA genes encoding the **HA1** substitutions **Y159N, T160I** (resulting in the loss of a glycosylation site), **L164Q, G184D** and **D190N;** the other less common group (Cambodia-like) includes viruses from Cambodia, Laos, Timor-Leste and several other countries, that have HA genes encoding the **HA1** substitutions **G186S** and **S198P** in **HA1** with many encoding a reversion at position 171 (**K171N**);
  - previously, viruses in the **+T131K-B** subgroup, carrying substitutions **S219F** in **HA1** and **V18M** in **HA2**, many of these also having **Q197R** in **HA1** and **E155G** in **HA2** sometimes with **K207R** in **HA1**, had been co-circulating.
- Group **3C.2a1b+T135K** viruses have the substitutions **T128A** and **T135K** (both resulting in the loss of glycosylation sites), with most now having **A138S** and **F193S** in **HA1**. Within this group two main genetic subgroups have emerged;
  - viruses in the **+T135K-A** subgroup, most recently seen in West Africa, have the substitutions **G186D**, **D190N, I192F** and **S198P** in **HA1**;
  - those in the **+T135K-B** subgroup have an **S137F** substitution in **HA1**.

Figure 8 shows an HA amino acid sequence alignment for a representative selection of the viruses used to generate the phylogenies. The vaccine viruses A/Kansas/14/2017 (clade 3C.3a), A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1), A/Hong Kong/2671/2019 (subgroup 3C.2a1b+T135K-B) and A/Cambodia/e0826360/2020 (subgroup 3C.2a1b+T131K-A) are shown in red, glycosylation motifs are highlighted, reference viruses are coloured blue and the HA1/HA2 proteolytic cleavage site is highlighted. The clade/subclade/group/subgroup to which each of the HA sequences belongs is also shown.

Figures 9a and **9b** show the locations on a 2005 H3 HA structure of amino acid substitutions that define clades and recent groups/subgroups. **Figure 9a** shows the substitutions seen in group 3C.2a1b+T135K, and subgroups thereof, compared to the HA of a previous vaccine virus, A/Singapore/INFIMH/16-0019/2016 (subclade 3C.2a1). **Figure 9b** shows those substitutions seen in group 3C.2a1b+T131K-A compared to A/Singapore/INFIMH/16-0019/2016.

Figure 10 shows a NA phylogenetic tree for representative viruses with their HA genetic groups indicated. **Figure 11** shows a NA amino acid sequence alignment for a representative selection of these viruses. As above, the current vaccine viruses are shown

in red, glycosylation motifs are highlighted, the reference viruses are coloured blue and the clade/subclade/group/subgroup to which the corresponding HA gene sequences belong is shown.

The NA gene sequences of viruses with HA genes within clades **3C.3a** and **3C.2a** and its subclades, show generally similar subclade/group clustering. All current viruses share the substitutions **S245N** (creating a glycosylation site) and **S247T**, **T267K**, **D339N**, **I380V**, **T392I** and **P468H**. Recently collected viruses with HA genes in subclade **3C.2a1b** share the **NA** amino acid substitutions **P126L, K220N, V303I** and **N329S** (resulting in the loss of a glycosylation site). Viruses with HA genes in subgroups **3C.2a1b+T131K-A** and **3C.2a1b+T135K-A** have **E344K** in the **NA.** Those in subgroup **T131K-A** also have **S315R, G346K** and **D463N** with **N465S** (together forming a potential glycosylation site). The cluster from Cambodia, Laos, Timor Leste and several other countries have NA genes encoding an **I62M** substitution in the stalk domain of the **NA**. Those in subgroup **T135K-A**, from West Africa and elsewhere, share the substitution **V263I**.

Antiviral resistance

Susceptibility to the neuraminidase inhibitors (NAIs) oseltamivir and zanamivir was assessed phenotypically and by full NA gene sequencing, for 30 A(H3N2) viruses detected and received within the course of the 2020-2021 influenza season (**Table 11**). All showed normal inhibition (NI: no reduced susceptibility) by both antivirals.

All of the 39 A(H3N2) full-length PA gene sequences generated at the Crick, from individual viruses detected in the course of the 2020-2021 influenza season, encoded isoleucine at position 38 (I38) and showed no evidence of other substitutions associated with reduced susceptibility to baloxavir marboxil.

Conclusion.

Received A(H3N2) samples with collection dates after 2021-01-31 have HAs in subclade 3C.2a1b. Viruses in subclade 3C.2a1b fell into two main genetic subgroups (3C.2a1b+T131K-A and 3C.2a1b+T135K-A). Those in the ‘Bangladesh’ cluster, within subgroup 3C.2a1b+T131K-A, were more common than those in the ‘Cambodia’ cluster. Each of the two subclade 3C.2a1b subgroups (T131K-A and T135K-A) were best recognised by post-infection ferret antisera raised against viruses within the same subgroup, with those raised against cell culture-propagated viruses giving better recognition than those raised against egg-propagated viruses. The viruses falling into the ‘Bangladesh’ cluster were better recognised by antisera raised against viruses in the same cluster than antisera raised against viruses from the ‘Cambodia’ cluster. All A(H3N2) viruses characterised were sensitive to the neuraminidase inhibitors and the PA inhibitor baloxavir marboxil.

Table 6. Summary of influenza A(H3N2) viruses collected after 2021-01-31, analysed by HI

MONTH	H3N2																
			3C.2a1: Egg-propagated A/Singapore/INFIMH-16-0019/2016			3C.2a1b+T131K-B: Egg-propagated A/Hong Kong/2671/2019			3C.2a1b+T131K-B: Cell-propagated A/Hong Kong/2671/2019			3C.3a1b+T131K-A: Egg-propagated A/Cambodia/e0826360/2020			3C.3a: Egg-propagated NYMC X-327 A/Kansas/14/2017		
Country	Number received	Number propagated[1,2]	≤2 fold[3]	4 fold[3]	≥8 fold[3]	≤2 fold[4]	4 fold[4]	≥8 fold[4]	≤2 fold[5]	4 fold[5]	≥8 fold[5]	≤2 fold[6]	4 fold[6]	≥8 fold6[6]	≤2 fold[7]	4 fold[7]	≥8 fold[7]
2021																	
FEBRUARY																	
Sweden	1	1			1			1			1			1			1
MARCH																	
Sweden	1	1			1			1			1			1			1
APRIL																	
Norway	1	1		1				1			1		1				1
Sweden	2	2			2			2			2			2			2
MAY																	
JUNE																	
JULY																	
France	1	1		1				1		1				1			1
Ghana	5	3		1	2			3	1	2				3			3
Qatar	6	0															
AUGUST																	
Netherlands	1	1			1			1			1			1			1
Norway	2	2			2			2			2			2			2
Qatar	46	12			12			12			12			12			12
Russia	1	0															
	67	24	0	3	21	0	0	24	1	3	20	0	1	23	0	0	24
7 Countries			0.0%	12.5%	87.5%	0.0%	0.0%	100.0%	4.2%	12.5%	83.3%	0.0%	4.2%	95.8%	0.0%	0.0%	100.0%

1. Numbers shown in red indicate that not all of the specimens received had been propagated at the time this report was prepared
2. Propagated to sufficient titre to perform HI assay in presence of 20nM oseltamivir
3. Compared to homologous titres for ferret antisera raised egg-propagated A/Singapore/INFIMH-16-0019/2016 (3C.2a1)
4. Compared to homologous titres for ferret antisera raised against egg-propagated A/Hong Kong/2671/2019 (3C.2a1b+T131K-B)
5. Compared to homologous titres for ferret antisera raised against tissue culture-propagated A/Hong Kong/2671/2019 (3C.2a1b+T131K-B)
6. Compared to homologous titres for ferret antisera raised against egg-propagated A/Cambodia/e0826360/2020 (3C.2a1b+T131K-A)
7. Compared to homologous titres for ferret antisera raised against egg-propagated NYMC X-327 A/Kansas/14/2017 (3C.3a)

As of 2021-09-10

Table 7-1. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-02-25

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre															
					Post-infection ferret antisera															
											NEW		NEW				NEW			
					A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Finland 183/20	A/Finland 183/20	A/Tasmania 503/20	A/Tasmania 503/20	A/Tasmania 503/20	A/Camb 925256/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kan/14/17	A/Kansas 14/17
		Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	SIAT	Egg	Egg	Egg	SIAT	SIAT	SIAT	SIAT	Egg	SIAT
		Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F39/20[*1]	F05/21[*1]	AUS F10039916/20[*1]	F06/21[*1]	AUS F10039780/20[*1]	F03/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
		Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES																			
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	40	40	40	40	160	40	40	80	160	40	320	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	80	320	80	80	<	<	1280	<	80	40	160	<	40	<	<
A/Denmark/3264/2019		3C.2a1b+T135K-A	2019-10-25	SIAT3/SIAT3	160	320	320	160	160	320	640	160	160	320	640	320	160	80	160
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	E8/E3	<	80	160	1280	320	40	1280	80	160	40	160	160	160	640	80
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	80	160	320	320	160	320	640	80	80	320	640	320	160	80	80
A/Finland/183/2020		3C.2a1b+T131K-A	2020-03-02	MDCK1/SIAT2	80	160	160	80	80	320	640	80	80	640	1280	320	160	80	80
A/Finland/183/2020		3C.2a1b+T131K-A	2020-03-02	E6	<	80	80	80	<	40	1280	160	320	80	160	160	80	40	<
A/Tasmania/503/2020		3C.2a1b+T131K-A	2020-02-16	E5/E1	40	160	160	160	40	80	>5120	640	1280	160	320	320	320	80	80
A/Tasmania/503/2020		3C.2a1b+T131K-A	2020-02-16	E5/E2	80	160	320	320	80	80	>5120	640	2560	320	320	320	320	160	160
IVR-122 (A/Tasmania/503/2020)		3C.2a1b+T131K-A	2020-02-16	E5/D6/E1	80	320	320	320	80	80	>5120	640	1280	320	640	320	160	160	80
A/Cambodia/925256/2020		3C.2a1b+T131K-A	2020-03-02	SIAT3	40	80	80	<	40	160	320	40	40	320	640	80	80	40	40
A/Bangladesh/4005/2020		3C.2a1b+T131K-A	2020-10-04	SIAT2	40	40	160	160	40	80	320	160	160	80	160	640	320	160	160
A/Cambodia/e0826360/2020		3C.2a1b+T131K-A	2020-07-18	E5/E1	<	40	40	40	<	<	640	160	320	40	40	80	80	<	<
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	<	40	<	<	<	40	40	<	40	<	40	40	640	80	160
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	Ex/E1	<	<	<	80	<	<	40	<	40	<	<	40	160	320	320
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	<	40	40	40	<	80	40	<	40	<	40	40	640	160	320
TEST VIRUSES																			
A/Saitama/92/2020		3C.2a1b+T131K-A	2020-03-04	MDCK1/Hck2/SIAT1	40	80	80	40	40	160	320	80	40	320	320	80	160	>	40
A/Bangladesh/1006/2020		3C.2a1b+T131K-A	2020-08-26	S3/SIAT1	<	40	80	80	<	40	160	80	80	40	80	640	160	80	80
A/Dakar/10B/2020		3C.2a1b+T135K-A	2020-10-16	C1/MDCK3	40	40	80	40	40	80	ND	80	ND	160	160	ND	80	80	80
A/Dakar/03/2020		3C.2a1b+T135K-A	2020-10-18	C1/SIAT1	40	80	160	40	80	80	80	40	40	160	320	80	80	80	40
A/Dakar/02/2020		3C.2a1b+T135K-A	2020-10-21	C1/SIAT1	40	40	160	40	80	160	80	40	40	160	320	80	80	<	40
A/Dakar/01/2020		3C.2a1b+T135K-A	2020-11-02	C1/SIAT1	<	40	160	40	40	80	80	40	40	160	320	160	80	<	40
						Vaccine SH 2018 NH 2018-19		Vaccine NH 2020-21 SH 2021										Vaccine NH 2019-20		

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-2. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-03-05

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre												
					Post-infection ferret antisera												
					A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Finland 183/20	A/Finland 183/20	A/Tasmania 503/20	A/Camb 925256/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
		Passage history			MDCK	Egg 10[-4]	SIAT	Egg	Cell	SIAT	Egg	Egg	SIAT	SIAT	SIAT	Egg	SIAT
		Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F39/20[*1]	F05/21[*1]	F06/21[*1]	F03/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
		Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES																	
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	40	40	40	40	160	40	160	40	320	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E2	80	320	80	80	<	<	640	80	80	<	40	<	40
A/Denmark/3264/2019		3C.2a1b+T135K-A	2019-10-25	SIAT3/SIAT3	160	320	320	160	320	640	640	160	1280	320	320	160	160
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	E8/E3	40	160	160	2560	320	80	1280	160	320	160	320	640	160
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	160	320	320	320	320	640	80	640	160	160	80	80
A/Finland/183/2020		3C.2a1b+T131K-A	2020-03-02	MDCK1/SIAT2	ND	ND	160	40	40	320	640	160	1280	320	ND	ND	80
A/Finland/183/2020		3C.2a1b+T131K-A	2020-03-02	E6	<	80	80	80	<	40	1280	320	160	160	160	80	40
A/Tasmania/503/2020		3C.2a1b+T131K-A	2020-02-16	E5/E2	80	320	320	320	40	80	>5120	2560	640	320	320	160	80
A/Cambodia/925256/2020		3C.2a1b+T131K-A	2020-03-02	SIAT3	ND	ND	ND	ND	ND	320	640	80	640	ND	ND	ND	40
A/Bangladesh/4005/2020		3C.2a1b+T131K-A	2020-10-04	SIAT2	ND	ND	ND	ND	ND	80	320	160	160	640	ND	ND	ND
A/Cambodia/e0826360/2020		3C.2a1b+T131K-A	2020-07-16	E5/E1	<	160	160	160	80	40	1280	640	160	160	160	80	80
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	<	40	40	40	40	80	40	40	80	40	640	160	320
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	Ex/E1	<	<	<	320	40	<	40	40	<	40	320	1280	320
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	<	40	40	40	40	80	40	40	80	40	640	160	320
TEST VIRUSES																	
IVR-224 (A/Cambodia/e0826360/2020)		3C.2a1b+T131K-A	2020-07-16	E5/D7/E1	40	80	160	160	40	40	2560	1280	160	160	160	80	80
A/Bangladesh/3005/2020		3C.2a1b+T131K-A	2020-09-05	E3/E1	<	<	80	80	80	<	320	320	80	640	160	80	160
A/Bangladesh/4002/2020		3C.2a1b+T131K-A	2020-10-05	E3/E1	<	40	160	160	80	40	320	320	160	640	160	80	160
						Vaccine SH 2018 NH 2018-19		Vaccine NH 2020-21 SH 2021								Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-3. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-04-23

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
	Passage history			A/HK 5738/14 MDCK	A/Singapore 0019/16 Egg 10^{-4}	A/Denmark 3264/19 SIAT	A/HK 2671/19 Egg	A/HK 2671/19 Cell	A/Camb e0826360/20 Egg	A/Eng 538/18 SIAT	NYMC X-327 A/Kansas/14/17 Egg	A/Kansas 14/17 SIAT
	Ferret number			St Judes F60/17*1	F13/19*1	F19/20*1	F44/19*1	St Judes F21/20*1	F10/21*1	F31/18*1	F16/19*1	F17/19*1
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES												
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	<	<	40	80	160	320	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	80	320	80	80	<	40	40	40	<
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT5	160	320	320	160	320	320	160	320	160
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E3	<	160	160	1280	320	320	160	640	160
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	160	320	320	320	320	160	80	80
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	160	160	160	<	2560	320	160	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT4	<	40	<	<	<	40	320	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	<	40	<	160	<	80	160	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	80	40	40	40	80	640	320	640
TEST VIRUSES												
A/Stockholm/1/2021	3C.2a1b+T131K-A	2021-01-08	SIAT0/SIAT1	40	160	160	160	80	320	320	320	320
A/Egypt/7113/2019	3C.2a1b+T135K-B	2019-12-21	SIAT1	40	80	160	80	320	<	40	<	<
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22		Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-4. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-05-21

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre											
				Post-infection ferret antisera											
	Passage history			A/HK 5738/14 MDCK	A/Singapore 0019/16 Egg 10^{-4}	A/Denmark 3264/19 SIAT	A/HK 2671/19 Egg	A/HK 2671/19 Cell	A/Camb e0826360/20 Egg	A/Bang 4005/20 SIAT	A/Eng 538/18 SIAT	NYMC X-327 A/Kansas/14/17 Egg	A/Kansas 14/17 SIAT	A/Bang 911009/20 SIAT	A/Cal 55/20 SIAT
	Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F10/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]	CDC F2021-048	CDC F2021-047
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a	3C.2a1b+T131K-A	3C.2a1b+T131K-A
REFERENCE VIRUSES															
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	320	320	40	40	40	80	80	320	320	160	80	80
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	160	320	80	80	<	40	<	40	40	<	<	40
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT5	160	320	320	80	160	160	160	160	160	160	160	160
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E3	40	160	80	1280	160	160	80	160	640	80	80	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	320	160	160	320	160	160	160	80	160	160	160
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	80	80	<	1280	160	160	80	40	80	160
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2020-10-04	SIAT2	80	80	160	80	40	160	640	320	160	160	160	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	80	<	40	<	40	40	640	160	320	40	40
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	40	<	<	320	<	80	<	320	1280	320	80	40
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	80	40	40	<	80	40	640	320	320	40	40
TEST VIRUSES															
A/Bangladesh/911009/2020	3C.2a1b+T131K-A	2020-09-03	SIAT3	80	80	160	160	40	320	640	320	160	160	160	160
A/California/55/2020	3C.2a1b+T131K-A	2020-10-12	SIAT2	80	80	80	<	40	80	80	40	40	40	80	160
A/Cameroon/16996/2020	3C.2a1b+T135K-A	2020-12-15	SIAT3	40	80	80	80	40	160	320	160	160	80	160	160
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22			Vaccine NH 2019-20			

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-5. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-05-28

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
	Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	Egg	SIAT
	Ferret number			St Judes F60/17*1	F13/19*1	F19/20*1	F44/19*1	St Judes F21/20*1	F10/21*1	F07/21*1	F31/18*1	F16/19*1	F17/19*1
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	320	320	40	40	40	80	80	320	320	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	160	320	80	80	<	40	<	40	40	<
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT5	160	320	320	80	160	160	160	160	160	160
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E3	40	160	80	1280	160	160	80	160	640	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	320	160	160	320	160	160	160	80	160
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	160	160	<	1280	160	160	80	40
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2020-10-04	SIAT2	80	80	160	80	40	160	640	320	160	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	40	80	<	40	<	40	40	640	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	40	<	<	320	<	80	<	320	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	80	40	40	<	80	40	640	320	320
TEST VIRUSES													
A/Norway/10230/2021	3C.2a1b+T131K-A	2021-04-14	SIAT1	40	80	320	160	40	320	640	320	160	160
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22			Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-6. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-06-18

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre: Post-infection ferret antisera						NEW					
				A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Calif 55/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kan/14/17	A/Kansas 14/17
	Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F10/21[*1]	F24/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES														
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	320	320	<	<	40	40	80	80	320	160	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	160	320	40	40	<	40	40	<	40	<	<
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT3/SIAT3	160	160	160	80	160	80	320	160	160	80	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E1	40	80	80	1280	160	160	80	80	160	640	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	160	160	160	160	80	320	80	160	80	160
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	80	80	<	1280	80	160	160	80	80
A/California/55/2020	3C.2a1b+T131K-A	2020-10-12	SIAT2/SIAT1	80	80	80	<	80	40	320	80	80	40	40
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2020-10-04	SIAT2	40	40	80	80	40	160	160	320	160	160	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	<	40	<	<	<	40	<	40	640	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	40	<	<	320	<	40	40	<	320	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	40	<	<	<	40	40	40	640	160	320
TEST VIRUSES														
A/Darwin/6/2021	3C.2a1b+T131K-A	2021-03-16	E4 /E1	<	<	80	40	<	160	40	160	80	40	40
A/Darwin/9/2021	3C.2a1b+T131K-A	2021-04-17	E3/E1	<	<	80	80	<	320	80	320	160	80	40
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22				Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-7. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-06-29

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
					A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
		Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	Egg	SIAT
		Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F10/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
		Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES														
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	<	<	40	40	80	160	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	80	320	40	40	<	<	<	80	<	<
A/Denmark/3264/2019		3C.2a1b+T135K-A	2019-10-25	SIAT5	80	160	80	40	160	80	160	160	40	80
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	E8/E2	<	80	80	640	160	160	80	320	320	80
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	80	160	160	160	160	80	160	160	40	80
A/Cambodia/e0826360/2020		3C.2a1b+T131K-A	2020-07-16	E5/E2	<	80	80	80	<	1280	160	160	80	80
A/Bangladesh/4005/2020		3C.2a1b+T131K-A	2020-10-04	SIAT2	<	40	80	80	<	160	320	320	80	160
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	<	40	<	<	<	<	40	640	160	320
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	Ex/E1	<	<	<	160	<	40	40	320	1280	320
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT2	40	40	<	<	<	<	40	640	160	320
TEST VIRUSES														
A/Stockholm/2/2021		3C.2a1b+T131K-A	2021-01-23	SIAT0/SIAT1	<	40	80	80	<	160	320	320	80	80
A/Stockholm/3/2021		3C.2a1b+T131K-A	2021-02-19	SIAT0/SIAT1	40	40	80	80	<	80	640	320	80	80
A/Stockholm/4/2021		3C.2a1b+T131K-A	2021-03-11	SIAT0/SIAT1	<	40	80	80	<	160	320	160	80	80
A/Stockholm/5/2021		3C.2a1b+T131K-A	2021-04-16	SIAT0/SIAT1	<	<	40	40	<	40	160	80	40	<
A/Stockholm/6/2021		3C.2a1b+T131K-A	2021-04-23	SIAT0/SIAT1	<	<	<	<	<	80	320	160	80	<
						Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22			Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-8. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-08-13

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre									
				Post-infection ferret antisera									
				A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Bang 4005/20	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
	Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	Egg	SIAT
	Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F10/21[*1]	F07/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES													
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	<	<	40	40	80	320	160	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	160	320	40	40	<	40	<	40	<	<
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT5	160	160	160	80	160	80	160	160	80	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E2	40	80	80	1280	160	160	80	160	640	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	160	160	160	160	80	80	160	80	160
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	80	80	<	640	160	160	80	80
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2020-10-04	SIAT2	40	40	80	80	40	160	640	160	160	160
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT3	<	40	<	<	<	40	40	640	160	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	40	<	<	320	<	40	<	320	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT2	40	40	<	<	<	40	40	640	160	640
TEST VIRUSES													
A/Nepal/NPWR-05637/2021	3C.2a1b+T131K-A	2021-04-08	hCK2/SIAT1	<	<	80	80	<	80	320	160	80	80
A/Abidjan/456/2021	3C.2a1b+T135K-A	2021-07-07	MDCK3/SIAT1	40	80	40	<	40	80	80	80	40	40
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021-22			Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-9. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-09-02

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										
												NEW			
					A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Bang 4005/20	A/Stock 5/21	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
		Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	SIAT	Egg	SIAT
		Ferret number			St Judes F60/17[*1]	F13/19[*1]	F19/20[*1]	F44/19[*1]	St Judes F21/20[*1]	F10/21[*1]	F07/21[*1]	F35/21[*1]	F31/18[*1]	F16/19[*1]	F17/19[*1]
		Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
REFERENCE VIRUSES															
A/Hong Kong/5738/2014		3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	<	<	40	40	80	80	320	160	160
A/Singapore/INFIMH-16-0019/2016		3C.2a1	2016-04-14	E5/E3	160	320	40	40	<	40	<	40	40	<	<
A/Denmark/3264/2019		3C.2a1b+T135K-A	2019-10-25	SIAT5	160	160	160	80	160	80	160	160	160	80	80
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	E8/E3	40	80	80	1280	160	160	80	160	160	640	80
A/Hong Kong/2671/2019		3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	160	160	160	160	160	80	80	80	160	80	160
A/Cambodia/e0826360/2020		3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	80	80	<	1280	160	320	160	80	80
A/Bangladesh/4005/2020		3C.2a1b+T131K-A	2020-10-04	SIAT2	40	40	80	80	40	160	640	320	160	160	160
A/Stockholm/5/2021		3C.2a1b+T131K-A	2021-04-16	S0/S2	<	<	40	40	<	40	160	1280	80	40	<
A/England/538/2018		3C.3a	2018-02-26	MDCK1/SIAT3	<	40	<	<	<	40	40	80	640	160	320
NYMC X-327 (A/Kansas/14/17)		3C.3a	2017-12-14	Ex/E1	40	<	<	320	<	40	<	40	320	1280	320
A/Kansas/14/2017		3C.3a	2017-12-14	SIAT3/SIAT1	40	40	<	<	<	40	40	80	640	160	320
TEST VIRUSES															
A/Ghana/1352/2021		3C.2a1b+T135K-A	2021-07-08	SIAT1	<	80	40	<	40	40	40	40	40	<	<
A/Ghana/1948/2021		3C.2a1b+T135K-A	2021-07-26	SIAT1	<	40	<	<	40	40	40	40	40	<	<
						Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021				Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 7-10. Antigenic analyses of influenza A(H3N2) viruses (Guinea Pig RBC with 20nM Oseltamivir) 2021-09-10

