GISHN report of activity prior to the WHO Consultation on the Composition of Influenza Virus Vaccines for use in the 2025 southern Hemisphere Influenza Season.

Report prepared the 18h of September 2024

1 - Description of the network

GIHSN is collecting clinical and virological information from hospitalized cases through a network of sites (20) located in different regions of the world (figure 1). This combined clinical and virological surveillance allows the identification of viruses responsible for severe influenza. This severity is assessed by the oxygen requirement of cases registered by the sites. In this report, viruses detected and sequenced from cases requiring oxygen supplementation are identified in the phylogenetic trees provided, to determine if specific lineages or clades or sub-clades are associated with more frequent severe presentation. It has been noted in the GIHSN report of the 2023 surveillance for the southern hemisphere VCM that O2 requirement seemed to be more frequently reported in the A(H3N2) 3C.2a1b.2a.3a HA lineage. This was not confirmed in the 2023-2024 Northern Hemisphere report.

For the SH 2024 surveillance period in GIHSN, influenza activity was mainly due to Influenza A viruses in most countries, with co-circulation of A(H1N1)pdm09 and A(H3N2) in different relative proportions.

Regarding the Influenza B viruses, as for the NH 2023-2024 surveillance, it has been reported for this SH 2024 surveillance a very limited number of detections of B/Victoria lineage viruses, and no B/Yamagata viruses have been detected by the network. This is the 3rd year of GIHSN surveillance with no detection of B/Yamagata viruses. Due to the very limited data available on influenza B viruses, no analysis regarding severity can be done at this stage.

This report is colliding the available sequencing data from 12 sites collected on patients admitted in hospital between February 1st, 2024 and August 31st, 2024: *Brazil (4), Kenya (25), Pakistan (50), Peru (21), Romania (63), Russia Moscow (12), Senegal (15), Spain (84), South Africa (175), Türkiye (9), Ukraine (80), USA (65).* All 603 sequences, from hospitalized cases only, have been uploaded in the GISAID database with a GIHSN tag.

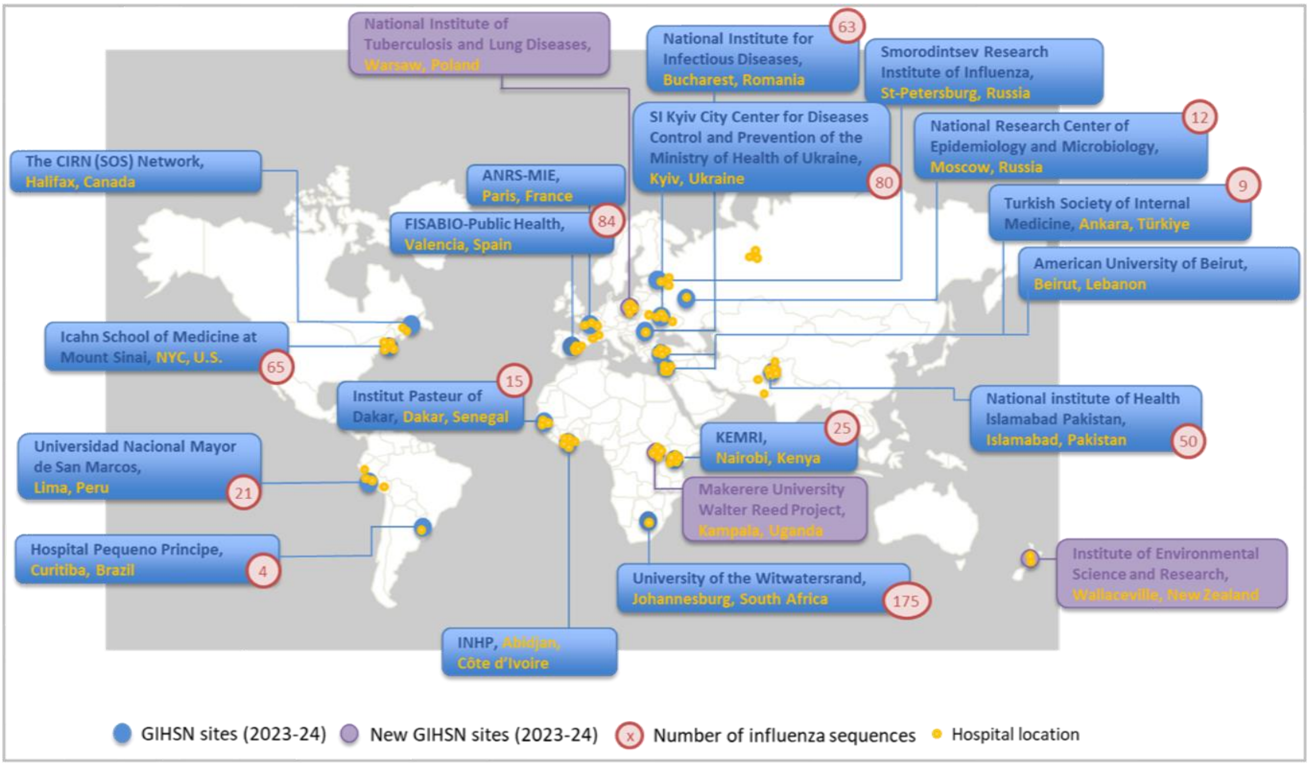

Fig. 1 Map showing the repartition of the participating countries, between February 1st, 2024 and August 31st, 2024. Three new sites are identified in purple. The number of sequences provided by the sites are indicated in the red circles.

