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Influenza virus surveillance in Switzerland
Season 2021–2022

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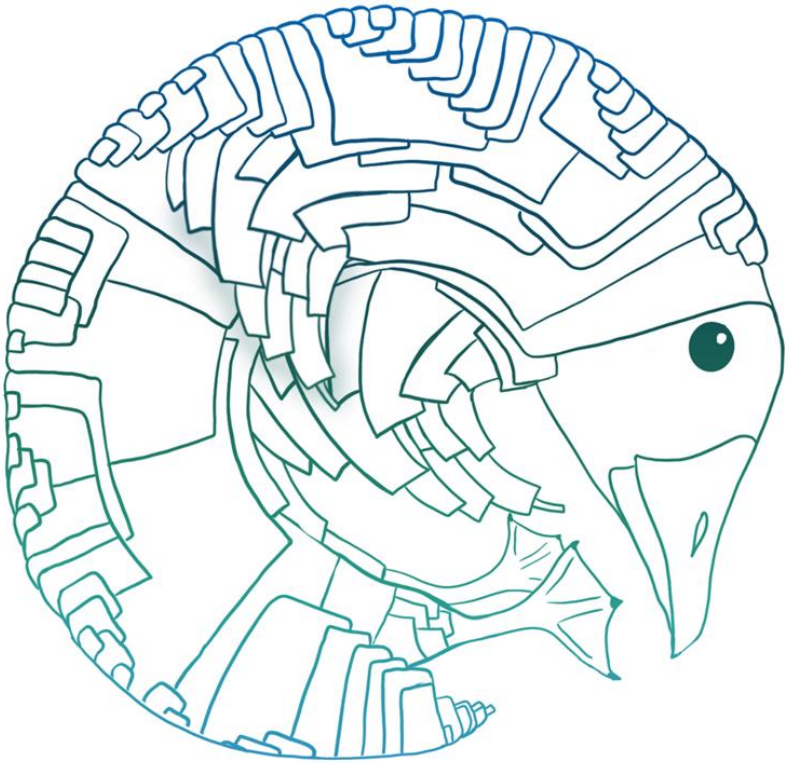

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Phylogenetic tree representing a wild goose.
Image definition: 2000x2000 pixels

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Abbreviations and Acronyms

CDC	centers for disease control and prevention
COVID-19	coronavirus disease 2019
CPE	cytopathic effect
Ct	cycle threshold
ECDC	European centre for disease prevention and control
EEA	European economic area
EEIQAP	European external influenza virus quality assessment programme
EQAP	external quality assessment programme
EU	European union
FOPH	federal office of public health
GISAID	global initiative on sharing all influenza data
HA	hemagglutinin
HAI	hemagglutinin inhibition
HAdV	human adenovirus
HBoV	human bocavirus
HCoV	human coronavirus
HEF	hemagglutinin-esterase-fusion
H/LPAI	high/low pathogenic avian influenza
HMPV	human metapneumovirus
HPIV	human parainfluenza
ILI	influenza-like illness(es)
M	matrix
MDCK	Madin-Darby canine kidney cells
MDCK-SIAT1	sialic acid-enriched MDCK cells
NA	neuraminidase
NAI	neuraminidase inhibitor
NEP	nuclear export protein
NRCI	national reference centre of influenza
NS	non-structural
PA, PB	acidic protein, basic protein
PRNA	plaque-reduction neutralisation assay
RBC	red blood cell
RNA	ribonucleic acids
RNP	ribonucleoprotein
RV/EV	rhinoviruses/enteroviruses
RSV	respiratory syncytial virus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
rRT-PCR	real-time reverse-transcription polymerase chain reaction
Vic, Yam	victoria, yamagata
WHO	world health organization
WIC	worldwide influenza centre
URTI	upper respiratory tract infection(s)

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Résumé – Zusammenfassung – Summary

Résumé de la surveillance de l'activité grippale 2021/2022

Pour la deuxième année consécutive au sein du réseau de surveillance Sentinelle, les 2688 prélèvements nasopharyngés reçus par CNRI (n= 2688 pour la période entre la semaine 17/2021 à la semaine 16/2022), ont non seulement été dépistés pour le virus de la grippe mais aussi pour le SARS-CoV-2, RSV, HCoV NL63, HCoV HKU1, HCoV OC43, HCoV 229E, HPIV1-4, HBoV, HAdV, RV/EV et HMPV. Parmi les 2688 échantillons reçus, 1772 étaient positifs pour au moins un virus respiratoire. Le SARS-CoV-2 et le RV/EV étaient les virus les plus fréquemment détectés durant cette saison.

La grippe a fait sa première apparition au sein du réseau Sentinelle en semaine 47/2021. Sur les 2688 échantillons testés, nous avons détecté 282 virus de la grippe, ce qui représente environ 15.9% des prélèvements positifs. Les virus de l'influenza A étaient prédominants. La majorité des influenza A détectés étaient de sous-type A(H3N2) et appartenaient au groupe génétique 3C.2a1b.2a.2 ; ces derniers étaient par ailleurs bien reconnus par l'antisérum dirigé contre la souche vaccinale 2022 de l'hémisphère sud A/Darwin/9/2021 (3C.2a1b.2a.2). Peu de virus de l'influenza A(H1N1)pdm09 et B ont été détectés en Suisse cette saison. Les virus A(H1N1)pdm09 étaient antigénétiquement proches des souches vaccinales 2020/2021 A/GuangdongMaonan/SWL1536/2019 et 2019/2020 A/Brisbane/02/2018, respectivement. Seuls les virus influenza de la lignée B/Victoria/2/1987 ont été identifiés en Suisse. Ces derniers ont été antigénétiquement caractérisés comme étant similaires à la souche B/Brisbane/60/2008 ou à la souche vaccinale 2022 de l'hémisphère sud B/Austria/1359417/2021.

Un seul prélèvement du virus de la grippe A(H3N2) a été testé phénotypiquement pour la résistance à l'oseltamivir. Le séquençage du génome a révélé la présence de la mutation E119V, associée à une sensibilité réduite à cet inhibiteur de la neuraminidase.

L'activité grippale 2021/2022 chez l'Homme était plus élevée que la saison 2020/2021 mais restait tout de même inférieure aux années précédant l'émergence de la COVID-19. Aucune infection grippale zoonotique n'a été recensée en Suisse. Chez les oiseaux sauvages mais également chez la volaille, l'activité grippale a été particulièrement importante dans plusieurs pays d'Europe, d'Amérique et d'Asie.

Zusammenfassung der Grippeüberwachung 2021/2022

Im zweiten Jahr in Folge wurden im Rahmen des Sentinella-Überwachungsnetzes die beim NRZI eingegangenen Nasopharynxproben (n=2688 für den Zeitraum zwischen Woche 17/2021 und Woche 16/2022) nicht nur auf Influenzaviren, sondern auch auf SARS-CoV-2, RSV, HCoV NL63, HCoV HKU1, HCoV OC43, HCoV 229E, HPIV1-4, HBoV, HAdV, RV/EV und HMPV getestet. Von den 2688 eingegangenen Proben waren 1772 positiv für mindestens ein respiratorisches Virus. SARS-CoV-2 und RV/EV waren die am häufigsten nachgewiesenen Viren in dieser Saison.

In der Woche 47/2021 trat die Grippe zum ersten Mal im Sentinella-Netzwerk auf. Von den 2688 getesteten Proben wiesen wir 282 Influenzaviren nach, was etwa 15.9% der positiven Proben entspricht. Influenza-A-Viren waren vorherrschend. Die meisten der nachgewiesenen Influenza-A-Viren waren vom Subtyp A(H3N2) und gehörten der genetischen Gruppe 3C.2a1b.2a.2 an; letztere wurden zudem gut von dem Antiserum erkannt, das gegen den Impfstamm 2022 der südlichen Hemisphäre A/Darwin/9/2021 (3C.2a1b.2a.2) gerichtet war. In der Schweiz wurden in dieser Saison nur wenige Influenza A(H1N1)pdm09- und B-Viren nachgewiesen. Die A(H1N1)pdm09-Viren waren antigenetisch eng mit den Impfstämmen 2020/2021 A/GuangdongMaonan/SWL1536/2019 bzw. 2019/2020 A/Brisbane/02/2018 verwandt. In der Schweiz wurden nur Influenzaviren der B-Victoria-Linie identifiziert. Diese wurden antigenetisch so charakterisiert, dass sie dem Stamm B/Brisbane/60/2008 oder dem Impfstamm 2022 der südlichen Hemisphäre B/Austria/1359417/2021 ähnlich sind.

Eine einzige Probe des Influenza-A(H3N2)-Virus wurde phänotypisch auf Resistenz gegen Oseltamivir getestet. Die Sequenzierung des Genoms dieses Virus ergab das Vorhandensein der Mutation E119V, die mit einer verminderten Empfindlichkeit gegenüber diesem Neuraminidasehemmer einhergeht.

Die Influenzaaktivität 2021/2022 beim Menschen war deutlich höher als in der Saison 2020/2021, blieb aber dennoch niedriger als in den Jahren vor dem Auftreten von COVID-19. In der Schweiz wurden keine zoonotischen Influenzainfektionen festgestellt. Bei Wildvögeln, aber auch bei Geflügel, war die Influenzaaktivität in mehreren Ländern Europas, Amerikas und Asiens besonders hoch.

Summary of the 2021/2022 influenza surveillance

For the second consecutive year within the Sentinel surveillance network, the 2688 nasopharyngeal swabs received by the NRCI (n=2888 for the period between week 17/2021 and week 16/2022), were not only screened for influenza virus but also for SARS-CoV-2, RSV, HCoV NL63, HCoV HKU1, HCoV OC43, HCoV 229E, HPIV1-4, HBoV, HAdV, RV/EV and HMPV. Of the 2688 samples, 1772 were positive for at least one respiratory virus. SARS-CoV-2 and RV/EV were the most frequently detected viruses this season.

Influenza appeared for the first time of this season in week 47/2021 in the Sentinel network. Out of 2688 samples tested, we detected 282 influenza viruses from weeks 17/2021 to 16/2022, which represents about 15.9% of the positive samples. A strong predominance of influenza A was observed compared with influenza B. The majority of influenza A detected were of subtype A(H3N2) and belonged to the 3C.2a1b.2a.2 genetic group with strong recognition of antiserum to the 2022 southern hemisphere vaccine strain A/Darwin/9/2021 (3C.2a1b.2a.2). Few influenza A(H1N1)pdm09 and influenza B viruses have been detected in Switzerland this season. The A(H1N1)pdm09 viruses were rather antigenically close to the previous vaccine strains 2020/2021 A/GuangdongMaonan/SWL1536/2019 and 2019/2020 A/Brisbane/02/2018, respectively. Only influenza viruses of the B-Victoria lineage have been identified in Switzerland. These were antigenically characterized as similar to the B/Brisbane/60/2008-like strain and the 2022 southern hemisphere vaccine strain B/Austria/1359417/2021.

A single influenza A(H3N2) virus sample was phenotypically tested for oseltamivir resistance. Genome sequencing of this virus revealed the presence of the E119V mutation, associated with reduced susceptibility to neuraminidase inhibitors.

The 2021/2022 influenza activity in humans was much higher than the previous season 2020/2021 but still lower than the years prior to the emergence of COVID-19, when the epidemic threshold for influenza in Switzerland had not been exceeded. No zoonotic influenza infections have been recorded in Switzerland. Influenza activity In wild birds and in poultry was particularly high in several countries in Europe, America and Asia.

1 Introduction

Influenza virus infections are a major clinical and economic burden worldwide.[1] In Switzerland, the sentinel surveillance system (Sentinella) is a community-based network of primary care medical practitioners who report influenza-like illness (ILI) or COVID-19 cases to the Federal Office of Public Health (FOPH). A subgroup of sentinel practitioners collects respiratory samples from patients presenting with ILI and/or COVID-19 suspicion, which are sent to the National Reference Centre of Influenza (NRCI) in Geneva for further characterization.

Since week 40 of the year 2020, in addition to influenza, SARS-CoV-2, respiratory syncytial virus (RSV), human coronavirus (HCoV) (NL63/HKU1/OC43/229E), human parainfluenza (HPIV) 1-4 viruses, human bocavirus (HBoV), human adenovirus (HAdV), human rhinovirus/enterovirus (RV/EV) and human metapneumovirus (HMPV) screening was performed during the annual surveillance.

This report summarizes the demographic, epidemiological and virological data gathered from samples processed and analysed by the NRCI during 2021/2022 surveillance (week 17/2021 to week 16/2022).

2 Influenza viruses

Influenza viruses are Orthomyxoviruses, a family of enveloped, negative, single-stranded ribonucleic acid (RNA) viruses (Figure 1), known to be causative agents of respiratory tract infections and referred to as influenza disease or “flu”. Influenza viruses are divided into four types, A, B, C and D. They are transmitted via airborne and contact routes.[1,2]

Influenza A viruses have a wide host tropism, while influenza B viruses are mainly found in humans[3] and in harbour seals[4]. These two influenza types are responsible for the annual influenza epidemics. Influenza C viruses can be isolated from swine and humans in whom they cause mostly limited mild to moderate symptoms, particularly in children. Influenza C’s epidemiological pattern has not been well studied. Influenza D viruses are mainly found in swine and cattle.[5] Even if the pathogenic potential of influenza D virus in humans remains unknown, specific influenza D antibodies can be found in high proportions in individuals regularly in contact with cattle.[6]

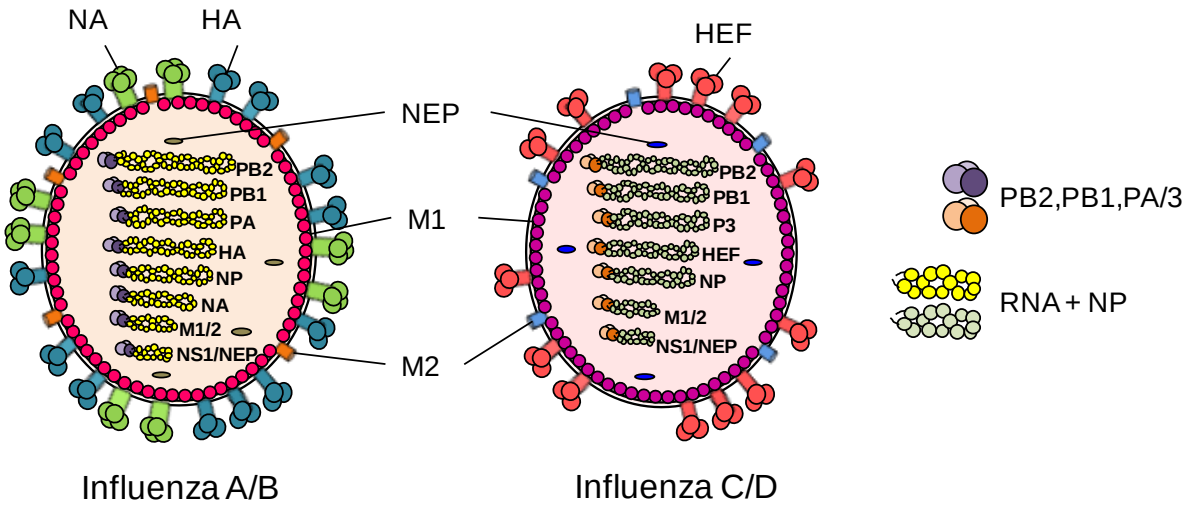

Figure 1. The structure of influenza viral particles. Basic protein 2 (PB2), 1 (PB1) and acidic protein or 3 (PA or P3) form a complex that corresponds to the RNA-dependent polymerase. The hemagglutinin (HA) and the hemagglutinin-esterase-fusion (HEF) play a role in virus attachment to sialic acids present at the surface of host cells and in fusion. The neuraminidase (NA) is crucial for virion detachment from the cellular surface by cleaving the HA on the virus surface. In influenza B, the NA gene also encodes the NB ion channel (not shown). The matrix protein 1 (M1) protein forms the viral capsid. The ion channel M2 allows virion acidification required for fusion. The nuclear export protein (NEP), also named "non-structural (NS) protein 2", is implicated in the export of the virus polymerase + RNA + nucleoprotein (NP) complex to the cell nucleus. The RNA + NP is also called ribonucleoprotein (RNP). The RNA segments PB1, PB2, PA/3, HA or HEF, NP, NA (not present in influenza C and D), M and NS are present inside the viral capsid, protected by NPs. Only non-structural protein 1 is not present in the viral particle, but it is expressed upon infection of the host cell. Influenza D is structurally closer to influenza C than to A and B.

Influenza viruses are known to evolve rapidly through two major mechanisms called antigenic drift and shift. The first is the consequence of the accumulation of mutations in the hemagglutinin (HA) and neuraminidase (NA) genes encoding the two major surface glycoproteins targeted by neutralizing antibodies produced against the virus. The antigenic drift drives the annual evolution of the virus and is therefore responsible for the necessity to regularly adapt the seasonal influenza vaccine strains. The antigenic shift results from the exchange (reassortment) of the influenza A HA and NA genes from different non-human species. It drives the emergence of new variants with high pandemic potential.[7]

Human infection with seasonal influenza A and B viruses can be asymptomatic or cause mild to severe diseases, which can sometimes be lethal. These viruses are of major concern in vulnerable individuals, such as the elderly (≥65 years old), pregnant women, persons with underlying chronic diseases and young children, in whom they represent an important health threat.

3 Other respiratory viruses

A majority of respiratory viruses other than influenza infections are often associated with mild or moderate acute respiratory diseases. Nevertheless, they can also be linked to more severe syndromes and increased morbidity[8] in particular subpopulations.

3.1 RSV

RSV belongs to the *Pneumoviridae* family, genus *Orthopneumovirus*. This enveloped virus contains a non-segmented, single-stranded, negative sense RNA genome of ten genes coding for 11 proteins.[9]

RSV is considered to be an important threat for children under 5 years old, adults with underlying medical conditions, the immunocompromised[10], and the elderly.[11] Each year, RSV infections are estimated to be responsible for more than 3 million hospitalizations and more than 118'000 deaths globally[12], a large proportion in low income countries. Considering the high public health impact of RSV, the WHO is currently building a global RSV surveillance programme similar to the one already existing for influenza (https://www.who.int/influenza/rsv/en/).[13]

During RSV upper respiratory tract infections (URTI), clinical manifestations are generally mild with symptoms like runny nose, cough, nasal congestion, low-grade fever and decreased appetite. Most infants with RSV will present an URTI, whereas 20-30% will develop potentially severe lower respiratory tract infection such as bronchiolitis, pneumonia, sometimes leading to respiratory failure. RSV infections at early age are also suspected to be linked to the development of asthma. Older children mostly present URTI symptoms. In adults and elderly, RSV symptoms can be similar to those caused by influenza virus.[11] Cases of RSV associated encephalitis[14], myocarditis[15,16], and hepatitis[17] have also been reported.

3.2 HMPV

Like RSV, HMPV are enveloped single-stranded, negative-sense non-segmented RNA viruses, which belong to the *Pneumoviridae* family, albeit to a distinct genus, namely the *Metapneumovirus* . Their 13kb genome encodes for eight genes encoding for nine proteins. HMPV are divided in two genotypes and two sub-genotypes.[18]

HMPV infections are prevalent in young children <5 years old; and are second in terms of association with a hospitalisation requirement after RSV infection. Reinfection throughout life is common but disease is generally milder in young adults. HMPV have a tropism for the upper and lower respiratory tracts, and can lead to bronchiolitis, pneumonia, as well as acute asthma and chronic obstructive pulmonary disease exacerbations in adults. HMPV infections, as well as all the respiratory viruses described above, can be a major threat in vulnerable individuals and in the elderly, in whom they can also be fatal.[18]

3.3 HCoVs

Coronaviruses are enveloped, single-strand, positive-sense 5′-capped and 3′-polyadenylated RNA viruses belonging to the subfamily *Orthocoronavirinae* of the Coronaviridae family. Their 30kb genome encodes more than 20 proteins.[19] *Orthocoronavirinae* are divided in four genera *: α-coronavirus, β-coronavirus, γ-coronavirus* and *δ-coronavirus. Alpha-* and *β-coronaviruses* infect mammalian species while *γ-* and *δ*-coronaviruses are avian viruses.[20]

Before the emergence of SARS-CoV-2 in 2019, four coronaviruses were known to cause, in general, mild to moderate diseases in humans, i.e. HCoV 229E, NL63, OC43, and HKU1, and two were associated with more severe lower respiratory tract infections, i.e. severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Most HCoVs seem to peak during winter[21] and to display biannual epidemic patterns.[22] The first cases of SARS-CoV and MERS-CoV were respectively identified in 2002 and 2012. SARS-CoV is currently not circulating in the human population, while there are sporadic laboratory-confirmed MERS-CoV infections reported to the WHO as of December 2021.[23]

HCoV 229E, NL63, OC43, and HKU1 can infect the upper and lower respiratory tracts of both adults and children, and are, as many other respiratory viruses, often associated with common colds of mild to moderate intensity depending on the viral species. Nevertheless, in vulnerable individuals, both in children and adults, HCoV 229E, NL63, OC43, and HKU1 may exhibit more severe diseases as bronchiolitis and pneumonia.[22] Neurological manifestations have also been reported.[24]

SARS-CoV-2 is a *β-coronavirus* responsible for the current coronavirus disease pandemic (COVID-19) that emerged in China in December 2019.[25] Most of the first identified cases of COVID-19 were linked to a wet market in Wuhan city where live-wild animals were also traded. However, the origin of the index case(s) remains unknown.

Clinical manifestations of SARS-CoV-2 range from mild to severe diseases with non-specific symptoms similar to that caused by other respiratory viruses. Other manifestations concern the brain, kidneys, heart, and blood vessels.[26-30] Asymptomatic cases have also been described.[19] As of August 2nd 2022, 3'972'610 cases (577'018'226 in the EU/EEA, as of August 3rd 2022) and 13'534 deaths (6'401'046 in the EU/EEA, as of August 3rd 2022) have been reported in Switzerland.[31,32]

SARS-CoV-2 can be transmitted from human-to-human via respiratory droplets, fomites and by aerosols.[33] SARS-CoV-2 RNA has also been detected in blood[34], urine and faeces.[35] Some studies have observed viral RNA fragments in breast milk, raising the concern regarding the possibility of mother to child transmission via breastfeeding.[36] Wild and domestic animals infections by human SARS-CoV-2 have also been observed.[37-39]

SARS-CoV-2 virus has evolved into several genetic clades and subclades. Some genetic lineages were specifically identified as higher public health threats and classified in four risk groups, i.e. variant of concern (VOC), variant of interest (VOI) and variant under monitoring (VUM). VOI is defined by the WHO as "a variant with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape, and identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global health". VOC variant is defined as a VOI and shares additional characteristics at a global public health scale: "increase in transmissibility or detrimental change in covid-19 epidemiology; or increase in virulence or change in clinical disease presentation; or decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics." Omicron subvariants under monitoring represent " variants, which according to phylogenetic analysis,

belong to a currently circulating VOC and show signals of transmission advantage compared to other circulating VOC lineages, and have additional amino acid changes that are known or suspected to confer the observed change in epidemiology and fitness advantage as compared to other circulating variants. VUM definition is “a variant with genetic changes that are suspected to affect virus characteristics with some indication that it may pose a future risk, but evidence of phenotypic or epidemiological impact is unclear, requiring enhanced monitoring and repeat assessment pending new evidence.”[40]

3.4 HPIV

HPIV are enveloped, non-segmented, single-stranded, negative-sense RNA viruses belonging to the *Paramyxoviridae* family. Their 15’000 base-pair genome only encodes six proteins. HPIV are divided in four genotype. Genotype 4 is further subdivided into a and b genotypes. HPIV 1 and 3 belong to the *Respirovirus* genus, while HPIV 2 and 4 to the *Rubulavirus* genus.

HPIV can infect both the upper and lower respiratory tracts of children, often with ages <5 years old, and adults. HPIV, with RSV, infections are major causes of morbidity and mortality in young children worldwide.[41] Even if generally considered as mild in healthy individuals, HPIV infections can also result in more severe respiratory diseases in immunocompromised individuals as well as in children.[42] HPIV 1 and HPIV 2 cause croup and cold-like symptoms, while HPIV 3 often results in bronchiolitis, bronchitis and pneumonia.[43] HPIV 4 is less well studied but seems to exhibit symptoms similar to HPIV 3 in children.[44]

3.5 HBoV

Human bocaviruses (HBoV) 1 to 4 are non-enveloped, non-segmented, single-stranded DNA viruses belonging to the family *Parvoviridae,* subfamily within the *Parvovirinae* family. Their approximately 5’000 base-pair genome encodes at least eight proteins.[45]

With parvovirus B19, HBoV is the second parvovirus known to be pathogenic to humans. HBoV 1 is more commonly found in respiratory specimens of young

children[45], but can also be detected in adults.[46] HBoV 2, 3 and 4 are commonly identified in stools samples.[47] They are also often found as co-infections. Their clinical presentation is similar to other respiratory viruses leading to either asymptomatic or mild URTI in HBoV1. However more severe clinical manifestations as encephalitis, myocarditis[48], idiopathic lung fibrosis, as well as yet to be confirmed carcinogenesis have also been associated with HBoV, particularly type 1.[49]

3.6 HAdV

Adenoviruses are non-enveloped, double-stranded DNA viruses of more than 26'000 base-pairs encoding for several non-structural and structural proteins, that infect both animals and humans. HAdV belong to the *Mastadenovirus* genus of the Adenoviridae family, and are further divided into species A to G and more than 50 different genotypes infect humans. HAdV B and E both infect the conjunctiva as well as the upper and lower respiratory tracts, while D and C are specific to only one of these anatomical sites, respectively. Finally, types F and G have a tropism for the gastrointestinal tract. Most HAdV infections are either asymptomatic or mild, particularly in young children. However, in vulnerable individuals (e.g. immunocompromised), the clinical manifestations are broader and more severe with possible fatal outcome.[50,51] Of note, HAdv have recently been suggested being linked to acute hepatitis of unknown aetiology in children.[52]

3.7 RV/EV

Picornaviruses can be pathogenic for both animals and humans. They are non-enveloped, single-stranded, positive-sense RNA viruses with genomes ranging from 7'200 to 8'500 bases long. RV (A-C) and EV (A-D) are species of the Enterovirus genus of the Picornaviridae family that are responsible for a high number of human infections annually.[53,54]

Due to their resistance to low pH and high temperatures (37°C), enteroviruses can survive the gastric acidic environment and infect the small intestine. In contrast, rhinoviruses are pH-sensitive and replicate optimally at the neutral pH and slightly lower temperature (~33°C) found in the nasal mucosa. While rhinoviruses usually

cause mild upper respiratory infections and enteroviruses benign diseases, such as hand, foot and mouth disease, these viruses can sometimes also cause more severe manifestations as pancreatitis, hepatitis, myocarditis, encephalitis, flaccid myelitis, paralysis and even death.[53] It is notably the case of poliovirus, the causative agent of major poliomyelitis epidemics before the initiation of the Global Polio Eradication Initiative by the WHO in 1988.