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre – Post-infection ferret antisera											
	Passage history			MDCK	Egg 10^{-4}	SIAT	Egg	Cell	Egg	SIAT	SIAT	SIAT	SIAT	Egg	SIAT
	Ferret number			St Judes F60/17*1	F13/19*1	F19/20*1	F44/19*1	St Judes F21/20*1	F10/21*1	F03/21*1	F07/21*1	F35/21*1	F31/18*1	F16/19*1	F17/19*1
	Genetic group			3C.2a	3C.2a1	3C.2a1b+T135K-A	3C.2a1b+T135K-B	3C.2a1b+T135K-B	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.2a1b+T131K-A	3C.3a	3C.3a	3C.3a
				A/HK 5738/14	A/Singapore 0019/16	A/Denmark 3264/19	A/HK 2671/19	A/HK 2671/19	A/Camb e0826360/20	A/Camb 925256/20	A/Bang 4005/20	A/Stock 5/21	A/Eng 538/18	NYMC X-327 A/Kansas/14/17	A/Kansas 14/17
REFERENCE VIRUSES															
A/Hong Kong/5738/2014	3C.2a	2014-04-30	MDCK1/MDCK2/SIAT2	160	320	40	<	40	40	160	80	80	320	160	160
A/Singapore/INFIMH-16-0019/2016	3C.2a1	2016-04-14	E5/E3	80	320	80	40	<	<	160	<	<	40	<	<
A/Denmark/3264/2019	3C.2a1b+T135K-A	2019-10-25	SIAT5	80	160	320	40	160	160	640	320	320	320	80	160
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	E8/E2	<	80	160	640	80	160	160	80	160	160	320	80
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2019-06-17	MDCK1/SIAT4	80	160	320	160	160	80	640	160	160	160	80	80
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2020-07-16	E5/E2	40	80	160	80	<	1280	160	320	320	160	80	80
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2020-09-25	SIAT4	40	160	160	<	80	80	1280	160	160	160	40	80
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2020-10-04	SIAT2	40	40	160	80	<	80	160	640	640	160	80	160
A/Stockholm/5/2021	3C.2a1b+T131K-A	2021-04-16	S0/S2	<	40	80	80	<	80	80	320	640	160	80	<
A/England/538/2018	3C.3a	2018-02-26	MDCK1/SIAT4	<	40	40	<	<	40	40	40	80	320	80	320
NYMC X-327 (A/Kansas/14/17)	3C.3a	2017-12-14	Ex/E1	<	<	40	320	<	40	<	<	40	320	1280	320
A/Kansas/14/2017	3C.3a	2017-12-14	SIAT3/SIAT1	<	40	80	<	<	40	80	40	80	640	160	320
TEST VIRUSES															
A/Norway/16606/2021	3C.2a1b+T131K-A	2021-08-02	hCK1/SIAT1	<	<	40	<	<	<	40	80	320	40	<	<
A/Norway/16960/2021	3C.2a1b+T131K-A	2021-08-07	SIAT1	<	<	80	40	<	40	40	160	320	80	40	<
A/Qatar/24-VI-21-4043041/2021	3C.2a1b+T131K-A	2021-08-08	SIAT1	<	<	80	40	<	80	80	320	640	160	80	<
A/Qatar/16-VI-21-4036102/2021	3C.2a1b+T131K-A	2021-08-08	SIAT1	<	<	160	40	<	160	40	320	320	160	40	40
A/Qatar/47-VI-21-3991750/2021	3C.2a1b+T131K-A	2021-08-09	SIAT1	<	<	160	40	<	160	80	320	320	160	80	40
A/Qatar/24-VI-21-3986733/2021	3C.2a1b+T131K-A	2021-08-09	SIAT1	<	<	160	80	<	160	80	320	320	160	80	40
A/Qatar/10-VI-21-3994025/2021	3C.2a1b+T131K-A	2021-08-09	SIAT1	<	<	160	40	<	160	40	320	320	160	80	40
A/Qatar/10-VI-21-3976292/2021	3C.2a1b+T131K-A	2021-08-10	SIAT1	<	<	160	40	<	160	40	320	320	160	80	40
A/Qatar/24-VI-21-3948134/2021	3C.2a1b+T131K-A	2021-08-10	SIAT1	<	<	160	40	<	160	40	320	320	160	80	40
A/Qatar/16-VI-21-3956954/2021	3C.2a1b+T131K-A	2021-08-11	SIAT1	<	<	160	40	<	160	40	320	320	160	40	40
A/Qatar/24-VI-21-3942752/2021	3C.2a1b+T131K-A	2021-08-11	SIAT1	<	<	160	40	<	160	80	320	320	160	80	40
A/Qatar/16-VI-21-3936112/2021	3C.2a1b+T131K-A	2021-08-11	SIAT1	<	<	160	80	<	160	80	320	320	160	80	40
A/Qatar/10-VI-21-3914545/2021	3C.2a1b+T131K-A	2021-08-11	SIAT1	<	<	40	40	<	40	40	160	320	80	<	<
A/Qatar/24-VI-21-3909543/2021	3C.2a1b+T131K-A	2021-08-13	SIAT1	<	<	160	40	<	160	80	320	320	160	80	40
A/Netherlands/00007/2021	3C.2a1b+T131K-A	2021-08-13	SIAT1	<	<	40	40	<	40	40	160	320	80	40	<
A/Ghana/1344/2021	3C.2a1b+T135K-A	2021-07-05	SIAT1	40	80	320	40	80	80	320	160	160	160	<	40
					Vaccine NH 2018-19 SH 2018		Vaccine NH 2020-21 SH 2021		Vaccine NH 2021					Vaccine NH 2019-20	

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 8-1. Antigenic analysis of influenza A(H3N2) viruses - Plaque Reduction Neutralisation (MDCK-SIAT) 2021-07-19

Viruses	Passage history Ferret number Genetic group	Collection Date	Passage History	Neutralisation Titre[1] Post-infection ferret antisera A/Norway 3275/2018 SIAT F03/19 3C.2a1b+T131K		A/Cambodia 925256/2020 SIAT F03/21 3C.2a1b+T131K-A		A/Cambodia e0826360/2020 Egg F10/21 3C.2a1b+T131K-A		A/Bangladesh 4005/2020 SIAT F07/21 3C.2a1b+T131K-A		A/Bangladesh 2004/2020 Egg F11/21 3C.2a1b+T131K-A		NIB-127B A/Darwin 06/2021 Egg F34/21 3C.2a1b+T131K-A		NIB-126A A/Darwin 09/2021 Egg F33/21 3C.2a1b+T131K-A		A/Denmark 3264/19 SIAT F19/20 3C.2a1b+T135K-A		A/Hong Kong 2671/19 SIAT F33/19 3C.2a1b+T135K-B		A/Kansas 14/2017 SIAT F17/19 3C.3a		HA1 substitutions for 3C.2a/3a viruses compared to A/Norway/3275/2018: Egg adaptation HA substitutions compared to the corresponding cell culture propagated virus
				2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	
REFERENCE VIRUSES																								
A/Norway/3275/2018	3C.2a1b+T131K	2019-08-01	SIAT2 10^{-3}	320	371	80	70	<	<	<	<	<	<	<	<	<	<	80	90	40	45	<	<	
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2021-01-21	SIAT3 10^{-3}	80	70	320	243	<	<	<	<	<	<	<	<	<	<	80	85	80	89	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-02-25	E5/E2 10^{-5}	<	<	<	<	320	436	40	54	160	180	320	253	80	116	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2021-05-10	SIAT2 10^{-3}	<	<	40	41	40	54	320	350	320	401	320	435	640	512	<	<	<	<	40	54	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Bangladesh/2004/2020	3C.2a1b+T131K-A	2021-02-16	E5 (Am3AI2) (ls2) 10^{-5}	<	<	320	291	1280	1224	2560	2334	2560	3551	2560	3456	5120	3934	320	408	<	<	320	301	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-127B (A/Darwin/6/2021)	3C.2a1b+T131K-A		E4/E1/E5	<	<	80	98	160	125	320	245	320	343	640	789	1280	960	80	65	<	<	<	<	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-126A (A/Darwin/9/2021)	3C.2a1b+T131K-A		E3/E1/E5	<	<	160	173	160	225	640	567	640	597	1280	1320	2560	1994	160	124	<	<	40	49	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
A/Denmark/3264/2019	3C.2a1b+T135K-A	2020-07-16	SIAT3/SIAT2 10^{-3}	40	52	320	254	<	<	<	<	<	<	<	<	40	40	320	273	160	163	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, F193S, S198P
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2020-03-19	MDCK1/SIAT4 10^{-3}	40	50	320	345	<	<	<	<	<	<	<	<	<	<	320	310	320	290	<	<	V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, F193S
A/Kansas/14/2017	3C.3a	2019-11-18	SIAT3/SIAT2 10^{-3}	<	<	<	<	<	<	<	<	40	40	320	258	<	<	<	<	<	<	160	132	G62E, S91N, R92K, V106A, K121N, T128A(-cho), K131T, A138S, S144K, Y159S, T160K(-cho), K171N, F193S, K326R
TEST VIRUSES																								
A/Bangladesh/911009/2020	3C.2a1b+T131K-A	2020-09-03	SIAT4	<	<	40	47	80	61	320	301	320	312	320	312	320	312	<	<	<	<	80	60	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Stockholm/1/2021	3C.2a1b+T131K-A	2021-01-08	SIAT1	<	<	80	60	160	133	320	457	640	550	640	800	640	485	80	119	<	<	80	77	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, R201I
A/Norway/10230/2021	3C.2a1b+T131K-A	2021-04-14	SIAT1	<	<	40	40	80	93	320	315	320	438	640	524	320	414	80	87	<	<	40	58	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, R201I
A/Cameroon/16996/2020	3C.2a1b+T135K-A	2020-12-15	SIAT3	<	<	80	71	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	V106A, T128A(-cho), K131I, T135K(-cho), A138S, Q173K, G186D, D190N, I192F, F193S, S198P

[1] Antiserum dilution value (2-fold), equivalent to HI reading, closest to the actual computer read value from a digitized image (Read) causing 50% reduction in plaque formation. In both columns, < indicates titres of <40.

Table 8-2. Antigenic analysis of influenza A(H3N2) viruses - Plaque Reduction Neutralisation (MDCK-SIAT) 2021-07-29

Viruses	Passage history Ferret number Genetic group	Collection Date	Passage History	Neutralisation Titre[1] Post-infection ferret antisera A/Norway 3275/2018 SIAT F03/19 3C.2a1b+T131K		A/Cambodia 925256/2020 SIAT F03/21 3C.2a1b+T131K-A		A/Cambodia e0826360/2020 Egg F10/21 3C.2a1b+T131K-A		A/Bangladesh 4005/2020 SIAT F07/21 3C.2a1b+T131K-A		A/Bangladesh 2004/2020 Egg F11/21 3C.2a1b+T131K-A		NIB-127B A/Darwin 06/2021 Egg F34/21 3C.2a1b+T131K-A		NIB-126A A/Darwin 09/2021 Egg F33/21 3C.2a1b+T131K-A		A/Denmark 3264/19 SIAT F19/20 3C.2a1b+T135K-A		A/Hong Kong 2671/19 SIAT F33/19 3C.2a1b+T135K-B		A/Kansas 14/2017 SIAT F17/19 3C.3a		HA1 substitutions for 3C.2a/3a viruses compared to A/Norway/3275/2018: Egg adaptation HA substitutions compared to the corresponding cell culture propagated virus
				2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	
REFERENCE VIRUSES																								
A/Norway/3275/2018	3C.2a1b+T131K	2019-08-01	SIAT2 10^{-3}	320	371	80	70	<	<	<	<	<	<	<	<	<	<	80	90	40	45	<	<	
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2021-01-21	SIAT3 10^{-3}	80	70	320	243	<	<	<	<	<	<	<	<	<	<	80	85	80	89	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-02-25	E5/E2 10^{-5}	<	<	<	<	320	436	40	54	160	180	320	253	80	116	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2021-05-10	SIAT2 10^{-3}	<	<	40	41	40	54	320	350	320	401	320	435	640	512	<	<	<	<	40	54	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Bangladesh/2004/2020	3C.2a1b+T131K-A	2021-02-16	E5 (Am3Al2) (ls2) 10^{-5}	<	<	320	291	1280	1224	2560	2334	2560	3551	2560	3456	5120	3934	320	408	<	<	320	301	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-127B (A/Darwin/6/2021)	3C.2a1b+T131K-A		E4/E1/E5	<	<	80	98	160	125	320	245	320	343	640	789	1280	960	80	65	<	<	<	<	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-126A (A/Darwin/9/2021)	3C.2a1b+T131K-A		E3/E1/E5	<	<	160	173	160	225	640	567	640	597	1280	1320	2560	1994	160	124	<	<	40	49	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
A/Denmark/3264/2019	3C.2a1b+T135K-A	2020-07-16	SIAT3/SIAT2 10^{-3}	40	52	320	254	<	<	<	<	<	<	<	<	40	40	320	273	160	163	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, F193S, S198P
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2020-03-19	MDCK1/SIAT4 10^{-3}	40	50	320	345	<	<	<	<	<	<	<	<	<	<	320	310	320	290	<	<	V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, F193S
A/Kansas/14/2017	3C.3a	2019-11-18	SIAT3/SIAT2 10^{-3}	<	<	<	<	<	<	<	<	40	40	320	258	<	<	<	<	<	<	160	132	G62E, S91N, R92K, V106A, K121N, T128A(-cho), K131T, A138S, S144K, Y159S, T160K(-cho), K171N, F193S, K326R
TEST VIRUSES																								
A/Stockholm/2/2021	3C.2a1b+T131K-A	2021-01-23	SIAT2	<	<	<	<	80	77	320	273	320	364	320	298	320	298	40	40	<	<	40	40	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, R201I
A/Stockholm/3/2021	3C.2a1b+T131K-A	2021-02-19	SIAT2	<	<	40	49	40	46	320	269	320	268	320	310	320	272	<	<	<	<	<	<	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, K315R
A/Stockholm/4/2021	3C.2a1b+T131K-A	2021-03-11	SIAT2	<	<	40	53	40	46	160	218	320	249	160	175	160	222	<	<	<	<	<	<	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, K315R
A/Stockholm/5/2021	3C.2a1b+T131K-A	2021-04-16	SIAT2	<	<	<	<	<	<	80	72	80	113	320	260	320	422	<	<	<	<	<	<	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Stockholm/6/2021	3C.2a1b+T131K-A	2021-04-23	SIAT2	<	<	<	<	<	<	80	72	80	87	320	240	320	375	<	<	<	<	<	<	D53N, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F

[1] Antiserum dilution value (2-fold), equivalent to HI reading, closest to the actual computer read value from a digitized image (Read) causing 50% reduction in plaque formation. In both columns, < indicates titres of <40.

Table 8-3. Antigenic analysis of influenza A(H3N2) viruses - Plaque Reduction Neutralisation (MDCK-SIAT) 2021-08-26

Viruses	Passage history Ferret number Genetic group	Collection Date	Passage History	Neutralisation Titre[1] Post-infection ferret antisera A/Norway 3275/2018 SIAT F03/19 3C.2a1b+T131K		A/Cambodia 925256/2020 SIAT F03/21 3C.2a1b+T131K-A		A/Cambodia e0826360/2020 Egg F10/21 3C.2a1b+T131K-A		A/Bangladesh 4005/2020 SIAT F07/21 3C.2a1b+T131K-A		A/Bangladesh 2004/2020 Egg F11/21 3C.2a1b+T131K-A		NIB-127B A/Darwin 06/2021 Egg F34/21 3C.2a1b+T131K-A		NIB-126A A/Darwin 09/2021 Egg F33/21 3C.2a1b+T131K-A		A/Denmark 3264/19 SIAT F19/20 3C.2a1b+T135K-A		A/Hong Kong 2671/19 SIAT F33/19 3C.2a1b+T135K-B		A/Kansas 14/2017 SIAT F17/19 3C.3a		HA1 substitutions for 3C.2a/3a viruses compared to A/Norway/3275/2018: Egg adaptation HA substitutions compared to the corresponding cell culture propagated virus
				2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	
REFERENCE VIRUSES																								
A/Norway/3275/2018	3C.2a1b+T131K	2019-08-01	SIAT2 10^{-3}	320	371	80	70	<	<	<	<	<	<	<	<	<	<	80	90	40	45	<	<	
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2021-01-21	SIAT3 10^{-3}	80	70	320	243	<	<	<	<	<	<	<	<	<	<	80	85	80	89	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-02-25	E5/E2 10^{-5}	<	<	<	<	320	436	40	54	160	180	320	253	80	116	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2021-05-10	SIAT2 10^{-3}	<	<	40	41	40	54	320	350	320	401	320	435	640	512	<	<	<	<	40	54	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Bangladesh/2004/2020	3C.2a1b+T131K-A	2021-02-16	E5 (Am3AI2) (Is2) 10^{-5}	<	<	320	291	1280	1224	2560	2334	2560	3551	2560	3456	5120	3934	320	408	<	<	320	301	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-127B (A/Darwin/6/2021)	3C.2a1b+T131K-A		E4/E1/E5	<	<	80	98	160	125	320	245	320	343	640	789	1280	960	80	65	<	<	<	<	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-126A (A/Darwin/9/2021)	3C.2a1b+T131K-A		E3/E1/E5	<	<	160	173	160	225	640	567	640	597	1280	1320	2560	1994	160	124	<	<	40	49	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
A/Denmark/3264/2019	3C.2a1b+T135K-A	2020-07-16	SIAT3/SIAT2 10^{-3}	40	52	320	254	<	<	<	<	<	<	<	<	40	40	320	273	160	163	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, F193S, S198P
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2020-03-19	MDCK1/SIAT4 10^{-3}	40	50	320	345	<	<	<	<	<	<	<	<	<	<	320	310	320	290	<	<	V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, F193S
A/Kansas/14/2017	3C.3a	2019-11-18	SIAT3/SIAT2 10^{-3}	<	<	<	<	<	<	<	<	40	40	320	258	<	<	<	<	<	<	160	132	G62E, S91N, R92K, V106A, K121N, T128A(-cho), K131T, A138S, S144K, Y159S, T160K(-cho), K171N, F193S, K326R
TEST VIRUSES																								
A/Yamagata/1/2021	3C.2a1b+T131K-A	2021-02-09	hCK2/SIAT1	40	49	160	233	<	<	<	<	<	<	<	<	<	<	80	78	80	75	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/California/55/2020	3C.2a1b+T131K-A	2021-06-14	SIAT2/SIAT1	80	67	160	227	<	<	<	<	<	<	<	<	<	<	80	106	80	84	<	<	G5V, K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
IVR-224 A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-03-01	E5/D7/E1 10^{-6}	<	<	<	<	320	310	80	75	320	256	320	348	160	151	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, S186R, S193*, Y195F, S198P, S219*
A/Nepal/NPWR-05637/2021	3C.2a1b+T131K-A	2021-04-08	hCK2/SIAT1	<	<	40	42	40	57	320	272	320	254	320	276	320	282	40	44	<	<	40	56	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, I300V
A/Michigan/173/2020	3C.2a1b+T131K-A	2021-07-13	E5 (Am1AI4) Is1	<	<	640	484	2560	2447	2560	3600	>5120	>5120	>5120	>5120	>5120	>5120	1280	1280	40	40	640	665	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, D186N, D190N, F193S, Y195F, R201I, D225G
A/Darwin/6/2021	3C.2a1b+T131K-A	2021-06-11	E4	<	<	80	85	80	117	320	267	640	570	1280	1062	1280	1783	80	73	<	<	40	40	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F, D225G
A/Darwin/9/2021	3C.2a1b+T131K-A	2021-06-11	E3	<	<	640	480	1280	1088	1280	1242	1280	1520	2560	3368	5120	4053	320	248	<	<	160	126	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, D186N, D190N, F193S, Y195F, D225G
A/Dakar/01/2020	3C.2a1b+T135K-A	2020-11-02	C1/SIAT1	<	<	160	221	<	<	<	<	<	<	<	<	80	103	320	247	80	80	<	<	S54N, V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, I192F, F193S, S198P
A/Dakar/02/2020	3C.2a1b+T135K-A	2020-10-21	C1/SIAT1	<	<	320	302	<	<	<	<	<	<	NA	NA	NA	NA	320	291	80	100	<	<	S54N, Q57H, V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, I192F, F193S, S198P
A/Dakar/03/2020	3C.2a1b+T135K-A	2020-10-18	C1/SIAT1	<	<	160	213	<	<	<	<	<	<	<	<	80	70	160	143	80	62	<	<	V106A, T128A(-cho), V130A, K131T, T135K(-cho), A138S, G186D, D190N, I192F, F193S, S198P, R299K
A/Abidjan/456/2021	3C.2a1b+T135K-A	2021-07-07	MDCK3/SIAT1	<	<	80	84	<	<	<	<	<	<	<	<	<	<	80	60	<	<	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, V182I, G186D, D190N, I192F, F193S, S198P, R261Q, V309I
A/Nepal/20FL1005/2020	3C.2a1b+T135K-B	2020-03-20	hCK1/SIAT1	<	<	160	141	<	<	<	<	<	<	<	<	<	<	80	78	80	117	<	<	E50K, V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, S144N(+cho), F193S

[1] Antiserum dilution value (2-fold), equivalent to HI reading, closest to the actual computer read value from a digitized image (Read) causing 50% reduction in plaque formation. In both columns, < indicates titres of <40.

Table 8-4. Antigenic analysis of influenza A(H3N2) viruses - Plaque Reduction Neutralisation (MDCK-SIAT) 2021-09-06

Viruses	Passage history Ferret number Genetic group	Collection Date	Passage History	Neutralisation Titre[1] Post-infection ferret antisera A/Norway 3275/2018 SIAT F03/19 3C.2a1b+T131K		A/Cambodia 925256/2020 SIAT F03/21 3C.2a1b+T131K-A		A/Cambodia e0826360/2020 Egg F10/21 3C.2a1b+T131K-A		A/Bangladesh 4005/2020 SIAT F07/21 3C.2a1b+T131K-A		A/Bangladesh 2004/2020 Egg F11/21 3C.2a1b+T131K-A		NIB-127B A/Darwin 06/2021 Egg F34/21 3C.2a1b+T131K-A		NIB-126A A/Darwin 09/2021 Egg F33/21 3C.2a1b+T131K-A		A/Denmark 3264/19 SIAT F19/20 3C.2a1b+T135K-A		A/Hong Kong 2671/19 SIAT F33/19 3C.2a1b+T135K-B		A/Kansas 14/2017 SIAT F17/19 3C.3a		HA1 substitutions for 3C.2a/3a viruses compared to A/Norway/3275/2018: Egg adaptation HA substitutions compared to the corresponding cell culture propagated virus
				2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	
REFERENCE VIRUSES																								
A/Norway/3275/2018	3C.2a1b+T131K	2019-08-01	SIAT2 10^{-3}	320	371	80	70	<	<	<	<	<	<	<	<	<	<	80	90	40	45	<	<	
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2021-01-21	SIAT3 10^{-3}	80	70	320	243	<	<	<	<	<	<	<	<	<	<	80	85	80	89	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-02-25	E5/E2 10^{-5}	<	<	<	<	320	436	40	54	160	180	320	253	80	116	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2021-05-10	SIAT2 10^{-3}	<	<	40	41	40	54	320	350	320	401	320	435	640	512	<	<	<	<	40	54	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Bangladesh/2004/2020	3C.2a1b+T131K-A	2021-02-16	E5 (Am3Al2) (ls2) 10^{-5}	<	<	320	291	1280	1224	2560	2334	2560	3551	2560	3456	5120	3934	320	408	<	<	320	301	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-127B (A/Darwin/6/2021)	3C.2a1b+T131K-A		E4/E1/E5	<	<	80	98	160	125	320	245	320	343	640	789	1280	960	80	65	<	<	<	<	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-126A (A/Darwin/9/2021)	3C.2a1b+T131K-A		E3/E1/E5	<	<	160	173	160	225	640	567	640	597	1280	1320	2560	1994	160	124	<	<	40	49	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
A/Denmark/3264/2019	3C.2a1b+T135K-A	2020-07-16	SIAT3/SIAT2 10^{-3}	40	52	320	254	<	<	<	<	<	<	<	<	40	40	320	273	160	163	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, F193S, S198P
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2020-03-19	MDCK1/SIAT4 10^{-3}	40	50	320	345	<	<	<	<	<	<	<	<	<	<	320	310	320	290	<	<	V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, F193S
A/Kansas/14/2017	3C.3a	2019-11-18	SIAT3/SIAT2 10^{-3}	<	<	<	<	<	<	<	<	40	40	320	258	<	<	<	<	<	<	160	132	G62E, S91N, R92K, V106A, K121N, T128A(-cho), K131T, A138S, S144K, Y159S, T160K(-cho), K171N, F193S, K326R
TEST VIRUSES																								
NYMC X-361-A (A/Cambodia/e082630/2020)	3C.2a1b+T131K-A	2021-03-30	Ex	<	<	<	<	320	255	40	52	80	94	160	155	80	66	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P, S219F

[1] Antiserum dilution value (2-fold), equivalent to HI reading, closest to the actual computer read value from a digitized image (Read) causing 50% reduction in plaque formation. In both columns, < indicates titres of <40.