2 - Description of the virus sequenced in the GIHSN

2.1 – international context

Globally, influenza detections reached a peak in December 2023 and have decreased since then until falling below the epidemic levels in March 2024. The relative proportions of A/H1N1, A/H3N2 and B/Victoria varied by geographic region with predominance of A/H1N1 in Europe and North and Central America and some predominance of A/H3N2 in Asia, Africa and Australia. Some countries in South America showed predominance of B/Victoria, as well as South Africa and Madagascar.

2.2 - Influenza A viruses

A(H1N1)pdm09 viruses

6B.1A.5a.2a and 6B.1A.5a.2a.1 clade viruses both continued to circulate with differing relative proportions depending on region, with a global predominance of 5a.2a viruses.

Sequencing results indicated that 15% of these viruses belonged to 6B.1A.5a.2a.1 clade close to reference strains A/Victoria/4897/2022 and A/Wisconsin/67/2022, while 85% belonged to 6B.1A.5a.2a clade (Fig. 2). The diversity of origin of these clade 6 B.1A.5a.2a viruses was larger, as compared to the clade 6B.1A.5a.2a1 viruses.

Among 5a.2a clade, most of the viruses belonged to C.1.9 subclade (68%), with other minor subclades detected: C.1 (18%), C.1.8 (11%), C.1.7.2 (3%) and C.1.7 (1%).

Viruses from clade 5a.2a.1 belonged mostly to subclade D1 (37%). Clade 5a.2a.1 viruses were closer to A/Victoria/4897/2022 reference strain than A/Wisconsin/67/2022, and were characterized by HA1: T216A substitution. Additional HA1 substitutions in some viruses included: R45K, S85P and R113K.

The frequency of report of Oxygen requirement does not seems to be more frequent in cases with specific sub clades of H1N1 viruses (Fig. 2).

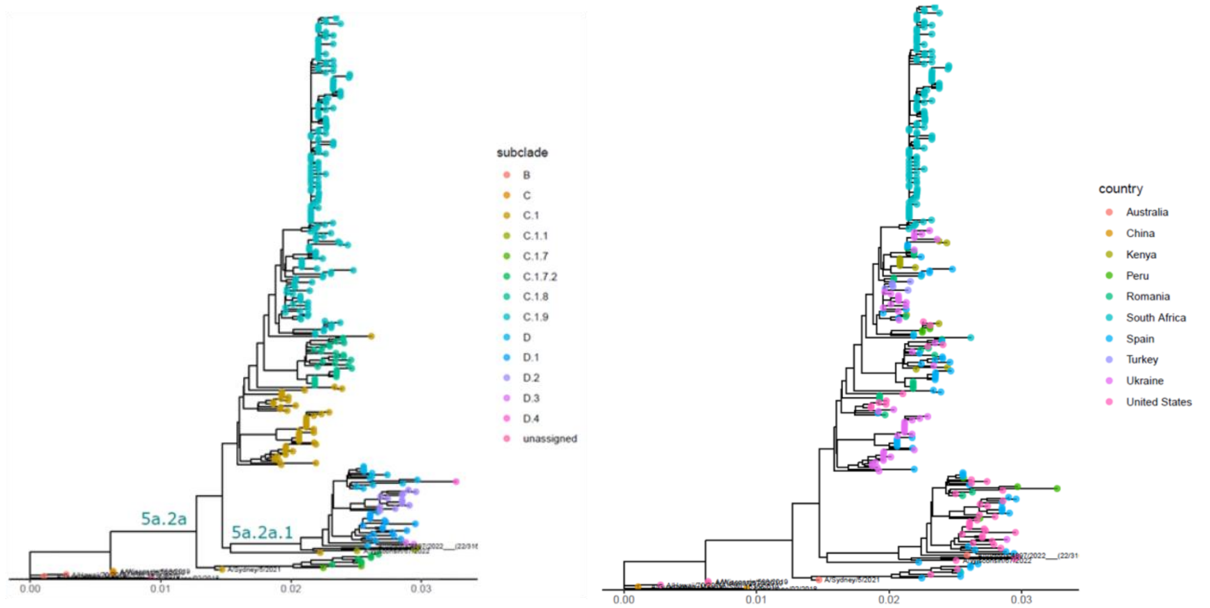

Fig 2a

Fig 2b

Fig 2: Phylogenetic tree of the ***A(H1N1pdm09)*** *viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R.*

Fig 2a provide the phylogenetic tree with clade and sub clade distribution;

Fig 2b provide the geographic origin of the viruses sequenced by the laboratories of GIHSN, with vaccine reference strains displayed in black.