4 Methodology

4.1 Clinical identification of influenza cases

Primary care practitioners, usually 150 to 250, voluntarily participate in the epidemiological national influenza surveillance network on a yearly basis. They are requested to report each week ILI and COVID-19 suspected cases.

Within the Swiss Sentinel system, ILI cases are defined as sudden high-grade fever (>38°C) onset and cough or sore throat. The presence of other symptoms, such as malaise, myalgia, joint pain and headache, as well as gastrointestinal symptoms is not required. Patients presenting with a secondary disease (pneumonia, bronchitis, otitis, etc.) consecutive to an unreported influenza are also expected to be reported.

COVID-19 suspected cases are defined as symptoms of acute respiratory tract disease (i.e. cough, sore throat, shortness of breath, chest pain), and/or acute confusional state or deterioration of general condition with no other aetiology in the elderly, and/or fever with no other aetiology, and/or sudden onset of anosmia, and/or ageusia. Of note, the circulation of COVID-19 still has a major impact on ILI data collection within the Sentinella network as, despite the fact that different case definitions are used, COVID-19 and influenza symptoms remain often similar. Therefore, it seems most likely that some clinically reported ILI were in fact COVID-19 cases and vice versa.

A subgroup of sentinel practitioners collects nasopharyngeal swabs from patients fitting the ILI and COVID-19 case definitions for subsequent viral detection and further characterization, in particular for influenza.

4.2 Sentinella population

The sentinel practitioners who send samples to the NRCI are asked to complete a brief case report form. The following data are collected: patient identity, address and phone number (necessary for mandatory reporting only); sample type; age; gender; time of symptom onset; pneumonia; hospitalization; travel within the previous 14 days upon symptoms onset; and influenza and COVID-19 vaccination status.

4.3 Molecular detection of respiratory viruses other than influenza and SARS-CoV-2

All nasopharyngeal swabs sent to the NRCI for influenza and SARS-CoV-2 detection were also screened for common respiratory viruses using a PCR panel already used by the Geneva University Hospitals Laboratory of Virology. RSV, HCoVs NL63/HKU1/OC43/229E, HPIV, HBoV, HAdV, RV/EV and HMPV were detected using a combination of seven custom manufactured rRT-PCR mixes produced by Eurogentec. Mixes' targets are grouped as follows: 1. RSV/ canine distemper virus (CDV, our extraction efficiency control), 2. HCoV NL63/OC43, 3. HCoV 229E/HKU1, 4. HBoV/HPIV2-4 (does not distinguish between HPIV 2 and 4), 5. HMPV/HPIV1-3 (does not distinguish between HPIV 1 and 3), 6. RV/EV, and 7. HAdV/CDV.

4.4 Molecular detection of SARS-CoV-2 viruses

SARS-CoV-2 was diagnosed daily by PCR using the Cobas® SARS-CoV-2 on a Cobas® 6800 instrument. In some rare cases the Xpert® Xpress SARS-CoV-2 (Cepheid) test was also used.

4.4.1 Genetic characterization of SARS-CoV-2 viruses

Genetic characterization of SARS-CoV-2 was undertaken by whole genome sequencing either by Microsynth AG (Balgach, Switzerland) or the Genome Center (Campus Biotech, Geneva, Switzerland). The resulting consensus sequences were shared internationally through submission to GISAID. In parallel, VOCs were discriminated searching specific mutations in the spike protein performed by a single nucleotide polymorphism (SNP) specific rRT-PCR (VirSNiP Mutation Assays, TIB Molbiol, Berlin). Following the emergence of SARS-CoV-2 Omicron variant, the detection failure of the S target (S drop out) of a multiplex rRT-PCR detecting S, N and Orf1ab of SARS-CoV-2 was used as a proxy for the detection of SARS-CoV-2 VOC Omicron.

4.5 Molecular detection of influenza viruses[1]

Nasopharyngeal swabs received at the NRCI are submitted to virus screening and subtyping tests. For screening, a one-step, real-time reverse transcription polymerase chain reaction (rRT-PCR) adapted from the 2009 USA Centers for Disease Prevention and Control (CDC) protocol is used to detect the presence of influenza A and B viral genomes in the clinical samples. The duplex rRT-PCR targets are the M protein and the non-structural (NS) protein genes for influenza A and B viruses, respectively.

Since the 2017/2018 season, influenza A positive samples are subtyped using an in-house-developed quadruplex rRT-PCR targeting the HA (H1 and H3) and the NA (N1 and N2) genes in order to discriminate between influenza A(H1N1)pdm09 and A(H3N2) strains. This new assay is a mix of already validated (in-house H1 and H3 CDC) and newly-designed (N2[2]) rRT-PCR combinations, adapted from the one used in the study by Henritzi *et al* [55] (N1). The quadruplex detection limit is similar to that of the diagnostic rRT-PCR. The N1 combination was able to detect the H1N1v[3], swH1N1[4] and H5N1[5] isolates tested during the assay validation process. The H3 and N2 rRT-PCR combinations are also able to detect the A/Wisconsin/12/2010 H3N2 triple reassortant (H3N2tr),[56] although the latter virus is not known to circulate in Switzerland. Nevertheless, if needed, additional tests are available at the NRCI to discriminate seasonal H3N2 from H3N2tr viruses. Influenza B/Yamagata/16/88-like (Yam) and B/Victoria/2/87-like (Vic) lineages are determined using a duplex rRT-PCR adapted from Schweiger et al. 2000.[57]

A random selection of rRT-PCR-negative specimens is inoculated on cells for viral culture. This strategy allows the detection of potential influenza strains that may have "escaped" rRT-PCR detection. For example, this could be the case in the presence of viruses carrying mutations in the genomic regions targeted by rRT-PCR screening. For

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1 The evaluation of the proficiency of the Laboratory of Virology at Geneva University Hospitals in performing molecular detection of influenza viruses is accessed through the World Health Organization (WHO) External Quality Assessment Programme for the Detection of Influenza Viruses by RT-PCR, and was initiated in 2007 by the WHO (https://www.who.int/influenza/gisrs_laboratory/external_quality_assessment_project/en/).

2 Human N2 sequences from 2009-2017 were used for the N2 rRT-PCR design.

3 H1N1v: A/Switzerland/***2244/2011 and A/Berne/****6552/2017, variants isolated from Swiss pig breeders.

4 swH1N1 35 (2008): virus isolated from a Swiss pig.

5 H5N1: A/Hong Kong/6841/2010 (EQAP panel 16) and A/goose/Qinghai/1A/05*A/PR8/34(INT).

biosafety reasons, only negative-SARS-CoV-2 samples were submitted to cell culture starting end of February 2020.

4.5.1 Antigenic and genetic characterization of influenza virus

A selection of influenza viruses are submitted to phenotypic and genotypic analysis. In general, five RT-PCR positive samples with cycle threshold (Ct) values <30 are chosen per week for further characterization samples with sufficient HA titers and are submitted to an hemagglutination inhibition (HAI) assay. The latter allows to assess the antigenic similarity between reference and circulating influenza strains. A microneutralisation (MN) assay can be used for samples that do not or poorly agglutinate red blood cells (RBC).

To assess the phylogeny of the circulating strains and to determine how genetically close they are to reference vaccine strains, the HA gene of influenza viruses is analysed. NA gene and, secondarily influenza A M and influenza B NS segments are also sequenced. NA gene sequencing allows the detection of key mutations previously described as conferring resistance to NA inhibitors (NAIs), while M and NS genes sequencing allows to check the adequacy of rRT-PCR primers and probes used for influenza A and B screening.

4.5.1.1 Cell culture

Both influenza positive and negative samples are cultured on MDCK and MDCK-SIAT1 cells. This allows to ensure that a low positivity rate is not due to a rRT-PCR detection defect.

In brief, 0.4 ml of transport medium containing nasopharyngeal swab are incubated for seven days at 33°C on MDCK cells and 37°C on MDCK-SIAT1. The presence of a cytopathic effect (CPE) is monitored for a period of 7 days. If CPE is present, samples are submitted to an hemagglutination. If CPE is absent or low after 7 days, the cells are screened for influenza viruses by immunofluorescence using monoclonal influenza A and B antibodies combined with mouse fluorescein isothiocyanate-conjugate (Merck-Millipore, Chemicon®, Schaffhausen, Switzerland).

As already mentioned, only negative-SARS-CoV-2 samples were submitted to cell culture. Of note, SARS-CoV-2 isolation/amplification by cell culture is also possible at the NRCI, but it was not requested during 2020-2022 surveillance. It is currently performed by our associated research group within our Biosafety level 3 laboratory.

4.5.2 Hemagglutination inhibition (HAI) assay

A two-fold serial dilution is performed using 50 µl of viral suspension buffer in SALK solution (5%) and 25 µl of glutaraldehyde-fixed guinea pig RBC (1.5%) are added for 1 h incubation at 4°C. HA titer is defined as the last dilution in which the complete hemagglutination is still observed. After titer determination, HAI is performed as follows: 25 µl of reference antisera are added in the first two wells of a 96-well plate. Two-fold dilutions are prepared by adding 25 µl of SALK solution (5%) in the second well. 25 µl are then collected from the same well and the procedure repeated to the end of each line. 25 µl of viral suspension containing 4 HA units are added to the antisera dilution and incubated for 1 h at room temperature. 25 µl of guinea pig RBC are then added to each well. The plates are incubated, then, for 1 h at 4°C. The HAI titer corresponds to the last antiserum dilution for which HA is still inhibited. This titer is compared to the homologous titer obtained with reference strains submitted to their corresponding antigenic antisera (antigenic table). The antigenic tables are influenza strain-specific (Figure 2) and are thereby, adjusted yearly. Since the serum is initially diluted 1/8, the titers provided in figure 2 should be multiplied by 8 to obtain the final titers.

Reference antisera and corresponding viral strains were kindly provided by the World Health Organisation (WHO) Collaborating Centre Reference Laboratory at the Francis Crick Worldwide Influenza Centre (WIC, London, UK). HAIs were performed with glutaraldehyde fixed guinea pig Red Blood Cells (RBC) (Charles River, Lyon, France).

a. H1N1pdm09	A/Brisbane/02/2018	A/Guangdong-Maonan/SWL1536/2019	A/Victoria/2570/2019	A/Denmark/3280/2019
A/Brisbane/02/2018	**64**	1024	<16	32
A/Guangdong-Maonan/SWL1536/2019	1024	**2048**	<16	16
A/Victoria/2570/2019	16	64	**256**	512
A/Denmark/3280/2019	32	256	256	**1024**

b. H3N2	A/England/538/2018	A/Hong Kong/2671/2019	A/Cambodia/e0826360/2020	A/Darwin/9/2021
A/England/538/2018	**512**	64	256	256
A/Hong Kong/2671/2019	256	**512**	512	256
A/Cambodia/e0826360/2020	512	128	**2048**	512
A/Darwin/9/2021	256	128	1024	**1024**

c. B	B/Brisbane/60/2008	B/Washington/02/2016	B/Austria/135941/2021	B/Phuket/3073/2013
B/Brisbane/60/2008	**2048**	128	<16	<16
B/Washington/02/2016	256	**256**	<16	<16
B/Austria/135941/2021	256	<16	**512**	<16
B/Phuket/3073/2013	<16	<16	<16	**1024**

Figure 2. Antigenic tables for the 2021/22 influenza season. These tables correspond to the HI titers of reference influenza strains (first column of the tables) incubated with ferret reference antisera (first row of the tables). The HI titers correspond to the highest dilution where an inhibition is still observed. The titer obtained after incubation of a given strain with the corresponding ferret antiserum is known as the homologous titer (in bold). In red: 2021/22 influenza vaccine strains. a, b and c correspond to A(H1N1pdm09), A(H3N2) and B (Victoria-lineage in orange, Yamagata-lineage in blue) influenza virus antigenic tables, respectively.

4.5.3 Influenza genes sequencing

At the NRCI, a subset of the influenza positive samples were genetically characterized by sequencing the HA 1 part of their HA genes. As HA genes tend to evolve rapidly, comparing HA sequences of the circulating strains with reference sequences, including those from the vaccine strains, allows to evaluate the viral diversity. The HA gene can either be sequenced by Sanger or through whole genome sequencing.

Positive samples, with a Ct value <30, selected for sequencing are processed as follows: 400 µl of the initial respiratory specimens are extracted using the NucliSens easyMAG magnetic bead system (BioMérieux, Geneva, Switzerland)and viral RNA is recovered in 50 µl elution volume. 10 to 12.5ul of RNA are used for the synthesis of cDNA using the SuperScript® II Reverse Transcriptase (Invitrogen, Carlsbad, CA, USA) with influenza-specific primers. HA1 cDNAs are further amplified using strain-specific primers. The amplified products are then sequenced with specific primers using the ABI 3500xL Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). A list of primers used for sequencing analysis is presented in Appendix 1. Similar sequencing procedures are applied for NA, M and NS, and PA genes sequencing but with gene-specific primers (Appendix 1).

HA1, NA, PA, M and NS sequences are edited and stored in the Smartgene ISDN database (SmartGene, Switzerland; www.smartgene.com). Sequences are analysed using the Geneious 6.1.6.[58] The MAFFT v7.017 program is used for sequence alignments and maximum-likelihood trees (Figures 12-14) are estimated using the PhyML programme.[59] Reference sequences used in the phylogenic trees were imported from the Global Initiative on Sharing Avian Influenza Data (GISAID) platform (http://platform.gisaid.org, restricted access). Whole genome sequencing for influenza A and B.

Whole genome sequencing of influenza is performed by Microsynth AG. Influenza A and B segments are pre-amplified using, for influenza A[60], a mix of two forward primers and a single reverse primer located in the conserved regions of the viral genome segments; and for influenza B[61], a primer cocktail of 13 different forward and reverse primers. Libraries were prepared using Illumina Nextera kits and were then run on the Illumina platform MiSeq using ≥2*150 reads. Data is quality-filtered and de-multiplexed by Microsynth AG before being sent to the NRCI for in-house sequence analysis. The best sequencing results are obtained for samples with Ct values <25.

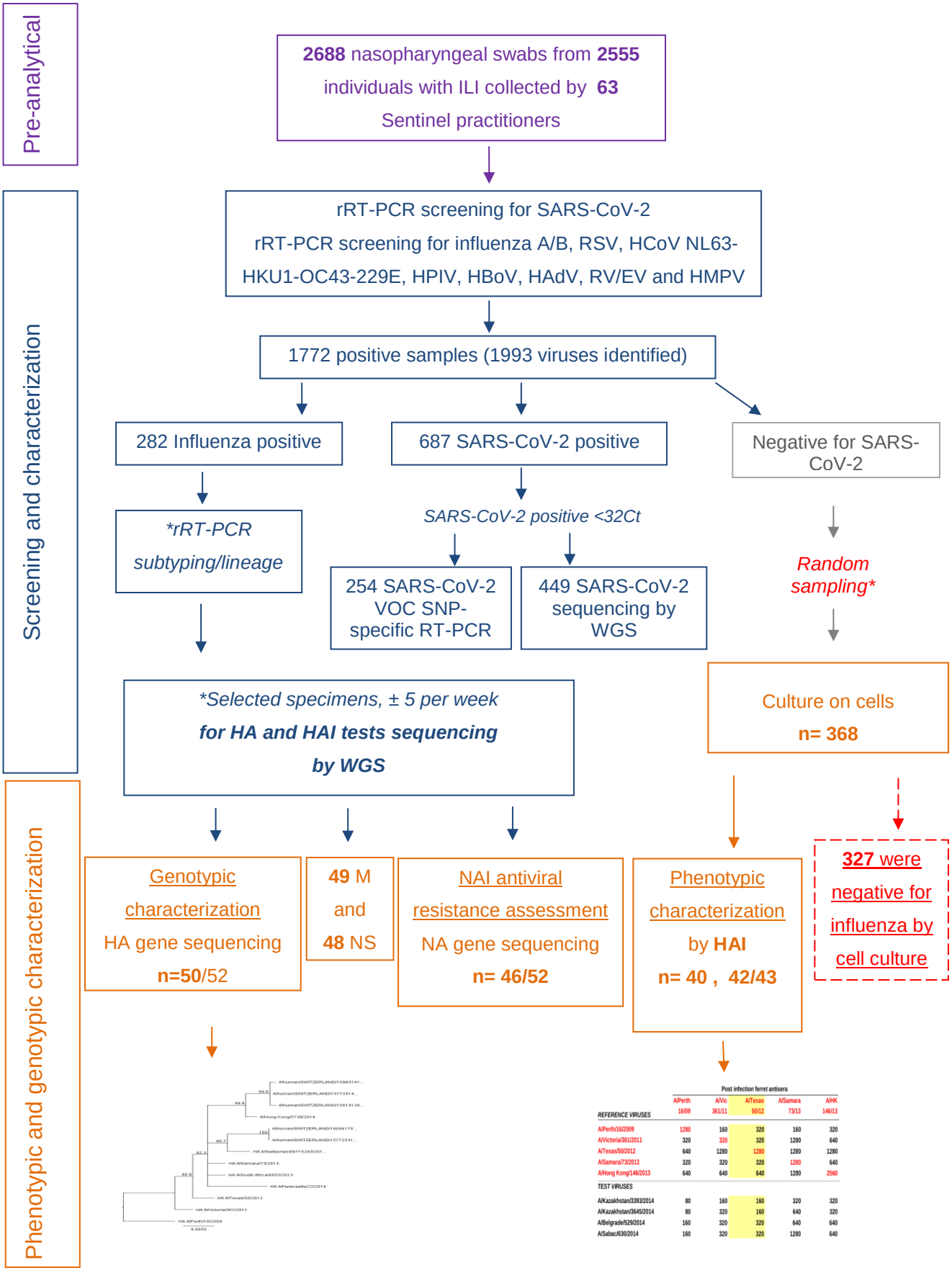


Figure 3. Flow chart of Sentinel samples collection and processing. Starting end of April 2021, only influenza positive and negative samples that were also negative for SARS-CoV-2 were submitted to cell culture. Subtyping, antigenic and genetic characterizations were only performed for influenza virus.

5 2021/2022 surveillance period

Data gathered in the present report corresponds to Sentinel samples received at the NRCI from April 24th 2021 (week 17/2021) to April 22nd 2022 (week 16/2022).

5.1 Population demographics

5.1.1 Annual NRCI surveillance (2021/2022)

From week 17/2021 to week 16/2022, 2555 individuals were sampled by 63 sentinel practitioners for further screening at the NRCI. Among those, 1336 (52.3%) were women and 1219 (47.7%) were men. Fifty-three men and sixty-five women were sampled twice. One man and three women were tested at least 3 times each during the surveillance period (Table 1).

5.1.2 Stratification by sex and age

Data on age was available for all individuals (median 37 years old, range [0 to 97 years]; 95% confidence interval (CI), 36-38 years old). Median age was 35 years old for males (range [0 days to 96 years]; 95% CI, 34-36 years old) and 39 years old for females (range [0 to 97 years]; 95% CI, 38-40 years old) (Figure 4). When further stratifying the population by age groups (i.e. 0-4, 5-14, 15-29, 30-64 and ≥65 years old), a slightly higher percentage of males in the 0-4 years old group and of females in the 15-29 and 30-64 groups could be observed (Table 1). The age distribution by sex was similar in-between male and female (Figure 4).

Table 1: Age and sex distribution of the tested Sentinella population, from weeks 17/2021 to 16/2022

	Male	*Female*	*Total*
Number of individuals	1219	1336	2555
Age group distribution			
0-4	148	110	258
	12.1%	*8.2%*	*10.1%*
5-14	142	115	257
	11.6%	*8.6%*	*10.1%*
15-29	227	275	502
	18.6%	*20.6%*	*19.6%*
30-64	528	623	1151
	43.3%	*46.6%*	*45.1%*
≥65	174	213	387
	14.3%	*15.9%*	*15.1%*

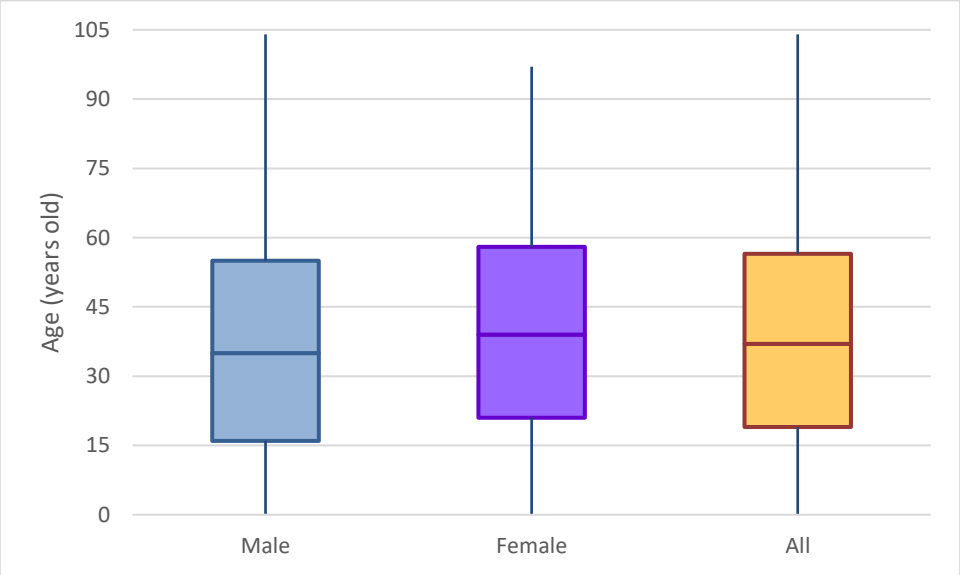


Figure 4. Age distribution by sex of the tested Sentinel population, from weeks 17/2021 to 16/2022. Distribution pattern for the entire population. Median ages and 25% and 75% quartiles are shown.

5.2 Detection of respiratory viruses in nasopharyngeal samples

From week 17/2021 to week 16/2022, 2688 nasopharyngeal samples (NPS) were screened by rRT-PCR for influenza, SARS-CoV-2, RSV, HCoV NL63, HCoV HKU1, HCoV OC43, HCoV 229E, HPIV, HBoV, HAdV, RV/EV and HMPV.

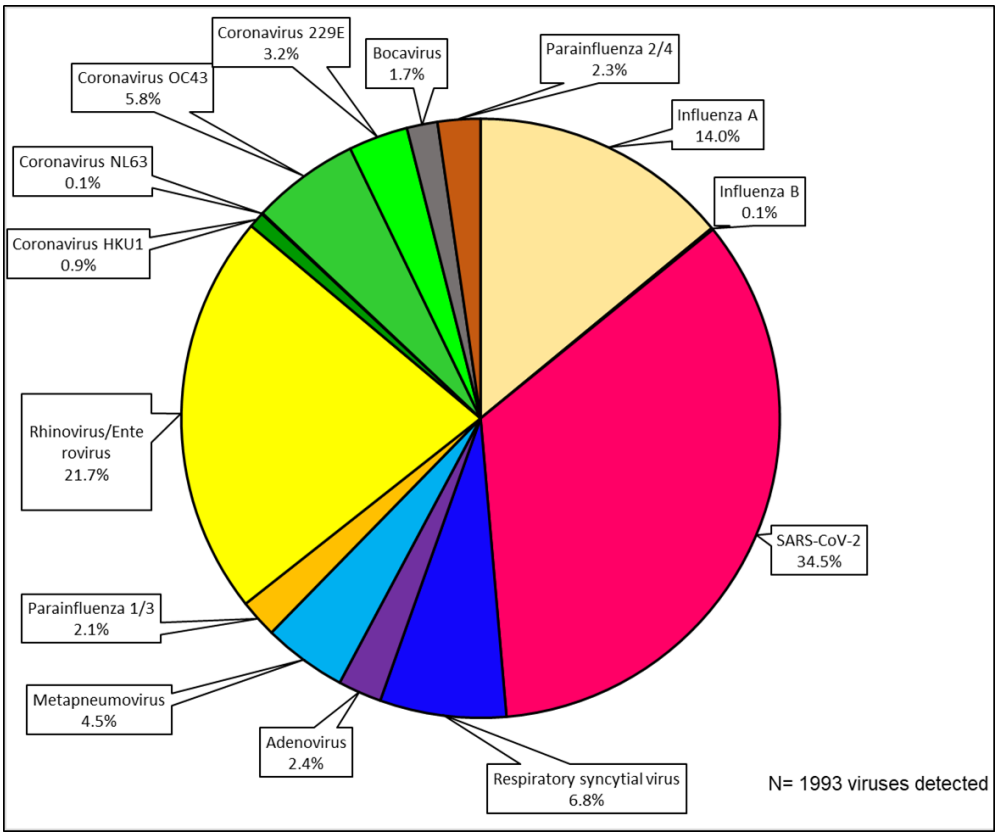
One thousand seven hundred and seventy-two samples (65.9%) were positive for at least one respiratory virus and 1993 viruses in total were detected. Among these, the following pathogens were detected: 687x SARS-CoV-2 (34.5%), 433x RV/EV (21.7%), 280x influenza A viruses (14%), 136x RSV(6.8%), 116x HCoV OC43 (5.8%), 90x HMPV (4.5%), 64x HCoV 229E (3.2%), 47x HAdV (2.4%), 46 HPIV 2/4 (2.3%), 41x HPIV 1/3 (2.1%), 33x HBoV (1.7%), 17x HCoV HKU1 (0.9%), 1x HCoV NL63 (0.05%), and two influenza B viruses (0.1%) (Figure 5a).

During the seasonal surveillance 2021/2022, we observed a maximum positivity rate of 81.9% during week 10/2022, that was close to the peak of ILI consultations for 2021/2022 in Switzerland (Appendix 2) and a minimum positivity rate of 36.7% during week 43/2021 (median positivity rate : 64.1%, range [36.7 to 81.9%]; 95% CI (63.6-64.6 %)) (Figure 5b).

SARS-CoV-2, RV/EV, RSV and HMPV, and other human coronaviruses were detected throughout the surveillance period. Similarly to data originating from the national mandatory SARS-CoV-2 reporting, a sharp increase in SARS-CoV-2 positive samples could also be seen in the Sentinel surveillance network starting at week 45/2021. A significant increase in HCoV 229E and HCoV OC43 detections could be observed from week 46/2021 to week 5/2022. While HPIV2/4 and HPIV1/3 were initially sporadically detected, they started to increase in prevalence beginning week 33/2021 and 13/2022, respectively (Figure 5b). Since week 44/2021, we observed a large increase in viruses detection, mainly due to the emergence of seasonal influenza.