Table 8-5. Antigenic analysis of influenza A(H3N2) viruses - Plaque Reduction Neutralisation (MDCK-SIAT) 2021-09-15

Viruses	Passage history Ferret number Genetic group	Collection Date	Passage History	Neutralisation Titre[1] Post-infection ferret antisera A/Norway 3275/2018 SIAT F03/19 3C.2a1b+T131K		A/Cambodia 925256/2020 SIAT F03/21 3C.2a1b+T131K-A		A/Cambodia e0826360/2020 Egg F10/21 3C.2a1b+T131K-A		A/Bangladesh 4005/2020 SIAT F07/21 3C.2a1b+T131K-A		A/Bangladesh 2004/2020 Egg F11/21 3C.2a1b+T131K-A		NIB-127B A/Darwin 06/2021 Egg F34/21 3C.2a1b+T131K-A		NIB-126A A/Darwin 09/2021 Egg F33/21 3C.2a1b+T131K-A		A/Denmark 3264/19 SIAT F19/20 3C.2a1b+T135K-A		A/Hong Kong 2671/19 SIAT F33/19 3C.2a1b+T135K-B		A/Kansas 14/2017 SIAT F17/19 3C.3a		HA1 substitutions for 3C.2a/3a viruses compared to A/Norway/3275/2018: Egg adaptation HA substitutions compared to the corresponding cell culture propagated virus
				2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	2-fold	Read	
REFERENCE VIRUSES																								
A/Norway/3275/2018	3C.2a1b+T131K	2019-08-01	SIAT2 10^{-3}	320	371	80	70	<	<	<	<	<	<	<	<	<	<	80	90	40	45	<	<	
A/Cambodia/925256/2020	3C.2a1b+T131K-A	2021-01-21	SIAT3 10^{-3}	80	70	320	243	<	<	<	<	<	<	<	<	<	<	80	85	80	89	<	<	K83E, Y94N, V106A, K171N, G186S, F193S, Y195F, S198P
A/Cambodia/e0826360/2020	3C.2a1b+T131K-A	2021-02-25	E5/E2 10^{-5}	<	<	<	<	320	436	40	54	160	180	320	253	80	116	<	<	<	<	<	<	K83E, Y94N, V106A, T160K(-cho), K171N, G186R, F193S, Y195F, S198P
A/Bangladesh/4005/2020	3C.2a1b+T131K-A	2021-05-10	SIAT2 10^{-3}	<	<	40	41	40	54	320	350	320	401	320	435	640	512	<	<	<	<	40	54	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Bangladesh/2004/2020	3C.2a1b+T131K-A	2021-02-16	E5 (Am3Al2) (Is2) 10^{-5}	<	<	320	291	1280	1224	2560	2334	2560	3551	2560	3456	5120	3934	320	408	<	<	320	301	K83E, Y94N, V106A, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-127B (A/Darwin/6/2021)	3C.2a1b+T131K-A		E4/E1/E5	<	<	80	98	160	125	320	245	320	343	640	789	1280	960	80	65	<	<	<	<	D53G, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
NIB-126A (A/Darwin/9/2021)	3C.2a1b+T131K-A		E3/E1/E5	<	<	160	173	160	225	640	567	640	597	1280	1320	2560	1994	160	124	<	<	40	49	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186N, D190N, F193S, Y195F, D225G
A/Denmark/3264/2019	3C.2a1b+T135K-A	2020-07-16	SIAT3/SIAT2 10^{-3}	40	52	320	254	<	<	<	<	<	<	<	<	40	40	320	273	160	163	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, G186D, D190N, F193S, S198P
A/Hong Kong/2671/2019	3C.2a1b+T135K-B	2020-03-19	MDCK1/SIAT4 10^{-3}	40	50	320	345	<	<	<	<	<	<	<	<	<	<	320	310	320	290	<	<	V106A, T128A(-cho), K131T, T135K(-cho), S137F, A138S, F193S
A/Kansas/14/2017	3C.3a	2019-11-18	SIAT3/SIAT2 10^{-3}	<	<	<	<	<	<	<	<	40	40	320	258	<	<	<	<	<	<	160	132	G62E, S91N, R92K, V106A, K121N, T128A(-cho), K131T, A138S, S144K, Y159S, T160K(-cho), K171N, F193S, K326R
TEST VIRUSES																								
A/Norway/16606/2021	3C.2a1b+T131K-A	2021-08-07	SIAT1	<	<	<	<	<	<	80	79	80	111	160	154	320	308	<	<	<	<	<	<	K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Norway/16960/2021	3C.2a1b+T131K-A	2021-08-08	SIAT1	<	<	<	<	<	<	80	116	160	132	160	184	320	381	<	<	<	<	<	<	G16X, N31X, K83E, Y94N, V106A, H156S, Y159N, T160I(-cho), L164Q, G186D, D190N, F193S, Y195F
A/Netherlands/00007/2021	3C.2a1b+T131K-A	2021-08-02	hCK1/SIAT1	<	<	<	<	<	<	80	71	80	98	320	274	320	270	<	<	<	<	<	<	D53G, K83E, Y94N, D104G, V106A, H156S, Y159N, T160I(-cho), L164Q, V182X, G186D, D190N, F193S, Y195F, K276R
A/Ghana/1352/2021	3C.2a1b+T135K-A	2021-07-08	SIAT1	<	<	80	61	<	<	<	<	<	<	<	<	<	<	40	40	<	<	<	<	I58V, V106A, T128A(-cho), K131I, T135K(-cho), A138S, G186D, D190N, I192F, F193S, S198P, K207R
A/Ghana/1948/2021	3C.2a1b+T135K-A	2021-07-26	SIAT1	<	<	40	57	<	<	<	<	<	<	<	<	<	<	40	48	<	<	<	<	I58V, V106A, T128A(-cho), K131I, T135K(-cho), A138S, G186D, D190N, I192F, F193S, S198P, K207R
A/Ghana/1344/2021	3C.2a1b+T135K-A	2021-07-05	SIAT2	<	<	80	75	<	<	<	<	<	<	<	<	<	<	80	60	<	<	<	<	V106A, T128A(-cho), K131T, T135K(-cho), A138S, V182I, G186D, D190N, I192F, F193S, S198P, R261Q, V309I

[1] Antiserum dilution value (2-fold), equivalent to HI reading, closest to the actual computer read value from a digitized image (Read) causing 50% reduction in plaque formation. In both columns, < indicates titres of <40.

Figure 6. HA phylogeny of A(H3N2) viruses used in VN assay

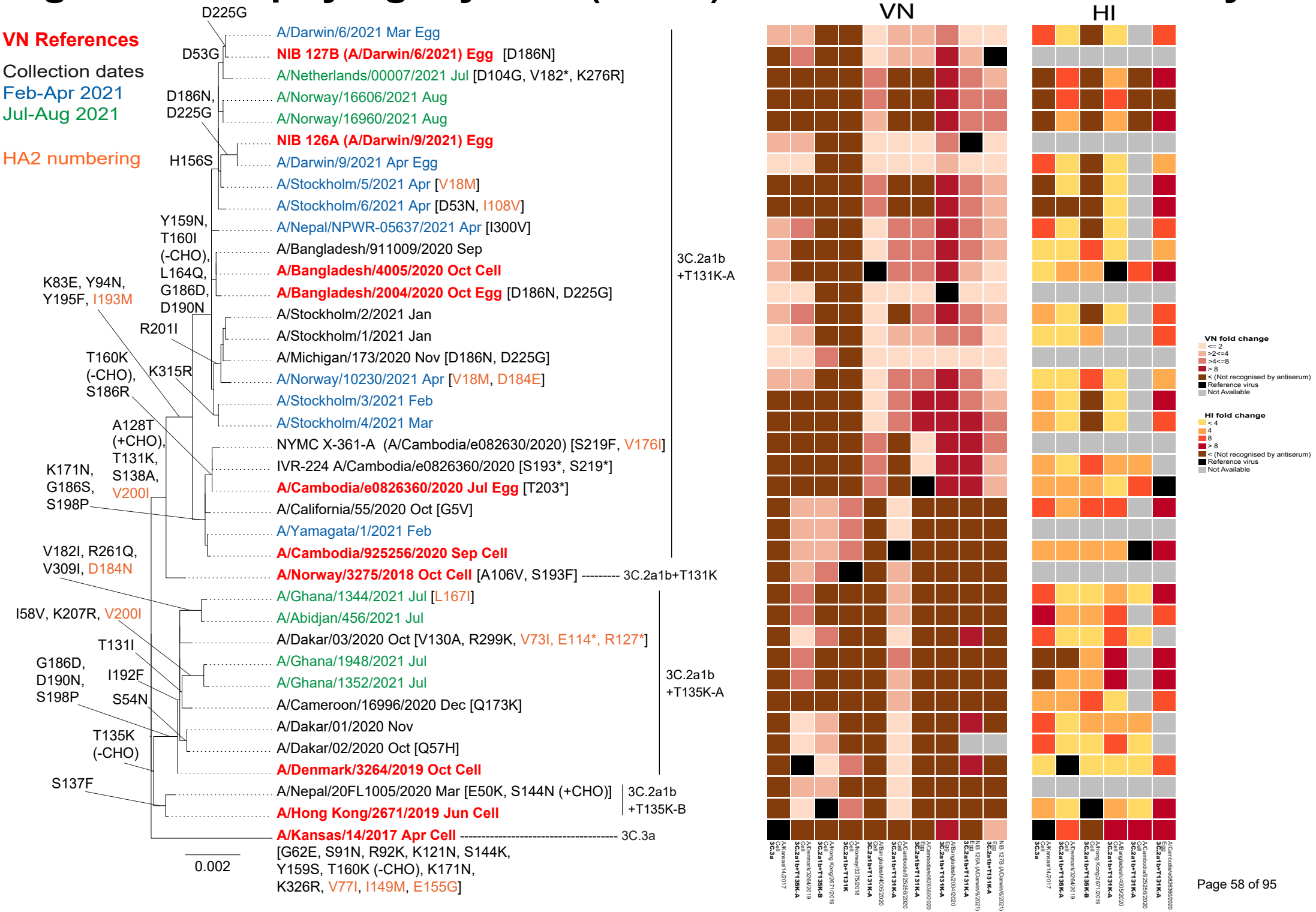


Figure 7. Phylogenetic comparison of A(H3N2) HA genes

Vaccine viruses
Reference viruses

Collection date
Aug 2021
Jul 2021
Jun 2021
May 2021
Apr 2021
Mar 2021
Feb 2021

HA2 numbering

recent Crick sequences

$ proposed serology antigens

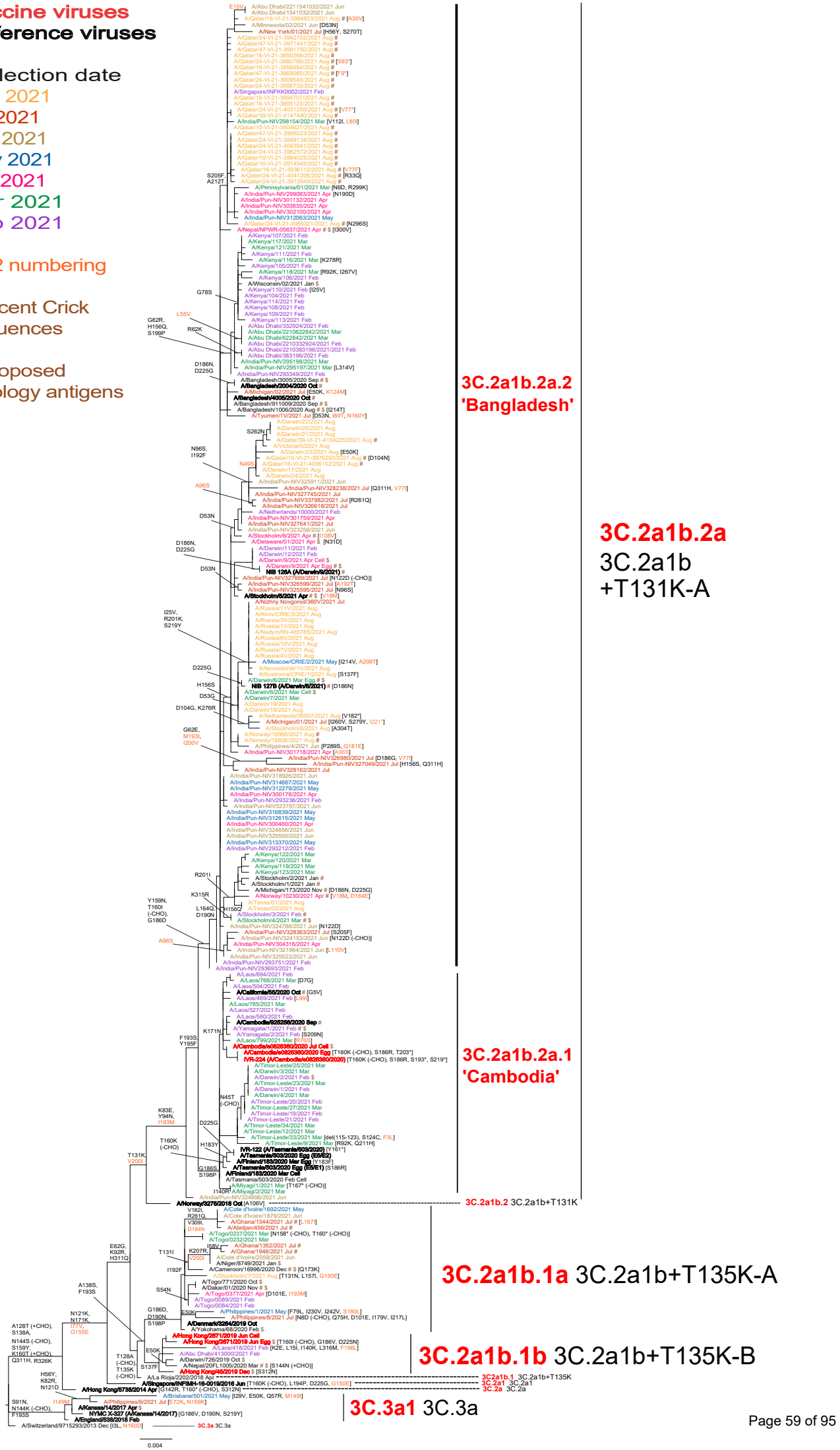
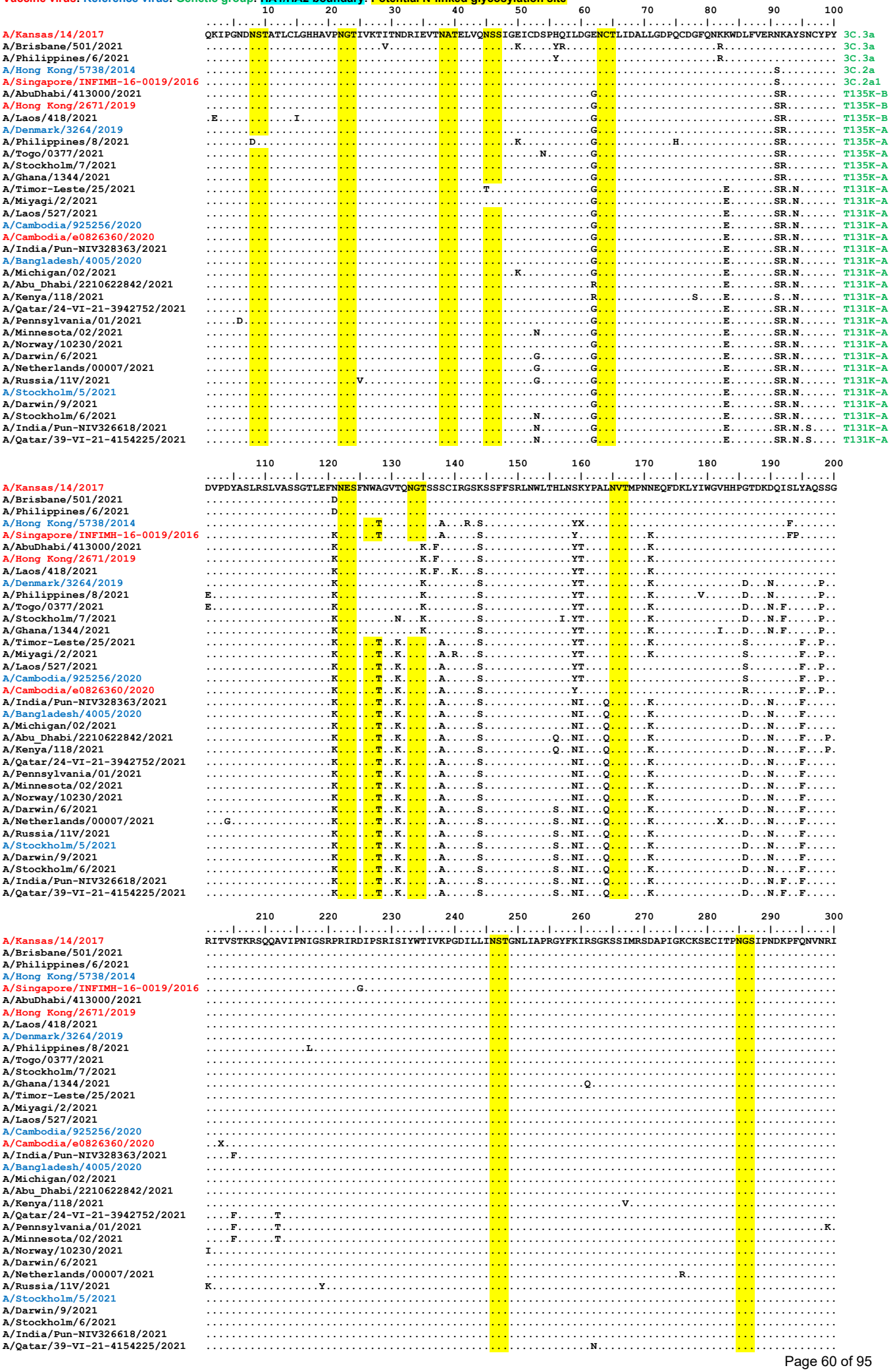
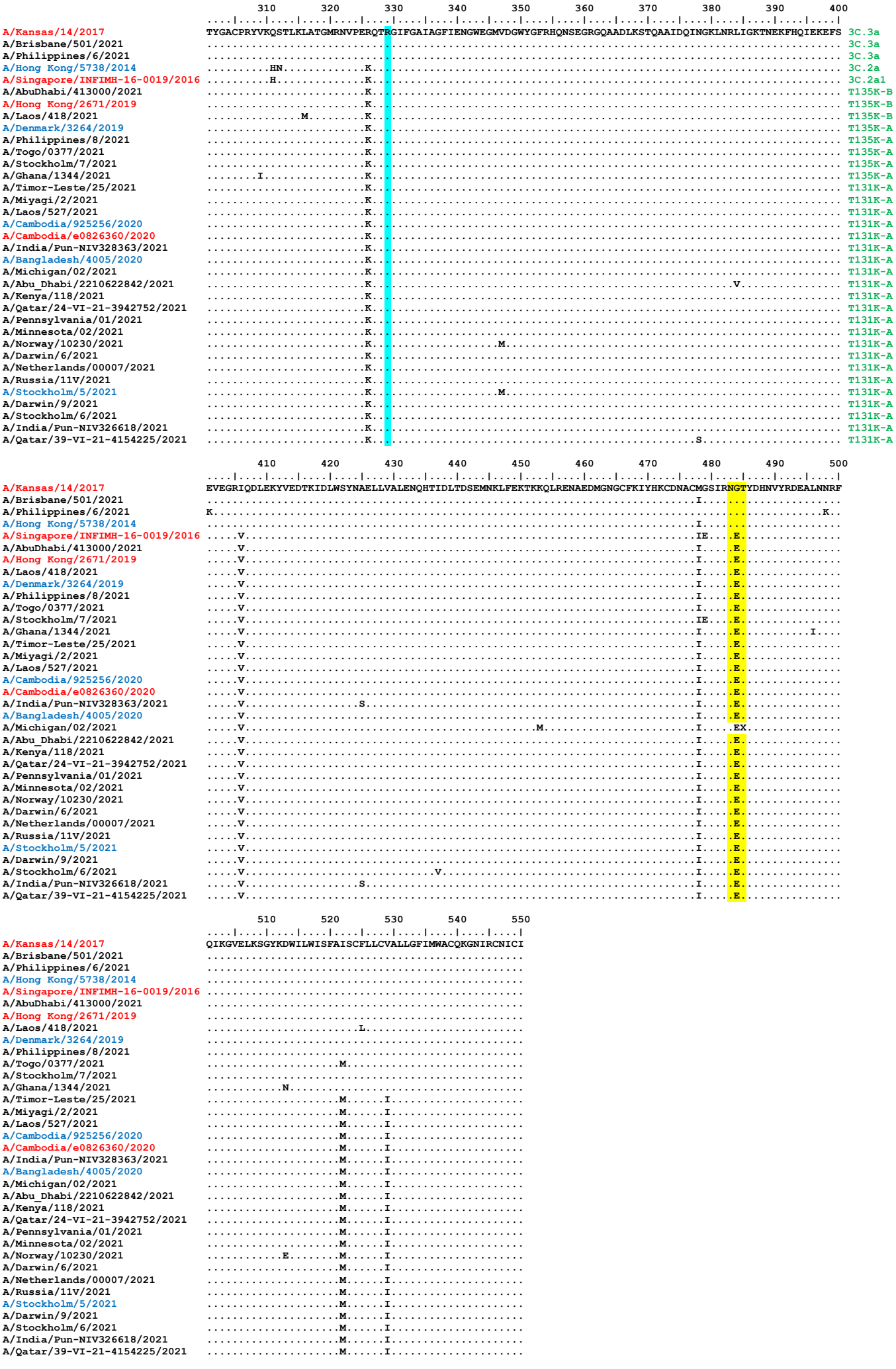