From week 17/2021 to week 16/2022, more than one virus was detected in 201 (11.3%) out of 1772 positive samples (Appendix 3). The highest number of co-detections (16) was observed in week 10/2022, which correlates with the highest positivity rate during the surveillance period (figure 5b). Not surprisingly, among the 201 co-detections, 108 concerned SARS-CoV-2 (53.7%); which was mostly observed with coronaviruses 229E or OC43 (30.6%), influenza A viruses (29.6%), and with RV/EV (21.3%). Of note, viral loads for coronaviruses 229E and OC43 were often low when SARS-CoV-2 was also present (Data not shown).

a.



b.

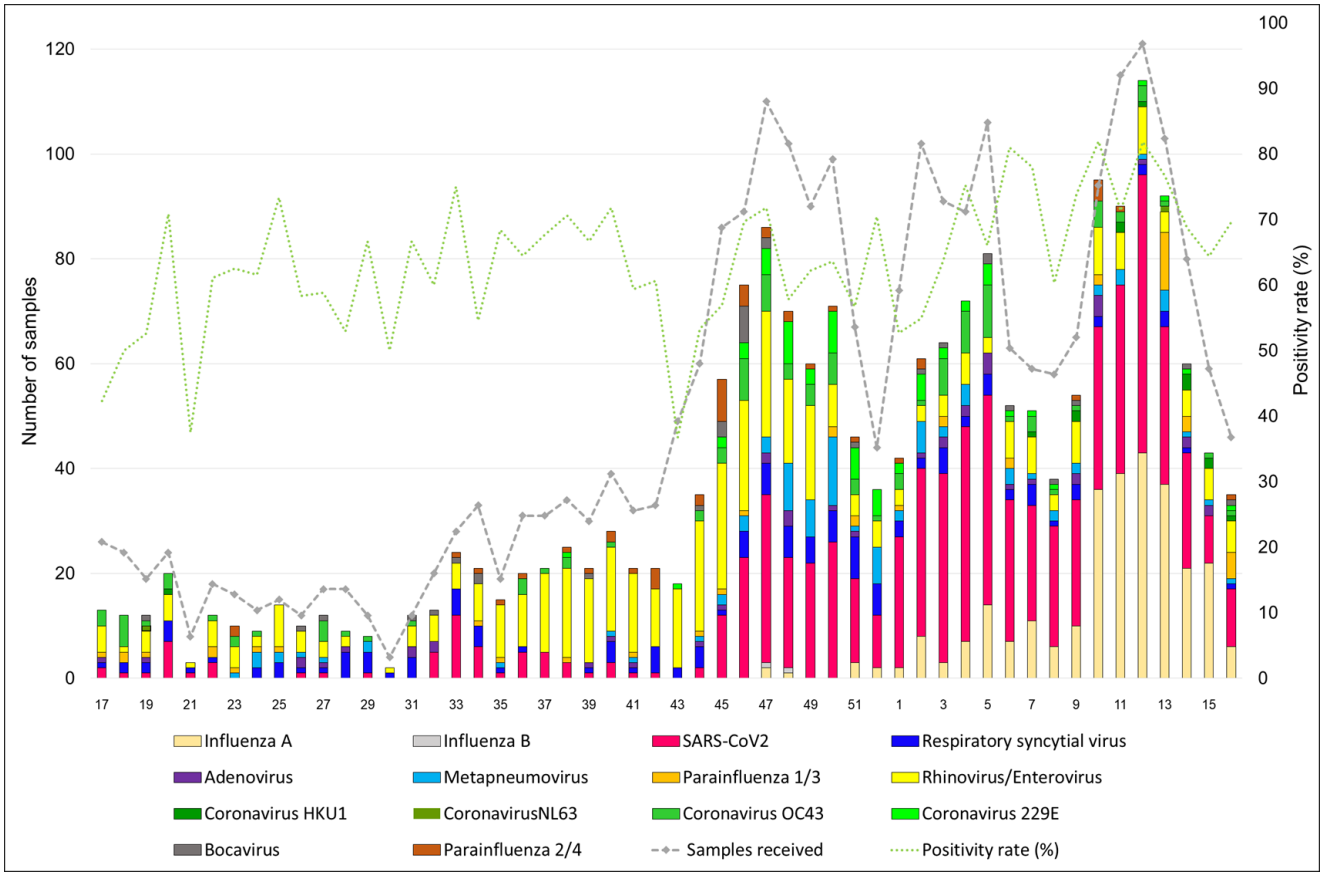
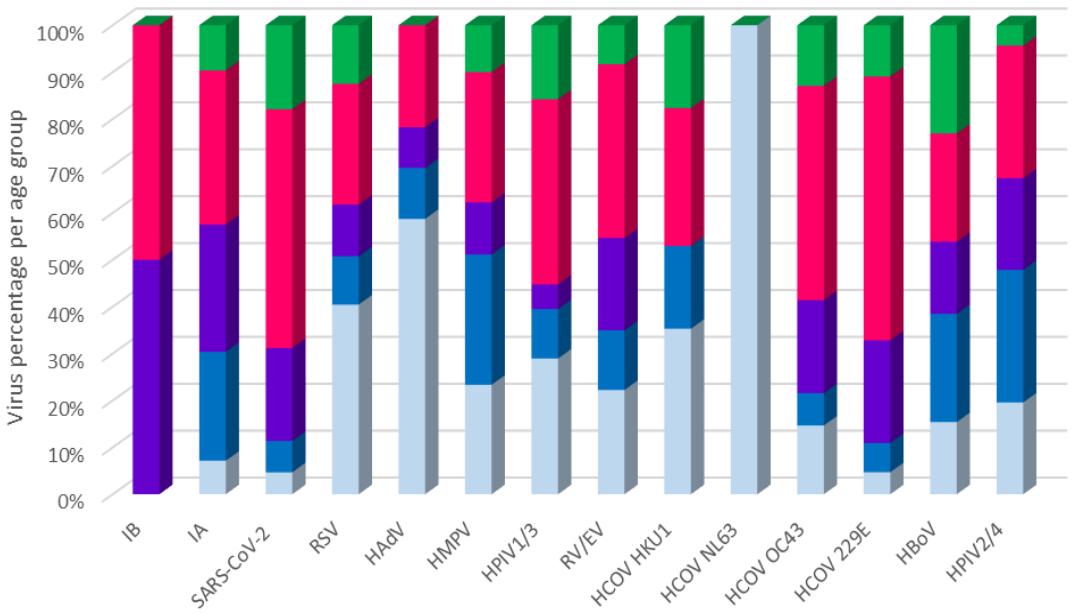


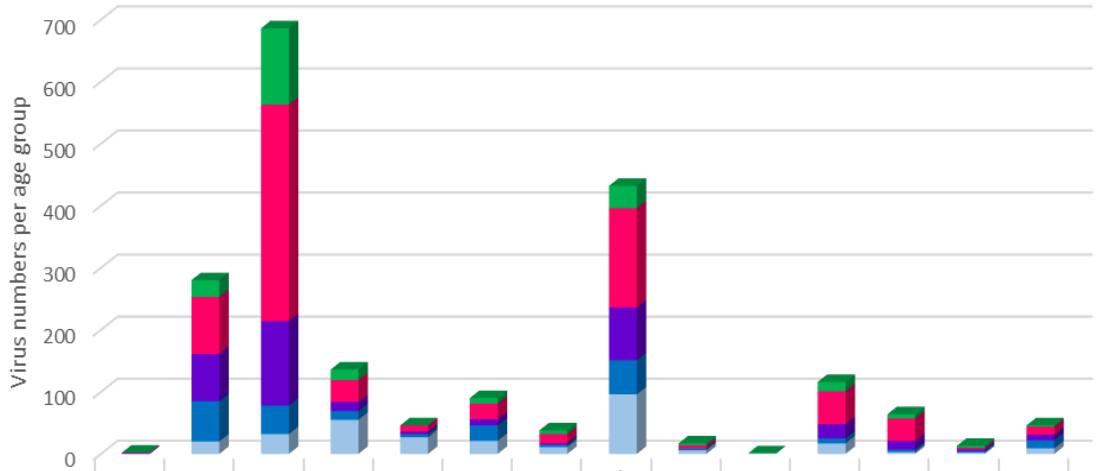
Figure 5. Percentage and temporal distribution of respiratory viruses detected in NPS collected from week 17/2021 to 16/2022. a. Percentages of the different respiratory viruses (N=1993) detected in 2688 NPS. **b**. Distribution of the samples tested and the detected pathogens throughout the surveillance period. Positivity rate is based on the number of positive samples per total number of samples received each week.

When stratifying positive samples by age groups, we observed that a majority of HAdV, RSV and HCoV HKU1 were found in infants and toddlers (Figure 6a,b). Indeed , in the 0-4 year-old group, they represented 58.7%, 40.4% and 35.3%, of the observed viruses respectively (Figure 6a). The only HCoV NL63 positive sample detected this season was also observed in the 0-4 year-old group. HMPV and HPIV2/4 were frequent in older children and teens, in whom they accounted for 45-50% of the positive samples. SARS-CoV-2 positives samples were present mostly in adults (Figure 6b) with 50.9%, 19.8% and 17,9% for the 30-64, 15-29, and ≥65 year-old groups, respectively. The 0-4 and 5-14 age groups accounted for 4.7% and 6.7% of the positive SARS-CoV-2 samples, respectively. Interestingly, the age groups distribution for HCoV 229E positive samples was similar to that of SARS-CoV-2. Influenza A virus was present mostly in the 30-64, 15-29, and 5-14 year-old groups, corresponding to 32.9%, 27.1%, and 23.2%, respectively. One influenza B virus was observed in the 15-29 years old group and the other in 30-64 years old group. RV/EV, HCoV OC43, HPIV1/3and more surprisingly HBoV, positive samples were more evenly detected throughout the age groups.

a.



b.



	IB	IA	SARS-CoV-2	RSV	HAdV	HMPV	HPIV1/3	RV/EV	HCOV HKU1	HCOV NL63	HCOV OC43	HCOV 229E	HBoV	HPIV2/4
≥65	0	27	123	17	0	9	6	36	3	0	15	7	3	2
30-64	1	92	349	35	10	25	15	160	5	0	53	36	3	13
15-29	1	76	136	15	4	10	2	85	0	0	23	14	2	9
5-14	0	65	46	14	5	25	4	55	3	0	8	4	3	13
0-4	0	20	32	55	27	21	11	96	6	1	17	3	2	9

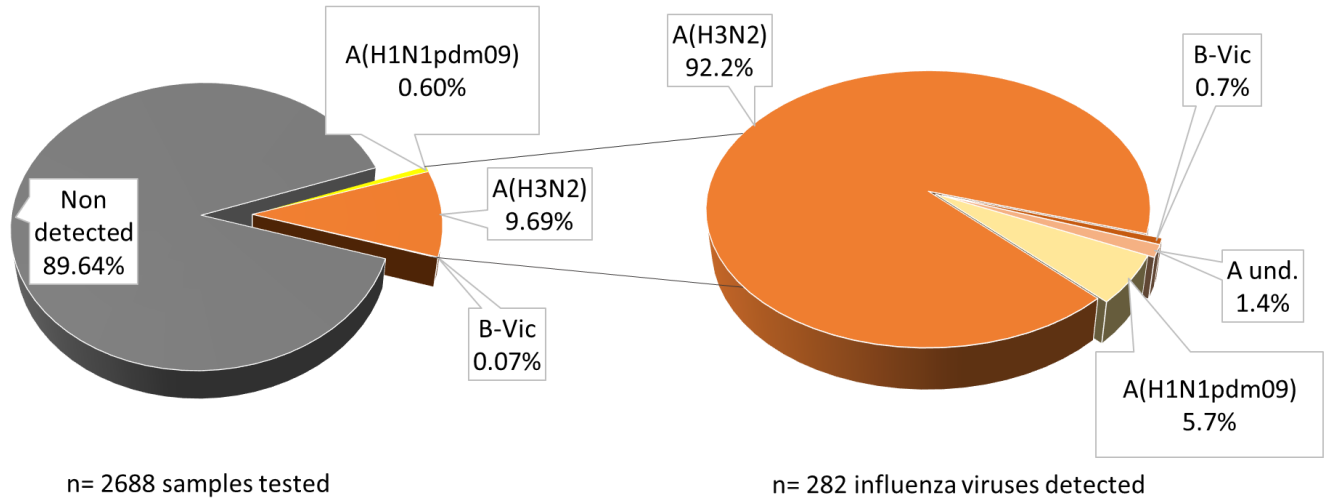
Figure 6. Respiratory viruses distribution: a. per age group in percent **b.** in absolute numbers of positive samples.

5.3 Detection of influenza in nasopharyngeal samples

Among the 2688 samples tested, we identified 280 influenza A viruses (14%) and 2 influenza B viruses (0.1%) (Figure 5a). A majority of 260 (92.2%) samples were subtyped as A(H3N2) and 16 (5.7%) as A(H1N1)pdm09 (Figure 10a). Four (1.4%) influenza A viruses could not be subtyped due to low viral load (Figure 7a).The two influenza B viruses identified, which represented only 0.7% of the influenza-positive samples, belonged to the B-Victoria lineage (Figures 5a and 7a).

During the sentinel surveillance from week 17/2021 to week 16/2022, the first influenza case was detected in week 47/2021. The two cases of influenza B were identified in week 47 and 48/2021, respectively. The median positivity rate for influenza was about 10.3%, range [0 to 38.3%]; 95% CI (4.8-15.9%) (Figure 7b), with a peak at 38.3% during week 10/2022, which is also consistent with the maximum positivity rate for the respiratory viruses surveillance and close to the peak of ILI consultations in week 10/2022 (Appendix 2).

a.



b.

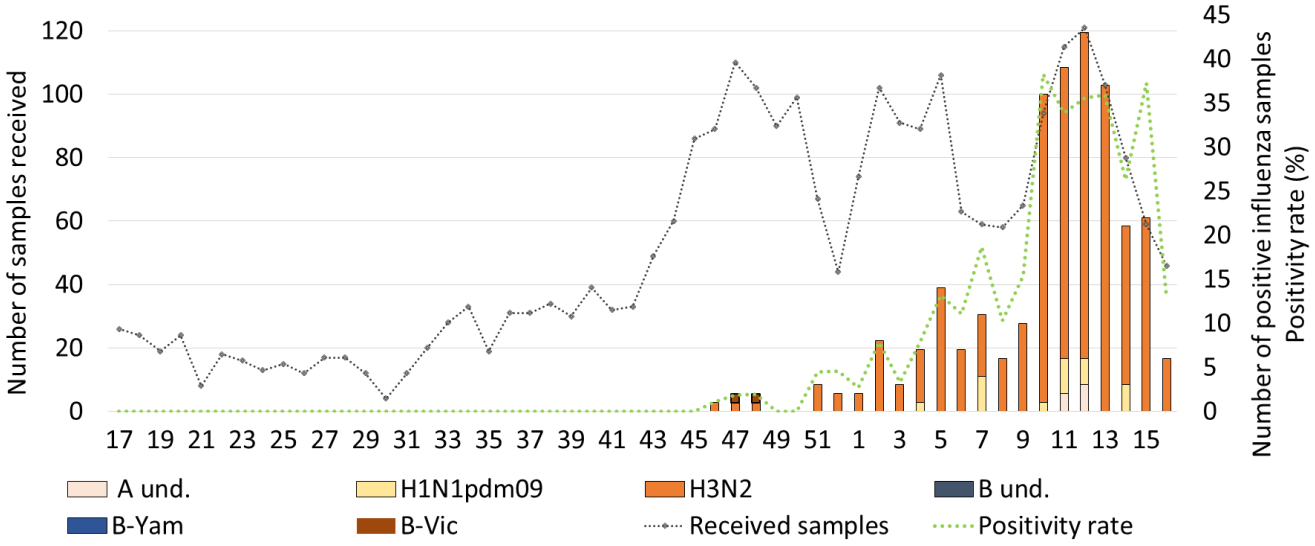


Figure 7. Percentage and temporal distribution of Influenza viruses detected in NPS collected from week 17/2021 to 16/2022. a. Percentages of influenza viruses, subtypes (FluA) and lineages (FluB). **b.** Distribution of the detected influenza viruses throughout the surveillance period. Influenza viruses typing and subtyping done by real-time rRT-PCR. A und. and B und.: influenza A and B viruses that could not be further subtyped. H1N1pdm09 and H3N2 refer to influenza A(H1N1)pdm09 and influenza A(H3N2), respectively. B-Yam: influenza B virus of Yamagata lineage. B-Vic: influenza B virus of Victoria lineage. Positivity rate is based on the number of weekly positive influenza samples per the number of samples received each week.

5.4 SARS-CoV-2 and influenza viruses characterisation (17/2021 to 16/2022)

5.4.1 SARS-CoV-2 variants identification and genetic analysis

SARS-CoV-2 positive samples identified from week 17/2021 to week 16/2022, with Ct values lower than 32, were further characterized by sequencing. The 254 sequenced samples, which were all submitted to GISAID, fell into 24 distinct Pangolin[62] lineages

(Table 2). One hundred sequences were identified as belonging to VOC Delta and 144 samples were attributed to VOC Omicron (Table 2). They represented, respectively, 39.4% and 56.7% of the sequenced samples. Nine VOC alpha (3.5%) and only one P1 lineage from VOC Gamma (0.4%) were detected in 2021. Primary cases of VOC Delta (B.1.1.617.2) and VOC Omicron were detected in Switzerland beginning April and December 2021, respectively.

As the sequencing time-to-results was over one week, and our national contact tracing strategy required variants' identification within 24 hours upon SARS-CoV-2 laboratory confirmation, all SARS-CoV-2 positive cases with Ct value <32 were also screened using an rRT-PCR targeting VOC-specific mutations in the spike gene. First detected in South Africa on 9 November 2021, VOC Omicron (B.1.1.529), carrying many more mutations than its predecessor, replaced the VOC Delta and became the major sequence worldwide and the most prevalent within the Sentinel surveillance starting from week 52/2021.

Later, the detection failure of the S target (S drop out) of a multiplex rRT-PCR detecting S, N and Orf1ab of SARS-CoV-2 was used as a proxy for detection of SARS-CoV-2 VOC Omicron. Since systematic screening for the S drop out was implemented on November 27 2021 to discriminate between VOC Omicron (BA.1, BA.1.1) and Delta, 367 samples were tested using this strategy (Data not shown). The S gene could not be detected for 92 samples (25.1%), which were therefore classified as VOC Omicron, while waiting for whole genome sequencing confirmation.

Table 2. List of the different SARS-CoV-2 Pangolin lineages within which Sentinel isolates were distributed

Pangolin[1] lineages (VOC)	Number of isolates	Pangolin lineages (VOC)	Number of isolates
AY.102 (Delta)	1	AY.46.6 (Delta)	10
AY.108 (Delta)	2	AY.7.1 (Delta)	1
AY.12 (Delta)	10	AY.9 (Delta)	3
AY.121 (Delta)	1	AY.9.2 (Delta)	2
AY.122 (Delta)	3	AY.98 (Delta)	1
AY.122.1 (Delta)	1	B.1.1.529 (Omicron)	1
AY.126 (Delta)	1	B.1.1.7 (Alpha)	9
AY.21 (Delta)	1	B.1.617.2 (Delta)	11
AY.39 (Delta)	1	BA.1 (Omicron)	52
AY.4 (Delta)	26	BA.1.1 (Omicron)	40
AY.43 (Delta)	20	BA.2 (Omicron)	51
AY.46 (Delta)	5	P1 (Gamma)	1
N	254		

[1] Web-based lineage assessment: https://github.com/cov-lineages/pangolin

5.4.2 Antigenic and genetic characterization of influenza viruses

Cell culture on MDCK and MDCK-SIAT1 cells was attempted on 368 negative-SARS-CoV-2 samples. Of note, SARS-CoV-2 was shown not to replicate in MDCK and MDCK-SIAT1 cells.[63,64]

Amongst the 368 samples, 78 were known to be influenza positive, but only 43 grew on MDCK and/or MDCK-SIAT cells. Forty-two of them further underwent antigenic characterization using the HAI assay. Forty-one out of 42 were antigenically characterized (Figure 8).

Fifty two samples were submitted for genetic characterization. Fifty out of 52 HA sequences were successfully recovered. Among these, 43 were A(H3N2), 5 A(H1N1)pdm09 and 2 B-Victoria (Figures 9-11). Forty-six NA sequences were successfully recovered: 40 were A(H3N2), 4 A(H1N1)pdm09, and two B-Victoria (Data not shown). Twenty samples were shared with the WIC for additional analysis and characterization. Corresponding phenotypic results are available in Appendixes 5-6; phylogenic results in Appendixes 7-12 and antiviral resistance assessment in Appendix 13.

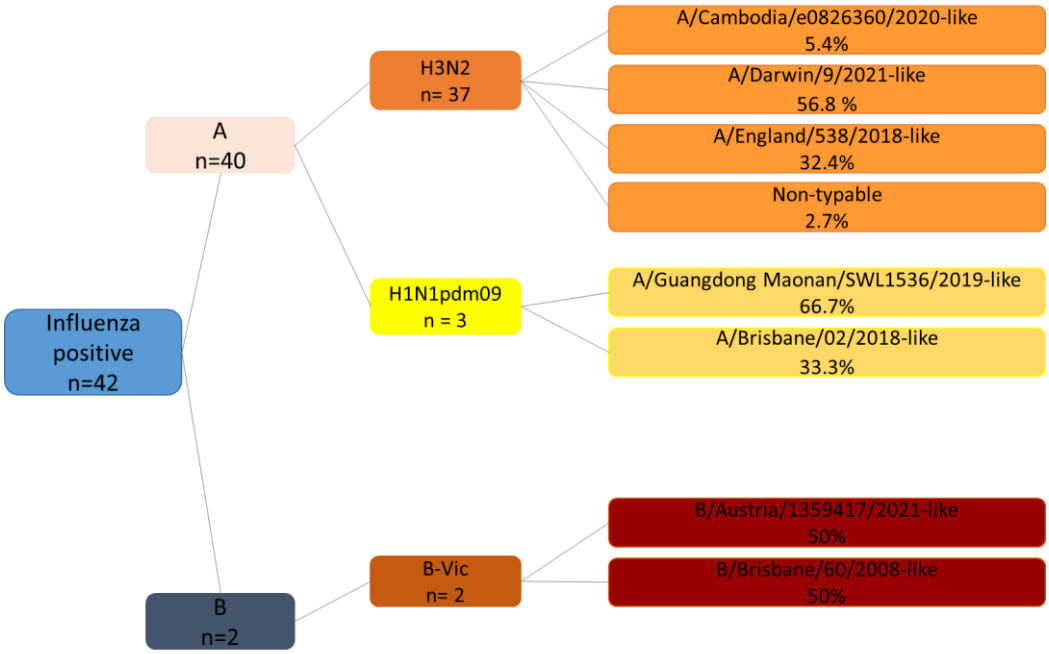


Figure 8. Antigenic characterization by HAI assay of selected influenza viruses isolated through the 2021/2022 season.

5.4.2.1 Characterization of influenza A(H3N2) viruses

As for previous years, the WIC reported that antigenic characterization of A(H3N2) viruses can be difficult by HAI assay due to variable agglutination of red blood cells (RBC) from guinea pigs and presence of NA-mediated agglutination of RBC. Interestingly, currently circulating A(H3N2) viruses of the genetic group, 3C.2a1b.2a.2, seemed to have regained the ability to bind to guinea pig RBCs. However, viruses belonging to genetic clade 3C.2a1b, continue to fail to agglutinate RBCs.

37 A(H3N2)(97.3%) were characterized by HAI. Two isolates reacted well with the antiserum against A/Cambodia/e0826360/2020 (recommended vaccine 2021/2022), 21 isolates were well recognized by antiserum raised against A/Darwin/9/2021 (recommended vaccine strain southern hemisphere 2022), and 12 isolates were poorly (≥8-fold titres reduction compared to the homologous) recognized by both the A/Cambodia/e0826360/2020 and A/Darwin/9/2021 reference antisera, but showed reactivity within 2- to 4-fold the homologous titer in presence of the antiserum raised against an A/England/538/2018 virus, a “recent” 3C.3a1. One isolate could not be further characterized due to the low titers obtained (Figure 8).

Twelve out of the 18 influenza A viruses sent to the WIC were recovered and characterized successfully. All samples showed good recognition by antisera raised against the cell culture-propagated reference virus A/Stockholm/5/2021 and cell culture-propagated A/Bangladesh/4005/2020, respectively. Eleven out of 12 viruses, all 3C.2a1b.2a.2, were recognized at reasonable levels by the antiserum raised against egg-propagated A/Darwin/9/2021. All viruses were poorly recognized by the antiserum raised against the egg-propagated A/Cambodia/e0826360/2020 (subclade 3C.2a1b.2a.1, 2021/2022 vaccine strain); and the antiserum raised against cell culture-propagated A/Cambodia/925256/2020 only recognized A/Switzerland/51230/2021 (3C.2a1b.1a) and A/Switzerland/42321/2021 (3C.2a1b.2a.2). None of the test viruses reacted with the antiserum raised against the cell culture-propagated cultivar A/Hong Kong/2671/2019 (subclade 3C.2a21b.1b). The antiserum raised against A/Denmark/3264/2019 (subclade 3C.2a1b.1a) recognised the 3C.2a1b.1a virus A/Switzerland/51230/2021 poorly. However, the latter reacted well with 5 of the 3C.2a1b.2a.2 viruses. As expected, all viruses were poorly recognised by the antiserum raised against the cell culture-propagated cultivar of the former vaccine virus A/Kansas/14/2017 (Appendix 5).

At the genetic level, 43 A(H3N2) HA1 (Figure 9) and 40 NA (A(H3N2)) (Data not shown) sequences were successfully recovered. Forty-two fell into the genetic group 3C.2a1b.2a.2 (A/Bangladesh/4005/2020) and carried this subclade typical substitutions: Y159N, T160I, L164Q, G186D and D190N in HA1. We observed several sub-clusters characterised by specific mutations within the 3C.2a1b.2a.2 subclade (Figure 9). However, one isolate, the A/Switzerland/51230/2021 virus clustered into the 3C.2a1b.1a subclade (A/Denmark/3264/2019) and exhibited T131K, G186D, D190N,S198P, and R207K substitutions in HA1, with some viruses also having S205F or I192F substitutions in HA1.