Figure 8. HA protein alignment for A(H3N2) viruses

Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site





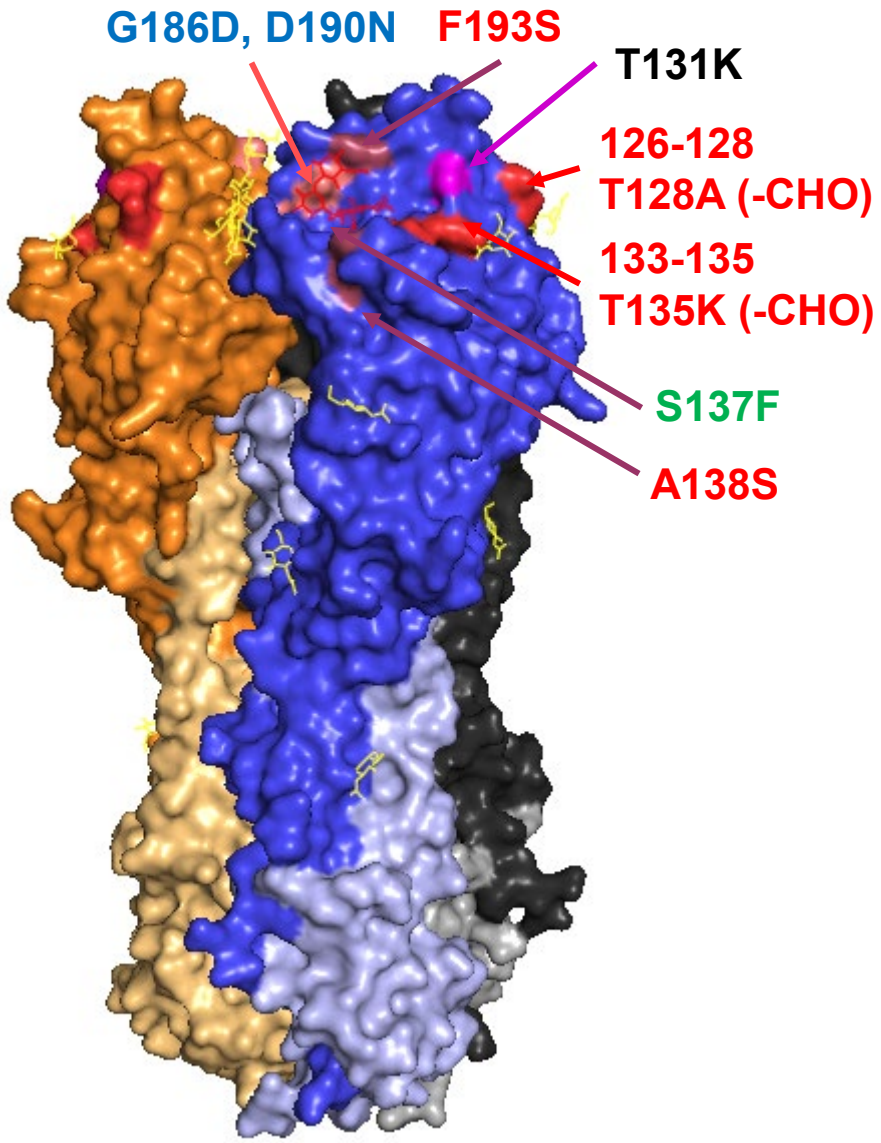
Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site

Figure 9a. Amino acid substitutions in the HA of recently detected A(H3N2) viruses

Substitutions in group 3C.2a1b+T135K HAs compared to the HA of A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1)

Substitutions defining:
Group 3C.2a1b+T135K
Subgroup 3C.2a1b+T135K-A
Subgroup 3C.2a1b+T135K-B

In addition group 3C.2a1b viruses have HA1 substitutions E62G, K92R and H311Q



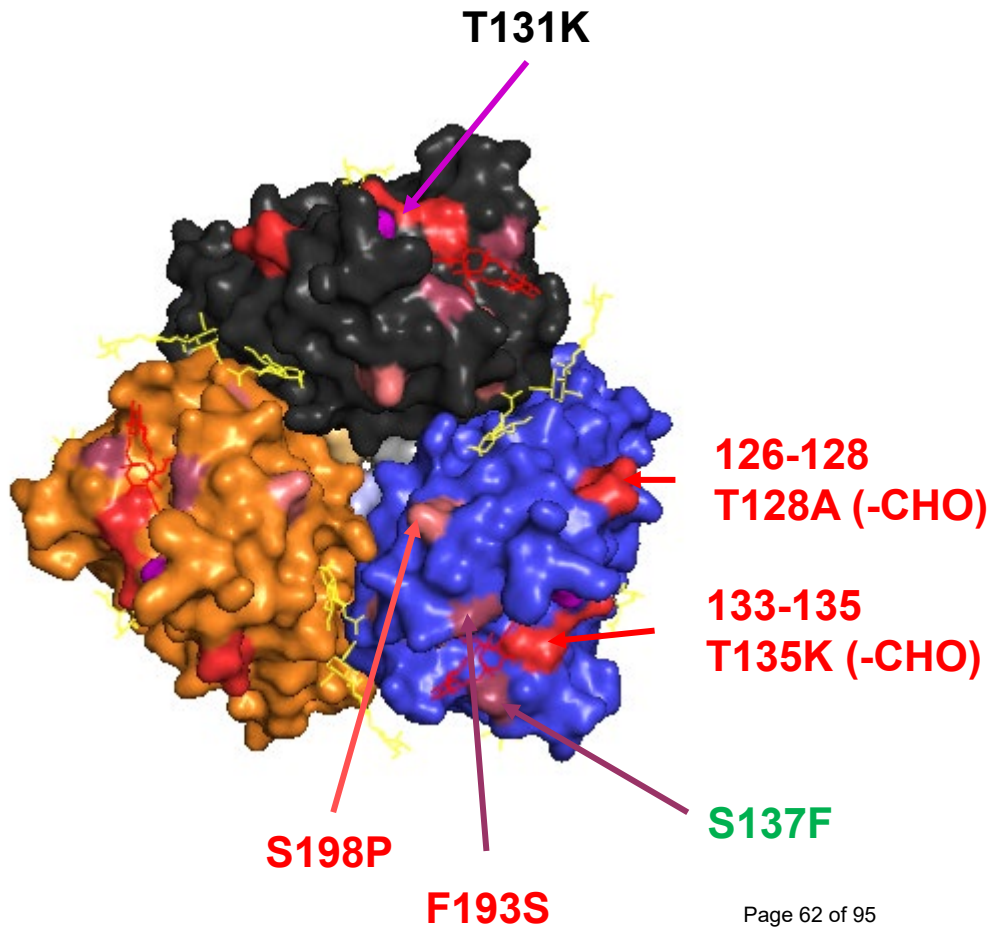
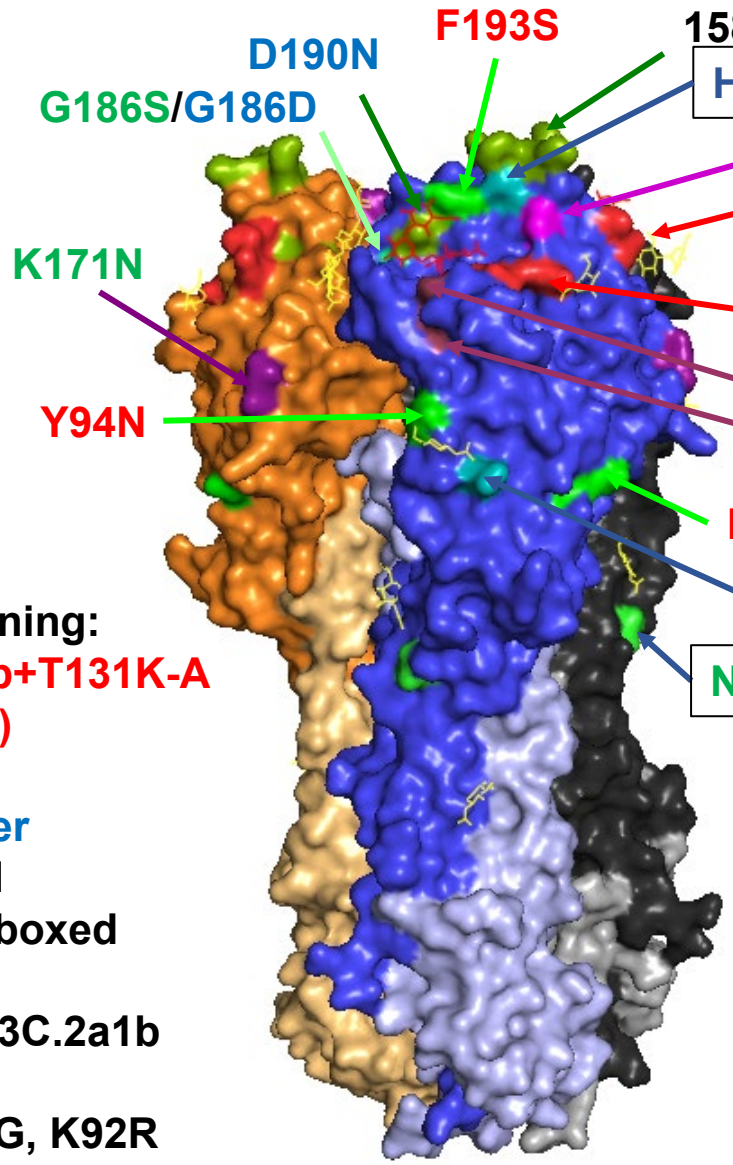


Figure 9b. Amino acid substitutions in the HA of recently detected A(H3N2) viruses

Substitutions in subgroup 3C.2a1b+T131K-A HAs compared to the HA of A/Singapore/INFIMH-16-0019/2016 (subclade 3C.2a1)



Substitutions defining:
Subgroup 3C.2a1b+T131K-A (Y195F not visible)
Cambodia cluster
Bangladesh cluster
Recently emerged substitutions are boxed

In addition group 3C.2a1b viruses have HA1 substitutions E62G, K92R and H311Q

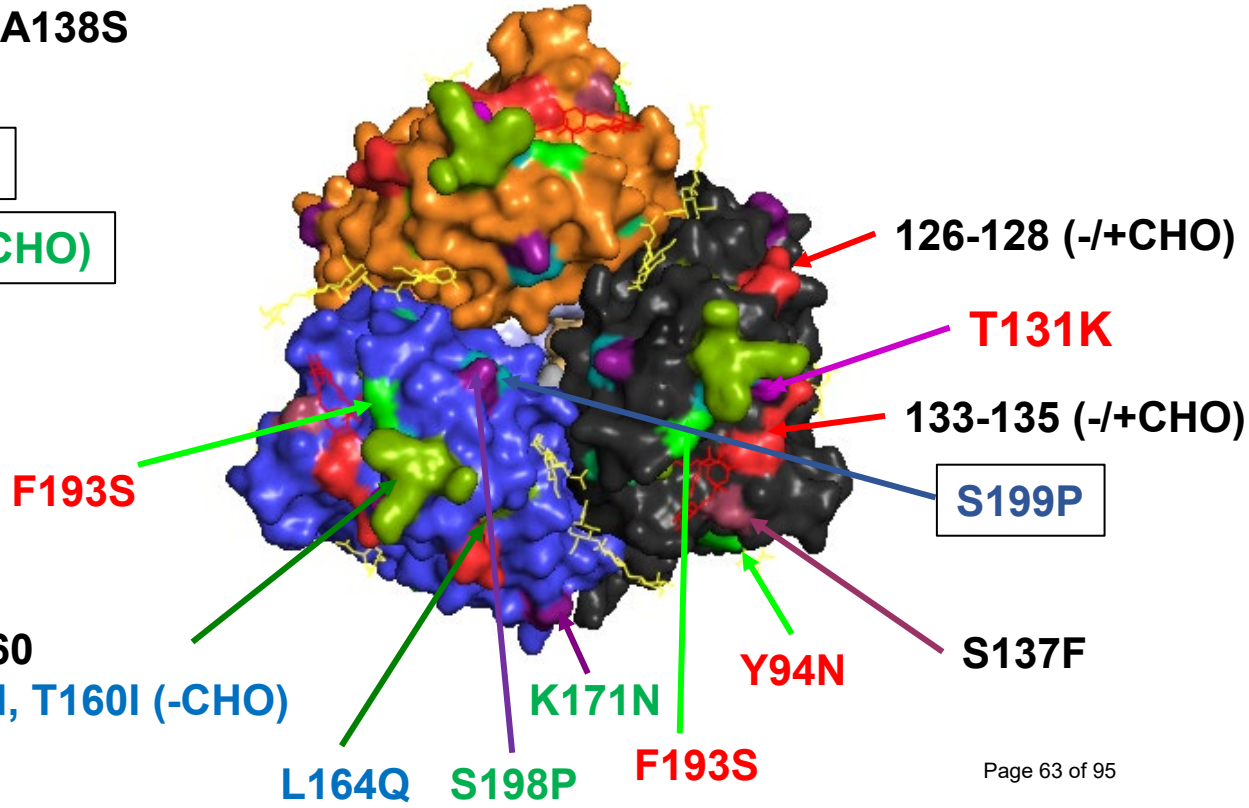


Figure 10. Phylogenetic comparison of A(H3N2) NA genes

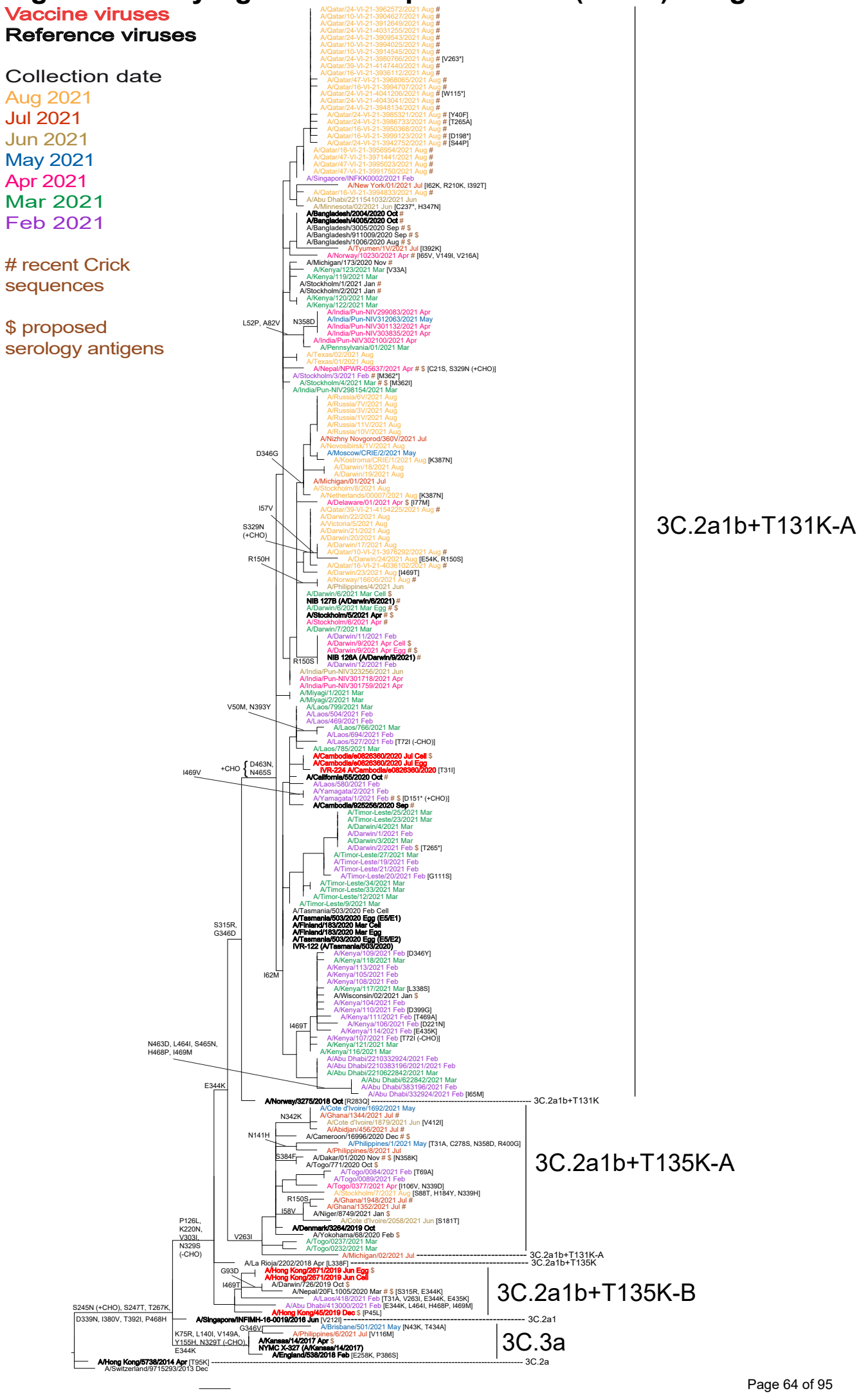
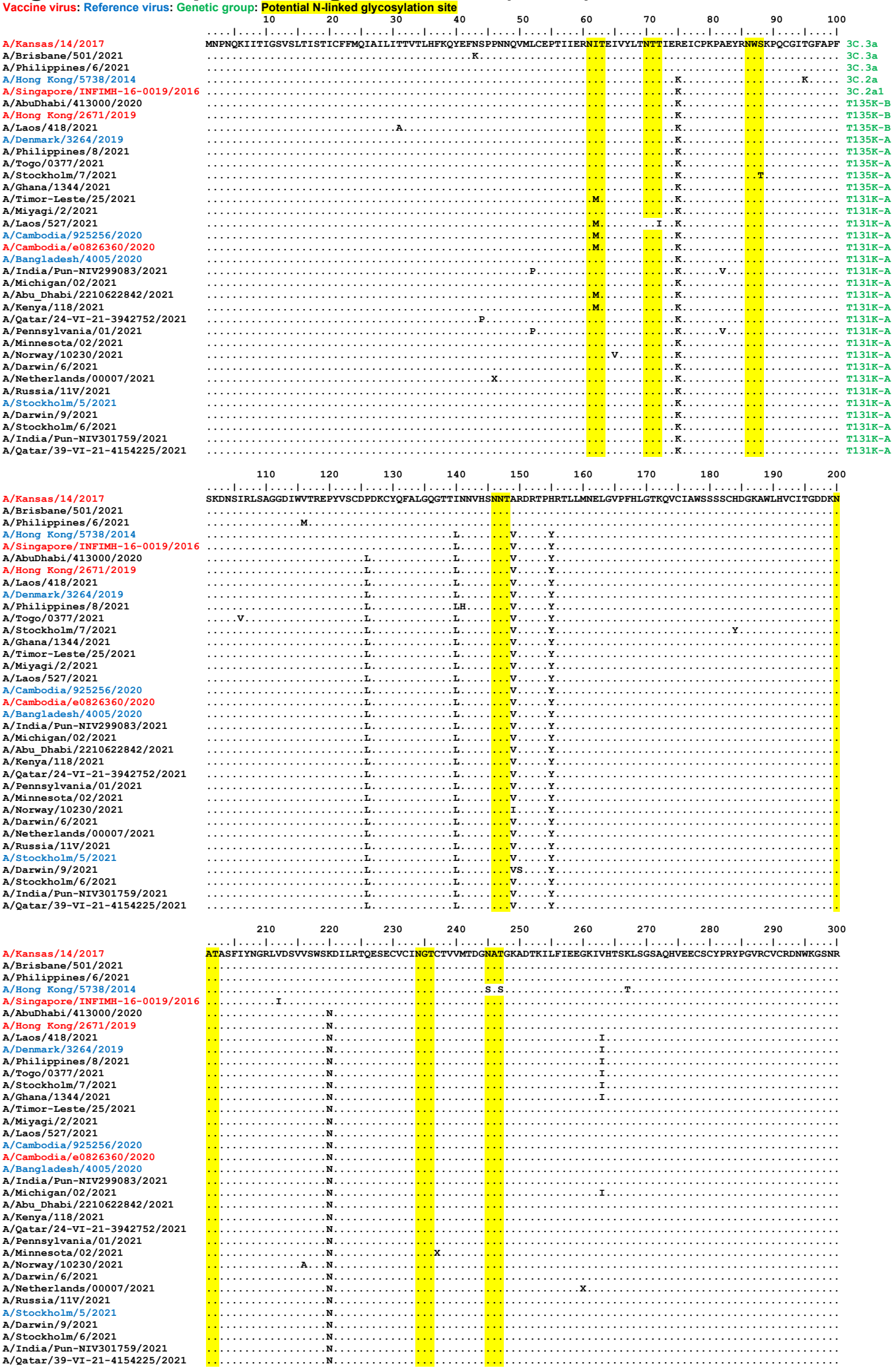
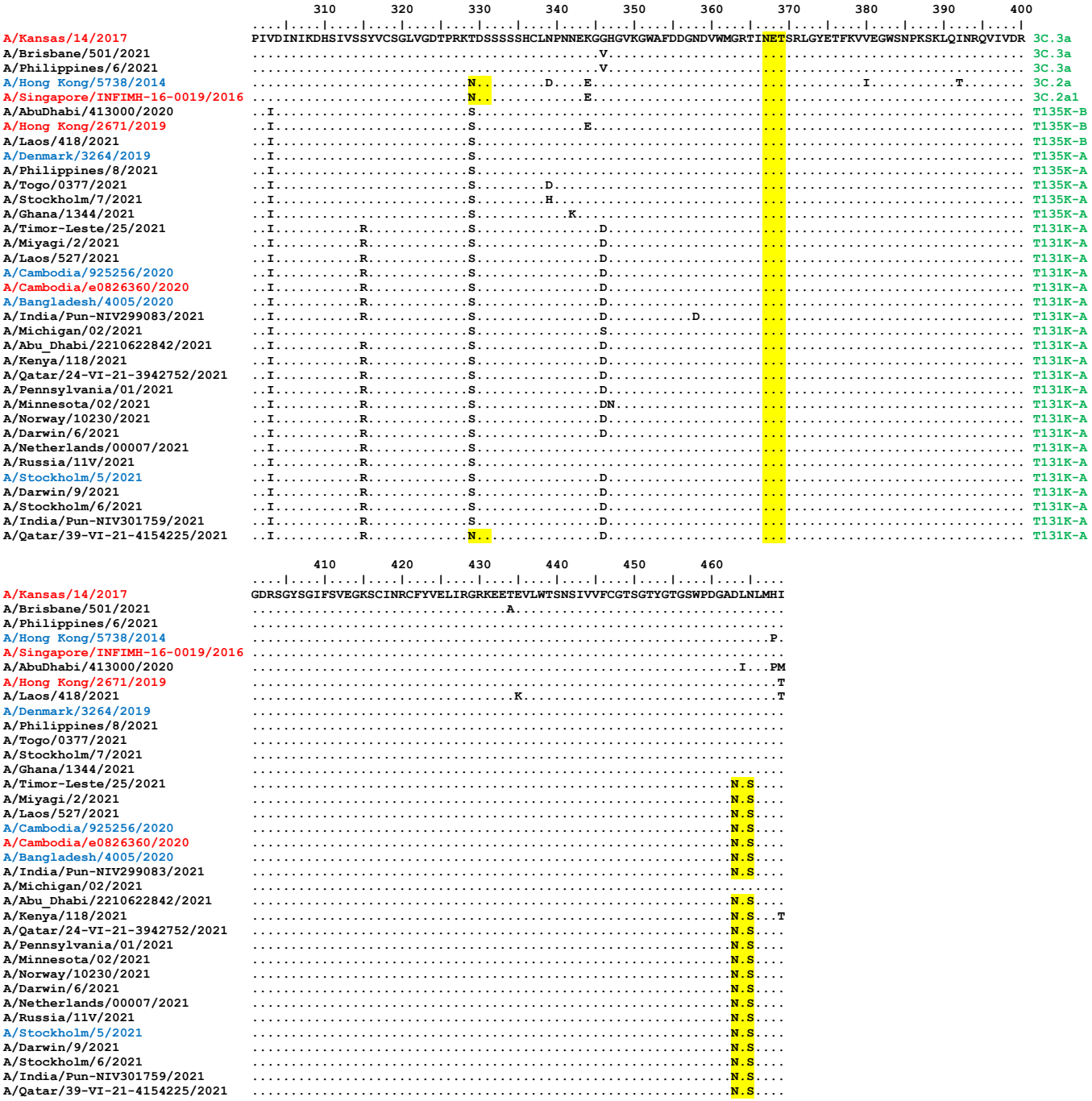


Figure 11. NA protein alignment for A(H3N2) viruses

Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site





Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site

Influenza B virus analyses.

Influenza B viruses with collection dates after 2021-01-31 were received from three NICs in two WHO Regions: the European (France and Sweden) and the Eastern Mediterranean (Qatar). They represented 19% of the samples received with collection dates after 2021-01-31 (**Table 1**) and, of those ascribed to a lineage, all were B/Victoria. All of the six clinical specimens and four virus isolates subjected to virus propagation at the time of preparing this report were recovered (**Table 2**) and a summary of the HI results obtained for these ten viruses is shown in **Table 3**. Since the February VCM influenza B viruses represented 14% of the samples received: all were B/Victoria-lineage.

B/Victoria-lineage.

HI analyses

The collection details and summary results for the ten viruses with collection dates after 2021-01-31 that were assayed by HI, up to 2021-09-10, are shown in **Table 9**.

HI results for all propagated viruses analysed since the February 2021 report are shown in **Tables 10-1** to **10-9**, test viruses in each table are sorted by date of collection and those with collection dates after 2021-01-31 are indicated in **Tables 10-5 to 10-7 (**below the red horizontal lines). The HA genetic group is indicated. **Table 10-1** includes the results of three viruses received from CDC, **Table 10-6** includes two viruses from VIDRL, **Tables 10-3, 10-4** and **Table 10-9** includes results of viruses sent by CNIC with some corresponding antisera. **Tables 10-1** to **10-7** show primary analyses of viruses from NICs, some of which were chosen to be reanalysed with a different set of antisera (shown in **Table 10-8**).