The HA and NA genes of 14 of the 17 A(H3N2) isolates sent to the WIC were recovered successfully. Thirteen out of 14 viruses had HA genes belonging to subclade 3C.2a1b.2a.2, while the remaining virus' HA gene belonged to subclade 3C.2a1b.1a. The HA gene of the 3C.2a1b.1a virus, A/Switzerland/51230/2021, encoded substitutions T131K, I192F and R207K in HA1 both at the WIC and NRCI. SubstitutionI58V was only observed by the WIC .Indeed, at the NRCI, both Sanger and WGS A/Switzerland/51230/2021 HA gene had I58 residue. The latter virus clustered

with A/Denmark/3264/2019. Two viruses (A/Switzerland/69954/2021 and A/Switzerland/28536/2022) clustered close to A/Bangladesh/4005/2020 but encoded the additional substitutions S205F and A121T in HA1. The other eleven viruses shared the amino acid substitution H156S in HA1 with the vaccine viruses A/Darwin/6/2021 and A/Darwin/9/2021 and the reference virus A/Stockholm/5/2021. Seven also had the substitutions: D53N, N96S, I192F in HA1 and N49S in HA2 (N378S) (Appendix 7). The NA genes clustered in a similar fashion (Appendix 8).

The genetic characterisation and subsequent cluster/sub-cluster attribution for the different Swiss A(H3N2) isolates analysed by both the NRCI and the WIC was concordant (Figure 9; Appendixes 7-8).

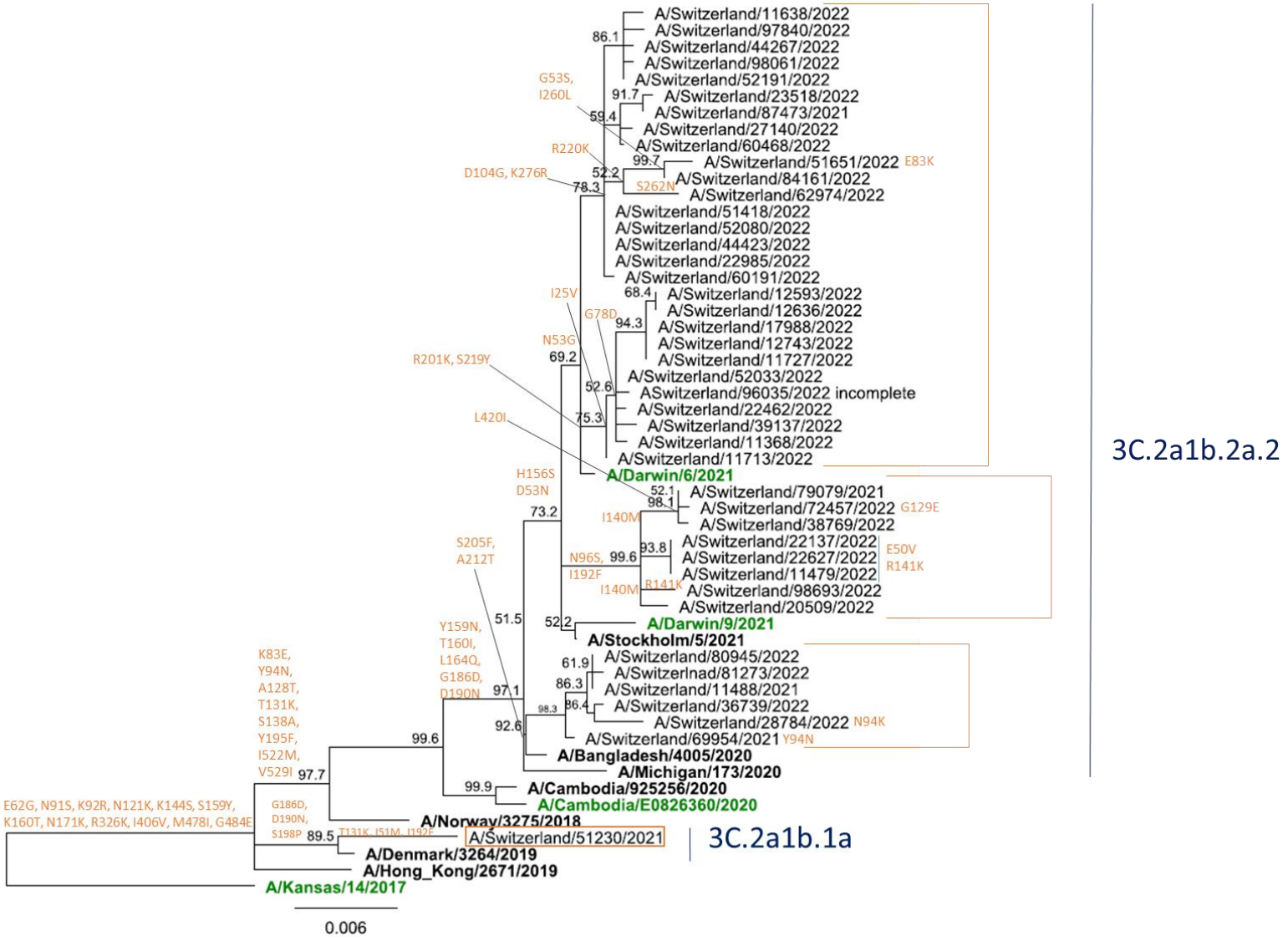


Figure 9. Phylogenetic analysis of the HA1 gene of A(H3N2) viruses. Black: influenza viruses detected in the Sentinel network during the 2021/2022 season. Green: vaccine strains for NH 19/20 A/Kansas/14/2017, 21/22 A/Cambodia/E0826360/2020, SH 22 A/Darwin/9/2021 (egg-based), SH 22 A/Darwin/6/2021 (cell-based). Bold: reference strains. Orange: some typical substitutions characterizing the respective clusters described by the WIC and Nexclade V.1.14.1. Blue: genetic groups/sub-groups. Sequences were aligned using Geneious 6.1.8 MAFT alignment (v7.017) with default settings. A consensus tree was built from 1000 original trees in maximum likelihood (70% support threshold) using Geneious 6.1.8 PHYML default settings.

5.4.2.2 Characterization of influenza A(H1N1pdm09) viruses

Among the 41 isolates successfully characterized by HAI assay, 3 were A(H1N1)pdm09 viruses. Two of these isolates were well recognized by the reference antiserum directed against the egg-based vaccine strain 2020/2021 A/Guangdong Maonan/SWL1536/2019, but reacted poorly with the antiserum raised against the recommended egg-based vaccine strain 2021/2022 A/Victoria/2570/2019. One isolate was well recognized by the antiserum raised against the A/Brisbane/02/2018 virus (egg-based recommended vaccine 2019/2020) but showed a reduction of reactivity within 8 to 32-fold in presence of the antiserum raised against the recommended egg-based vaccine strain 2021/2022 A/Victoria/2570/2019 and the vaccine strain 2020/2021 A/Guangdong Maonan/SWL1536/2019 (Figure 8). No A(H1N1)pdm09 isolates were available to be sent to the WIC in February 2022.

At the genetic level, 5 HA1 and 4 NA genes were successfully sequenced (Figure 10; data not shown). All A(H1N1)pdm09 sequenced at the NRCI fell into the 6B.1A.5a.1 subclade (A/Guangdong-Maonan/SWL1536/2019) and carried the typical amino acid substitutions D187A and Q189E in HA1 related to this subgroup (Figure 10).

According to the WIC reports for 2021/2022[65], most of the currently circulating A(H1N1)pdm09 tested were attributed to a subgroup of the 6B.1A.5a subclade(Appendixes 9-10). This is concordant with what we observed at the NRCI.

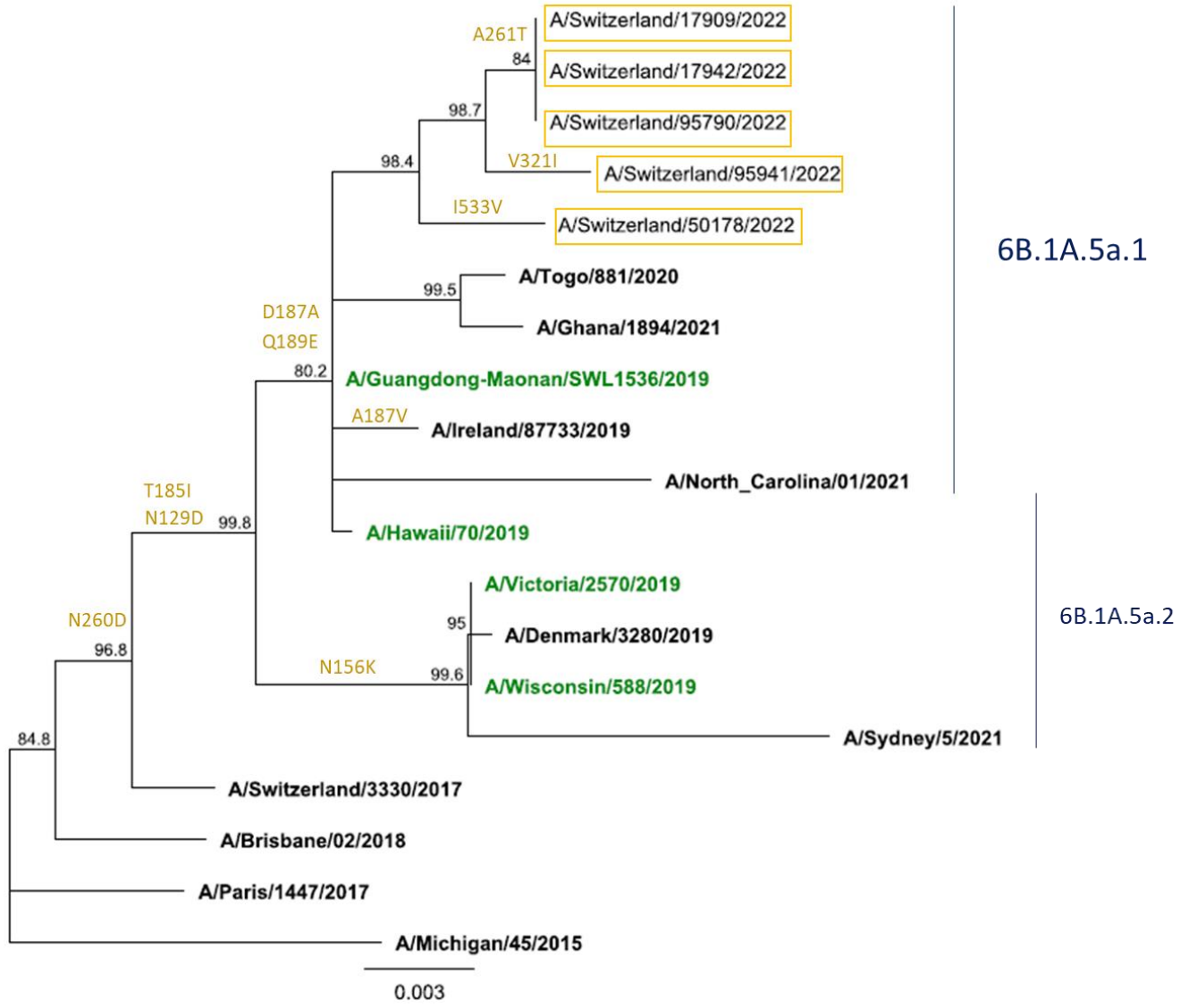


Figure 10. Phylogenetic analysis of the HA1 gene of A(H1N1)pdm09 viruses. Black: influenza viruses detected in the Sentinel network during the 2021/2022 season. Green: vaccine strains for 2020/2021 A/Guangdong-Maonan/SWL1536/2019 (egg-based), 2020/2021 A/Hawaii/70/2019 (cell-based), 2021/2022 A/Victoria/2570/2019 (egg-based), 2021/2022 A/Wisconsin/588/2019 (cell-based). Bold: reference strains. Yellow: some typical mutations characterizing the respective clusters described by the WIC and Nexclade V.1.14.1. Blue: genetic groups/sub-groups. Sequences were aligned using Geneious 6.1.8 MAFT alignment (v7.017) with default settings. A consensus tree was built from 1000 original trees in maximum likelihood (70% support threshold) using Geneious 6.1.8 PHYML default settings.

5.4.2.3 Characterization of influenza B(Victoria) viruses

Only two B/Victoria viruses were identified by the NRCI from week 17/2021 to week 16/2022. They were both characterized by HAI assay. One isolate reacted poorly with the reference antisera raised against the recommended vaccine 2020/2021 B/Washington/02/2019 (subclade V1A.3) strain but was recognized at titers within 2- to 4-fold the homologous titer by the B/Brisbane/60/2008 (recommended vaccine 2018) antiserum. The other isolate reacted well with the antiserum raised against B/Austria/1359417/2021 virus (recommended vaccine southern hemisphere 2022, subclade V1A.3a.2) (Figure 11).

The 2 isolates analyzed by the WIC were recognized at titers equal to and 2-fold lower than the homologous titers of the antisera raised against, respectively, the cell culture-propagated and an “early”- egg-propagated cultivar of B/Austria/1359417/2021. In contrast, the antiserum raised against the egg-propagated former vaccine virus B/Washington/02/2019 recognized both test viruses poorly. B/Switzerland/11488/2021 and B/Switzerland/57945/2021 reacted at titers only 4-fold lower than the homologous titer of the antiserum raised against the Δ162-163 variant of the egg-propagated former vaccine virus B/Colorado/06/2017. The antiserum raised against the Δ162-163 variant of the (subclade V1A.1) egg-propagated former vaccine virus B/Colorado/06/2017 also recognised B/Switzerland/11488/2021 and B/Switzerland/57945/2021 at titers only 4-fold lower than the homologous titre of the antiserum (Appendix 6).

Sequence analysis of the HA gene and the NA gene on the both isolates has been carried out (Figure 11; data not shown; appendixes 11-12). Similar to the WIC results, both B-Victoria viruses clustered in the V1A.3a.2 subclade (B/Austria/1359417/2021), but in the group carrying the HA1 substitution D197E (Figure 11; appendixes 11-12).

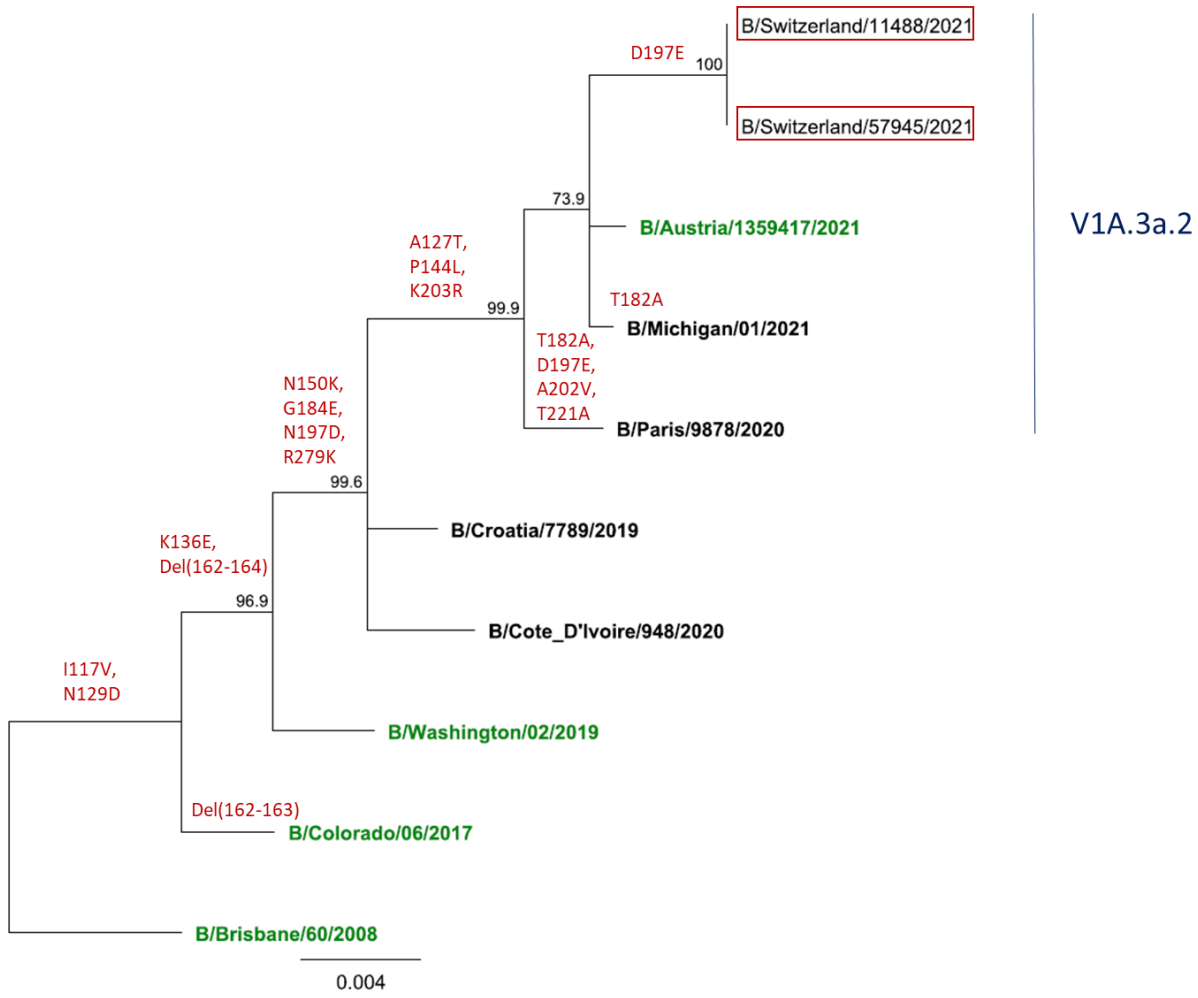


Figure 11. Phylogenetic analysis of the HA1 gene of B-Victoria viruses. Black: influenza viruses detected in the Sentinel network during the 2021/2022 season. Green: vaccine strains for 2012-18 B/Brisbane/60/2008, 19/20 B/Colorado/06/2017, 2020-22 B/Washington/02/2019, and 22/23 B/Austria/1359417/2021. Bold: reference strains. Red: some typical mutations characterizing the respective clusters described by the WIC V.1.14.1. Blue: genetic groups/sub-groups. Sequences were aligned using Geneious 6.1.8 MAFT alignment (v7.017) with default settings. A consensus tree was built from 1000 original trees in maximum likelihood (70% support threshold) using Geneious 6.1.8 PHYML default settings.

5.4.3 Antiviral resistance

Fifty-two viruses (45 A(H3N2), 5 A(H1N1)pdm09, and 2 B-Victoria) were submitted to NA, and PA gene sequencing analysis to search for the antiviral resistance-associated mutations. None of the 46 isolates successfully sequenced for PA displayed any mutations associated with a decreased susceptibility to Baloxavir marboxil (Data not shown) and none of these isolates displayed any mutations in the NA gene associated with decrease susceptibility to neuraminidase inhibitors (Data not shown). Phenotypic tests for antiviral resistance assessment were not performed at the NRCI.

Fourteen (12 A(H3N2), 2 B-Victoria) of 20 sentinel influenza viruses sent to the WIC had sufficient neuraminidase activity and were therefore eligible for phenotypic antiviral resistance testing. They were all sensitive to both oseltamivir and zanamivir (Appendix 13).

Of note, one non-sentinel influenza A/H3N2 sample, originating from a hospitalized patient not improving under oseltamivir treatment, exhibited the E119V substitution in the NA (Data not shown).

5.4.4 Whole genome sequencing of Influenza A and B

The National Influenza Centre collaborates with Microsynth AG for whole genome sequencing (WGS) of Influenza A and B viruses. SARS-CoV-2 sequencing is also possible at Microsynth AG but for 2021/2022, it was mainly performed though the National genomic SARS-CoV-2 surveillance program, a collaborative project with the Genome Centre in Geneva. Fifty-two influenza positive samples were submitted to WGS.

WGS protocols of Zhou *et al*.[60,61] were applied to 50 IA (both subtypes) and 2 IB (B-Victoria lineage) samples with Ct values <29 (Table 3). Whereas complete or near complete sequences were obtained for the majority of the samples, some showed incomplete segments despite a decent viral load. However, all failed sequencing attempts were also associated with a Ct value > 25 Ct. Moreover, failed sequencing attempts were missing nucleotides within the target genes, whereas incomplete sequences were often missing 2 to-5 amino acids at the beginning or the end of a segment (Data not shown).

Table 3. List of samples used for the first WGS run. 52 influenza A and B samples were batched. Failed sequencing attempts are in red.

ID	Isolate	PB2	PB1	PA	HA	NP	NA	M	NS	PB2	PB1	PA	HA	NP	NA	M	NS	Ct	Subptype
11368	A/Switzerland/11368/2022	2279	2289	2152	1701	1540	1331	1005	814									26.2	H3N2
11479	A/Switzerland/11479/2022	2312	2341	2202	1701	1542	1416	1006	815									21.7	H3N2
11488	B/Switzerland/11488/2021									2389	2321	2287	1886	1770	1546	1150	1042	24.6	Bvic
11638	A/Switzerland/11638/2022	2117	2285	2113	1701	1410	838	980	764									25.1	H3N2
11713	A/Switzerland/11713/2022	2275	2331	2153	1701	1513	1405	1013	814									24.9	H3N2
11727	A/Switzerland/11727/2022	2312	2341	2176	1701	1560	1418	1003	815									21.8	H3N2
12204	A/Switzerland/12204/2022	2302	2270	2172	1701	1541	1379	1002	839									23.1	H3N2
12252	A/Switzerland/12252/2022							934										27.8	H3N2
12593	A/Switzerland/12593/2022				1701			927	782									25.4	H3N2
12636	A/Switzerland/12636/2022	2304	2337	2211	1624	1548	1419	1013	805									21.5	H3N2
12743	A/Switzerland/12743/2022		2245	2146	1701		1326	1005	804									27.8	H3N2
17909	A/Switzerland/17709/2022	2297	2337	2227	1694	1523	1379	993	890									18.4	H1N1pdm09
17942	A/Switzerland/17942/2022	2297	2326	2217	1701	1516	1362	991	890									24.4	H1N1pdm09
17988	A/Switzerland/17988/2022	2335	2342	2208	1701	1532	1419	1008	815									15.9	H3N2
20509	A/Switzerland/20509/2022	2312	2342	2204	1701	1565	1418	1010	815									20.5	H3N2
22137	A/Switzerland/22137/2022	2251	2291	2152	1701	1523	1333	1013	846									23.1	H3N2
22462	A/Switzerland/22462/2022	2252	2299	2129	1701	1517	1335	981	847									24.5	H3N2
22627	A/Switzerland/22627/2022	2303	2299	2191	1701	1561	1336	1007	805									22.4	H3N2
22985	A/Switzerland/22985/2022	2312	2342	2199	1701	1562	1420	1015	815									18.9	H3N2
23518	A/Switzerland/23518/2022	2330	2342	2191	1701	1566	1418	1017	814									19.6	H3N2
27140	A/Switzerland/27140/2022	2334	2342	2187	1701	1562	1410	1027	815									20	H3N2
28784	A/Switzerland/28784/2022	2312	2337	2196	1701	1564	1418	1013	842									20.9	H3N2
31039	A/Switzerland/31039/2022																	27	H3N2
36739	A/Switzerland/36739/2022	2240	2274	2125	1701	1527	1403	1004	825									25	H3N2
38769	A/Switzerland/38769/2022	2312	2340	2200	1701	1562	1417	1008	814									25	H3N2
39137	A/Switzerland/39137/2022	2335	2344	2207	1701	1562	1418	1014	817									16.9	H3N2
44267	A/Switzerland/44267/2022	2302	2342	2197	1701	1532	1408	1014	814									25.7	H3N2
44423	A/Switzerland/44423/2022	2315	2342	2212	1701	1562	1419	1013	865									16.9	H3N2
50178	A/Switzerland/50178/2022	2225	2268	2032	1701	1517	1163	1021	889									25.7	H1N1pdm09
51230	A/Switzerland/51230/2021	2304	2342	2200	1701	1561	1417	1006										22.5	H3N2
51418	A/Switzerland/51418/2022	2304	2337	2201	1701	1562	1418	1015	812									21.5	H3N2
51651	A/Switzerland/51651/2022	2242	2298	2110	1701	1534	1395	998	803									24.3	H3N2
52033	A/Switzerland/52033/2022	2315	2342	2185	1701	1540	1418	1014	815									18.8	H3N2
52080	A/Switzerland/52080/2022				1583			927	773									27.6	H3N2
52191	A/Switzerland/52191/2022	2328	2344	2209	1701	1535	1403	1018	811									19.1	H3N2
57945	B/Switzerland/57945/2021									2383	2257	2277	1783	1700	1546			23.1	BVic
60191	A/Switzerland/60191/2022	2307	2321	2204	1701	1551	1403	1008	812									25.7	H3N2
60468	A/Switzerland/60468/2022	2315	2342	2229	1701	1540	1420	1023	885									16.8	H3N2
62974	A/Switzerland/62974/2022	2307	2325	2175	1701	1553	1323	1006	804									22.3	H3N2
69954	A/Switzerland/69954/2021	2302	2291	2160	1701	1477	1385	998	817									24.6	H3N2
72457	A/Switzerland/72457/2022	2315	2342	2198	1701	1540	1417	1016	889									19.8	H3N2
79079	A/Switzerland/79079/2021	2265	2237	2127	1694	1550	1329	993	786									26.7	H3N2
80945	A/Switzerland/80945/2022	2334	2342	2208	1701	1562	1419	1019	857									16.3	H3N2
81273	A/Switzerland/81273/2022	2301	2342	2198	1701	1558	1419	1019	846									23.7	H3N2
84161	A/Switzerland/84161/2022	2312	2342	2206	1701	1559	1400	1019	816									20.6	H3N2
87473	A/Switzerland/87473/2021	2308	2337	2196	1701	1548	1404	1006	812									24.1	H3N2
95790	A/Switzerland/95790/2022	2135	2047	1956	1701	1510		991	886									26.5	H1N1pdm09
95941	A/Switzerland/95941/2022	2300	2337	2227	1701	1537	1391	991	890									18.5	H1N1pdm09
96035	A/Switzerland/96035/2022				1701				606									28.3	H3N2
97840	A/Switzerland/97840/2022	2318	2346	2207	1701	1535	1419	1014	816									15.8	H3N2
98061	A/Switzerland/98061/2022	2035	2225	2104	1701	1512	1330	1001	787									26.1	H3N2
98693	A/Switzerland/98693/2021	2314	2342	2205	1701	1530	1419	1013	808									19.6	H3N2

In summary, genetic segments of 47 out of 52 viruses were submitted to GISAID (Table 3 and appendix 14). 43 HA (86%), 20 NA (40%) and 22 PA (44%) influenza A genes had complete sequences. Additionally, known antiviral drug resistance-associated positions were covered in 44 PA and 43 NA genes. When looking at the two influenza B isolates, NA and PA genes for both samples, and the HA gene for one of them, were fully recovered. M and NS genes, the influenza diagnostic rRT-PCR targets were also available for a majority of the samples.