In the HI analyses no test viruses were recognised at titres within 2-fold of the homologous titre by the antiserum raised against the former vaccine virus egg-propagated B/Brisbane/60/2008 and only a single virus, B/Dakar/09/2020, was recognised at a titre within 4-fold of the homologous titre. None of the test viruses analysed with antisera raised against cell culture-propagated viruses with no deletion in the HA, B/South Australia/81/2012, B/Ireland/3154/2016, B/Nordrhein-Westfalen/1/2016 and B/Norway/2409/2017, were recognised.

An antiserum raised against the former vaccine virus egg-propagated B/Colorado/06/2017, with the two amino acid deletion in HA1 (Δ2), recognised twelve of the test viruses at titres within 4-fold of the homologous titre, but only three within 2-fold.

An antiserum raised against the current egg-propagated vaccine virus B/Washington/02/2019, with the three amino acid deletion in HA1 (Δ3), recognised seven of the tested viruses at titres within 4-fold of the homologous titre, but none within 2-fold. An antiserum raised against the cell culture-propagated cultivar of B/Washington/02/2019 had a low homologous titre and recognised three of the analysed viruses. An additional antiserum, shared by CDC, raised against the cell culture-propagated cultivar of B/Washington/02/2019 had a higher homologous titre but

it also recognised none of the viruses against which it was tested bar the egg- and cell culture-propagated cultivars of B/Washington/02/2019 (**Table 10-9**).

Antisera raised against both egg-propagated and cell culture-propagated cultivars of B/Austria/1359417/2021 and the cell culture-propagated cultivar of B/Paris/9878/2020 recognised 16 test viruses of 19 examined (84%) in **Tables 10-1** to **10-7** at titres within 4-fold of the homologous titres of the antisera, and similar proportions (84%, 79% and 84% respectively) of these viruses at titres within 2-fold of the homologous titres. The exceptions were four viruses from China (**Tables 10-3** and **10-4**). Three of these viruses from China (**Table 10-3**) had HAs that fell into the **150K** group with the additional **HA1** substitutions **V220M** and **P241Q**, unlike the three reference viruses which belong to the **150K** group with additional **HA1** substitutions **A127T, P144L** and **K203R**.

An antiserum raised against B/Cote d'Ivoire/948/2020, with a HA gene in the **150K** group with additional **HA1** substitutions **V220M** and **P241Q,** was used in **Table 10-2**. It recognised three viruses in the same genetic group at titres equal to the homologous titre, but test viruses in the **150K** group with additional **HA1** substitutions **A127T, P144L** and **K203R,** or the **150K** group with these three substitutions along with further **HA1** substitutions **T182A**, **D197E** and **T221A**, somewhat less well, but recognising all the viruses (n = 6) at titres within 4-fold, and three within 2-fold, none at titres equal to that seen with the homologous virus.

An antiserum raised against cell culture-propagated B/Croatia/7789/2019 was used in **Table 10-7**. The HA gene of B/Croatia/7789/2019 encoded the **150K** group substitutions in **HA1** (**N150K, G184E, N197D** (resulting in loss of a glycosylation site) and **R279K**) without the additional substitutions. This antiserum recognised the six test viruses, all from Qatar, at titres 2-fold lower than the homologous titre.

Table 10-8 shows a selection of test viruses reanalysed with a wider panel of antisera. The test viruses chosen had HA genes that fell into the **150K** group with the additional **HA1** substitutions **V220M** and **P241Q**, the **150K** group with the additional **HA1** substitutions **A127T, P144L** and **K203R,** or the **150K** group with the latter three substitutions along with further **HA1** substitutions **T182A**, **D197E** and **T221A.** The antisera used were raised against egg- or cell culture-propagated viruses in each of these three genetic groups.

The antiserum raised against B/Croatia/7789/2019 recognised viruses in the **N150K** group with the substitutions **V220M** and **P241Q** very well, but those with HA genes with the **HA1** substitutions **A127T, P144L** and **K203R** along with **T182A**, **D197E** and **T221A** less well, but those with **A127T, P144L** and **K203R** only were recognised well with six of eight test viruses being recognised at titres within 2-fold of the homologous titre and all eight within 4-fold.

The antisera raised against the egg- or cell culture-cultivars of B/Cote d'Ivoire/948/2020 recognised viruses in the same genetic group very well, but those with the additional **HA1** substitutions **A127T, P144L** and **K203R** less well with 4-fold (n = 6 or n = 8, for the antisera *versus* the egg- or cell culture-based antigens, respectively) or 8-fold (n = 1 for both antisera) reductions being seen. Viruses with the further substitutions **T182A**,

D197E and **T221A** were also recognised less well by these antisera but with 2-fold (n = 3 for that raised against the egg-based antigen), 4-fold (n = 5, for both antisera) or 8-fold reductions (n = 3 for that raised against the cell-based antigen) being seen.

The antisera raised against egg- and cell culture-propagated B/Austria/1359417/2021 (**150K** group with the additional **HA1** substitutions **A127T, P144L** and **K203R**) and cell culture-propagated B/Paris/9878/2020 (**150K** group with **HA1** substitutions **A127T, P144L** and **K203R** along with **T182A**, **D197E** and **T221A**), recognised most of the tested viruses in the 'basal' **150K** group (**HA1** substitutions **N150K, G184E, N197D** and **R279K**) or those in the **150K** group with the additional **HA1** substitutions **V220M** and **P241Q** poorly. This was irrespective of whether the reference viruses were propagated in cell culture or in eggs. These antisera recognised **150K** group viruses with the additional **HA1** substitutions **A127T, P144L** and **K203R,** and those with the further substitutions **T182A**, **D197E** and **T221A**, much better.

Antisera raised against two egg-propagated isolates of B/Paris/9878/2020 were also generated. B/Paris/9878/2020 **EIs1** had a polymorphism acquired on culture of **G141G/R** in **HA1** and B/Paris/9878/2020 **EIs2** had the substitution **G141V**. The antiserum raised against B/Paris/9878/2020 **EIs1** was used in **Tables 10-3** to **10-5**, and that raised against B/Paris/9878/2020 **EIs2** was used in Tables **10-6**, **10-7** and **10-9**. Both antisera were used in **Table 10-8**. The antisera raised against both recognised viruses in the 'basal' **150K** group with substitutions **N150K, G184E, N197D** and **R279K** alone or with the additional substitutions **V220M** and **P241Q** poorly. The antiserum raised against B/Paris/9878/2020 **EIs2** did not recognise well (at titres within 2-fold of the homologous titre) any of the viruses in the **150K** group with the additional **HA1** substitutions **A127T, P144L** and **K203R** and those with the further substitutions **T182A, D197E** and **T221A** although it recognised 19 of 27 viruses (70%) at titres only 4-fold lower than the homologous titre. However, the antiserum raised against B/Paris/9878/2020 **EIs1** recognised all the test viruses in these genetic groups, the **150K** group with the additional **HA1** substitutions **A127T, P144L** and **K203R** and those with the further substitutions **T182A, D197E** and **T221A**, at titres within 2-fold of the homologous titre.

Table 10-9 includes viruses and antisera from CNIC. The antisera were all raised against viruses in the **150K** group with the additional **HA1** substitutions **A127T, P144L** and **K203R** and also **H122Q** observed frequently in China. Two of the antisera were generated against viruses with a codon insertion in the HA gene encoding a **+167N** amino acid insertion in **HA1**. The antisera recognised viruses in the same genetic groups very well, as was the case with antisera raised against egg- and cell culture-propagated B/Austria/1359417/2021 and the cell culture-propagated cultivar of B/Paris/9878/2020. These antisera recognised viruses in the **150K** group with **V220M** and **P241Q** substitutions less well, although many of the viruses were recognised at titres only 4-fold lower than the homologous titres. That said, the antiserum raised against B/Gansu-Baiyin/1281/2021 showed a very similar pattern of reactivity to those antisera raised at the Crick. It appears that the **HA1 H122Q** substitution and the insertion of an amino acid, **+167N**, has limited antigenic impact.

One of the test viruses B/Gansu-Baiyin/1293/2021 had acquired the glycosylation site at residues **197-199** in **HA1** and was recognised poorly by most of the antisera, although the antisera raised against the egg- and cell culture-propagated cultivars of B/Henan-Xigong/1118/2021 recognised B/Gansu-Baiyin/1293/2021 at titres only 4-fold lower than the homologous titres.

Genetic analysis

Phylogenetic analysis of the HA genes of B/Victoria-lineage viruses sequenced at the Crick, together with those of viruses having collection dates after 2021-03-31 analysed elsewhere and deposited in the EpiFlu™ database of GISAID, is shown in **Figure 12.** An alignment of the HA glycoproteins of a selection of these viruses is shown in **Figure 13**. All recently circulating viruses analysed carried HA genes that fell into genetic clade **1A**, the B/Brisbane/60/2008 genetic clade, but with two **HA1** amino acid substitutions compared with B/Brisbane/60/2008: **I117V** and **N129D**. While a few clade **1A** viruses with full-length HA genes have been detected in China recently, the remainder with collection dates after 2021-03-31 have a three amino acid deletion in **HA1** (**Δ162-164**) with **K136E** substitution (genetic subclade **1A(Δ3)B**) and the vast majority fall into a large genetic group defined by **HA1** substitutions **N150K, G184E, N197D** (resulting in the loss of the glycosylation motif at **197-199**) and **R279K.** Within this group two main subgroups can be seen: one with HA genes encoding the **HA1** substitutions **V220M** and **P241Q** (e.g. B/Cote d'Ivoire/948/2020 and a great many viruses from China), and another encoding the **HA1** substitutions **A127T, P144L** and **K203R** (e.g. B/Austria/1359417/2021) a subset of which also encode the **HA1** substitutions **T182A, D197E** and **T221A** (e.g. B/Paris/9878/2020). Viruses in the **150K** group from China, with additional **HA1** substitutions **A127T, P144L** and **K203R,** fall in a large genetic cluster encoding an **HA1 H122Q** substitution.

Figure 14 shows the locations of amino acid substitutions that define the groups/subgroups within subclade **1A(Δ3)B** viruses on a B/Brisbane/60/2008 HA structure.

Figure 15 shows a phylogenetic tree for the NA gene of viruses with collection dates after 2021-03-31, as for **Figure 12**. **Figure 16** shows a corresponding amino acid sequence alignment for a selection of NA glycoproteins. The NA gene phylogeny is largely congruent with the HA phylogeny and the vast majority of viruses in subclade **1A(Δ3)B** have NA genes that fall into two main groups. Some reassortment of HA and NA genes is evident: viruses from China with HA genes encoding **HA1 H122Q** amino acid substitution have NA genes encoding NA substitutions **D53N, N59S** and **G233E**. A large group of viruses from Singapore, Bangladesh and elsewhere, including B/Paris/9878/2020 and B/Austria/1359417/2021, have NA genes encoding the substitutions **P42Q**, **V71A**, **K343E**, **A395V** and **V401R**.

B/Yamagata-lineage.

While detection of a single B/Yamagata-lineage virus was reported to TESSy from non-sentinel sources (**Table E-1**) during the 2020-2021 influenza season, no B/Yamagata-lineage viruses with collection dates after March 2020 have been received at the Crick.

Phylogenetic analyses for HA (**Figure 17**) and NA (**Figure 19**) gene sequences derived from B/Yamagata viruses detected in 2020 are shown, along with glycoprotein alignments of HA (**Figure 18**) and NA (**Figure 20**) for representative viruses.

Antiviral Analysis.

Susceptibility to the neuraminidase inhibitors (NAIs) oseltamivir and zanamivir was assessed phenotypically and by full NA gene sequencing, for 25 B/Victoria-lineage viruses detected and received within the course of the 2020-2021 influenza season (**Table 11**). All showed normal inhibition (NI: no reduced susceptibility) by both antivirals.

All of the 26 B/Victoria-lineage full-length PA gene sequences generated at the Crick, from individual viruses detected in the course of the 2020-2021 influenza season, encoded isoleucine at position 38 (I38) and showed no evidence of other substitutions associated with reduced susceptibility to baloxavir marboxil.

Conclusion.

Viruses of the B/Victoria-lineage predominated and all viruses sequenced had HAs with a three amino acid deletion in **HA1** (∆**162-164**) with the additional **HA1** amino acid substitution **K136E** (subclade **1A(∆3)B**). Most recent viruses had amino acid substitutions **N150K, G184E, N197D** (resulting in the loss of a glycosylation site) and **R279K**. B/Victoria-lineage viruses with collection dates after 2021-01-31 received at the Francis Crick Institute, in shipments from National Influenza Centres, also encoded **HA1** substitutions **A127T, P144L, K203R**, many also encoding further **T182A, D197E** and **T221A** substitutions in **HA1**. These recently collected viruses were poorly recognised by antisera raised against the cell culture- and egg-propagated cultivars of B/Washington/02/2019.

No viruses of the B/Yamagata-lineage with collection dates after 2021-01-31 have been received.

All influenza B viruses showed normal inhibition by the NAIs oseltamivir and zanamivir. Viruses yielding full-length PA gene sequences (n = 26) all encoded proteins likely to be well inhibited by baloxavir marboxil.

Table 9. Summary of influenza B (Victoria-lineage) viruses analysed, collected after 2021-01-31

MONTH			B Victoria lineage												
			Post-infection ferret antisera raised against												
			Clade 1A(Δ3)B virus			Clade 1A(Δ3)B virus			Clade 1A(Δ3)B virus			Clade 1A(Δ3)B virus		
Country	Number received	Number propagated[1,2]	≤2 fold[3]	4 fold[3]	≥8 fold[3]	≤2 fold[4]	4 fold[4]	≥8 fold[4]	≤2 fold[5]	4 fold[5]	≥8 fold[5]	≤2 fold[6]	4 fold[6]	≥8 fold[6]
2021 FEBRUARY														
MARCH														
Sweden	3	3	3			2	1				3			3
APRIL														
Qatar	1	1	1			1					1			1
MAY														
Qatar	5	3	3			3					3			3
JUNE														
Qatar	2	1	1			1					1			1
JULY														
France	1	1	1			1					1			1
Qatar	3	1	1			1					1			1
AUGUST														
Qatar	1	0												
	16	10	10	0	0	9	1	0	0	0	10	0	0	10
3 Countries			100.0%	0.0%	0.0%	90.0%	10.0%	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%

1 Numbers shown in red indicate that not all of the specimens received had been propagated at the time this report was prepared
2 Propagated to sufficient titre to perform HI assay
3 Compared to homologous titres for ferret antisera raised against tissue culture-propagated B/Austria/1359417/2021 - Clade 1A(Δ3)B N150K gp + A127T, P144L, K203R
4 Compared to homologous titres for ferret antisera raised against egg-propagated B/Austria/1359417/2021 - Clade 1A(Δ3)B N150K gp +A127T, P144L, K203R
5 Compared to homologous titres for ferret antisera raised against tissue culture-propagated B/Washington/02/2019 - Clade 1A(Δ3)B
6 Compared to homologous titres for ferret antisera raised against egg-propagated B/Washington/02/2019 - Clade 1A(Δ3)B

As of 2021-09-10

Table 10-1. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-02-16

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
					Post-infection ferret antisera									
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Sth Aus 81/12 Egg	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Norway 2409/17 MDCK	B/Colorado 06/17 MDCK	B/Colorado 06/17 Egg	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F25/16[*2]	F12/18[*2]	F38/17[*2]	F40/17[*2]	F21/18[*4]	F11/18[*4]	F37/19[*2]	F20/20[*2]
		Genetic group			1A	1A	1A	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES														
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	1280	640	40	80	<	<	80	<	80
B/South Australia/81/2012		1A	2012-11-28	E4/E2	2560	1280	640	40	80	<	<	80	<	80
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	2560	80	20	40	160	<	<	<	<	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	2560	80	20	80	160	<	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	40	<	<	<	<	20	40	40	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	MDCK1/MDCK2	80	10	<	<	<	40	40	80	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	320	80	<	<	40	80	320	<	160
B/Washington/02/2019		1A(Δ3)B	2019-01-19	C2/MDCK3	640	160	40	<	<	<	<	80	20	160
B/Washington/02/2019		1A(Δ3)B	2019-01-19	E3/E2	1280	320	80	<	<	<	<	160	40	320
TEST VIRUSES														
B/Maryland/24/2019	E128K	1A(Δ3)B	2019-11-06	C2/MDCK1	40	40	<	<	<	<	<	<	40	160
B/Lebanon/16/2020	D129N, N233S (-CHO), K272R	1A(Δ3)B	2020-02-02	C2/MDCK1	40	40	<	<	<	<	<	<	10	40
B/Florida/09/2020	N126K	1A(Δ3)B	2020-02-10	C1/MDCK1	<	20	<	<	<	<	<	<	<	20
B/Cote d'Ivoire/2703/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-13	MDCK1	640	80	<	<	<	<	<	80	<	<
B/Cote d'Ivoire/2705/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-18	MDCK1	640	160	<	<	<	<	<	80	<	<
B/Cote d'Ivoire/2862/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-28	MDCK1	640	160	<	<	<	<	<	80	<	<
B/Austria/1359417/2021	N150K group + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	SIAT1/MDCK2	640	160	10	<	<	<	<	40	<	<
B/Salalah/7211353/2021	N150K group + A127T, P144L, K203R	1A(Δ3)B	2021-01-17	MDCK1	640	80	<	<	<	<	<	40	<	<

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

Vaccine
SH 2019
NH 2019-20

Vaccine
SH 2020
NH 2020-21
SH 2021
NH 2021-22

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-2. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-02-25

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre										
					Post-infection ferret antisera										NEW
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Sth Aus 81/12 Egg	B/Ireland 3154/16 MDCK	B/Nord-West 1/16 MDCK	B/Norway 2409/17 MDCK	B/Colorado 06/17 MDCK	B/Colorado 06/17 Egg	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg	B/CIV 948/20 MDCK
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F25/16[*2]	F12/18[*2]	F38/17[*2]	F40/17[*2]	F21/18[*4]	F11/18[*4]	F37/19[*2]	F20/20[*2]	F08/21[*2]
		Genetic group			1A	1A	1A	1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES															
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	5120	1280	640	40	80	<	<	160	<	80	<
B/South Australia/81/2012		1A	2012-11-28	E4/E2	2560	1280	640	40	80	<	<	160	<	80	<
B/Ireland/3154/2016		1A	2016-01-14	MDCK1/MDCK4	5120	80	40	80	160	<	<	<	<	<	<
B/Nordrhein-Westfalen/1/2016		1A	2016-01-04	C2/MDCK2	2560	40	40	40	160	<	<	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	10	<	<	<	40	80	80	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	MDCK1/MDCK2	80	20	<	<	<	40	80	80	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	320	80	<	<	40	80	640	<	160	<
B/Washington/02/2019		1A(Δ3) B	2019-01-19	C2/MDCK3	1280	80	80	<	<	<	<	160	40	160	<
B/Washington/02/2019		1A(Δ3) B	2019-01-19	E3/E2	1280	160	80	<	<	<	<	320	40	320	<
B/Cote d'Ivoire/948/2020		1A(Δ3) B	2020-05-28	MDCK2	320	320	80	<	<	<	<	40	<	80	640
TEST VIRUSES															
B/Dakar/01/2020	N150K group + V220M, P241Q	1A(Δ3) B	2020-01-18	C1/MDCK1	640	80	40	<	<	<	<	40	<	80	640
B/Dakar/03/2020	N150K group + D197E, V220M, P241Q	1A(Δ3) B	2020-01-28	C1/MDCK1	640	80	20	<	<	<	<	40	<	80	640
B/Dakar/02/2020	N150K group + D197E, V220M, P241Q	1A(Δ3) B	2020-01-29	C1/MDCK1	640	80	20	<	<	<	<	40	<	80	640
B/Dakar/07/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3) B	2020-10-10	C1/MDCK1	1280	160	<	<	<	<	<	160	<	20	160
B/Dakar/04/2020		1A(Δ3) B	2020-10-18	C1/MDCK1	1280	160	<	<	<	<	<	160	<	20	320
B/Dakar/08/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3) B	2020-11-07	C1/MDCK1	1280	160	<	<	<	<	<	160	<	20	160
B/Dakar/06/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3) B	2020-11-14	C1/MDCK1	1280	160	10	<	<	<	<	160	<	20	320
B/Dakar/09/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3) B	2020-11-15	C1/MDCK1	1280	320	<	<	<	<	<	320	<	20	320
B/Dakar/05/2020	N150K group + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3) B	2020-11-16	C1/MDCK1	1280	160	<	<	<	<	<	160	<	20	160

[1] Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20

Vaccine
SH 2019
NH 2019-20

Vaccine
SH 2020
NH 2020-21
SH 2021
NH 2021-22

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-3. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-04-28

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Norway 2409/17 MDCK	B/Colorado 06/17 Egg	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg	B/Austria 1359417/21 MDCK	B/Austria 1359417/21 Egg	B/Paris 9878/20 MDCK	B/Paris 9878/20 Egg Isl 1
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F40/17[*2]	F11/18[*4]	F37/19[*2]	F20/20[*2]	NIB F01/21[*1]	F15/21[*1]	F12/21[*1]	F14/21[*1]
		Genetic group			1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)
REFERENCE VIRUSES														
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	640	<	80	<	40	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	10	40	160	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	160	20	320	<	80	<	<	<	<
B/Washington/02/2019		1A(Δ3) B	2019-01-19	C2/MDCK3	1280	80	<	160	20	80	<	<	<	<
B/Washington/02/2019		1A(Δ3) B	2019-01-19	E3/E2	1280	160	<	320	20	160	40	40	<	<
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3) B	2021-01-09	SIAT1/MDCK3	640	80	<	40	<	<	1280	1280	640	1280
B/Austria/1359417/2021 Isolate 1	N150K grp + A127T, P144L, K203R	1A(Δ3) B	2021-01-09	E2	1280	80	10	80	20	10	1280	1280	640	1280
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	MDCK1/MDCK3	1280	80	<	160	<	10	1280	1280	640	1280
B/Paris/9878/2020 Isolate 1 (G141G/R)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	E2	1280	80	<	160	10	10	1280	1280	640	2560
TEST VIRUSES														
B/Austria/1359417/2021 Isolate 1	N150K grp + A127T, P144L, K203R	1A(Δ3) B	2021-01-09	E3	640	40	<	80	10	<	2560	1280	640	1280
B/Paris/9878/2020 Isolate 1 (G141R)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	E3	640	40	<	80	<	<	640	640	320	2560
B/Paris/9878/2020 Isolate 2 (G141V)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	E3	640	80	<	160	10	10	1280	1280	320	1280
B/Jiangxi-Yuanzhou/12007/2020	N150K grp + V220M, P241Q	1A(Δ3) B	2020-12-01	C3/MDCK1	320	40	<	40	<	40	80	80	40	80
B/Guizhou-Douyun/11021/2020	N150K grp + V220M, P241Q	1A(Δ3) B	2020-12-03	C4/MDCK1	640	80	<	40	<	40	80	80	80	160
B/Jiangxi-Yushui/386/2020	N150K grp + V220M, P241Q	1A(Δ3) B	2020-12-04	C4/MDCK1	640	80	<	40	<	40	160	160	80	160
								Vaccine SH 2019 NH 2019-20		Vaccine SH 2020 NH 2020-21 SH 2021 NH 2021-22				

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

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-4. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-05-19

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
		Passage history			B/Bris 60/08	B/Bris 60/08	B/Norway 2409/17	B/Colorado 06/17	B/Wash'ton 02/19	B/Wash'ton 02/19	B/Austria 1359417/21	B/Austria 1359417/21	B/Paris 9878/20	B/Paris 9878/20
					Egg	Egg	MDCK	Egg	MDCK	Egg	MDCK	Egg	MDCK	Egg Isl 1
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F40/17[*2]	F11/18[*4]	F37/19[*2]	F20/20[*2]	NIB F01/21[*1]	F15/21[*1]	F12/21[*1]	F14/21[*1]
		Genetic group			1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES														
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	640	<	80	<	20	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	40	<	10	80	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	640	160	20	320	<	40	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	C2/MDCK3	640	40	<	160	20	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	E3/E2	640	80	<	160	10	80	<	<	<	<
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	SIAT1/MDCK3	640	80	<	80	<	<	2560	1280	640	1280
B/Austria/1359417/2021 Isolate 1	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	E2	640	40	<	40	10	<	2560	1280	320	1280
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	MDCK1/MDCK3	640	80	<	160	<	<	1280	1280	640	2560
B/Paris/9878/2020 Isolate 1 (G141G/R)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	E2	1280	80	<	160	10	<	1280	1280	640	1280
TEST VIRUSES														
B/Yunnan-Qilin/1121/2020	HA1-N233K (-cho), HA2-T201A	1A(Δ3)B	2020-03-10	E3/E1	320	20	<	40	<	20	<	<	<	<
B/Saudi Arabia/1157663012/2020	N150K grp + A127T, P144L, D197E, K203R	1A(Δ3)B	2020-10-31	MDCK2	1280	80	<	160	<	<	2560	2560	1280	2560
B/Saudi Arabia/1039371032/2020	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2020-11-15	MDCK1	640	80	<	40	<	<	2560	2560	640	1280
B/Saudi Arabia/2455317608/2020	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2020-12-04	MDCK1	640	40	<	40	<	<	1280	640	320	1280
B/Saudi Arabia/1071894032/2020	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2020-12-15	MDCK1	1280	80	<	80	10	<	2560	1280	640	1280
B/Saudi Arabia/1163435488/2020	N150K grp + A127T, P144L, D198K, K203R	1A(Δ3)B	2020-12-25	MDCK1	640	80	<	40	<	<	1280	1280	320	1280
B/Saudi Arabia/1194203376/2021	N150K grp + A127T, P144L, D197E, K203R	1A(Δ3)B	2021-01-03	MDCK1	1280	80	<	160	<	<	1280	1280	640	2560
								Vaccine SH 2019 NH 2019-20		Vaccine SH 2020 NH 2020-21 SH 2021 NH 2021-22				