In conclusion, the current influenza A and B WGS option at Microsynth AG is acceptable for epidemiological surveillance purposes. In addition, we were able to

obtain information on segments that is not at all available via Sanger sequencing at the NRCI.

5.4.5 Influenza circulation Worldwide

The global circulation of influenza viruses across the WHO regions was higher than in the 2020/2021 season, albeit substantially lower than before the COVID-19 pandemic in most areas. Both influenza A and B were detected, although there was less type B, with a dominance of A(H3N2) and B/Victoria lineage viruses across all the monitoring systems. In contrast, influenza type B dominates in Eastern and South-East Asia, particularly in China.[66] According to the European WHO surveillance, these distributions were largely consistent across the rest of the world. [66] Data below originate from the February 2022 report from the London WHO Collaborating Centre at Francis Crick Worldwide Influenza Centre (WIC). In the Western Europe region co-dominance of A(H3N2) and A(H1N1)pdm09 was observed and accounted for 57% and 43% of the detections, respectively (Table 4 and 5).

Table 4. Influenza season in the WHO European Region: weeks 40/2021-05/2022 (data from the *WIC report 21st-24th February 2022*)[65]

	Sentinel sources			Non-sentinel sources			Totals		
Virus type/subtype/lineage	2021/22 season	2020/21 season	2019/20 season	2021/22 season	2020/21 season	2019/20 season	2021/22 season	2020/21 season	2019/20 season
Influenza A	**2,121 (99%)**	**42 (69%)**	**11,277 (64%)**	**32,975 (96%)**	**445 (50%)**	**108,445 (74%)**	**35,096 (96%, 24.5:1)**	**487 (51%,1.1:1)**	**119,722 (73%, 2.6:1)**
A(H1N1)pdm09	96 (6%)	13 (65%)	6,112 (59%)	704 (6%)	28 (35%)	20,180 (57%)	800 (6%)	41 (41%)	26,292 (56%)
A(H3N2)	1,399 (94%)	9 (35%)	4,171 (41%)	11,756 (94%)	52 (65%)	16,539 (43%)	13,155 (94%, 16.4:1)	61 (59%,1.4:1)	20,710 (44%, 0.8:1)
A not subtyped	626	20	994	20,515	365	71,726	21,141	385	72,720
Influenza B	**29 (1%)**	**18 (31%)**	**6,402 (36%)**	**1,405 (4%)**	**442 (50%)**	**39,070 (26%)**	**1,434 (4%)**	**460 (49%)**	**44,472 (27%)**
Victoria lineage	5	3	2,492	8	12	2,067	13 (100%, NA)	15 (94%,30.1:1)	4,559 (98%, 51.8:1)
Yamagata lineage	0	0	23	1	1	65	0 (0%)	1 (6%)	88 (2%)
Lineage not ascribed	24	15	3,887	1,397	429	36,938	1,421	444	40,825
Total detections	**2,150**	**60**	**17,679**	**34,380**	**887**	**147,515**	**36,530**	**947**	**165,194**
Total tested	**30,627**	**43,499**	**52,491**	**1,458,697**	**881,400**	**860,760**	**1,389,324**	**924,899**	**913,251**

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.

Table 5. Laboratory confirmed influenza from sentinel and non-sentinel sources by geographic sub-region and influenza type and subtype/lineage (data from the *WIC report 21st-24th February 2022*)

Influenza type	South West Europe	Western Europe	Eastern Europe	Northern Europe	West Asia	Central Asia	WHO European Region
Influenza A	**2,922 (97%)**	**7,912 (99%)**	**8,996 (99%)**	**13,862 (92%)**	**1,205 (100%)**	**199 (96%)**	**35,096 (96%)**
Influenza A subtyped	1,232	1646	8,094	1601	1,204	178	13,955
A(H1N1)pdm09	30 (2%)	701 (43%)	12 (0%)	57 (4%)	0 (0%)	0 (0%)	800 (6%)
A(H3N2)	1,202 (98%)	945 (57%)	8,082 (100%)	1,544 (96%)	1,204 (100%)	178 (100%)	13,155 (94%)
Influenza B	**76 (3%)**	**85 (1%)**	**119 (1%)**	**1,142 (8%)**	**3 (0%)**	**9 (4%)**	**1,434 (4%)**
Influenza B lineage determined	0	9	0	3	1	0	13
B/Yamagata-lineage	0	0	0	0	0	0	0 (0%)
B/Victoria-lineage	0	9	0	3	1	0	13 (100%)
Total	**2,998**	**7,997**	**9,115**	**15,004**	**1,208**	**208**	**36,530**

Influenza activity has strongly increased since March 2022 in the southern hemisphere, particularly in Australia.[67] More than 87,989 cases were reported to the Australian National Notifiable Diseases Surveillance System. Influenza A accounted for 90% of the cases reported, of which 4.6% were A(H3N2) subtype and about 0.9% for A(H1N1)pdm09 subtype. In accordance with the Northern Hemisphere, influenza B also remained at a low level (0.1%). The great majority of influenza A(H3N2) and A(H1N1)pdm09 viruses antigenically characterized were similar to the 2022 vaccine strain A/Darwin/9/2021 and A/Victoria/2570/2019 strain, respectively. In contrast, influenza B samples characterized antigenically were not similar to the actual vaccine 2022 components (B/Austria/1359417/2021 nor B/Phuket/3073/2013).

6 *WHO recommendation for the composition of influenza virus vaccines for the 2022/2023 influenza season*

Influenza vaccine recommendations are based on the Global Influenza Surveillance Response System network data, virus antigenic and genetic characterization data, human serology data, virus fitness forecasting data, antiviral resistance data, vaccine effectiveness, and the availability of candidate vaccine viruses.

The vaccine strains recommended for the 2022/2023 northern hemisphere influenza vaccine by the WHO experts are depicted in table 6.

Table 6. Recommended influenza vaccine composition for the 2022/2023 influenza season.
a: for egg-based vaccines. b: for cell-based vaccines

a	Vaccine strains 2022/23
A(H1N1)pdm09	A/Victoria/2570/2019 (H1N1)pdm09-like virus
A(H3N2)	A/Darwin/9/2021 (H3N2)-like virus
B/Victoria lineage	B/Austria/1359417/2021 (B/Victoria lineage)-like virus *
B/Yamagata lineage	B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

** B strain included in the trivalent vaccine*

b	Vaccine strains 2022/23
A(H1N1)pdm09	A/Wisconsin/588/2019 (H1N1)pdm09-like virus
A(H3N2)	A/Darwin/6/2021 (H3N2)-like virus
B/Victoria lineage	B/Austria/1359417/2021 (B/Victoria lineage)-like virus *
B/Yamagata lineage	B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

**B strain included in the trivalent vaccine*

7 Human infection with influenza viruses of zoonotic origin

Transmission of zoonotic influenza viruses to humans often leads to infections limited to a single individual and sometimes to their close contacts. However widespread outbreaks and pandemics are also possible in the case of efficient human-to-human transmission. Recombination events between porcine/avian and human viruses due to concomitant circulation can drive human adaptation of zoonotic strains. In order to allow for the early identification and rapid containment of new potential animal-to-human transmission events, several countries, including Switzerland, have introduced the regular screening of animals such as poultry, wild birds and farm pigs for the presence of the respective influenza strains.

7.1.1 Swine-to-human influenza virus transmission

Human infections with influenza A viruses of porcine origin are identified as “variant” viruses and denoted with a letter “v”, such as A(H1N2)v, A(H3N2)v and A(H1N1)v.

7.1.1.1 In Switzerland

In 2001, the Federal Food Safety and Veterinary Office initiated a collaborative project with the Federal Office of Public Health project, the Institute of Virology of the

Vetsuisse Faculty of the University of Zurich and the Pig Health Service (SSP) of SUISAG, which aimed at monitoring the swine flu circulation in Switzerland. The project is named “Surveillance of swine influenza in pigs and humans”. In this context, specimens from farm pigs with respiratory symptoms are sent to, and analysed by, the National Veterinarian Institute (Vetvir, Zurich). In parallel, samples from pig breeders (or their employees), who have been in contact with influenza-infected animals and present with ILI symptoms, are sent to the NRCI. The latter are analysed using a rRT-PCR with the capacity to distinguish influenza A viruses of human and animal origin, both avian and porcine. Positive samples are further characterized by sequencing. No samples were sent to the NRCI during the week 17/2021 to week 16/2022 for suspicion of zoonotic transmission.

7.1.1.2 Worldwide

Since 2010, 482 [434 A(H3N2)v, 18 A(H1N1)v and 30 A(H1N2)v] human cases of variant influenza have been reported in several states in the USA. These cases were often mild with no evidence of further human-to-human transmission. One case of A(H1N2)v and one case of H3N2v were reported in 2021/2022.[68]

In 2021/2022, A(H1N1)v infections were also reported from China, Denmark and Germany.[69,70]

7.1.2 Avian influenza A subtypes in human[71]

As with porcine influenza, human cases of infection with various avian influenza viruses are sporadically reported. As of May 2022 a total of 864 laboratory-confirmed human cases of A(H5N1), including 456 deaths, have been reported from 18 countries since 2003. The last confirmed case was reported in April 2022 by the United States of America.

Since February 2014, 78 cases of highly pathogenic avian influenza (HPAI) A(H5N6), including 32 deaths, have been reported. The three last cases date back to February 2022 and were reported from China.

One A(H7N4) virus was also reported since February 2018. A laboratory-confirmed case of A(H3N8) virus was reported to the WHO on 25th April 2022. They both came from China.

No human cases of A(H7N9) were reported since 2019. To date, 74 laboratory-confirmed human cases of A(H9N2) infections, and 2 deaths, have been reported, mainly in mainland China since December 2015.

8 Avian influenza A in animals[72]

The reservoirs for L/HPAI influenza A viruses are wild birds. Both virus types can cause moderate to large outbreaks in poultry worldwide. While it could be expected that virtually all existing influenza A subtypes would be found within the bird population, most of the detected outbreaks are due to viruses of the H5, H7 and H9 subtypes.

The 2021/2022 avian influenza situation did not improve when compared to 2020/2021. Indeed the prevalence of avian influenza strains circulating was even higher than during the previous year. There was an increase of the reporting outbreaks in poultry and the number of detection in wild birds, particularly in Africa and Asia. For the first time HPAI infections were detected in Moldova and the Faroe Islands. A(H5N1) virus was more abundant than during 2021 and, along with the A(H5N8) subtypes, and was considered to be in persistent circulation.

9 Discussion

For the second consecutive year, the NRCI monitored not only influenza viruses circulating in Switzerland but also a rRT-PCR panel targeting the main respiratory viruses, which are human pathogens, including SARS-CoV-2. The number of samples received at the NRCI was more than 2-fold higher during this season compared with the 2020/2021 season. This was not surprising taking into account the ongoing SARS-CoV-2 pandemic, but with less sanitary measures compared with the previous season.

Among the participants included in the monitoring system, sex and age group distributions were comparable to previous years.

In concordance with the amount of samples analysed, the median positivity rate during week 40/2021 to 16/2022 was higher (66%) this season compared with the previous season (week 40/2020 to week 16/2021, (49.2%)). The increase in the positivity rate for 2021/2022 may be explained by the re-emergence of influenza viruses, the continuing SARS-CoV-2 circulation, and the increase of other respiratory viruses circulation, particularly during week 39/2021 to 16/2022.

Overall influenza activity has increased during the current surveillance period. Reduction of protective and hygiene measures against SARS-CoV-2 and opening of countries borders may have accounted for this rebound. Nevertheless, influenza activity in Switzerland has not yet reached the “normal” epidemic threshold established before COVID-19 pandemic. A possible explanation may be reduced testing for influenza due to screening procedures prioritizing SARS-CoV-2 diagnosis. However, as mentioned previously, the number of swabs tested within the sentinel surveillance during 2021/2022 was similar or even higher than previous seasons and all samples tested for SARS-CoV-2 were also tested for influenza. Hence, this does not explain the low influenza activity in Switzerland. Consistently, the influenza testing within the GISRS was also comparable to previous years. Furthermore, SARS-CoV-2 interference with influenza can also be hypothesized as a cause for reduced influenza circulation.[73-75] Nevertheless, the latter hypothesis is not supported by the remarkable rebound of influenza in the 2022 southern hemisphere despite SARS-CoV-2 circulation.

Influenza scarcity during the COVID-19 pandemic was a relief, as concomitant circulation of two viruses, which have a major public health impact, may have worsened the already substantial hospitalization and death burden. Nevertheless, this situation raises the concern that the proportion of influenza susceptible individuals may increase in the population foreshadowing a potential “higher than normal” number of hospitalized cases for 2022/2023 influenza season. Indeed, people that would have had their immunity boosted by natural infection were not exposed to the virus, even if vaccination rates against influenza may have been higher than usual in adults in some countries[76] during 2021/2022. Therefore one may expect that the population will be less immune to influenza infection and an increase in disease severity is possible.

Of note, in parallel to the lack of exposure to influenza is also a lack of immune pressure, potentially limiting viral evolution by antigenic drift. Indeed if influenza does not circulate, or at very low levels, the virus would be less subjected to selection for immune escape variants. If the genetic diversity of various subtypes/lineages decreases, some strains may not re-emerge again.[77,78] In contrast, viruses of subtypes that have persisted this year, may have a "fitness advantage enabling ongoing circulation"[75] and would be pushed by the genetic drift to re-emerge and to persist.

As already mentioned, rRT-PCR detection data on respiratory viruses other than influenza is only available since 2019/2020 within the Sentinel network, and the emergence of SARS-CoV-2 was shown to significantly impact the circulation of other respiratory viruses.[79,80] Before COVID-19 emergence, RSV was shown to alternate between low prevalence directly followed by high prevalence annual epidemics in Switzerland.[81] Last year, RSV circulation was unusual as this virus was delayed by around 20 weeks. This phenomenon was not only observed in Switzerland but also in other countries.[82-85] However, as with influenza, RSV circulation in Switzerland was detected again from week 40/2021 to week 7/2022 with a peak in week 51/2021, corresponding to observed detection before COVID-19 emergence in the EU/EEA region.[86,87]

HMPV detections were also infrequent in 2020/2021, accounting for 4.5% of the positive samples from week 17/2021 to 16/2022. Its positivity rate increased from week 40/2021 onwards to reach 13.1% at week 50/2021. Hence, this season, HMPV seems to have come back with a similar pattern of biannual circulation observed in epidemiological studies in China, Israel or Switzerland.[88-90]

SARS-CoV-2 viruses were regularly detected from week 17/2021 to week 16/2022 and represented, together with RV/EV, the most prevalent virus, reaching a peak at week 12/2022 (n=53, 43.8%). In general, an increase in detection at the NRCI fit well with an increase in the number of cases identified in the Swiss population (Figure 5b; appendix 2). Consistently, the detection rate of the SARS-CoV-2 Delta and Omicron BA.1 variants, that became predominant beginning July 2021, and December 2021, respectively, in the Swiss population, matched within the sentinel network as shown by the data of the national SARS-CoV-2 genomic surveillance[91] (Appendix 4). A continuous update of SARS-CoV-2 variants evolution in Switzerland can be found on Covariants (https://covariants.org/per-country?region=Switzerland) and CoV-

Spectrum[92] (https://cov-spectrum.ethz.ch/explore/Switzerland/AllSamples/AllTimes). The rise to dominance of the SARS-CoV-2 Omicron variant coincided with the decline and replacement of the Delta variant in Switzerland. The Omicron BA.1 variant is known to be more transmissible than the Delta VOC, which it replaced in several European countries within only weeks after its first detection.[93-95] While *in vitro* studies showed a reduced neutralization capacity from vaccinated sera[96], real-life data indicate that SARS-CoV-2 mRNA vaccines available in Switzerland still provided a good protection against severe disease caused by the Delta variant, with a slight diminution of protection against infection.[97] The Omicron variant, which is actually grouped in several sublineages, may exhibit variable sublineage-specific, transmissibility and immunogenicity patterns. This impact both risk of infection and vaccine effectiveness and some studies demonstrated that mRNA vaccines may provide less protective immunity against the BA.1 variant.[98] Regarding vaccine effectiveness on other subvariants (eg. BA.5, BA.4, BA.2.75), further investigation is required. Of note, when assessing vaccine effectiveness against any sub-lineage, estimates may vary with the type of vaccine administered, as well as the number of doses, the scheduling, and the time elapsed since the last received dose. Similarly, preliminary studies showed a rapid waning of protection by prior Omicron BA.1 and/or BA.2 infection[99], with timing since the last infection being the major risk factor for reinfection. Indeed, a substantial proportion of the population is vulnerable to reinfection by different Omicron sub-lineages in half a year or less[100]. As existing variants evolve and new ones emerge, scientific knowledge on the different viruses is constantly being updated.

RV/EV were the second most commonly detected viruses after SARS-CoV-2 during 2020/2021 and 2021/2022. This is consistent with data already published for in- and out- patients in Geneva.[101] As expected RV/EV detection was consistent throughout the year with a peak of positivity reaching 27.9% at week 45/2021 (n=24).

HCoVs HKU1, NL63, OC43 and HCoVs NL63/OC43 were present during the two last seasons, 2019/2020 and 2020/2021, respectively. During the 2021/2022 surveillance, only HCoV OC43 virus was continuously detected. HCoV 229E was first detected at week 38/2021, while HCoV HKU1 was first identified at week 20/2021, with a large gap until week 7/2022, when it circulated at a low rate. Of note, only one HCoV NL63, was detected as late as week 19/2021, while it represented 2.9% and 11.3% of the virus identified during 2019/2020, and 2020/2021, respectively. Despite the fact that HCoVs

tend to exhibit seasonal circulation, with peaks mostly in winter in Northern Hemisphere, the prevalence pattern of each HCoV strains varies in-between countries and from year to year.[102,103]

While they were only sporadically detected from week 40/2019 to week 51/2019 and in contrast regularly detected in 2020/2021, HPIV 1/3 positive samples were sporadically found again during 2021/2022 period. As our rRT-PCR does not differentiate between type 1 and 3, the discrepancy in prevalence may potentially be due to alternate circulation of different viruses types as it has been shown in Autralia.[104]

HPIV 2/4 were not commonly detected in general for the three last time periods (2019/2020, 2020/2021, and 2021/2022). However, we observed an increased number of positive samples from week 40/2021 to week 2/2022, with a peak of 8 positive HPIV 2/4 viruses (2.8%) in week 45/2021. As for HPIV1/3, our HPIV2/4 rRT-PCR does not discriminate between HPIV type 2 and 4.

Consistent with what we observed in prevalence in Europe[105], HBoV had a very low detection rate during the three last study periods. As could be expected, they were mainly found in children.[106]

Co-detections represented 11.3% and 7.2% of the positive samples in 2021/2022 and 2020/2021 respectively. This observation is consistent with previous publications.[107,108] The rRT-PCR respiratory panel used at the NRCI does not target bacterial or fungal pathogens. However, the latter are also often detected along with respiratory viruses, particularly in hospitalized patients.[108] The most common virus found in co-detections for both surveillance periods was SARS-CoV-2, which was mostly present with coronaviruses 229E or OC43 (30.6%), influenza A viruses (29.6%), and with RV/EV (21.3%). Of note, viral loads for coronaviruses 229E and OC43 were often low when combined with SARS-CoV-2. This finding was similar to what Lansbury et al.[108] observed. A high co-infection rate with SARS-CoV-2 was also observed in France in 2020.[109]

After two years of the SARS-CoV-2 pandemic, this season influenza viruses re-emergence, although at a lower detection rate than pre-COVID-19 pandemic seasons. emphases the importance of collecting and analysing influenza viruses circulation data as it is crucial in order to choose the most appropriated influenza vaccine candidate

strains. The ultimate goal being to mitigate as much as possible the burden linked to severe influenza cases.

Compared with the 2019/2020 and 2018/2019 seasons, antigenic and genetic data, as well as reporting of influenza cases in TESSY/ECDC in 2021/2022, appeared to remain low. This was probably due to the lack of laboratory resources caused by prioritizing SARS-CoV-2 analyses and biosafety concerns or cell-culture issues. Notably, at NRCI, the HAI assay was not performed on samples co-infected with SARS-CoV-2.[110]

The influenza season started from week 47/2021 at a low positivity rate (2.7%), which coincides with the detection of the new SARS-CoV-2 VOC omicron, and then rising sharply from week 4/2022 with a peak of positivity rate of 37.3% at week 15/2022 and then decreasing one week later (13%). This is consistent with what was observed in the WHO European region.[111]

Influenza A predominated over influenza B mainly in the northern hemisphere area, with a co-detection of influenza A and B in some regions of Asia. The great majority of type A viruses were subtype A(H3N2), except in France where A(H1N1)pdm09 was dominant.[112-114] The prevalence of influenza observed during 2021/2022 period was comparable to the previous pre-COVID-19 pandemic seasons at the NRCI level.

This season, only 7.1% of influenza A detection was attributed to the 0-4 years old age group, which is not consistent with the incidence observed in previous European epidemics.[115]

As expected for A(H3N2) viruses, a wide range of antigenic and phylogenetic variation was observed for A(H3N2) strains isolated during the 2021/2022 period. Up to 88% of the A(H3N2) strains in the world belonged to the 3C.2a1b.2a.2 clade (A/Bangladesh/4005/2020-like virus). This is comparable with what we observed at the NRCI. Except one that belonged to the 3C.2a1b.1a clade (A/Dennemark/3264/2019-like virus), all the isolates from the sentinel network belonged to the 3C.2a1b.2a.2 clade. As assessed by the HAI assay, a majority of isolates were well recognized by the antisera raised against the egg-propagated cultivar of the southern hemisphere 2022 A/Darwin/9/2021 recommended vaccine strain (58%), and 33% were poorly recognized at a titer within 8-fold of the homologous titer with the A/Cambodia/e0826360/2020 virus. In contrast, two isolates were antigenically characterized as A/Cambodia/e0826360/2020-like virus.

Only few influenza A(H1N1)pdm09 viruses circulated in Europe, including in Switzerland, and the USA this season. All the isolates belonged to the clade 6B.1A. About 80% of the test viruses from the WIC and all the isolates from NRCI belonged to the subclade 6B.1A.5a.1. Antigenic characterization on those viruses showed that they were antigenically close to A/GuangdongMaonan/SWL1536/2019, the recommended vaccine for 2020/2021. A third of the isolates were considered to be close to the 2019/2020 recommended vaccine virus A/Brisbane/02/2018.

This year, a very low proportion of B influenza circulated overall. Most of them belonged to the B-Victoria lineage, including those circulating in Switzerland. All B-Victoria viruses were genetically assigned to the clade V1A.3 and the vast majority belonged to the subclade V1A.3a.2, as the reference strain 2021/2022 B/Austria/1359417/2021. Of the two B-Victoria isolates antigenically characterized, one was related closely to the reference strain B/Austria/1359417/2021-like and the other was not recognized well (8-fold the homologous titer) by the antisera raised against B/Washington/02/2019, the reference vaccine for 2021/2022, but was determined to be B/Brisbane/60/08-like.

During the 2021/2022 season, none of the viruses sequenced at the NRCI in the context of the national surveillance exhibited mutations associated with reduced susceptibility to Baloxavir marboxyl and NA inhibitors. Our results are consistent with the tested viruses in Europe which do not show a decrease of the susceptibility of Oseltamivir, nor Baloxavir marboxil treatments. Of note, an A(H3N2) virus originating from an hospitalized patient contained the NA substitution E119V.

While the avian influenza transmissions remained high since last year, there was an additional increase of the number of outbreaks observed in poultry and in wild birds in Africa and Asia. Furthermore, HPAI infections were identified for the first time in Moldova and Faroe Islands, with a predominance of A(H5N1) subtype when compared with 2021. Zoonotic infection remains a major of concern for public health to determine potentially new host reservoirs.

To conclude, even if not at pre-pandemic levels, re-emergence of influenza viruses, despite SARS-CoV-2 circulation, was a major event for 2021/2022 season. Therefore, the dreadful possibility of a concomitantly circulation of influenza with ongoing SARS-CoV-2 VOC during 2022/2023 rises again.

10 Sharing of influenza cell-cultured isolates and/or reference strains

1. Shared material: *Original nasopharyngeal swabs (in UTM copan) positive for influenza A and B.*
    a. With whom: *Prof. Carmen Kurmann, Schweizer Paraplegiker-Zentrum, Labor, 6207 Nottwil.*
    b. Project: *Evaluation of Xpert® Xpress SARS-CoV-2/Flu/RSV detection cassettes from GeneXpert.*

2. Shared material: *Original nasopharyngeal swabs (in UTM copan) positive for influenza A, B or RSV.*
    a. With whom: *Synlab, 1003 Lausanne*
    b. Project: *Evaluation of Xpert® Xpress SARS-CoV-2/Flu/RSV detection cassettes from GeneXpert.*

3. Shared material: *Influenza A and B vaccine (reference) strains, MDCK/70 and MDCK-SIAT/13 cells.*
    a. With whom: SUPSI *Istituto Microbiologia, 6500 Bellinzona.*
    b. Project: *Development of a multiplex real time PCR system.*

4. Shared material: *RNA from nasopharyngeal swabs positive for influenza A and B, SARS-IA, SARS-229E, NL63, OC43, 229E, RSV-Pico, RSV, SARS-RSV, HMPV-ADV-Pico, P1-3-boca-OC43-Pico, P2-4, P1-3, OC43-Pico, HKU1*
    a. With whom: *The Health 2030 Genome Center, Campus Biotech Geneva.*
    b. Project: *Development of a "multipathogen" WGS protocol.*

5. Shared material: *Nasopharyngeal swabs positive for influenza A and B.*
    a. With whom: *Espace Lab, Biologie et Pathologie, 1201 Genève*
    b. Project: *Evaluation of the iPonatic-Portable Molecule Workstation for influenza detection*

6. Shared material: *B/Victoria-lineage isolate and MDCK-SIAT/13 cells*
    a. With whom: *Dr. Valeria Cagno, Institute of Microbiology, CHUV*
    b. Project: *Development of broad-spectrum antivirals against respiratory infections.*

11 Collaborative projects and publications

As for 2022, the NRCI continued to support the laboratory of virology and the National Reference Centre for Emerging Viral Infections (CRIVE), especially regarding SARS-CoV-2 variant detection.