[1] Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-5. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-06-25

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Norway 2409/17 MDCK	B/Colorado 06/17 Egg	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg	B/Austria 1359417/21 MDCK	B/Austria 1359417/21 Egg	B/Paris 9878/20 MDCK	B/Paris 9878/20 Egg Isl 1#
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F40/17[*2]	F11/18[*4]	F37/19[*2]	F20/20[*2]	NIB F01/21[*1]	F15/21[*1]	F12/21[*1]	F14/21[*1]
		Genetic group			1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES														
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	640	<	80	<	40	<	<	<	80
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	10	40	160	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	160	20	320	<	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	C2/MDCK3	1280	80	<	160	20	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	E3/E2	1280	160	<	320	20	160	<	<	<	<
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	SIAT1/MDCK3	640	80	<	40	<	<	2560	1280	640	1280
B/Austria/1359417/2021 Isolate 2	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	E3/E2	1280	80	10	80	20	10	2560	2560	640	2560
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	MDCK2	1280	80	<	160	<	10	1280	1280	640	1280
B/Paris/9878/2020 Isolate 2 (G141V)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	E3/E2	1280	80	<	160	10	10	1280	640	320	1280
TEST VIRUSES														
B/Stockholm/2/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-01	SIAT0/MDCK1	640	80	<	40	<	<	2560	1280	640	1280
B/Stockholm/3/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-05	SIAT0/MDCK1	640	40	<	40	<	<	2560	1280	320	640
B/Stockholm/4/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-15	SIAT0/MDCK1	640	40	<	40	<	<	1280	640	320	640

* Superscripts refer to antiserum properties (< relates to the lowest dilution of antiserum used):
[1] < = <40; [2] < = <10; [3] hyperimmune sheep serum; [4] < = <20
[#] G141G/R

Vaccine
SH 2019
NH 2019-20

Vaccine
SH 2020
NH 2020-21
SH 2021
NH 2021-22

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-6. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-08-17

Viruses	Other information		Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
		Passage history			B/Bris 60/08 Egg	B/Bris 60/08 Egg	B/Norway 2409/17 MDCK	B/Colorado 06/17 Egg	B/Wash'ton 02/19 MDCK	B/Wash'ton 02/19 Egg	B/Austria 1359417/21 MDCK	B/Austria 1359417/21 Egg	B/Paris 9878/20 MDCK	B/Paris 9878/20 Egg Isl 2
		Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F44/17[*4]	F40/17[*2]	F11/18[*4]	F37/19[*2]	F20/20[*4]	NIB F01/21[*1]	F15/21[*1]	F12/21[*1]	F23/21[*1]
		Genetic group			1A	1A	1A(Δ2)	1A(Δ2)	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B	1A(Δ3)B
REFERENCE VIRUSES														
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	2560	640	<	80	<	40	<	<	<	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	80	10	40	160	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	160	20	320	<	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	C2/MDCK3	1280	80	<	160	20	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	E3/E2	1280	160	<	320	20	160	<	<	<	<
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	SIAT1/MDCK4	640	80	<	40	<	<	1280	1280	640	320
B/Austria/1359417/2021 Isolate 2	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	E3/E2	1280	80	10	80	20	10	2560	1280	640	320
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	MDCK2	1280	80	<	160	<	10	1280	1280	640	320
B/Paris/9878/2020 Isolate 2 (G141V)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	E3/E2	1280	80	<	160	10	10	1280	640	320	1280
TEST VIRUSES														
B/Singapore/WUH0784/2021	N150K grp + A127T, P144L, A202V, K203R	1A(Δ3)B	2021-06-02	MDCK1/MDCK1	640	40	<	20	<	<	1280	640	320	160
B/Singapore/WUH0784/2021	N150K grp + A127T, P144L, A202V, K203R	1A(Δ3)B	2021-06-02	E3/E1	320	20	<	<	<	<	1280	640	320	320
B/Saint-Etienne/454/2021	N150K grp + K52N, A127T, P144L, A202V, K203R	1A(Δ3)B	2021-07-06	MDCK2/MDCK1	640	80	<	40	<	<	2560	1280	640	320

* 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

Vaccine SH 2019 NH 2019-20

Vaccine SH 2020 NH 2020-21 SH 2021 NH 2021-22

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-7. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-09-09

Viruses	Other information	Passage history / Ferret number / Genetic group	Collection date	Passage history	Haemagglutination inhibition titre									
						Post-infection ferret antisera								
					B/Bris 60/08	B/Norway 2409/17	B/Colorado 06/17	B/Wash'ton 02/19	B/Wash'ton 02/19	B/Croatia 7789/19	B/Austria 1359417/21	B/Austria 1359417/21	B/Paris 9878/20	B/Paris 9878/20
		Passage history			Egg	MDCK	Egg	MDCK	Egg	MDCK	MDCK	Egg	MDCK	Egg Isl 2
		Ferret number			Sn 539, 540, 543, 544, 570	F40/17[*2]	F11/18[*4]	F37/19[*2]	F20/20[*4]	F19/21[*1]	NIB F01/21[*1]	F15/21[*1]	F12/21[*1]	F23/21[*1]
		Genetic group			1A	1A(Δ2)	1A(Δ2)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)
REFERENCE VIRUSES														
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	40	40	80	<	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	1280	20	160	<	40	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)	2019-01-19	C2/MDCK3	640	<	80	20	80	80	<	<	<	<
B/Washington/02/2019		1A(Δ3)	2019-01-19	E3/E2	1280	<	160	20	80	160	<	<	<	<
B/Croatia/7789/2019		1A(Δ3)		MDCKx/MDCK2	640	<	160	<	80	640	80	80	<	<
B/Austria/1359417/2021		1A(Δ3)	2021-01-09	SIAT1/MDCK4	320	<	20	<	<	320	1280	640	320	160
B/Austria/1359417/2021 Isolate 2		1A(Δ3)	2021-01-09	E3/E2	320	<	20	<	<	320	1280	640	320	320
B/Paris/9878/2020		1A(Δ3)	2020-11-20	MDCK2	640	<	80	<	<	320	640	640	320	320
B/Paris/9878/2020 Isolate 2		1A(Δ3)	2020-11-20	E3/E2	640	<	160	<	<	160	1280	640	320	1280
TEST VIRUSES														
B/Qatar/24-VI-21-1993651/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)	2021-04-25	MDCK1	320	<	20	<	<	320	1280	640	320	160
B/Qatar/10-VI-21-2160110/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)	2021-05-05	MDCK1	320	<	20	<	<	320	1280	640	320	160
B/Qatar/21-VI-21-2331965/2021	N150K grp + H122Q, A127T, P144L, K203R	1A(Δ3)	2021-05-16	MDCK1	640	<	20	<	<	320	1280	1280	320	160
B/Qatar/11-VI-21-2542617/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)	2021-05-29	MDCK1	320	<	20	<	<	320	1280	1280	320	320
B/Qatar/10-VI-21-3067935/2021	pending	1A(Δ3)	2021-06-26	MDCK1	320	<	20	<	<	320	1280	1280	320	160
B/Qatar/16-VI-21-3744979/2021	N150K grp + K56E, A127T, P144L, K203R	1A(Δ3)	2021-07-31	MDCK1	320	<	10	<	<	320	1280	640	320	160

* 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

Vaccine
SH 2019
NH 2019-20

Vaccine
SH 2020
NH 2020-21
SH 2021
NH 2021-22

< 4-fold | 4-fold | 8-fold | > 8-fold | < not recognised by the antiserum | ≥ 160 (when homologous titre ≥ 2560) | ≥ 160 (no homologous titre)

Table 10-8. Antigenic analyses of influenza B viruses (Victoria lineage) - N150K group viruses

Viruses		Passage history Ferret number Genetic group	Collection date	Passage history	Haemagglutinin inhibition titre Post-infection ferret antiserum B/Croatia 7789/19 MDCK F19/21[*2] 1A(Δ3)B	B/CIV 948/20 Egg F20/21[*2] 1A(Δ3)B	B/CIV 948/20 MDCK F08/21[*2] 1A(Δ3)B	B/Austria 1359417/21 MDCK NIB F01/21[*1] 1A(Δ3)B	NEW B/Austria 1359417/21 MDCK F22/21*[1] 1A(Δ3)B	B/Austria 1359417/21 Egg F15/21[*1] 1A(Δ3)B	B/Paris 9878/20 MDCK F12/21[*1] 1A(Δ3)B	B/Paris 9878/20 Egg Isl 1[#] F14/21[*1] 1A(Δ3)B	NEW B/Paris 9878/20 Egg Isl 2[$] F23/21[*1] 1A(Δ3)B
REFERENCE VIRUSES													
B/Brisbane/60/2008		1A	2008-08-04	E4/E4	80	10	<	<	<	<	<	80	<
B/Norway/2409/2017		1A(Δ2)	2017-04-27	MDCK1/MDCK3	<	<	<	<	<	<	<	<	<
B/Colorado/06/2017		1A(Δ2)	2017-02-05	E5/E2	80	10	<	<	<	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	C2/MDCK3	40	20	20	<	<	<	<	<	<
B/Washington/02/2019		1A(Δ3)B	2019-01-19	E3/E2	80	20	20	<	<	<	<	<	<
B/Rhode Island/01/2019	N150K grp	1A(Δ3)B	2019-01-26	E3/E1	2560	320	320	160	ND	320	80	160	ND
B/Rhode Island/01/2019	N150K grp	1A(Δ3)B	2019-01-26	C1/MDCK1	1280	320	320	160	ND	320	80	160	ND
B/Croatia/7789/2019	N150K grp	1A(Δ3)B	2019-11-11	MDCKx/MDCK2	1280	320	320	320	160	160	80	160	80
B/Cote d'Ivoire/948/2020	N150K grp + V220M, P241Q	1A(Δ3)B	2020-05-28	MDCK2	2560	640	640	160	160	160	160	160	40
B/Cote d'Ivoire/948/2020	N150K grp + V220M, P241Q	1A(Δ3)B	2020-05-28	E3	2560	640	640	320	160	160	80	160	40
B/Moscow/44/2020	N150K grp + V220M, P241Q, V177I	1A(Δ3)B	2020-03-11	MDCK2/MDCK2	2560	640	640	160	160	80	80	160	ND
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	SIAT1/MDCK3	320	320	160	2560	1280	1280	640	1280	320
B/Austria/1359417/2021 Isl 2	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	E3/E2	640	320	320	2560	1280	2560	640	2560	320
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	MDCK2	320	160	160	1280	640	1280	640	1280	320
B/Paris/9878/2020 Isl 2 (G141V)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3)B	2020-11-20	E3/E2	160	320	160	1280	640	640	320	1280	1280
TEST VIRUSES													
B/Dakar/01/2020	N150K grp + V220M, P241Q	1A(Δ3)B	2020-01-18	C1/MDCK1	640	640	640	160	160	80	80	160	40
B/Dakar/03/2020	N150K grp + D197E, V220M, P241Q	1A(Δ3)B	2020-01-28	C1/MDCK1	640	320	640	80	80	80	80	160	40
B/Dakar/02/2020	N150K grp + D197E, V220M, P241Q	1A(Δ3)B	2020-01-29	C1/MDCK1	640	640	640	80	80	80	80	160	40
B/Saudi Arabia/1071894032/2020	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2020-12-15	MDCK1	640	160	160	2560	ND	2560	640	1280	ND
B/Norway/435/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-09	MDCK1	640	160	160	2560	ND	1280	640	1280	ND
B/Salalah/7211353/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-01-17	MDCK1	640	160	160	2560	ND	1280	640	1280	ND
B/Stockholm/2/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-01	SIAT0/MDCK1	640	160	160	2560	ND	1280	640	1280	ND
B/Stockholm/3/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-05	SIAT0/MDCK1	640	160	160	2560	ND	1280	320	640	ND
B/Stockholm/4/2021	N150K grp + A127T, P144L, K203R	1A(Δ3)B	2021-03-15	SIAT0/MDCK1	320	80	80	1280	ND	640	320	640	ND
B/Dakar/07/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-10-10	C1/MDCK1	160	160	160	1280	640	1280	640	1280	320
B/Dakar/04/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-10-18	C1/MDCK1	160	160	80	640	640	1280	640	1280	320
B/Dakar/08/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-07	C1/MDCK1	160	320	160	1280	640	1280	640	1280	320
B/Dakar/06/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-14	C1/MDCK1	320	160	80	1280	640	1280	640	1280	320
B/Dakar/09/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-15	C1/MDCK1	320	320	160	1280	640	1280	640	1280	320
B/Dakar/05/2020	N150K grp + A127T, P144L, T182A, D197E, K203R, T221A	1A(Δ3)B	2020-11-16	C1/MDCK1	160	160	80	640	640	1280	640	1280	320

[1] 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

[#]G141G/R; [$]G141V

≤2-fold

4-fold

≥8-fold

Table 10-9. Antigenic analyses of influenza B viruses (Victoria lineage) 2021-08-25 + 2021-09-08

Viruses	Other information		Collection date	Passage history	Haemagglutinin inhibition titre													
					Post-infection ferret antiserum													
		Passage history			B/Wash'ton 02/19	B/Wash'ton 02/19	B/Wash'ton 02/19	A/Croatia 7889/19	B/ClV 948/20	B/ClV 948/20	B/ClV 948/20	B/Austria 1359417/21	B/Austria 1359417/21	B/Hen-Xig 1118/21	B/Hen-Xig 1118/21	B/Gan-Baiy 1281/21	B/Gan-Baiy 1281/21	B/Paris 9878/20	B/Paris 9878/20
					MDCK	MDCK	Egg	MDCK	MDCK	MDCK	Egg	MDCK	Egg	Cell	Egg	Cell	Egg	MDCK	Egg Isl 2
		Ferret number			F37/19[-2]	CDC F2020-002[-2]	F20/20[-4]	F19/21[+1]	F08/21[+1]	F08/21[+1]	F20/21[-2]	NIB F01/21[-2]	F15/21[-2]	CNIC Ferret 2021-6-10[+1]	CNIC Ferret 2021-6-10[+1]	CNIC Ferret 2021-6-10[+1]	CNIC Ferret 2021-6-10[+1]	F12/21[-2]	F23/21[+1]
		Genetic group			1A(Δ3) B	1A(Δ3) B	1A(Δ3) B	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)	1A(Δ3)
REFERENCE VIRUSES					2021-09-08	2021-09-08	2021-09-08			2021-09-08									
B/Washington/02/2019		1A(Δ3) B	2019-01-19	C2/MDCK3	20	320	80	ND	ND	<	ND	<	<	ND	ND	ND	ND	<	<
B/Washington/02/2019		1A(Δ3) B	2019-01-19	E3/E2	20	640	80	ND	ND	<	ND	<	<	ND	ND	ND	ND	<	<
B/Croatia/7789/2019	N150K grp	1A(Δ3) B	2019-11-11	MDCKx/MDCK2	<	<	<	1280	320	320	320	320	160	160	160	80	640	<	40
B/Cote d'Ivoire/948/2020	N150K grp + V220M, P241Q	1A(Δ3) B	2020-05-28	MDCK2	<	<	<	1280	640	640	320	160	80	160	160	80	640	<	40
B/Cote d'Ivoire/948/2020	N150K grp + V220M, P241Q	1A(Δ3) B	2020-05-28	E3	<	<	<	1280	640	640	320	320	160	320	160	80	1280	<	80
B/Austria/1359417/2021	N150K grp + A127T, P144L, K203R	1A(Δ3) B	2021-01-09	SIAT1/MDCK4	<	<	<	320	160	160	160	1280	1280	640	640	640	1280	320	320
B/Austria/1359417/2021 Isl 2	N150K grp + A127T, P144L, K203R	1A(Δ3) B	2021-01-09	E3/E2	20	<	10	640	320	320	160	1280	1280	640	640	640	2560	320	320
B/Paris/9878/2020	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	MDCK2	<	<	10	320	80	80	80	640	1280	640	320	320	1280	640	320
B/Paris/9878/2020 Isl 2 (G141V)	N150K grp + A127T, P144L, T182A, D197E, A202V, K203R, T221A	1A(Δ3) B	2020-11-20	E3	10	<	10	160	80	80	160	1280	1280	640	320	320	1280	320	1280
TEST VIRUSES																			
B/Sichuan-Jingyang/12048/2019	N150K grp + V220M, P241Q	1A(Δ3) B	2019-11-26	C2/MDCK1	<	<	<	640	640	640	320	<	<	160	160	40	640	<	40
B/Sichuan-Jingyang/12048/2019	N150K grp + V220M, P241Q	1A(Δ3) B	2019-11-26	E2/E1	<	<	<	640	320	320	160	160	40	80	160	40	320	<	<
B/Shanghai-Songjiang/1193/2021	N150K grp + V220M, P241Q	1A(Δ3) B	2021-03-11	C1/C1/MDCK1	<	<	<	640	320	320	160	<	<	80	80	40	320	<	<
B/Fujian-Zhangpu/34/2021	N150K grp + V220M, P241Q	1A(Δ3) B	2021-03-22	C1/C1/MDCK1	<	<	<	640	320	320	320	80	<	160	160	40	640	<	40
B/Fujian-Zhangpu/34/2021	N150K grp + V220M, P241Q	1A(Δ3) B	2021-03-22	E1/E1/E2	<	<	<	640	320	320	320	80	<	160	160	40	640	<	40
B/Henan-Shanyang/37/2021	N150K grp + V220M, P241Q, R80K, E128K, I290V	1A(Δ3) B	2021-03-29	C1/C1/MDCK1	<	<	<	640	320	320	160	80	<	160	80	40	640	<	<
B/Henan-Shanyang/37/2021	N150K grp + V220M, P241Q, R80K, E128K, I290V	1A(Δ3) B	2021-03-29	E1/E1/E1	<	<	<	640	640	640	320	160	<	160	160	80	640	<	80
B/Hubei-Wujiagang/1299/2021	N150K grp + V220M, P241Q, R80K, H122N, A127T	1A(Δ3) B	2021-03-18	C2+1/MDCK1	<	<	<	640	320	320	320	160	<	160	80	40	640	<	40
B/Hubei-Wujiagang/1299/2021	N150K grp + V220M, P241Q, R80K, H122N, A127T	1A(Δ3) B	2021-03-18	E1/E1/E1	<	<	<	640	640	640	640	160	160	320	160	80	1280	<	80
B/Jiangxi-Zhushan/1164/2021	N150K grp + V220M, P241Q -185E	1A(Δ3) B	2021-03-01	C2/C1/MDCK1	<	<	<	640	320	320	160	<	<	80	80	40	320	<	<
B/Henan-Xigong/1118/2021	N150K grp + A127T, P144L, K203R, H122Q	1A(Δ3) B	2021-02-17	C1/C1/MDCK1	<	<	<	320	80	80	<	1280	1280	640	640	320	1280	320	320
B/Henan-Xigong/1118/2021	N150K grp + A127T, P144L, K203R, H122Q	1A(Δ3) B	2021-02-17	E1/E1/E1	<	<	<	320	160	160	160	1280	1280	640	640	640	2560	320	320
B/Hainan-Meilan/32/2021	N150K grp + A127T, P144L, K203R, R88K, H122Q	1A(Δ3) B	2021-03-17	C1/C1/MDCK1	<	<	<	320	80	80	<	1280	640	640	320	320	2560	320	160
B/Gansu-Baiyin/1281/2021	N150K grp + A127T, P144L, K203R, H122Q +167N	1A(Δ3) B	2021-04-13	C1/C1/MDCK1	<	<	<	640	160	160	160	1280	1280	640	640	640	2560	640	320
B/Gansu-Baiyin/1281/2021	N150K grp + A127T, P144L, K203R, H122Q +167N	1A(Δ3) B	2021-04-13	E1/E1	<	<	<	640	160	160	160	2560	1280	640	640	640	2560	640	320
B/Gansu-Chengguan/1515/2021	N150K grp + A127T, P144L, K203R, H122Q +167N, L115F	1A(Δ3) B	2021-03-30	C1/C1/MDCK1	<	<	<	320	160	160	160	2560	1280	640	640	640	2560	640	320
B/Gansu-Baiyin/1293/2021	N150K grp + A127T, P144L, K203R, H122Q +167N, D197N (+CHO)	1A(Δ3) B	2021-04-14	C1/C1/MDCK1	<	<	<	<	<	<	<	<	<	160	160	80	160	<	<

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

[1] < = <40; [2] < = <80; [3] hyperimmune sheep serum; [4] < = <20; ND = Not Done