Support for national surveillance and clinics in the context of SARS-CoV-2

Swiss public health measures associated with reduced SARS-CoV-2 transmission using genome data. Sarah A. Nadeau, Timothy G. Vaughan, Christiane Beckmann, Ivan Topolsky, Chaoran Chen, Emma Hodcroft, Tobias Schär, Ina Nissen, Natascha Santacroce, Elodie Burcklen, Pedro Ferreira, Kim Philipp Jablonski, Susana Posada Céspedes, Vincenzo Capece, Sophie Seidel, Noemi Santamaria de Souza, Julia M. Martinez-Gomaz, Phil Cheng, Philipp P. Bosshard, Mitchell P. Levesque, Verena Kufner, Stefan Schmutz, Maryam Zaheri, Michael Huber, Alexandra Trkola, Samuel Cordey, Florian Laubscher, Ana Rita Gonçalves, Sébastien Aeby, Trestan PIillonel, Damien Jacot, Claire Bertelli, Gilbert Greub, Karoline Leuzinger, Madlen Stange, Alfredo Mari, Tim Roloff, Helena Seth-Smith, Hans H. Hirsch, Adrian Egli, Maurice Redondo, Olivier Kobel, Christoph Noppen, Niko Beerenwinkel, Richard A. Neher, Christian Beisel, Tanja Stadler.

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Geneva, August 24th 2022

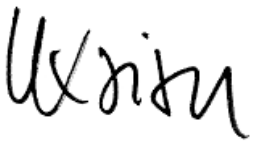
Mrs Tania Spedaliero

Dr Ana Rita Gonçalves Cabecinhas

Mrs Patricia Suter-Boquete

Dr Manuel Schibler

Professor Laurent Kaiser

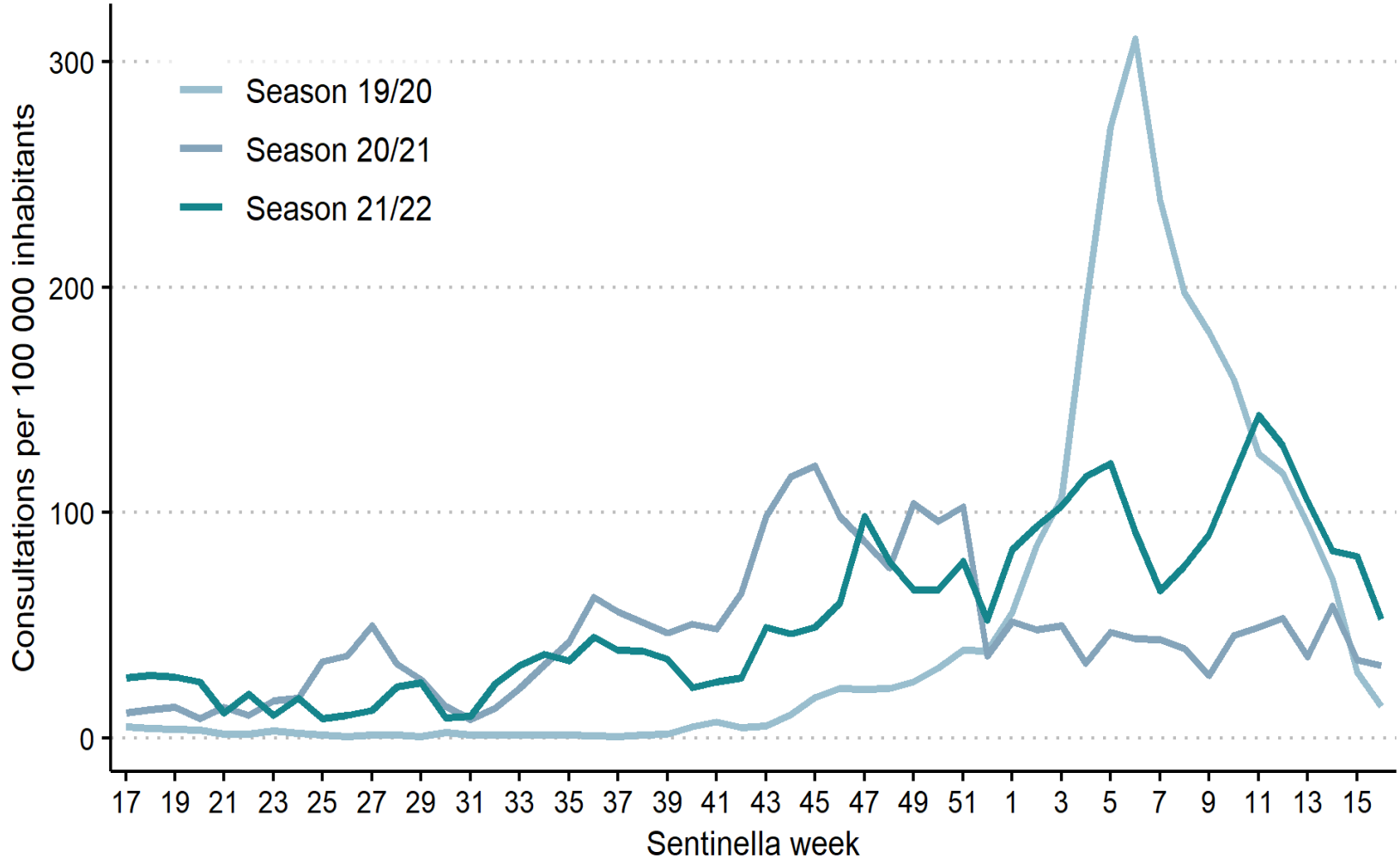


Appendix 1: Sequencing primers for influenza detection used during the 2021/2022 season

Primers used for classical RT-PCR detection of influenza viruses					
Influenza virus	**Origin**	**Target gene**	**Primer or probe**		**Origin and reference**
A (H1N1)pdm09	Human	Hemagglutinin (H1)	Forw ard	csw HAF1	R.Daniel, MRC-NIMR London Feb 2011
			Forw ard	csw HAF31	
			Forw ard	csw HAF451	
			Forw ard	csw HAF848	
			Reverse	csw HAR475	
			Reverse	csw HAR873	
			Forw ard	csw HAF1240	
			Reverse	csw HAR1264	
			Reverse	csw HAR1726	
			Reverse	csw HAR1777	
			Forw ard	AH1pdmF1	YT, CNRI, Geneva Mars 2014
			Forw ard	AH1p848F	
			Reverss	csw HAR873	
			Reverse	AH1p1200R	
			Reverse	csw HAR1264	
			Reverse	AH1p1313R	
			Forw ard	H1pGeF1	YT, CNRI, Geneva Dec 2010
			Reverse	H1pGeR1	
			Forw ard	H1pGeF2	
			Reverse	H1pGeR2	
			Reverse	H1pGeR3	
			Forw ard	H1pGeF523	
			Reverse	H1pGeR648	
	human	Hemagglutinin (H1)(mut 222)	Forw ard	1H1_MUT222F	YT, CNRI, Geneva Aug 2009
			Reverse	2H1_MUT222R	
			Forw ard	3H1_MUT222F	
			Reverse	4H1_MUT222R	
		Neuraminidase N1	Forw ard	sN1fw d PCR1	
			Reverse	sN1 Rev PCR1	
			Forw ard	sN1fw d nested*	
			Reverse	sN1 Rev nested*	
	Human	Neuraminidase N1	Forw ard	csw N1F1	R.Daniel, MRC-NIMR London
			Forw ard	csw N1F401	
			Reverse	csw N1R424	
			Forw ard	csw N1F1076	
			Reverse	csw N1R1099	
			Reverse	csw N1R1424	
			Reverse	csw N1R1440	
	human	Matrix (M1)	Forw ard	M93c	YT, CNRI, Geneva Aug 2009
			Reverse	M821Y	
			Reverse	Calif09Rev	

Primers used for classical RT-PCR detection of influenza viruses						
Influenza virus	Origin	Target gene	Primer or probe	Origin and reference	Sequence	Origin and reference
Influenza virus	Human	Hemaggutinin (Hf)	Reverse	AH1I		J. Ellis HPA, London Jan 2006
			Forward	AHfB		
			Reverse	AHfH		
			Reverse	AHfM		
			Forward	HfHAF552		
			Reverse	HfHAR823		
		Neuraminidase (N1)	Forward	N1F741		V. Gregory, MRC-NIMR London Jan 2006
			Reverse	H1N1R1		
		PA InfA	Forward	PA14M13	TGTAAAACGACGGCCAGT TGCGACAATGCTTCAATCC	Genève SP
			Reverse	PAIM13R	CAGGAAACAGCTATGACCGGYTCTTTCCAKCCAAAG	Deng &al. 2015
A (H3N2) seasonal	Human	Hemagglutinine (H3)	Forward	AH3G		J. Ellis London Jan 2006
			Reverse	AH3H		
			Forward	AH3B		
			Reverse	AH3CII		
			Reverse	AH3I		
			Forward	H3HAF552		
			Forward	AH3F348		YT, CNRI,Geneva Mars 2014
			Forward	AH3F476		
			Forward	AH3F567		
			Reverse	AH3R650		
		Neuraminidase (N2)	Forward	H3N2F1		V. Gregory , MRC-NIH London
			Reverse	N2R410		
			Forward	N2F387		
			Reverse	N2R778		
			Forward	N2F754		
			Reverse	N2R1104		
			Forward	N2F1083		
			Reverse	N2R1447		
		Matrix	Forward	M93c		YT, CNRI, Geneva Feb 2007
			Reverse	MF820		
B seasonal	Human	Hemagglutinin	Forward	BHA1F1		V.Gregory, MRC-NIMR London Jan 2006
			Reverse	BHA1RI		
			Forward	BHAF		
			Forward	BHA25		
			Forward	BHAF458		
			Reverse	BHAR652		
		Neuraminidase	Forward	BNAF1		V. Gregory , MRC-NIMR London
			Forward	BNAF336		modif YT, CNRI Geneva
			Reverse	BNAR359		
			Forward	BNAF725		
			Forward	BNAF1096		
			Reverse	BNAR1487		
			Reverse	BNAR1118		
			Reverse	BNAR748		
			Forward	BNAF5		YT, CNRI, Geneva Avril 2014
			Forward	BNA310F		
			Reverse	BNAR333		
			Reverse	BNA1496R		
		PA InfB	Forward	InfB PA 10F	GGTGCGTTTGATTTRTC	Genève SP 2019
			Reverse	InfB PA 945R	CTAGACATTCTTTGGC	
A (H5N1)	Human	Hemagglutinin (H5) Full length	Forward	H5Gen70F		YT, CNRI, Geneva May 2007
			Reverse	H5Gen1663R		
			Forward	H5Gen102F		
			Reverse	H5Gen1447R		
		Hemagglutinin (H5) Short	Forward	H5Gen819		YT, CNRI, Geneva May 2007
			Reverse	H5Gen1340		
			Forward	H5Gen887		
			Reverse	H5Gen1300		
		Matrix	Forward	H5-1		KY Yuen et al, Lancet 1998; 351: 467-471) and communicated by WHO

Appendix 2: Consultations due to influenza-like illness in Switzerland, FOPH



(https://www.bag.admin.ch/bag/fr/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/saisonale-grippe---lagebericht-schweiz.html)

Appendix 3: Detailed description of the observed co-infections (17/2021-16/2022)

Weeks	Co-infections																
17	RV-EV/HAdV/VRS																1
19	RV-EV/HAdV	HBoV/RV-EV															2
20	RV-EV/VRS																1
25	RV-EV/VRS	RV-EV/VRS	RV-EV/HMPV														3
26	RV-EV/HMPV	HBoV/RV-EV/HAdV															2
27	HCoVOC43/HAdV	HBoV/RV-EV															2
31	RV-EV/HAdV/VRS	HBoV/VRS/HAdV															2
32	HBoV/HAdV																1
33	HBoV/VRS	HPIV2-4/VRS															2
34	HBoV/RV-EV	RV-EV/VRS	HBoV/HPIV2-4														3
35	RV-EV/HMPV																1
38	HCoVOC43/RV-EV																1
39	HBoV/VRS																1
41	RV-EV/HAdV	VRS/SARS-CoV2															2
42	VRS/RV-EV																1
44	HBoV/RV-EV	RV-EV/HAdV	RV-EV/VRS														3
45	HBoV/RV-EV/HPIV1-3/HPIV2-4/SARS-CoV2	RV-EV/HMPV	HPIV2-4/HAdV	HMPV/HPIV2-4	HCoVOC43/SARS-CoV2	RV-EV/SARS-CoV2	HBoV/SARS-CoV2										7
46	HBoV/RV-EV	HBoV/RV-EV/SARS-CoV2	HBoV/VRS/SARS-CoV2	HCoVOC43/RV-EV	HPIV1-3/HBoV/HCoVOC43/RV-EV/SARS-CoV2	HBoV/SARS-CoV2	HBoV/SARS-CoV2	RV-EV/SARS-CoV2	HCoV229E/SARS-CoV2	HPIV2-4/SARS-CoV2							10
47	HCoVOC43/RV-EV	HCoVOC43/RV-EV	HBoV/RV-EV	RV-EV/VRS	HCoVOC43/HAdV/HBoV	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HAdV/SARS-CoV2	RV-EV/SARS-CoV2	RV-EV/SARS-CoV2	VRS/SARS-CoV2	HCoV229E/SARS-CoV2					12
48	RV-EV/HAdV/HMPV	RV-EV/HAdV/HMPV	HCoVOC43/HCoV229E	HAdV/VRS	HCoV229E/RV-EV	HCoV229E/RV-EV/SARS-CoV2	HMPV/HPIV2-4	VRS/SARS-CoV2									8
49	HCoV229E/HMPV	HCoVOC43/RV-EV	RV-EV/VRS	RV-EV/SARS-CoV2	HMPV/SARS-CoV2												5
50	HCoVOC43/HAdV	HCoVOC43/VRS/SARS-CoV2	RV-EV/HMPV/SARS-CoV2	HCoV229E/SARS-CoV2	RV-EV/SARS-CoV2	VRS/SARS-CoV2	HCoV229E/SARS-CoV2										7
51	HCoVOC43/SARS-CoV2	HPIV1-3/SARS-CoV2	HCoV229E/SARS-CoV2	IA/SARS-CoV2	VRS/SARS-CoV2	HCoVOC43/SARS-CoV2											6
52	HCoV229E/HMPV	HCoV229E/HMPV	RV-EV/IA	HCoV229E/SARS-CoV2	HCoV229E/SARS-CoV2	HCoV229E/SARS-CoV2											6
1	RV-EV/VRS	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	VRS/SARS-CoV2													4
2	HAdV/HMPV	HCoV229E/HBoV	HPIV2-4/HMPV	IA/SARS-CoV2													4
3	RV-EV/HBoV	HCoVOC43/HMPV	HCoVOC43/VRS	HCoVOC43/RV-EV	HCoVOC43/SARS-CoV2	HPIV1-3/SARS-CoV2	HAdV/SARS-CoV2	RV-EV/SARS-CoV2									8
4	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoV229E/SARS-CoV2	IA/HCoVOC43											6
5	IA/SARS-CoV2	IA/HAdV	VRS/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HCoVOC43/SARS-CoV2	HBoV/VRS	HCoVOC43/HBoV	VRS/SARS-CoV2						11
6	IA/SARS-CoV2	IA/HBoV	RV-EV/SARS-CoV2	RV-EV/SARS-CoV2	RV-EV/VRS	RV-EV/HAdV	RV-EV/HPIV1-3										7
7	HCoVOC43/SARS-CoV2	HCoVOC43/RV-EV	IA/SARS-CoV2	RV-EV/HAdV/IA													4
8	HBoV/SARS-CoV2	RV-EV/SARS-CoV2	RV-EV/HMPV														3
9	IA/SARS-CoV2	IA/SARS-CoV2	HCoVOC43/HAdV	RV-EV/SARS-CoV2	HBoV/RV-EV	RV-EV/IA	VRS/SARS-CoV2										7
10	IA/SARS-CoV2	HPIV2-4/SARS-CoV2	RV-EV/HAdV	HPIV2-4/HCoVOC43	RV-EV/SARS-CoV2	RV-EV/SARS-CoV2	HPIV2-4/SARS-CoV2/HCoVOC43	IA/SARS-CoV2	RV-EV/HAdV	HCoVOC43/SARS-CoV2	IA/HAdV	IA/HCoVOC43	RV-EV/SARS-CoV2	HPIV2-4/SARS-CoV2	IA/SARS-CoV2	RV-EV/HPIV1-3	16
11	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	RV-EV/SARS-CoV2	IA/HCoVOC43	RV-EV/SARS-CoV2	RV-EV/IA	HPIV2-4/IA									8
12	IA/SARS-CoV2	HCoVOC43/SARS-CoV2/IA	IA/SARS-CoV2	HCoVOC43/HMPV	RV-EV/HAdV	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	RV-EV/SARS-CoV2	RV-EV/IA	RV-EV/IA			14
13	RV-EV/IA	IA/SARS-CoV2/ HAdV	RV-EV/HAdV/HCoVHKU1	RV-EV/SARS-CoV2	RV-EV/HCoVHKU1	IA/SARS-CoV2/HBoV	IA/SARS-CoV2	IA/HCoVHKU1	IA/HCoVOC43	HPIV1-3/SARS-CoV2							10
14	IA/SARS-CoV2	IA/SARS-CoV2	RV-EV/IA	HPIV1-3/SARS-CoV2/IA													4
15	IA/SARS-CoV2	IA/SARS-CoV2	IA/SARS-CoV2	HCoVOC43/IA/HCoVHKU1													4
16	HPIV1-3/SARS-CoV2/IA	HCoVOC43/HBoV															2
Total																	201

Appendix 4: Lists of SARS-CoV-2 isolates submitted to GISAID (17/2021-16/2022)

Isolate name	Pangolin clade	Collection date	GISAID_ID
hCoV-19/Switzerland/AG-SNRCI-HUG-35992219/2021	AY.9	20211109	EPI_ISL_6512734
hCoV-19/Switzerland/BE-SNRCI-HUG-35991727/2021	AY.43	20211109	EPI_ISL_6512733
hCoV-19/Switzerland/VD-SNRCI-HUG-36003524/2021	AY.43	20211110	EPI_ISL_6512583
hCoV-19/Switzerland/ZH-SNRCI-HUG-36002985/2021	AY.46.6	20211110	EPI_ISL_6512580
hCoV-19/Switzerland/GR-SNRCI-HUG-36028023/2021	AY.46	20211112	EPI_ISL_6778020
hCoV-19/Switzerland/AG-SNRCI-HUG-36055180/2021	AY.102	20211115	EPI_ISL_6777972
hCoV-19/Switzerland/ZH-SNRCI-HUG-36055027/2021	B.1.617.2	20211115	EPI_ISL_6777794
hCoV-19/Switzerland/AG-SNRCI-HUG-36054934/2021	AY.43	20211115	EPI_ISL_6777316
hCoV-19/Switzerland/VD-SNRCI-HUG-36054733/2021	AY.46.6	20211115	EPI_ISL_6777697
hCoV-19/Switzerland/VD-SNRCI-HUG-36078646/2021	AY.46	20211116	EPI_ISL_6777699
hCoV-19/Switzerland/BE-SNRCI-HUG-36067436/2021	AY.46.6	20211116	EPI_ISL_6777803
hCoV-19/Switzerland/AG-SNRCI-HUG-36066960/2021	AY.43	20211116	EPI_ISL_6777317
hCoV-19/Switzerland/AG-SNRCI-HUG-36090585/2021	AY.43	20211117	EPI_ISL_7100636
hCoV-19/Switzerland/ZH-SNRCI-HUG-36090517/2021	AY.108	20211117	EPI_ISL_7095842
hCoV-19/Switzerland/GL-SNRCI-HUG-36078816/2021	AY.4	20211117	EPI_ISL_6777786
hCoV-19/Switzerland/BE-SNRCI-HUG-36078615/2021	AY.43	20211117	EPI_ISL_6777318
hCoV-19/Switzerland/GL-SNRCI-HUG-36078346/2021	AY.4	20211117	EPI_ISL_6777695
hCoV-19/Switzerland/GL-SNRCI-HUG-36090337/2021	AY.4	20211118	EPI_ISL_7094903
hCoV-19/Switzerland/VD-SNRCI-HUG-36103384/2021	AY.43	20211119	EPI_ISL_7096054
hCoV-19/Switzerland/ZH-SNRCI-HUG-36133461/2021	AY.43	20211122	EPI_ISL_7095036
hCoV-19/Switzerland/AG-SNRCI-HUG-36133353/2021	AY.122	20211122	EPI_ISL_7095133
hCoV-19/Switzerland/ZH-SNRCI-HUG-36133272/2021	AY.108	20211122	EPI_ISL_7095899
hCoV-19/Switzerland/BE-SNRCI-HUG-36132597/2021	AY.43	20211122	EPI_ISL_7100585
hCoV-19/Switzerland/BE-SNRCI-HUG-36132546/2021	B.1.617.2	20211122	EPI_ISL_7100561
hCoV-19/Switzerland/BE-SNRCI-HUG-36158762/2021	AY.43	20211123	EPI_ISL_7094152
hCoV-19/Switzerland/BE-SNRCI-HUG-36158216/2021	AY.43	20211123	EPI_ISL_7095022
hCoV-19/Switzerland/TG-SNRCI-HUG-36145078/2021	AY.43	20211123	EPI_ISL_7095281
hCoV-19/Switzerland/GR-SNRCI-HUG-36159005/2021	AY.21	20211124	EPI_ISL_7095303
hCoV-19/Switzerland/BE-SNRCI-HUG-36158599/2021	AY.46.6	20211124	EPI_ISL_7100609
hCoV-19/Switzerland/ZH-SNRCI-HUG-36157775/2021	AY.46.6	20211124	EPI_ISL_7095920
hCoV-19/Switzerland/VD-SNRCI-HUG-36238246/2021	AY.39	20211130	EPI_ISL_7546954
hCoV-19/Switzerland/VD-SNRCI-HUG-36239142/2021	AY.46.6	20211201	EPI_ISL_7546869
hCoV-19/Switzerland/FR-SNRCI-HUG-36237445/2021	AY.122	20211201	EPI_ISL_7546671
hCoV-19/Switzerland/ZH-SNRCI-HUG-36237818/2021	AY.4	20211201	EPI_ISL_7546871
hCoV-19/Switzerland/ZH-SNRCI-HUG-36238319/2021	AY.122.1	20211201	EPI_ISL_7546872
hCoV-19/Switzerland/TI-SNRCI-HUG-36239187/2021	AY.43	20211201	EPI_ISL_7546866
hCoV-19/Switzerland/SZ-SNRCI-HUG-36238562/2021	AY.43	20211201	EPI_ISL_7546865
hCoV-19/Switzerland/BE-SNRCI-HUG-36263601/2021	AY.98	20211203	EPI_ISL_7778918
hCoV-19/Switzerland/VD-SNRCI-HUG-36263785/2021	AY.46	20211203	EPI_ISL_7779093
hCoV-19/Switzerland/GL-SNRCI-HUG-36264135/2021	AY.121	20211203	EPI_ISL_7779090
hCoV-19/Switzerland/ZH-SNRCI-HUG-36299484/2021	AY.43	20211206	EPI_ISL_7779100
hCoV-19/Switzerland/ZH-SNRCI-HUG-36299537/2021	AY.43	20211206	EPI_ISL_7779101
hCoV-19/Switzerland/ZH-SNRCI-HUG-36299448/2021	AY.43	20211206	EPI_ISL_7779102
hCoV-19/Switzerland/VD-SNRCI-HUG-36299343/2021	AY.46	20211206	EPI_ISL_7779098
hCoV-19/Switzerland/BE-SNRCI-HUG-36328245/2021	AY.122	20211207	EPI_ISL_7779178
hCoV-19/Switzerland/GL-SNRCI-HUG-36328151/2021	AY.4	20211208	EPI_ISL_7779161
hCoV-19/Switzerland/SG-SNRCI-HUG-36328185/2021	AY.4	20211208	EPI_ISL_7779092
hCoV-19/Switzerland/VD-SNRCI-HUG-36328314/2021	AY.46	20211208	EPI_ISL_7779099
hCoV-19/Switzerland/ZH-SNRCI-HUG-36327885/2021	B.1.1.529	20211209	EPI_ISL_7779180
hCoV-19/Switzerland/NE-SNRCI-HUG-36327820/2021	AY.46.6	20211209	EPI_ISL_7779091

Isolate name	Pangolin clade	Collection date	GISAID_ID
hCoV-19/Switzerland/VD-SNRCI-HUG-36355598/2021	AY.4	20211210	EPI_ISL_7995682
hCoV-19/Switzerland/GL-SNRCI-HUG-36407630/2021	AY.43	20211213	EPI_ISL_7995820
hCoV-19/Switzerland/BL-SNRCI-HUG-36406335/2021	B.1.617.2	20211213	EPI_ISL_7995822
hCoV-19/Switzerland/BE-SNRCI-HUG-36406254/2021	AY.4	20211213	EPI_ISL_7995598
hCoV-19/Switzerland/NE-SNRCI-HUG-36406158/2021	AY.9.2	20211214	EPI_ISL_7995821
hCoV-19/Switzerland/NE-SNRCI-HUG-36406704/2021	AY.9.2	20211214	EPI_ISL_7995823
hCoV-19/Switzerland/AG-SNRCI-HUG-36406636/2021	AY.7.1	20211214	EPI_ISL_7995619
hCoV-19/Switzerland/TI-SNRCI-HUG-36449366/2021	AY.46.6	20211216	EPI_ISL_8466312
hCoV-19/Switzerland/TG-SNRCI-HUG-36470351/2021	AY.43	20211216	EPI_ISL_8466144
hCoV-19/Switzerland/GL-SNRCI-HUG-36449248/2021	AY.4	20211217	EPI_ISL_8466145
hCoV-19/Switzerland/VD-SNRCI-HUG-36484113/2021	BA.1	20211220	EPI_ISL_8466160
hCoV-19/Switzerland/FR-SNRCI-HUG-36579269/2021	AY.126	20211227	EPI_ISL_8466451
hCoV-19/Switzerland/ZH-SNRCI-HUG-36628556/2022	BA.1	20211230	EPI_ISL_8679337
hCoV-19/Switzerland/BE-SNRCI-HUG-36656500/2021	BA.1	20220103	EPI_ISL_8680341
hCoV-19/Switzerland/BE-SNRCI-HUG-36642372/2022	BA.1	20220103	EPI_ISL_8680339
hCoV-19/Switzerland/AG-SNRCI-HUG-36642162/2021	BA.1	20220103	EPI_ISL_8680343
hCoV-19/Switzerland/AG-SNRCI-HUG-36642127/2022	BA.1	20220103	EPI_ISL_8680342
hCoV-19/Switzerland/VD-SNRCI-HUG-36656717/2021	BA.1	20220104	EPI_ISL_8679342
hCoV-19/Switzerland/VD-SNRCI-HUG-36656458/2021	AY.4	20220104	EPI_ISL_8679343
hCoV-19/Switzerland/VS-SNRCI-HUG-36656333/2021	BA.1	20220104	EPI_ISL_8679339
hCoV-19/Switzerland/BE-SNRCI-HUG-36656158/2021	BA.1	20220104	EPI_ISL_8680340
hCoV-19/Switzerland/ZH-SNRCI-HUG-36656068/2021	BA.1	20220104	EPI_ISL_8679338
hCoV-19/Switzerland/ZH-SNRCI-HUG-36720273/2022	BA.1	20220107	EPI_ISL_8891953
hCoV-19/Switzerland/BE-SNRCI-HUG-36720341/2022	BA.1	20220108	EPI_ISL_8891678
hCoV-19/Switzerland/AG-SNRCI-HUG-36751734/2022	BA.1	20220111	EPI_ISL_8891676
hCoV-19/Switzerland/AG-SNRCI-HUG-36752215/2022	BA.1	20220111	EPI_ISL_8891677
hCoV-19/Switzerland/BE-SNRCI-HUG-36752097/2022	BA.1	20220111	EPI_ISL_8891679
hCoV-19/Switzerland/TI-SNRCI-HUG-36752249/2022	BA.1	20220111	EPI_ISL_8891944
hCoV-19/Switzerland/VD-SNRCI-HUG-36751767/2022	BA.1	20220112	EPI_ISL_8891952
hCoV-19/Switzerland/TI-SNRCI-HUG-36814289/2022	BA.1	20220114	EPI_ISL_9193437
hCoV-19/Switzerland/TI-SNRCI-HUG-36814364/2022	BA.1	20220114	EPI_ISL_9193439
hCoV-19/Switzerland/TI-SNRCI-HUG-36814402/2022	BA.1	20220114	EPI_ISL_9193438
hCoV-19/Switzerland/BE-SNRCI-HUG-36886358/2022	BA.1	20220120	EPI_ISL_9512577
hCoV-19/Switzerland/ZH-SNRCI-HUG-36886436/2022	BA.1.1	20220120	EPI_ISL_9512857
hCoV-19/Switzerland/VD-SNRCI-HUG-36884863/2022	BA.1	20220121	EPI_ISL_9512852
hCoV-19/Switzerland/VS-SNRCI-HUG-36921988/2022	BA.1.1	20220121	EPI_ISL_9512855
hCoV-19/Switzerland/BE-SNRCI-HUG-36886485/2022	BA.1	20220122	EPI_ISL_9512578
hCoV-19/Switzerland/ZH-SNRCI-HUG-36886526/2022	BA.1.1	20220122	EPI_ISL_9512858
hCoV-19/Switzerland/AG-SNRCI-HUG-36922020/2022	BA.1	20220124	EPI_ISL_9512575
hCoV-19/Switzerland/BE-SNRCI-HUG-36922068/2022	BA.1.1	20220124	EPI_ISL_9512579
hCoV-19/Switzerland/AG-SNRCI-HUG-36922181/2022	BA.1.1	20220124	EPI_ISL_9512573
hCoV-19/Switzerland/AG-SNRCI-HUG-36922207/2022	BA.1.1	20220124	EPI_ISL_9512574
hCoV-19/Switzerland/AG-SNRCI-HUG-36922846/2022	BA.1	20220124	EPI_ISL_9512576
hCoV-19/Switzerland/ZH-SNRCI-HUG-36940518/2022	BA.1	20220124	EPI_ISL_9512859
hCoV-19/Switzerland/GL-SNRCI-HUG-36939810/2022	BA.1.1	20220124	EPI_ISL_9512850
hCoV-19/Switzerland/TI-SNRCI-HUG-36940320/2022	BA.1	20220125	EPI_ISL_9512851
hCoV-19/Switzerland/VS-SNRCI-HUG-36939325/2022	BA.1	20220125	EPI_ISL_9512856
hCoV-19/Switzerland/ZH-SNRCI-HUG-36939453/2022	BA.1	20220125	EPI_ISL_9512860
hCoV-19/Switzerland/FR-SNRCI-HUG-36940574/2022	BA.1.1	20220125	EPI_ISL_9512581
hCoV-19/Switzerland/GL-SNRCI-HUG-36939899/2022	BA.1	20220125	EPI_ISL_9512849

Isolate name	Pangolin clade	Collection date	GISAID_ID
hCoV-19/Switzerland/NE-SNRCI-HUG-36997527/2022	BA.1.1	20220127	EPI_ISL_9752181
hCoV-19/Switzerland/GL-SNRCI-HUG-36997511/2022	BA.2	20220128	EPI_ISL_9752177
hCoV-19/Switzerland/GL-SNRCI-HUG-36997453/2022	BA.1	20220128	EPI_ISL_9752178
hCoV-19/Switzerland/AG-SNRCI-HUG-37011564/2022	BA.1.1	20220130	EPI_ISL_9751902
hCoV-19/Switzerland/TI-SNRCI-HUG-37012886/2022	BA.1.1	20220131	EPI_ISL_9752187
hCoV-19/Switzerland/TI-SNRCI-HUG-37012874/2022	BA.1.1	20220131	EPI_ISL_9752186
hCoV-19/Switzerland/AG-SNRCI-HUG-37012682/2022	BA.1.1	20220131	EPI_ISL_9751906
hCoV-19/Switzerland/AG-SNRCI-HUG-37012510/2022	BA.1	20220131	EPI_ISL_9751905
hCoV-19/Switzerland/VD-SNRCI-HUG-37012355/2022	BA.1	20220131	EPI_ISL_9752192
hCoV-19/Switzerland/VD-SNRCI-HUG-37012288/2022	BA.1.1	20220131	EPI_ISL_9752191
hCoV-19/Switzerland/ZH-SNRCI-HUG-37012171/2022	BA.1.1	20220131	EPI_ISL_9752198
hCoV-19/Switzerland/AG-SNRCI-HUG-37012024/2022	BA.1	20220131	EPI_ISL_9751904
hCoV-19/Switzerland/BE-SNRCI-HUG-37011927/2022	BA.1	20220131	EPI_ISL_9751910
hCoV-19/Switzerland/AG-SNRCI-HUG-37011754/2022	BA.1.1	20220131	EPI_ISL_9751903
hCoV-19/Switzerland/BE-SNRCI-HUG-37011586/2022	BA.1.1	20220131	EPI_ISL_9751909
hCoV-19/Switzerland/TI-SNRCI-HUG-37011438/2022	BA.1.1	20220131	EPI_ISL_9752185
hCoV-19/Switzerland/SG-SNRCI-HUG-37011805/2022	BA.1	20220131	EPI_ISL_9752184
hCoV-19/Switzerland/VD-SNRCI-HUG-37028473/2022	BA.1	20220201	EPI_ISL_9752195
hCoV-19/Switzerland/BE-SNRCI-HUG-37028455/2022	BA.1	20220201	EPI_ISL_9751912
hCoV-19/Switzerland/ZH-SNRCI-HUG-37028291/2022	BA.1.1	20220201	EPI_ISL_9752199
hCoV-19/Switzerland/AG-SNRCI-HUG-37028242/2022	BA.1.1	20220201	EPI_ISL_9751907
hCoV-19/Switzerland/BE-SNRCI-HUG-37028181/2022	BA.1.1	20220201	EPI_ISL_9751911
hCoV-19/Switzerland/GR-SNRCI-HUG-37027183/2022	BA.1.1	20220201	EPI_ISL_9752179
hCoV-19/Switzerland/NE-SNRCI-HUG-37027141/2022	BA.1	20220202	EPI_ISL_9752183
hCoV-19/Switzerland/ZH-SNRCI-HUG-37052351/2022	BA.1	20220203	EPI_ISL_10057831
hCoV-19/Switzerland/GE-SNRCI-HUG-37052105/2022	BA.1.1	20220203	EPI_ISL_10057832
hCoV-19/Switzerland/BE-SNRCI-HUG-37051965/2022	BA.1	20220203	EPI_ISL_10057833
hCoV-19/Switzerland/BE-SNRCI-HUG-37098051/2022	BA.1.1	20220204	EPI_ISL_10058000
hCoV-19/Switzerland/ZH-SNRCI-HUG-37098130/2022	BA.1	20220205	EPI_ISL_10057997
hCoV-19/Switzerland/BE-SNRCI-HUG-37097937/2022	BA.1.1	20220207	EPI_ISL_10058005
hCoV-19/Switzerland/VD-SNRCI-HUG-37098175/2022	BA.1	20220207	EPI_ISL_10057996
hCoV-19/Switzerland/VD-SNRCI-HUG-37098281/2022	BA.1	20220207	EPI_ISL_10058007
hCoV-19/Switzerland/FR-SNRCI-HUG-37098124/2022	BA.1.1	20220207	EPI_ISL_10057999
hCoV-19/Switzerland/SH-SNRCI-HUG-37097966/2022	BA.1.1	20220207	EPI_ISL_10058006
hCoV-19/Switzerland/VD-SNRCI-HUG-37098223/2022	BA.1.1	20220207	EPI_ISL_10057998
hCoV-19/Switzerland/GE-SNRCI-HUG-37098251/2022	BA.1.1	20220207	EPI_ISL_10057995
hCoV-19/Switzerland/VS-SNRCI-HUG-37111754/2022	BA.1	20220207	EPI_ISL_10058093
hCoV-19/Switzerland/FR-SNRCI-HUG-37111420/2022	BA.2	20220207	EPI_ISL_10058090
hCoV-19/Switzerland/AG-SNRCI-HUG-37111626/2022	BA.1	20220207	EPI_ISL_10058091
hCoV-19/Switzerland/BE-SNRCI-HUG-37111825/2022	BA.1	20220207	EPI_ISL_10058094
hCoV-19/Switzerland/TI-SNRCI-HUG-37111688/2022	BA.2	20220208	EPI_ISL_10058092
hCoV-19/Switzerland/VD-SNRCI-HUG-37111332/2022	BA.1.1	20220208	EPI_ISL_10058089
hCoV-19/Switzerland/TI-SNRCI-HUG-37111910/2022	BA.1.1	20220208	EPI_ISL_10058096
hCoV-19/Switzerland/BE-SNRCI-HUG-37111870/2022	BA.2	20220208	EPI_ISL_10058095
hCoV-19/Switzerland/VD-SNRCI-HUG-37148066/2022	BA.1.1	20220209	EPI_ISL_10356614
hCoV-19/Switzerland/LU-SNRCI-HUG-37135336/2022	BA.1.1	20220210	EPI_ISL_10356610
hCoV-19/Switzerland/ZH-SNRCI-HUG-37168333/2022	BA.2	20220210	EPI_ISL_10356621
hCoV-19/Switzerland/ZH-SNRCI-HUG-37147977/2022	BA.1.1	20220211	EPI_ISL_10356620
hCoV-19/Switzerland/GL-SNRCI-HUG-37181239/2022	BA.1	20220211	EPI_ISL_10356607
hCoV-19/Switzerland/GL-SNRCI-HUG-37181202/2022	BA.1	20220214	EPI_ISL_10356608

Isolate name	Pangolin clade	Collection date	GISAID_ID
hCoV-19/Switzerland/AG-SNRCI-HUG-37181102/2022	BA.2	20220214	EPI_ISL_10356395
hCoV-19/Switzerland/GR-SNRCI-HUG-37181019/2022	BA.1.1	20220214	EPI_ISL_10356609
hCoV-19/Switzerland/AG-SNRCI-HUG-37180970/2022	BA.1	20220214	EPI_ISL_10356396
hCoV-19/Switzerland/LU-SNRCI-HUG-37180919/2022	BA.2	20220214	EPI_ISL_10356611
hCoV-19/Switzerland/BE-SNRCI-HUG-37228720/2022	BA.1.1	20220218	EPI_ISL_10666447
hCoV-19/Switzerland/ZH-SNRCI-HUG-37272709/2022	BA.2	20220218	EPI_ISL_10666638
hCoV-19/Switzerland/NE-SNRCI-HUG-37260572/2022	BA.2	20220220	EPI_ISL_10666592
hCoV-19/Switzerland/AG-SNRCI-HUG-37260641/2022	BA.1.1	20220221	EPI_ISL_10666593
hCoV-19/Switzerland/GL-SNRCI-HUG-37260427/2022	BA.2	20220221	EPI_ISL_10666591
hCoV-19/Switzerland/LU-SNRCI-HUG-37260250/2022	BA.1.1	20220221	EPI_ISL_10666590
hCoV-19/Switzerland/AG-SNRCI-HUG-37260237/2022	BA.2	20220221	EPI_ISL_10666589
hCoV-19/Switzerland/AG-SNRCI-HUG-37260139/2022	BA.1	20220221	EPI_ISL_10666588
hCoV-19/Switzerland/TI-SNRCI-HUG-37272895/2022	BA.2	20220222	EPI_ISL_10666642
hCoV-19/Switzerland/GL-SNRCI-HUG-37272865/2022	BA.2	20220222	EPI_ISL_10666641
hCoV-19/Switzerland/GR-SNRCI-HUG-37272781/2022	BA.2	20220222	EPI_ISL_10666640
hCoV-19/Switzerland/BE-SNRCI-HUG-37272768/2022	BA.2	20220222	EPI_ISL_10666639
hCoV-19/Switzerland/AG-SNRCI-HUG-37272416/2022	BA.2	20220222	EPI_ISL_10666643
hCoV-19/Switzerland/VD-SNRCI-HUG-37294533/2022	BA.2	20220223	EPI_ISL_10926126
hCoV-19/Switzerland/GL-SNRCI-HUG-37305786/2022	BA.2	20220224	EPI_ISL_10926175
hCoV-19/Switzerland/AG-SNRCI-HUG-37294790/2022	BA.1	20220224	EPI_ISL_10926128
hCoV-19/Switzerland/ZH-SNRCI-HUG-37294762/2022	BA.2	20220224	EPI_ISL_10926127
hCoV-19/Switzerland/GL-SNRCI-HUG-37305770/2022	BA.2	20220225	EPI_ISL_10926174
hCoV-19/Switzerland/VD-SNRCI-HUG-37364720/2022	BA.2	20220302	EPI_ISL_11130601
hCoV-19/Switzerland/SG-SNRCI-HUG-37364677/2022	BA.2	20220303	EPI_ISL_11130600
hCoV-19/Switzerland/BE-SNRCI-HUG-37376325/2022	BA.2	20220304	EPI_ISL_11130661
hCoV-19/Switzerland/ZH-SNRCI-HUG-37449913/2022	BA.2	20220310	EPI_ISL_11348308
hCoV-19/Switzerland/BE-SNRCI-HUG-37449808/2022	BA.1.1	20220310	EPI_ISL_11348312
hCoV-19/Switzerland/ZH-SNRCI-HUG-37449662/2022	BA.2	20220310	EPI_ISL_11348309
hCoV-19/Switzerland/NE-SNRCI-HUG-37449861/2022	BA.2	20220311	EPI_ISL_11348313
hCoV-19/Switzerland/GL-SNRCI-HUG-37449781/2022	BA.1.1	20220311	EPI_ISL_11348311
hCoV-19/Switzerland/GR-SNRCI-HUG-37449716/2022	BA.2	20220311	EPI_ISL_11348310
hCoV-19/Switzerland/TI-SNRCI-HUG-37546280/2022	BA.2	20220321	EPI_ISL_11669236
hCoV-19/Switzerland/VD-SNRCI-HUG-37546254/2022	BA.2	20220321	EPI_ISL_11669238
hCoV-19/Switzerland/VD-SNRCI-HUG-37546224/2022	BA.2	20220321	EPI_ISL_11669237
hCoV-19/Switzerland/NE-SNRCI-HUG-37546189/2022	BA.2	20220321	EPI_ISL_11669242
hCoV-19/Switzerland/GL-SNRCI-HUG-37546138/2022	BA.2	20220321	EPI_ISL_11669243
hCoV-19/Switzerland/GE-SNRCI-HUG-37545910/2022	BA.2	20220321	EPI_ISL_11669241
hCoV-19/Switzerland/AG-SNRCI-HUG-37545868/2022	BA.2	20220321	EPI_ISL_11669240
hCoV-19/Switzerland/GR-SNRCI-HUG-37545667/2022	BA.2	20220321	EPI_ISL_11669244
hCoV-19/Switzerland/AG-SNRCI-HUG-37545806/2022	BA.2	20220321	EPI_ISL_11669239
hCoV-19/Switzerland/GR-SNRCI-HUG-37545667/2022	BA.2	20220321	EPI_ISL_11669244
hCoV-19/Switzerland/BE-SNRCI-HUG-37604425/2022	BA.2	20220324	EPI_ISL_11851664
hCoV-19/Switzerland/BE-SNRCI-HUG-37604741/2022	BA.2	20220324	EPI_ISL_11851667
hCoV-19/Switzerland/BE-SNRCI-HUG-37604857/2022	BA.2	20220324	EPI_ISL_11851669
hCoV-19/Switzerland/ZH-SNRCI-HUG-37604584/2022	BA.2	20220324	EPI_ISL_11851660
hCoV-19/Switzerland/VD-SNRCI-HUG-37604773/2022	BA.2	20220325	EPI_ISL_11851665
hCoV-19/Switzerland/BE-SNRCI-HUG-37604337/2022	BA.2	20220325	EPI_ISL_11851666
hCoV-19/Switzerland/BE-SNRCI-HUG-37604268/2022	BA.2	20220325	EPI_ISL_11851656
hCoV-19/Switzerland/BE-SNRCI-HUG-37604250/2022	BA.2	20220325	EPI_ISL_11851657
hCoV-19/Switzerland/BE-SNRCI-HUG-37604216/2022	BA.2	20220325	EPI_ISL_11851658

Appendix 5: Antigenic analyses of influenza A(H3N2) viruses (with 20nM Oseltamivir) 2022-03-18, WIC

Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
				Post-infection ferret antisera								
				A/Denmark	A/HK	A/Camb	A/Camb	A/Bang	A/Darwin	A/Stock	A/Eng	A/Kansas
				3264/19	2671/19	e0826360/20	925256/20	4005/20	9/21	5/21	214191723/21	14/17
	Passage history			SIAT	Cell	Egg	SIAT	SIAT	Egg	SIAT	SIAT	SIAT
	Ferret number			F19/20[*1]	St Judes F21/20[*1]	F10/21[*1]	F03/21[*1]	F07/21[*1]	F38/21[*1]	F35/21[*1]	F07/22[*1]	F17/19[*1]
	Genetic group			3C.2a1b.1a	3C.2a1b.1b	3C.2a1b.2a.1	3C.2a1b.2a.1	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.2a1b.2a.2	3C.3a1
REFERENCE VIRUSES												
A/Denmark/3264/2019	3C.2a1b.1a	2019-10-25	SIAT3/SIAT4	640	640	160	640	160	320	320	40	80
A/Hong Kong/2671/2019	3C.2a1b.1b	2019-06-17	MDCK1/SIAT4	320	640	160	640	320	320	160	40	160
A/Cambodia/e0826360/2020	3C.2a1b.2a.1	2020-07-16	E5/E2	320	40	2560	320	320	1280	320	640	160
A/Cambodia/925256/2020	3C.2a1b.2a.1	2020-09-25	SIAT5	160	160	160	640	160	320	160	40	160
A/Bangladesh/4005/2020	3C.2a1b.2a.2	2020-10-04	SIAT3	320	80	320	320	640	2560	640	640	320
A/Darwin/9/2021	3C.2a1b.2a.2	2021-04-17	E3/E2	320	40	320	160	320	2560	640	640	80
A/Stockholm/5/2021	3C.2a1b.2a.2	2021-04-16	S0/S3	160	40	80	160	320	2560	640	640	80
A/England/214191723/2021	3C.2a1b.2a.2	2021-10-12	MDCK1/SIAT2	40	<	40	80	160	1280	320	640	<
A/Kansas/14/2017	3C.3a1	2017-12-14	SIAT3/SIAT2	80	40	80	80	80	160	160	80	640
TEST VIRUSES												
A/Switzerland/51230/2021	3C.2a1b.1a	2021-12-02	MDCK1/SIAT1	80	80	160	320	160	160	160	640	<
A/Switzerland/44070/2022	3C.2a1b.2a.2	2022-01-04	SIAT1	40	<	40	40	160	640	160	640	80
A/Switzerland/42321/2021	3C.2a1b.2a.2	2022-01-03	MDCK1/SIAT1	320	40	320	160	320	2560	1280	320	80
A/Switzerland/28536/2022	3C.2a1b.2a.2	2022-01-03	SIAT1	160	40	320	80	320	640	320	320	<
A/Switzerland/12229/2022	3C.2a1b.2a.2	2022-01-02	SIAT1	80	<	80	40	160	640	160	320	<
A/Switzerland/87473/2021	3C.2a1b.2a.2	2021-12-28	SIAT1/SIAT1	80	<	40	40	160	1280	640	640	<
A/Switzerland/79079/2021	3C.2a1b.2a.2	2021-12-27	SIAT1/SIAT1	40	<	40	40	160	640	320	640	80
A/Switzerland/02353/2021	3C.2a1b.2a.2	2021-12-07	SIAT1	160	<	320	80	320	640	320	ND	<
A/Switzerland/11712/2021	3C.2a1b.2a.2	2021-12-22	MDCK1/SIAT1	40	<	80	80	160	320	320	ND	40
A/Switzerland/69954/2021	3C.2a1b.2a.2	2021-11-20	MDCK1/SIAT1	160	<	320	80	640	320	320	ND	80
A/Switzerland/06630/2021	3C.2a1b.2a.2	2021-11-02	MDCK1/SIAT1	40	<	40	40	160	640	320	ND	<
A/Switzerland/98693/2021	3C.2a1b.2a.2	2021-12-21	SIAT1/SIAT1	80	<	80	40	320	1280	640	ND	40

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

1 < = <40, ND = Not Done

Vaccine

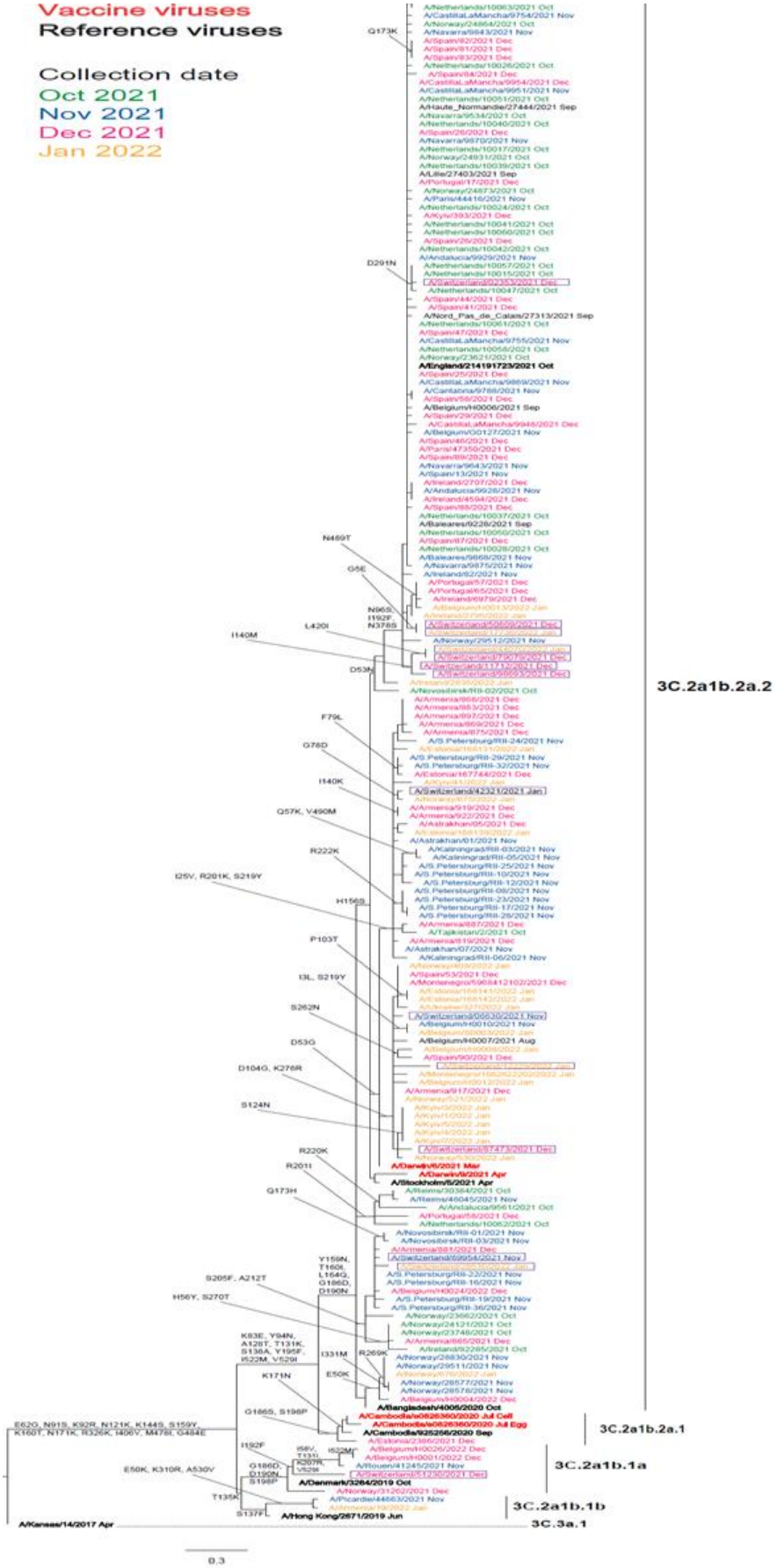
NH 2021

Appendix 6: Antigenic analyses of influenza B viruses (Victoria lineage) 2022-01-19, WIC