Additional substitutions in HA1

Additional substitutions in HA2

Amino acid insertions (+) or deletions (-) in HA1

Vaccine

SH 2020

NH 2020-21

SH 2021

NH 2021-22

Fold reductions compared to homologous titres

≤ 2-fold

4-fold

≥ 8-fold

Figure 12. Phylogenetic comparison of B(Victoria) HA genes

Vaccine viruses

Reference viruses

Collection date

Aug 2021

Jul 2021

Jun 2021

May 2021

Apr 2021

Mar 2021

Feb 2021

HA2 numbering

recent Crick sequences

$ proposed serology antigens

New insertions/deletions

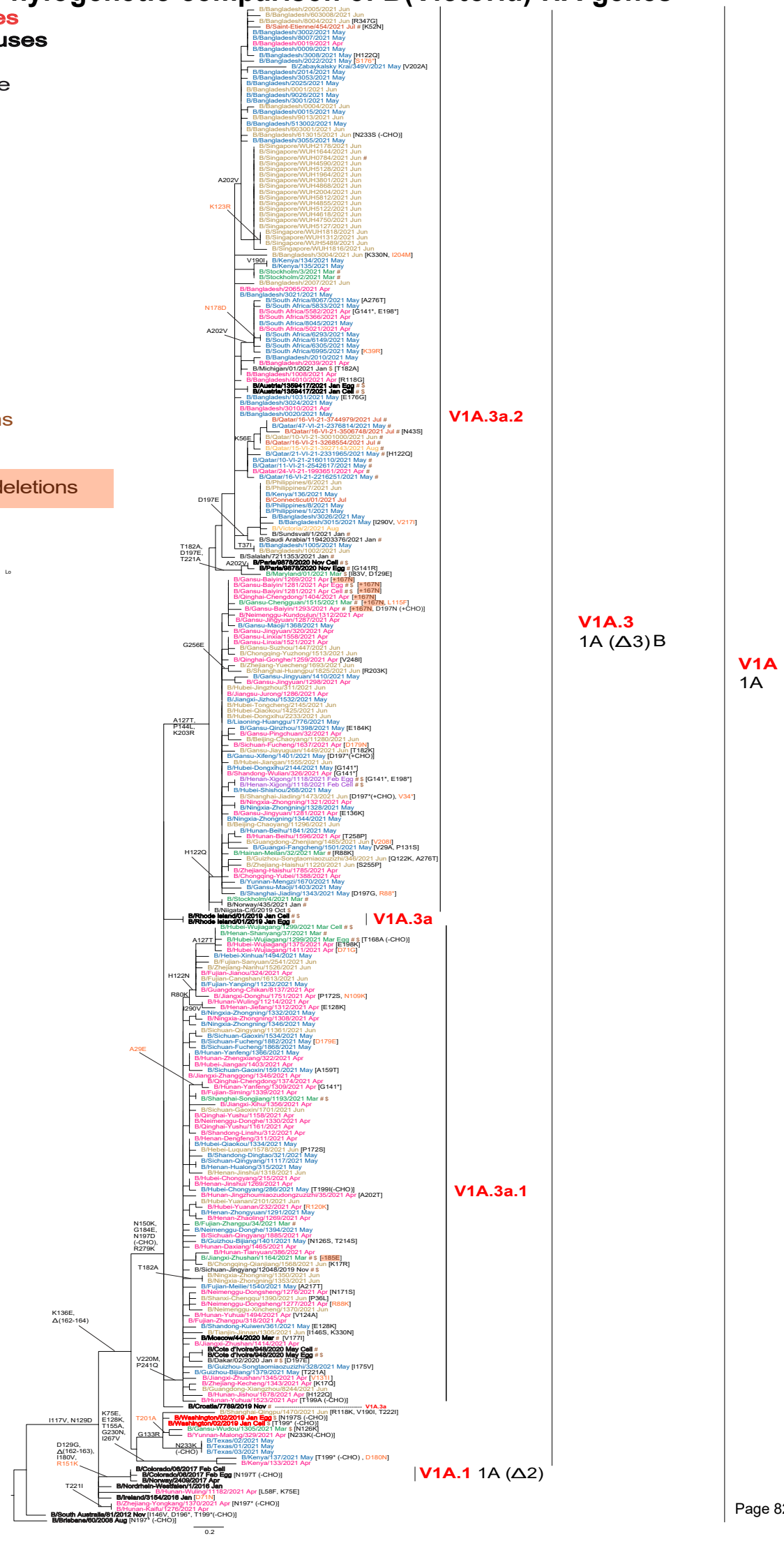
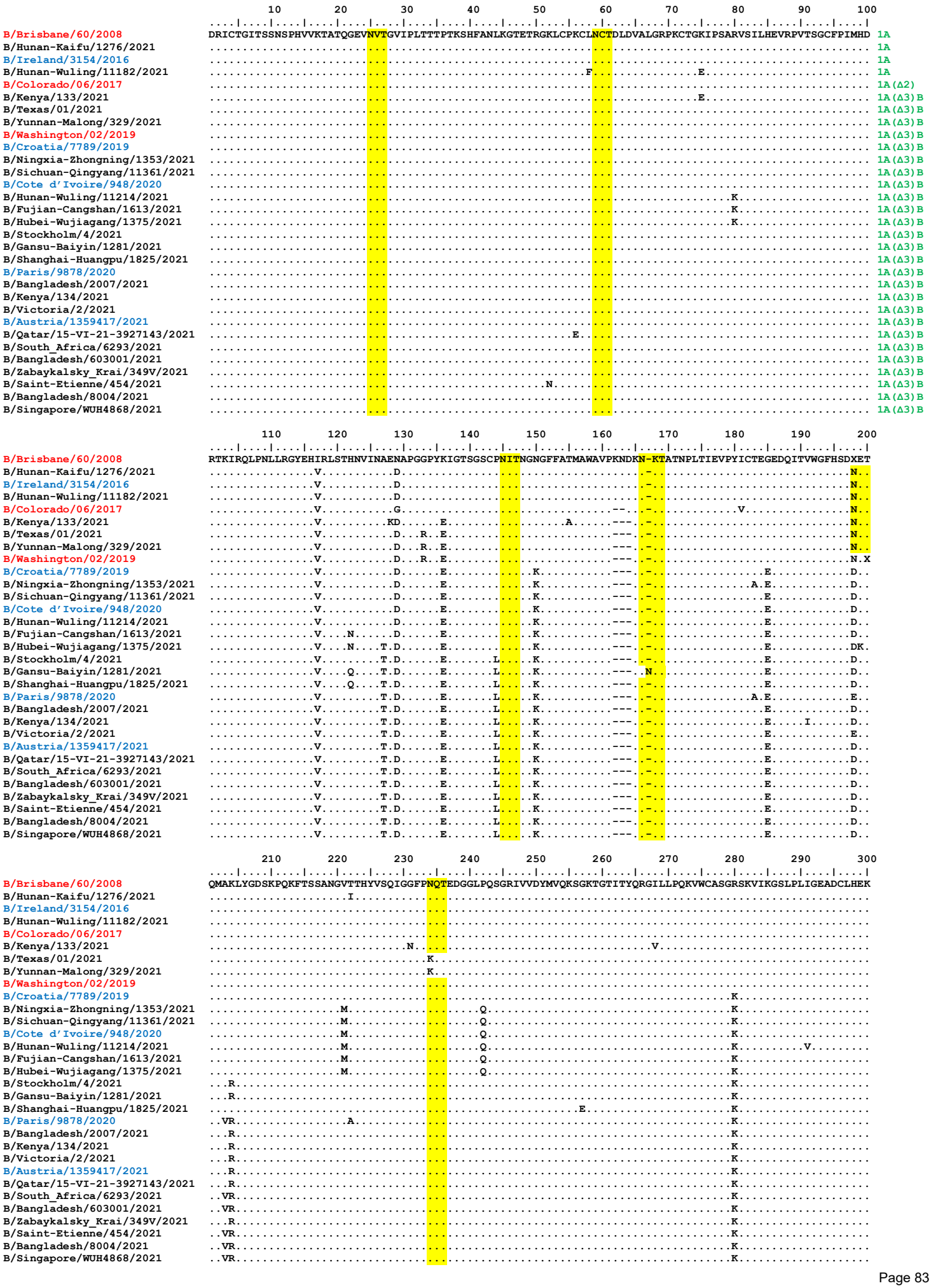
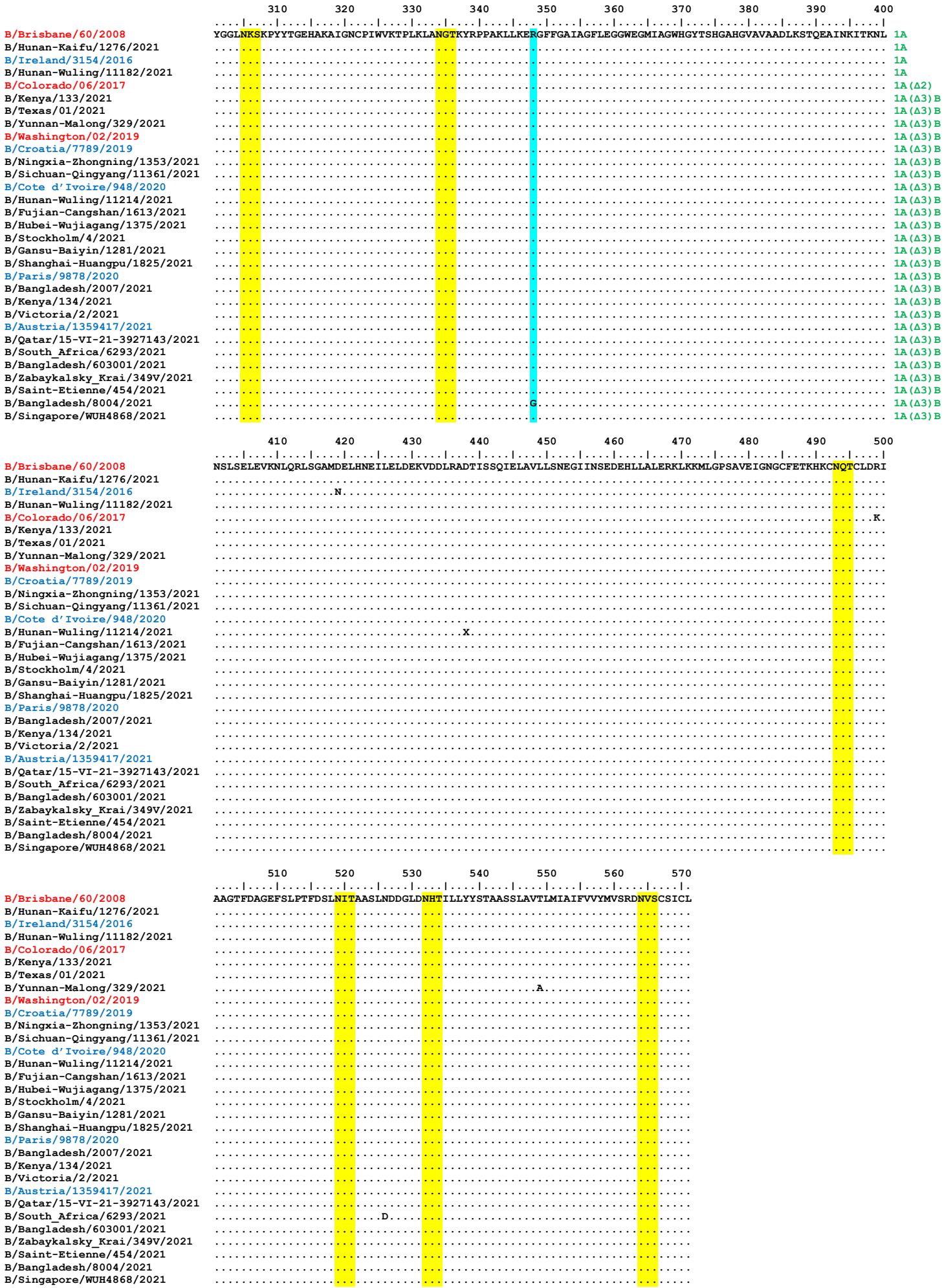


Figure 13. HA protein alignment for B (Victoria-lineage) viruses

Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site





Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site

Figure 14. Amino acid substitutions and deletions in the HA of recently circulating B/Victoria-lineage viruses mapped onto B/Brisbane/60/2008

Substitutions defining subclade 1A(△3)B viruses shown in Black

Viruses displaying low reactivity with antisera raised against B/Washington/02/2019:

The virus group (N150K) with 4 substitutions, has evolved in two directions V220M [hidden] + P241Q and A127T + P144L + K203R + (T182A + D197E + T221A [hidden]) with both subgroups displaying low reactivity

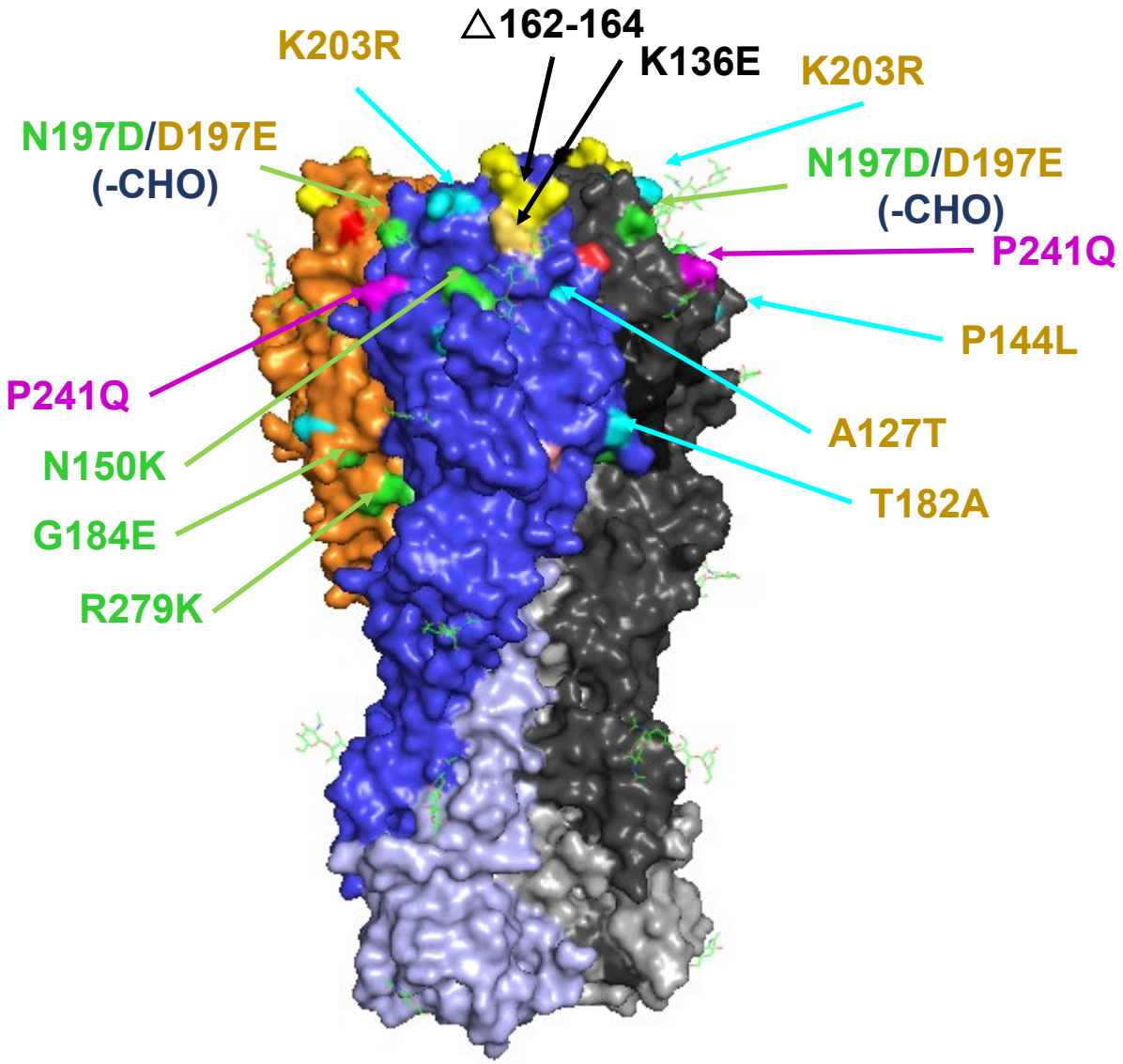


Figure 15. Phylogenetic comparison of B(Victoria) NA genes

Vaccine viruses
Reference viruses

Collection date
Aug 2021
Jul 2021
Jun 2021
May 2021
Apr 2021
Mar 2021
Feb 2021

recent Crick sequences

$ proposed serology antigens

New insertions

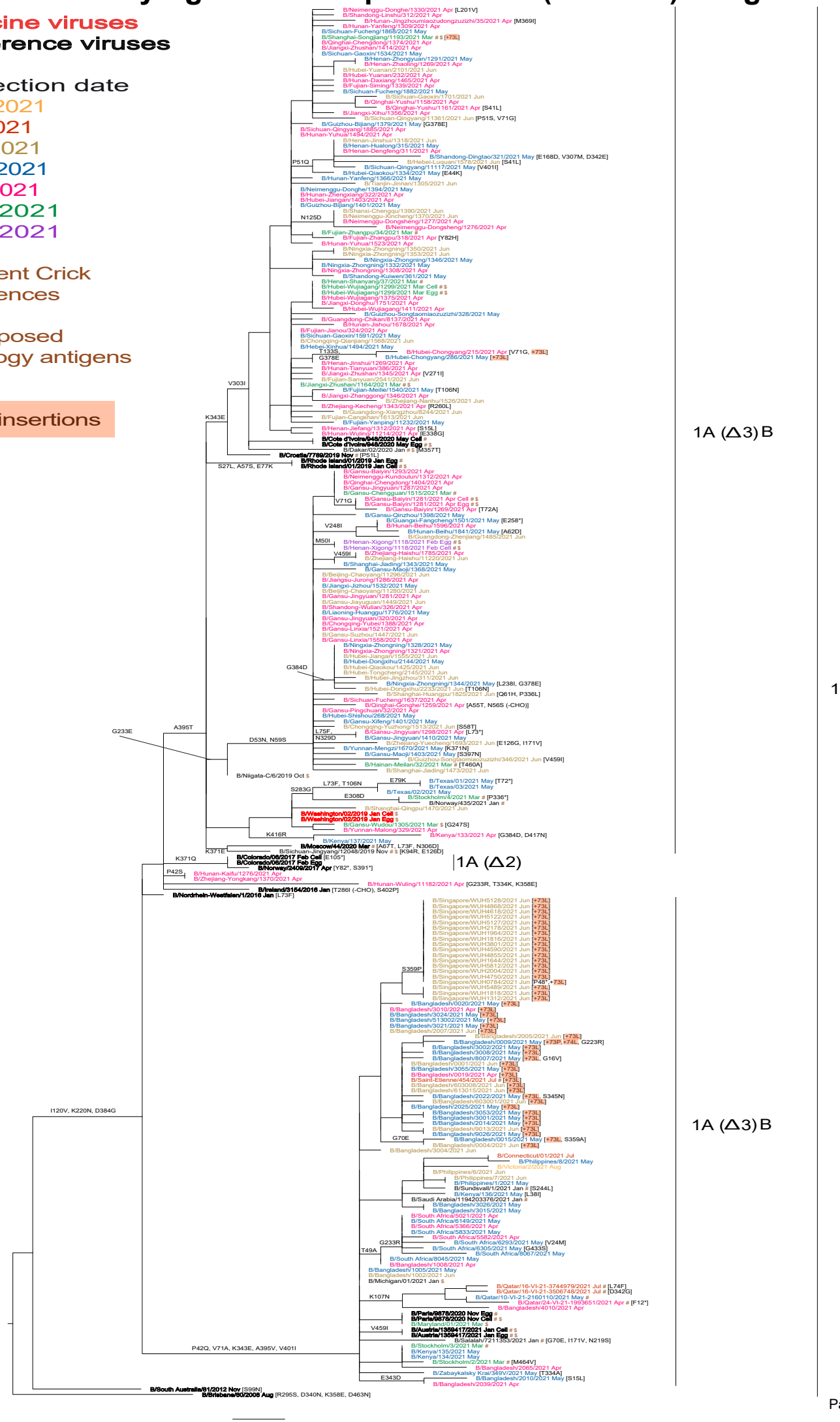
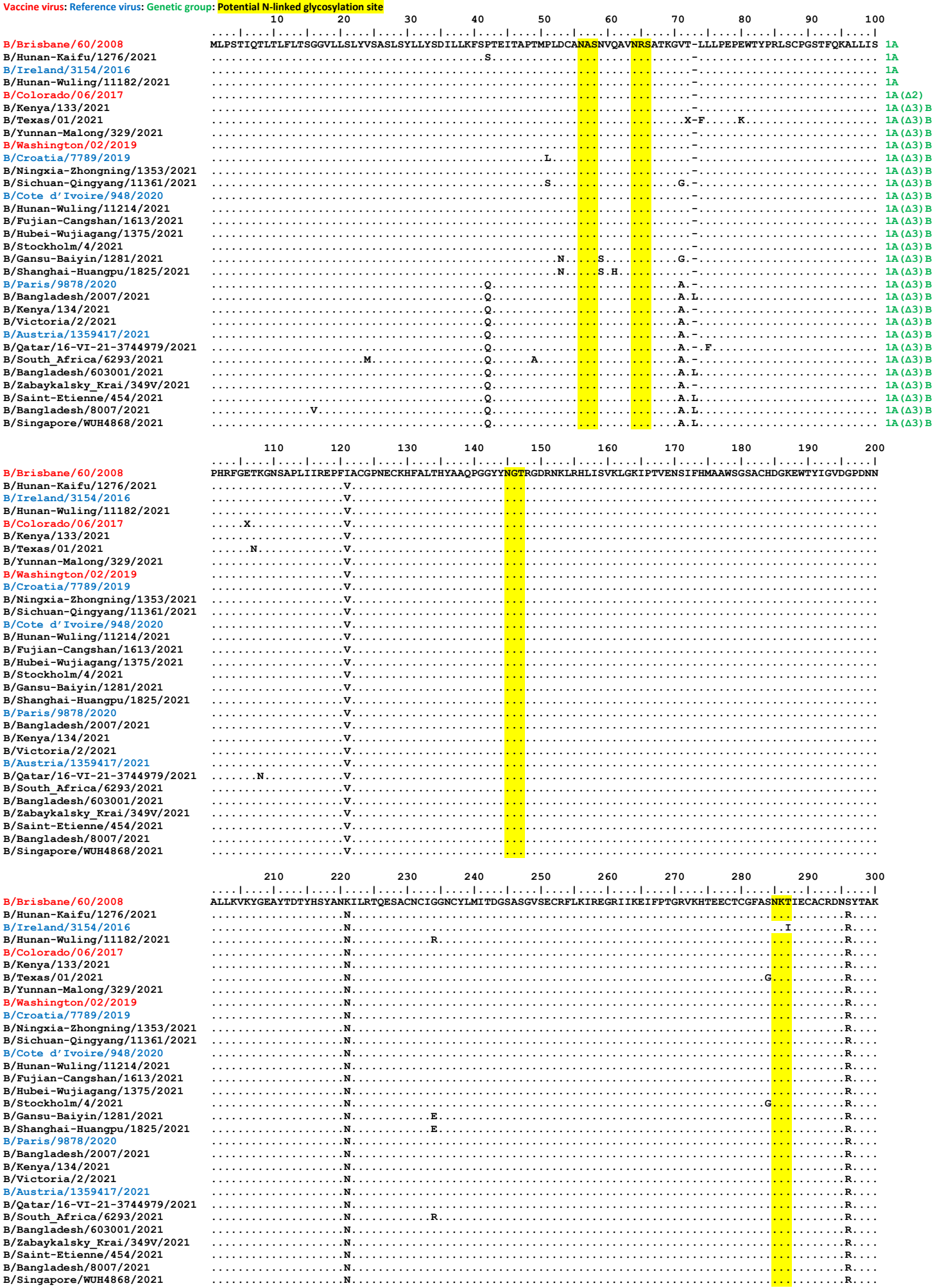
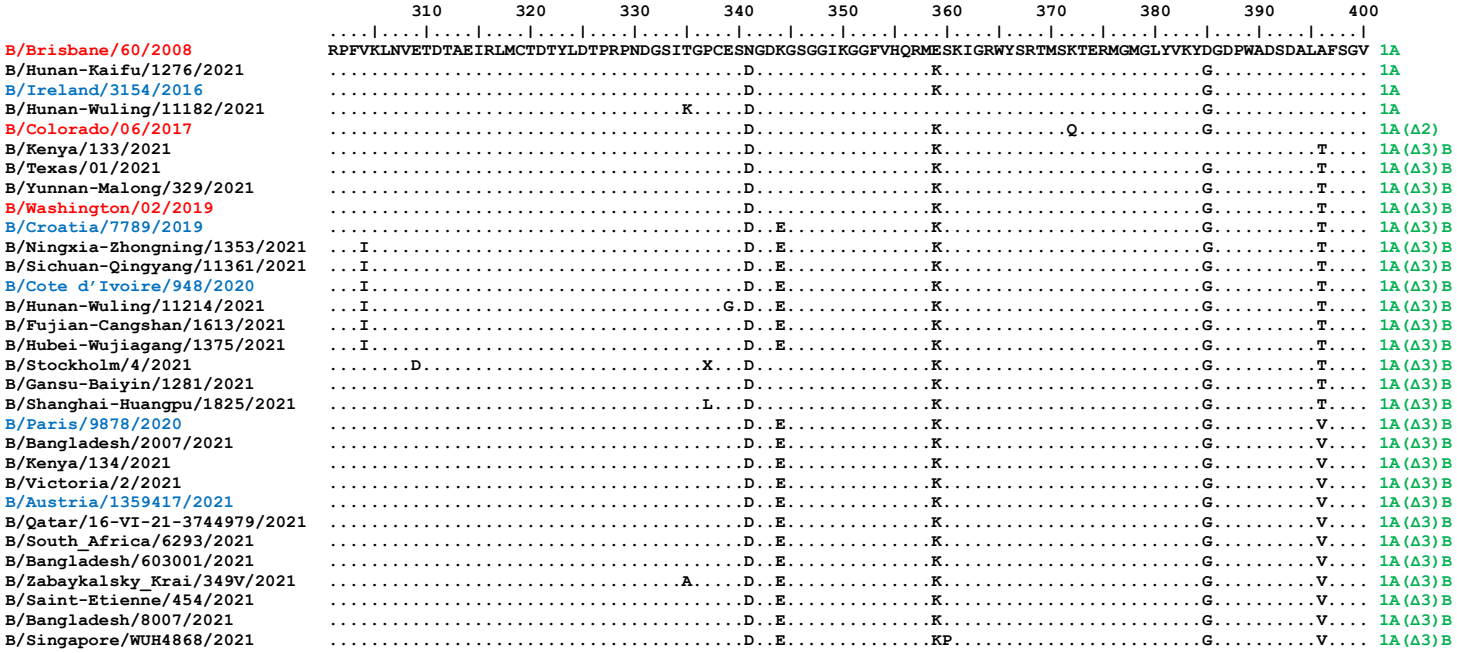


Figure 16. NA protein alignment for B (Victoria-lineage) viruses

Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site





Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site

Figure 17. Phylogenetic comparison of influenza B (Yamagata-lineage) HA genes

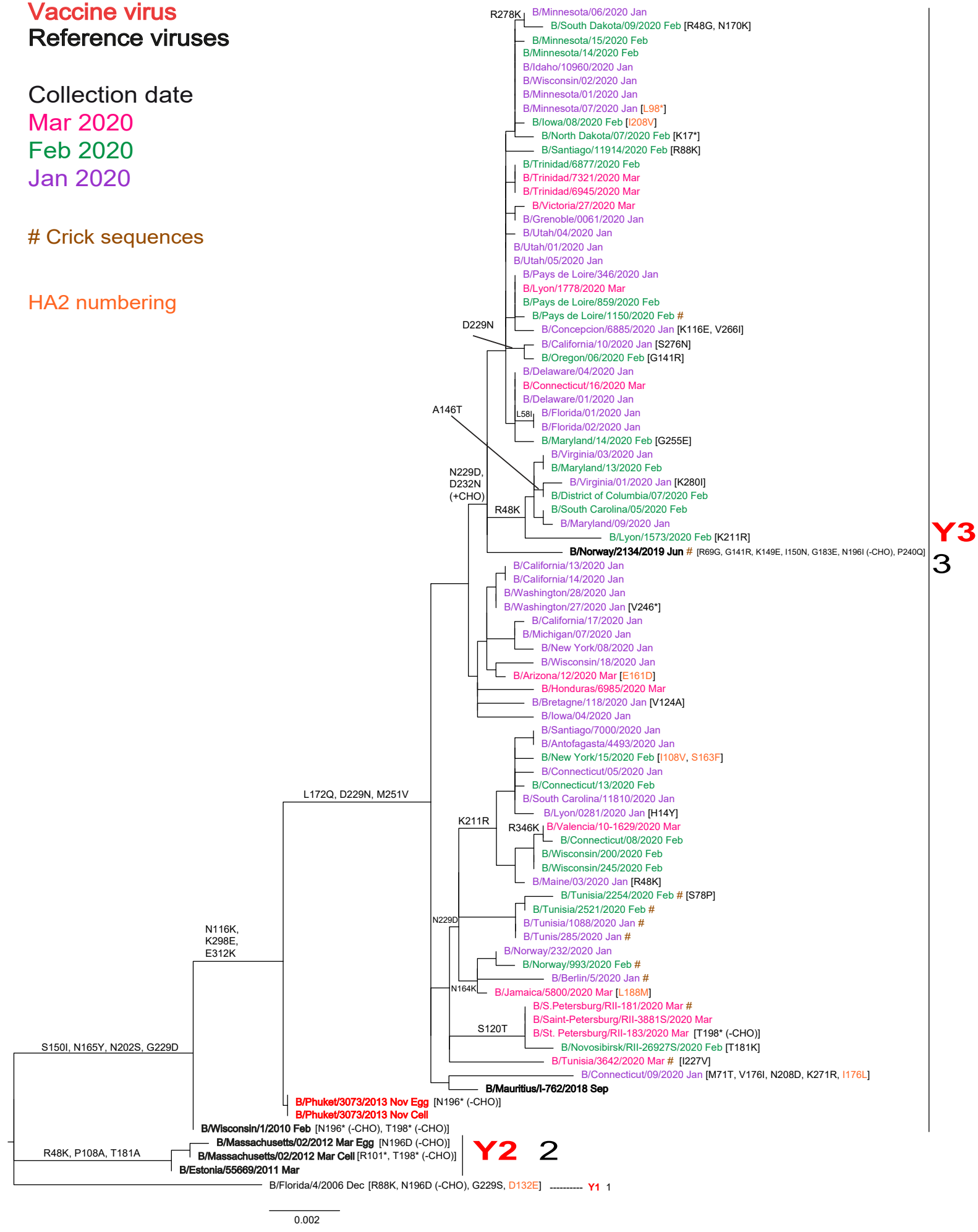
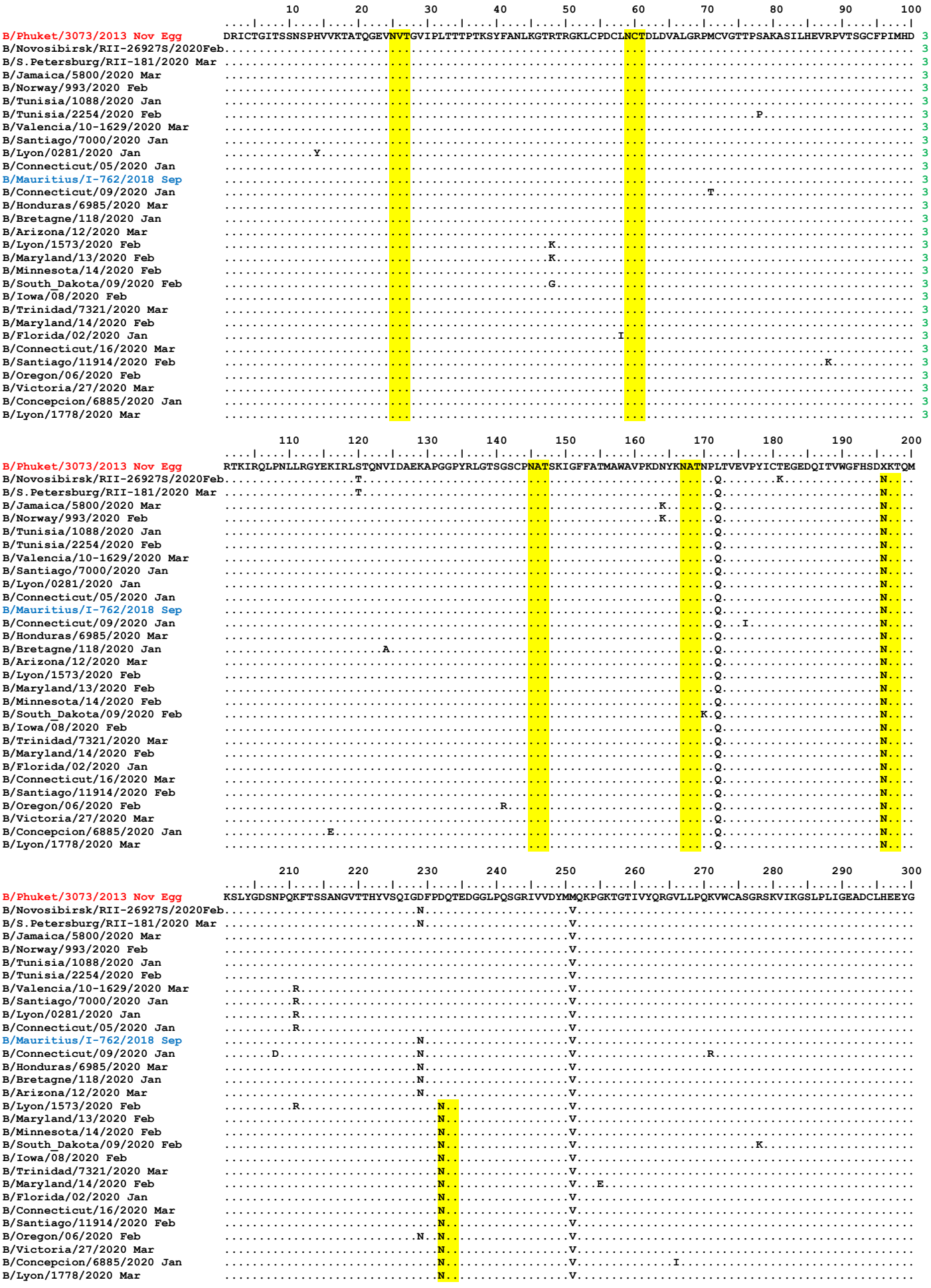
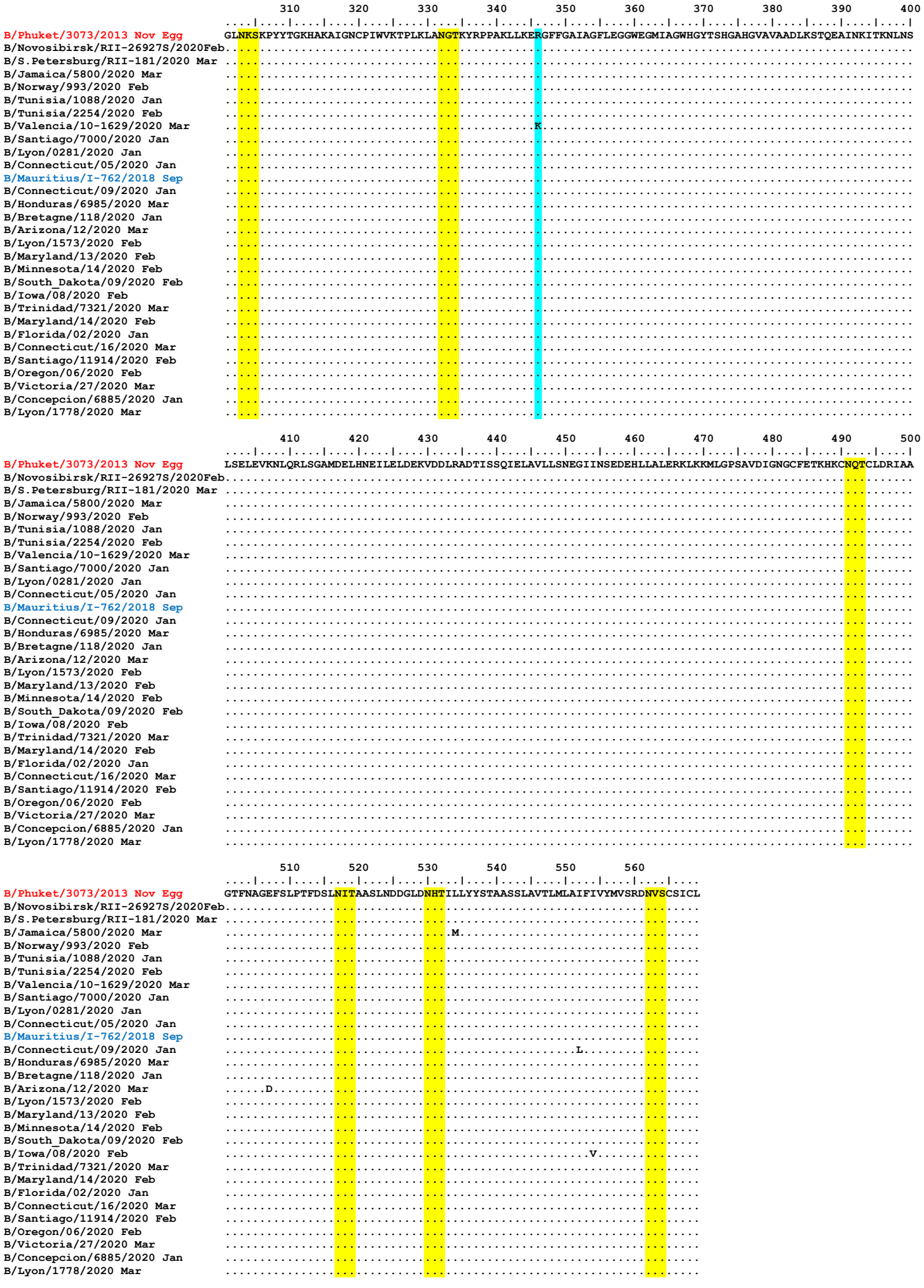


Figure 18. HA protein alignment for B (Yamagata-lineage) viruses

Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site





Vaccine virus: Reference virus: Genetic group: HA1/HA2 boundary: Potential N-linked glycosylation site

Figure 19. Phylogenetic comparison of influenza B (Yamagata-lineage) NA genes

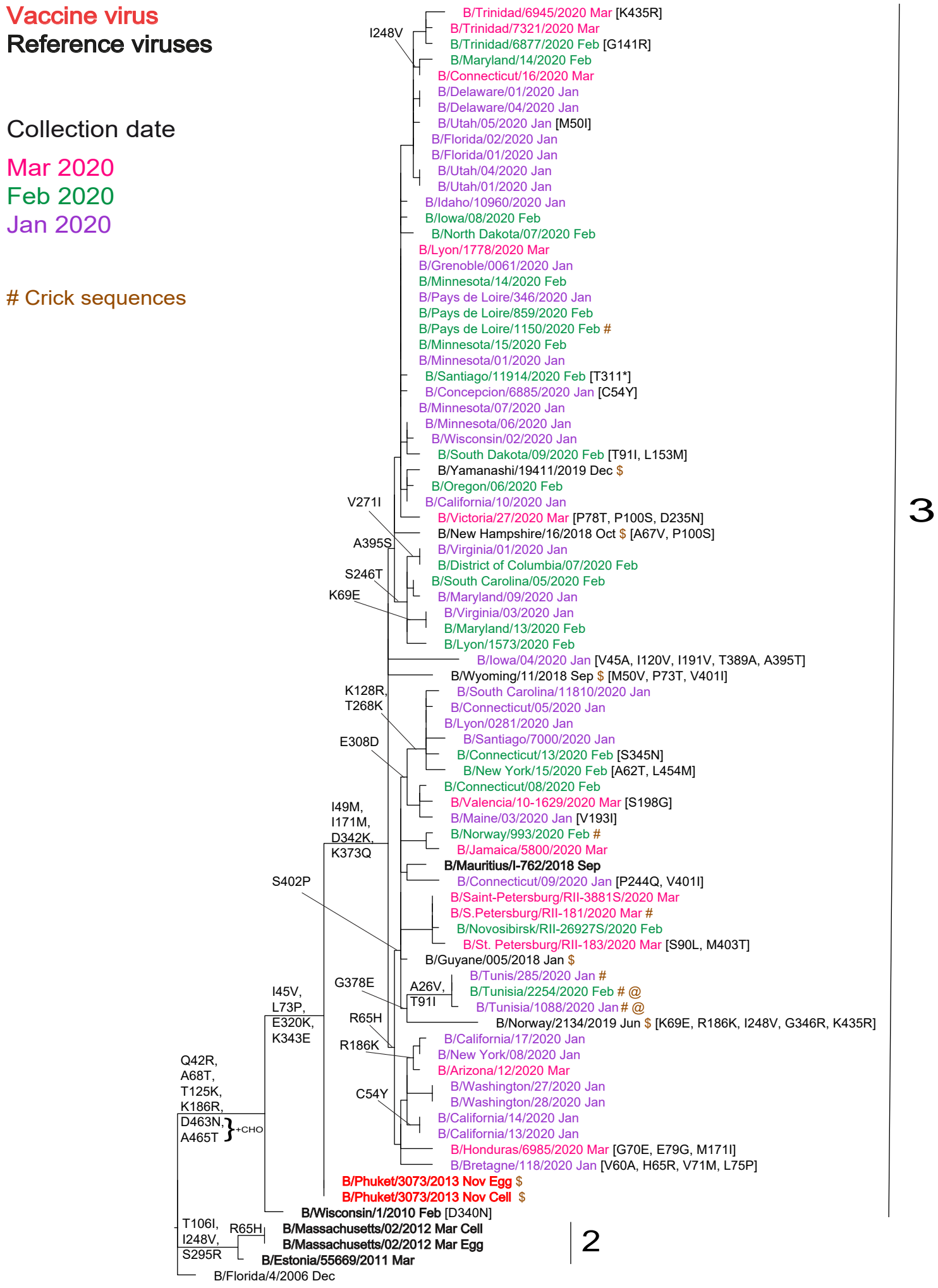
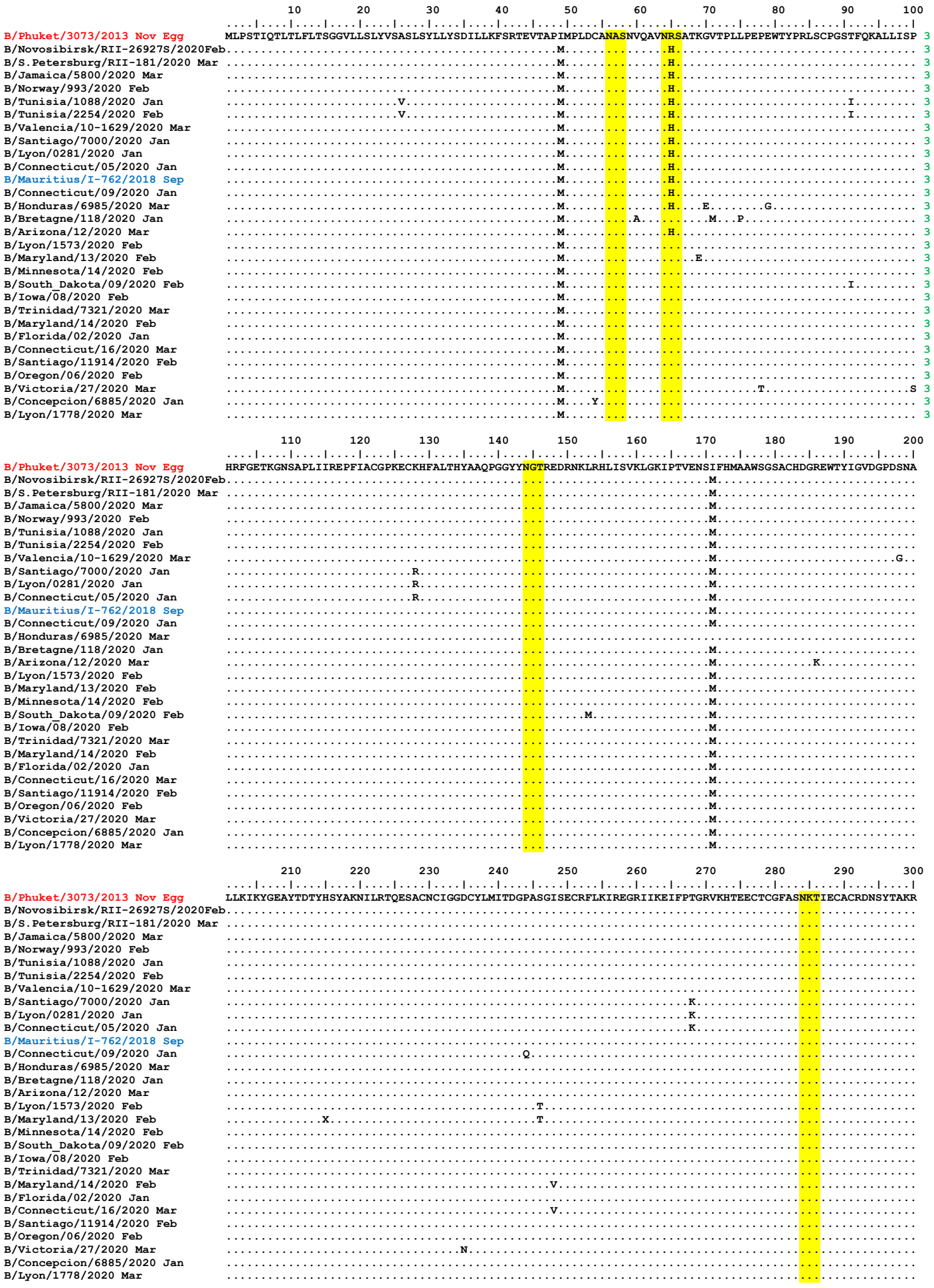
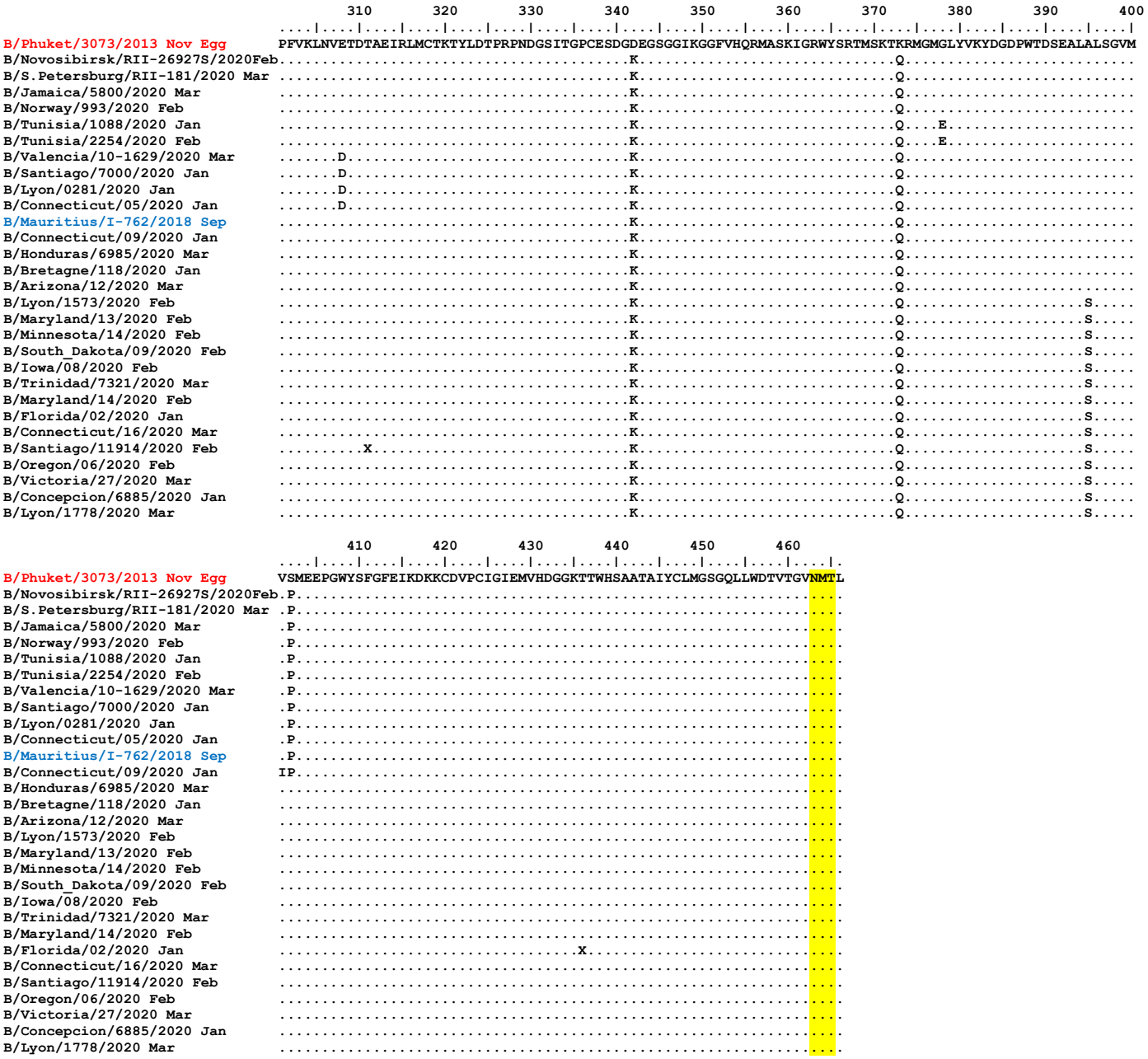


Figure 20. NA protein alignment for B (Yamagata-lineage) viruses

Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site





Vaccine virus: Reference virus: Genetic group: Potential N-linked glycosylation site

Table 11. Antiviral (NAI) testing of isolates with collection dates after 2019-08-31*

Month of Collection	Number of viruses tested for phenotype[1]								
	A(H1N1)pdm09		A(H3N2)		Influenza B-Victoria		Influenza B-Yamagata		
	NI	RI/HRI	NI	RI/HRI	NI	RI/HRI	NI	RI/HRI	Totals
2019-2020									
September-August	679	6	499	1	495	1	19	0	1700
2020-2021									
September-August	21	0	30	0	25	0	0	0	76
Totals	700	6	529	1	520	1	19	0	1776

[1] Phenotype: NI (normal inhibition), RI (reduced inhibition), HRI (highly reduced inhibition) as defined in WHO Wkly. Epidemiol. Rec. (2012) 87, 369-374

* As of 2021-09-10

Virus name[$]	Subtype/ Lineage	Collection date	Fold difference		NA substitution	
			Oseltamivir	Zanamivir		
NA sequence result					Clinical Sample	Virus
A/Salalah/6780/2019	A(H1N1)pdm09	2019-10-23	30.34(RI)		H275(Y90: H10)	H275(Y55: H45)
A/Sur/6980/2019	A(H1N1)pdm09	2019-10-27	232.1 (HRI)		H275(Y40: H60)	H275(Y85: H15)
A/Muscat/6997/2019	A(H1N1)pdm09	2019-10-29	369.97 (HRI)		H275Y	H275Y
A/Denmark/3295/2019	A(H1N1)pdm09	2019-11-15		142.56 (HRI)	NA	Q136K
A/Denmark/3311/2019	A(H1N1)pdm09	2019-11-16		280.06 (HRI)	NA	Q136K
A/Lund/4/2020	A(H1N1)pdm09	2020-02-17	418 (HRI)	0.64		
A/Limoges/2326/2019	A(H3N2)	2019-12-19		10.29(RI)	NA	T148I (-CHO)
B/Estonia/125782/2020	B Vic	2020-01-13		8.5(RI)	NA	I348V, V430I
Outliers						

[$] No information regarding vaccination status or antiviral treatment of patients was provided