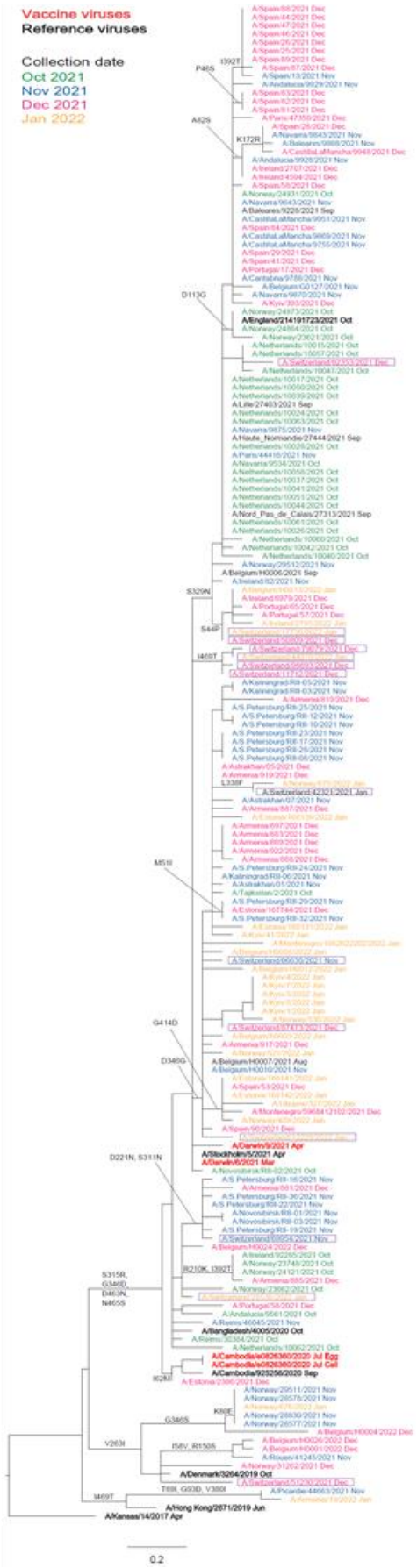
Viruses	Other information	Collection date	Passage history	Haemagglutination inhibition titre								
	Passage history			B/Bris 60/08 Egg	B/Colorado 06/17 Egg	B/Wash'ton 02/19 Egg	A/Croatia 7889/19 MDCK	B/CIV 948/20 MDCK	B/Austria 1359417/21 MDCK	B/Austria 1359417/21 Egg G141R	B/Austria 1359417/21 Egg G141X	B/Paris 9878/20 MDCK
	Ferret number			Sh 539, 540, 543, 544, 570, 571, 574[*1,3]	F11/18[*4]	F20/20[*2]	F19/21*[1]	F08/21*[2]	NIB F01/21[*1]	F44/21[*1]	F15/21[*1]	F12/21[*1]
	Genetic group			V1A	V1A.1	V1A.3	V1A.3a	V1A.3a.1	V1A.3a.2	V1A.3a.2	V1A.3a.2	V1A.3a.2
REFERENCE VIRUSES												
B/Brisbane/60/2008	V1A	2008-08-04	E4/E4	2560	40	40	80	<	<	<	<	<
B/Colorado/06/2017	V1A.1	2017-02-05	E5/E2	2560	160	80	80	<	<	<	<	<
B/Washington/02/2019	V1A.3	2019-01-19	E3/E2	1280	80	160	80	<	<	<	40	<
B/Croatia/7789/2019	V1A.3a	2019-11-11	MDCKx/MDCK3	640	80	80	640	160	160	80	160	40
B/Cote d'Ivoire/948/2020	V1A.3a.1	2020-05-28	MDCK2	640	<	80	640	640	80	160	160	80
B/Austria/1359417/2021	V1A.3a.2	2021-01-09	SIAT1/MDCK4	640	<	<	320	<	1280	640	2560	640
B/Austria/1359417/2021 Isolate 2G141	V1A.3a.2	2021-01-09	E3	ND	ND	ND	ND	ND	1280	1280	640	640
B/Austria/1359417/2021 Isolate 2G141R	V1A.3a.2	2021-01-09	E3/E4	320	10	<	320	160	1280	2560	>5120	640
B/Paris/9878/2020	V1A.3a.2	2020-11-20	MDCK2	1280	40	<	320	<	1280	640	1280	640
TEST VIRUSES												
B/Switzerland/11488/2021	V1A.3a.2	2021-11-29	SIAT1/MDCK1	640	40	<	320	<	1280	640	2560	640
B/Switzerland/57945/2021	V1A.3a.2	2021-11-24	MDCK1/MDCK1	640	40	<	160	<	1280	640	1280	640
					Vaccine SH 2019 NH 2019-20	Vaccine SH 2020 NH 2020-21 SH 2021					Vaccine SH 2021	

* 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

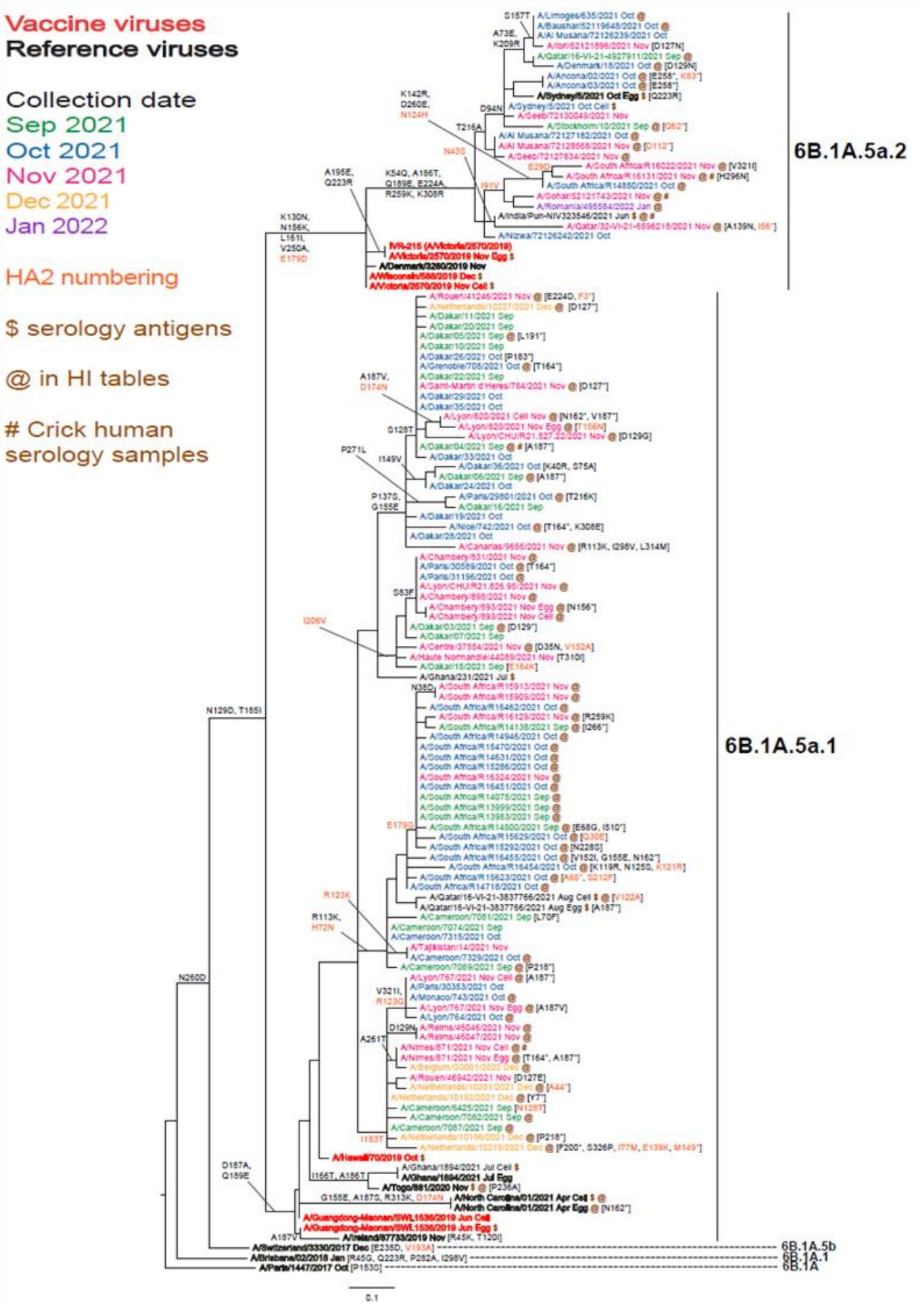
Appendix 7: Phylogenetic analysis of influenza A(H3N2), HA gene sequence, WIC



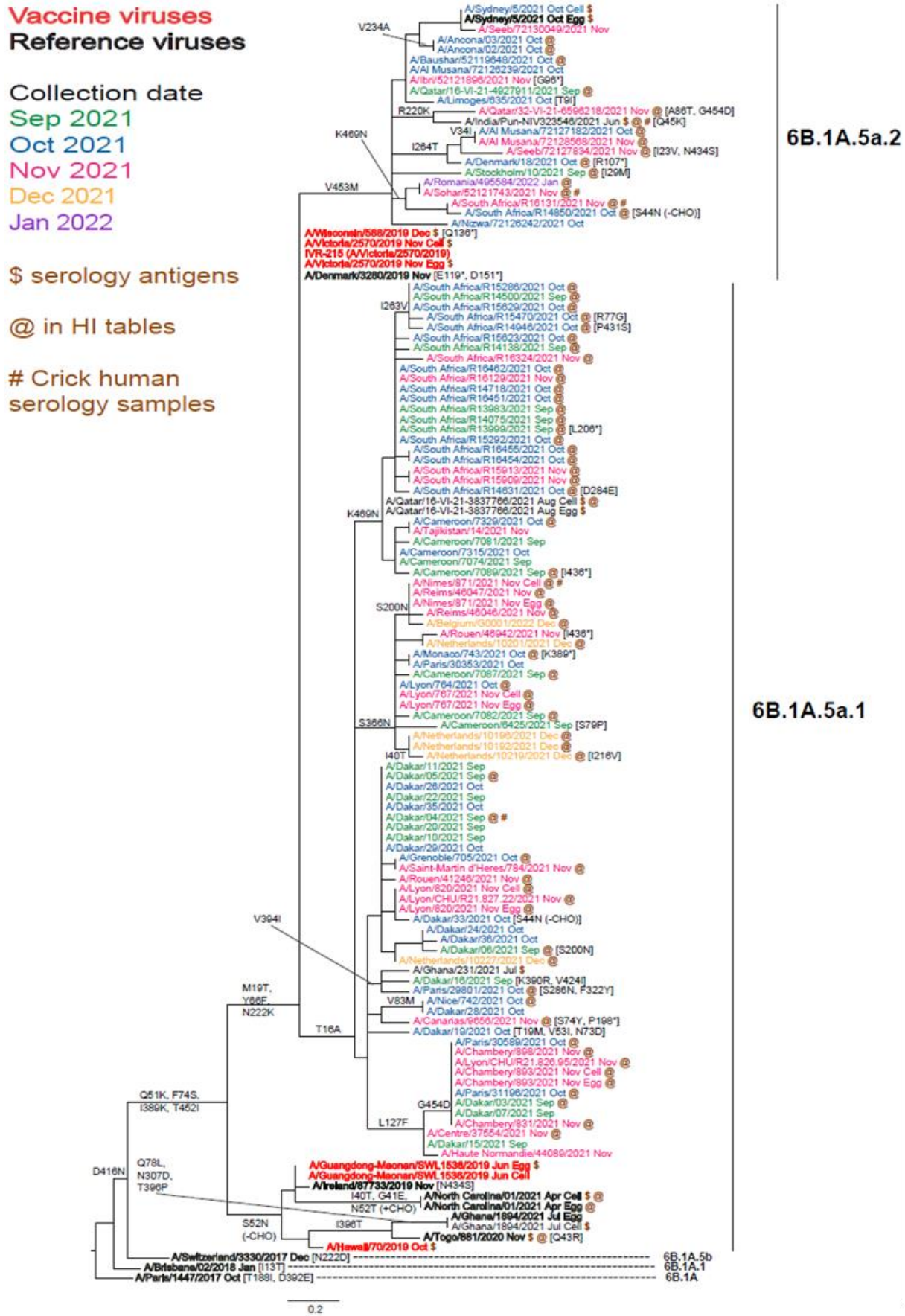
Appendix 8: Phylogenetic analysis of influenza A(H3N2), NA gene sequences, WIC



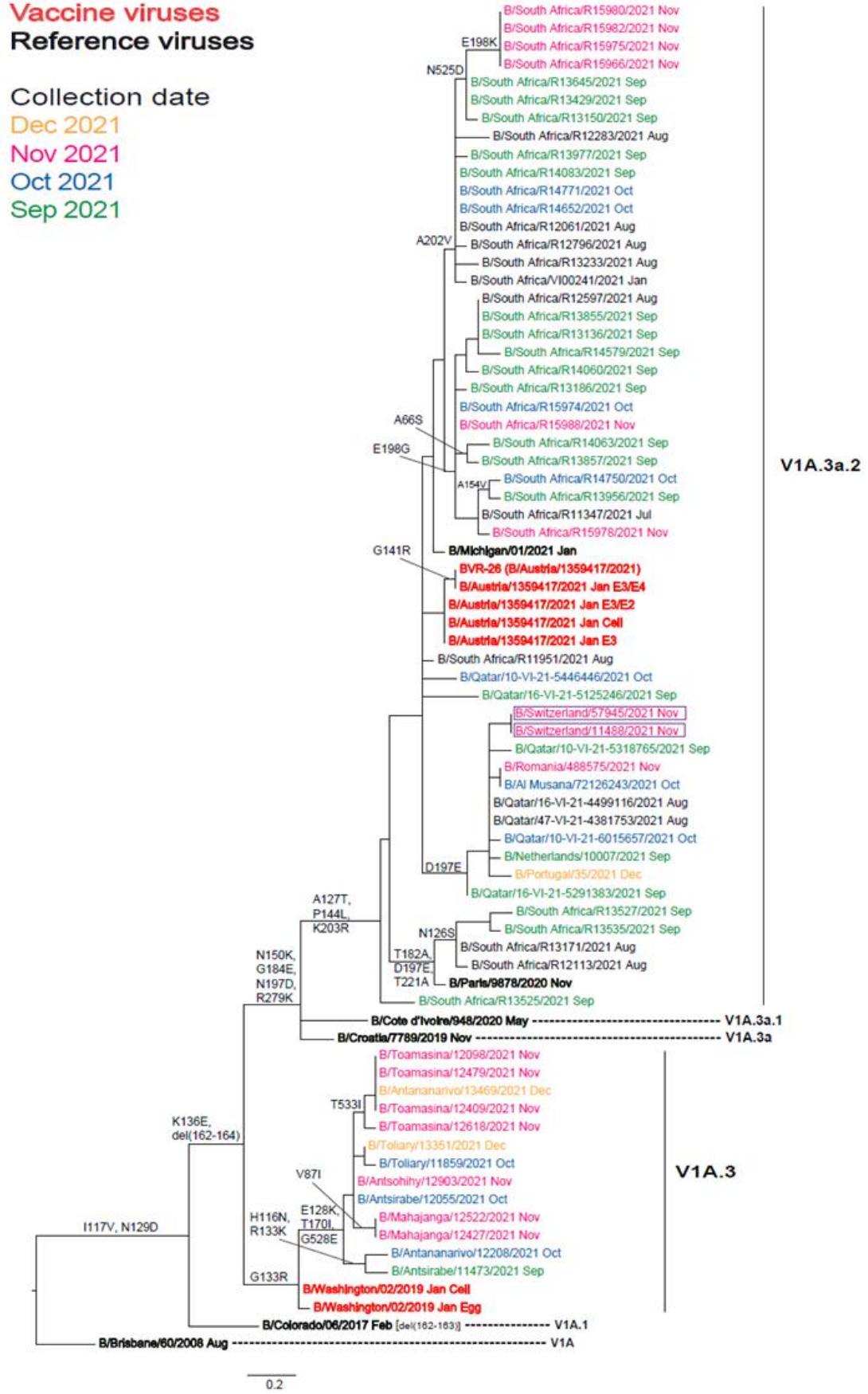
Appendix 9: Phylogenetic analysis of influenza A(H1N1)pdm09, HA gene sequences, WIC



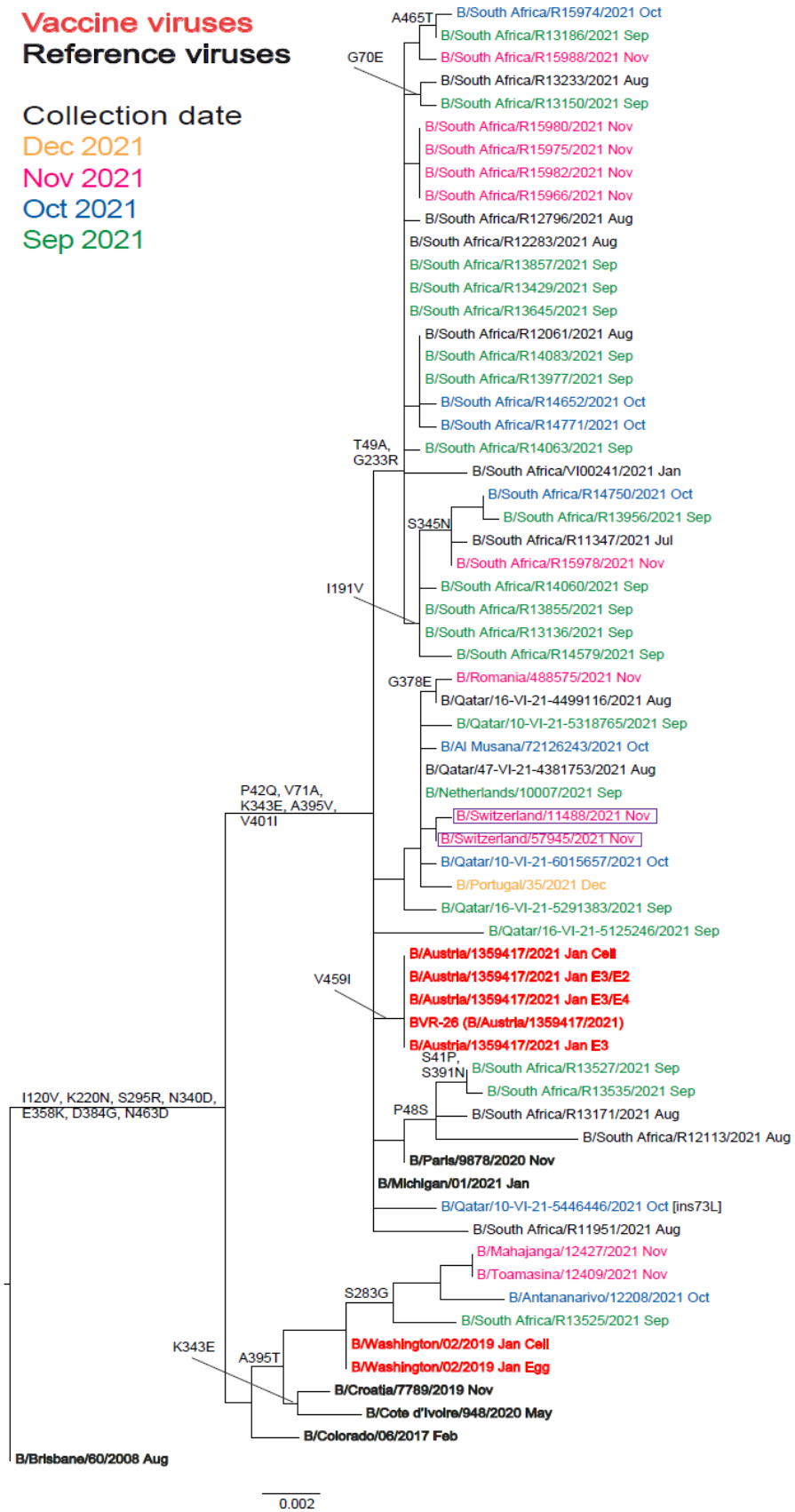
Appendix 10: Phylogenetic analysis of influenza A(H1N1)pdm09 NA gene sequences, WIC



Appendix 11: Phylogenetic analysis of influenza B-Victoria, HA gene sequences, WIC



Appendix 12: Phylogenetic analysis of influenza B-Victoria, NA gene sequences, WIC



Appendix 13: Antiviral sensitivity testing of Influenza A and B viruses, WIC

Virus name	Type/Subtype	OS IC50	OS sensitivity	Zan IC50	Zan sensitivity	HI result 1	Centre ID	Date received
A/Switzerland/01649/2021	A					Failed sequence – not cultured	CHE	13.janv.22
B/Switzerland/11488/2021	BV	37.06	Normal inhibition	5.31	Normal inhibition		CHE	13.janv.22
B/Switzerland/57945/2021	BV	38.85	Normal inhibition	2.60	Normal inhibition		CHE	13.janv.22
A/Switzerland/28605/2022	H3					Failed sequence – not cultured	CHE	13.janv.22
A/Switzerland/02423/2021	H3					Failed sequence – not cultured	CHE	13.janv.22
A/Switzerland/50809/2021	H3					Identical sequence – not cultured	CHE	13.janv.22
A/Switzerland/17736/2022	H3					Not cultured SAR-CoV2 positive	CHE	13.janv.22
A/Switzerland/51230/2021	H3	0.64	Normal inhibition	0.68	Normal inhibition		CHE	13.janv.22
A/Switzerland/44070/2022	H3	0.95	Normal inhibition	0.74	Normal inhibition		CHE	13.janv.22
A/Switzerland/42321/2021	H3	0.92	Normal inhibition	0.82	Normal inhibition		CHE	13.janv.22
A/Switzerland/28536/2022	H3	0.92	Normal inhibition	0.77	Normal inhibition		CHE	13.janv.22
A/Switzerland/12229/2022	H3	1.23	Normal inhibition	1.04	Normal inhibition		CHE	13.janv.22
A/Switzerland/87473/2021	H3	1.26	Normal inhibition	1.14	Normal inhibition		CHE	13.janv.22
A/Switzerland/79079/2021	H3	1.18	Normal inhibition	0.89	Normal inhibition		CHE	13.janv.22
A/Switzerland/11712/2021	H3	1.16	Normal inhibition	1.15	Normal inhibition		CHE	13.janv.22
A/Switzerland/98693/2021	H3	1.03	Normal inhibition	0.92	Normal inhibition		CHE	13.janv.22
A/Switzerland/69954/2021	H3	1.97	Normal inhibition	3.32	Normal inhibition		CHE	13.janv.22
A/Switzerland/06630/2021	H3	1.75	Normal inhibition	2.48	Normal inhibition		CHE	13.janv.22
A/Switzerland/02353/2021	H3	1.00	Normal inhibition	0.93	Normal inhibition		CHE	13.janv.22
A/Switzerland/14320/2021	H3					CT value high - not cultured	CHE	13.janv.22

Appendix 14: List of Influenza isolates submitted to GISAID (2021/2022)

Collection date	Isolate-ID	Isolate name
2021-Dec-02	EPI_ISL_13399693	A/Switzerland/51230/2021
2021-Dec-21	EPI_ISL_13331593	A/Switzerland/98693/2021
2021-Dec-27	EPI_ISL_13331586	A/Switzerland/79079/2021
2021-Dec-28	EPI_ISL_13331590	A/Switzerland/87473/2021
2021-Nov-20	EPI_ISL_13331584	A/Switzerland/69954/2021
2021-Nov-24	EPI_ISL_13332418	B/Switzerland/57945/2021
2021-Nov-29	EPI_ISL_13332417	B/Switzerland/11488/2021
2022-Feb-01	EPI_ISL_13331571	A/Switzerland/38769/2022
2022-Feb-02	EPI_ISL_13331594	A/Switzerland/27140/2022
2022-Feb-02	EPI_ISL_13331572	A/Switzerland/39137/2022
2022-Feb-03	EPI_ISL_13331580	A/Switzerland/52191/2022
2022-Feb-04	EPI_ISL_13331589	A/Switzerland/84161/2022
2022-Feb-07	EPI_ISL_13331592	A/Switzerland/98061/2022
2022-Feb-07	EPI_ISL_13331591	A/Switzerland/97840/2022
2022-Feb-08	EPI_ISL_13331595	A/Switzerland/11368/2022
2022-Feb-08	EPI_ISL_13331558	A/Switzerland/11727/2022
2022-Feb-09	EPI_ISL_13331568	A/Switzerland/23518/2022
2022-Feb-14	EPI_ISL_13331588	A/Switzerland/81273/2022
2022-Feb-14	EPI_ISL_13331553	A/Switzerland/95941/2022
2022-Feb-14	EPI_ISL_13331552	A/Switzerland/95790/2022
2022-Feb-15	EPI_ISL_13331587	A/Switzerland/80945/2022
2022-Feb-17	EPI_ISL_13331718	A/Switzerland/17909/2022
2022-Feb-17	EPI_ISL_13331569	A/Switzerland/28784/2022
2022-Feb-17	EPI_ISL_13331562	A/Switzerland/17988/2022
2022-Feb-17	EPI_ISL_13331551	A/Switzerland/17942/2022
2022-Feb-21	EPI_ISL_13331582	A/Switzerland/60468/2022
2022-Feb-21	EPI_ISL_13331581	A/Switzerland/60191/2022
2022-Feb-22	EPI_ISL_13331585	A/Switzerland/72457/2022
2022-Jan-07	EPI_ISL_13331563	A/Switzerland/20509/2022
2022-Jan-10	EPI_ISL_13331578	A/Switzerland/52033/2022
2022-Jan-10	EPI_ISL_13331576	A/Switzerland/51418/2022
2022-Jan-10	EPI_ISL_13331570	A/Switzerland/36739/2022
2022-Jan-11	EPI_ISL_13331577	A/Switzerland/51651/2022
2022-Jan-17	EPI_ISL_13331574	A/Switzerland/44423/2022
2022-Jan-17	EPI_ISL_13331573	A/Switzerland/44267/2022
2022-Jan-22	EPI_ISL_13331567	A/Switzerland/22985/2022
2022-Jan-23	EPI_ISL_13331565	A/Switzerland/22462/2022
2022-Jan-24	EPI_ISL_13331566	A/Switzerland/22627/2022
2022-Jan-24	EPI_ISL_13331564	A/Switzerland/22137/2022
2022-Jan-25	EPI_ISL_13331554	A/Switzerland/50178/2022
2022-Jan-26	EPI_ISL_13331583	A/Switzerland/62974/2022
2022-Jan-31	EPI_ISL_13399692	A/Switzerland/12743/2022
2022-Jan-31	EPI_ISL_13399691	A/Switzerland/12204/2022
2022-Jan-31	EPI_ISL_13331561	A/Switzerland/12636/2022
2022-Jan-31	EPI_ISL_13331557	A/Switzerland/11713/2022
2022-Jan-31	EPI_ISL_13331556	A/Switzerland/11638/2022
2022-Jan-31	EPI_ISL_13331555	A/Switzerland/11479/2022