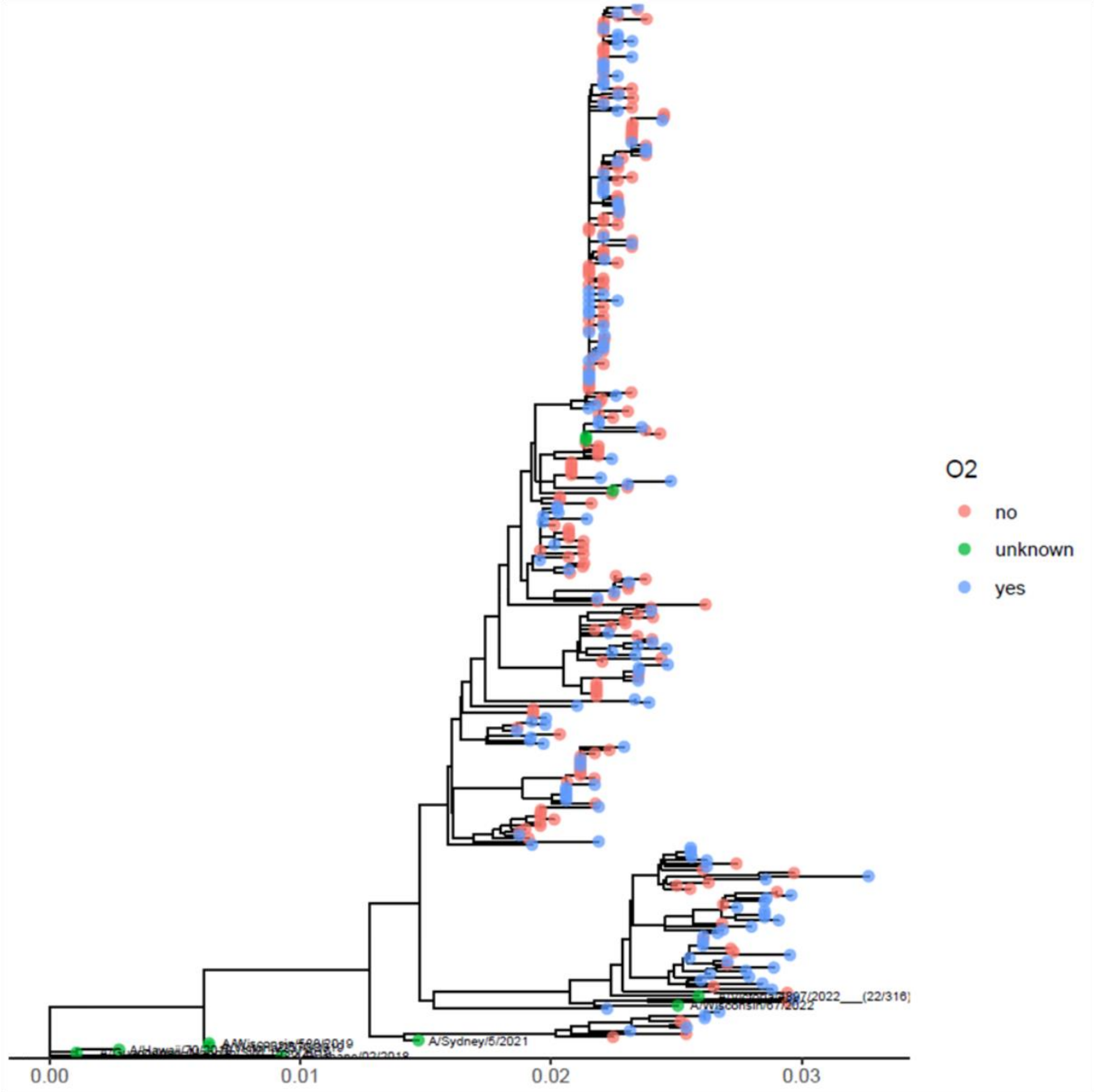

Fig 2c

Fig 2c: Phylogenetic tree of the ***A(H1N1pdm09)*** *viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red: no) with vaccine reference strains displayed in black. As stated in the text, no specific association could be observed between O2 requirement and any sub-clade*

A(H3N2) viruses

The HA genes of all A(H3N2) viruses sequenced into the GIHSN network belonged to 3C.2a1b.2a.2a.3a.1 clade, with A/Massachusetts/18/2022 and A/Thailand/8/2022 as reference viruses (Fig. 3). Most viruses were from J.2 subclade (71%) or from J.1 subclade (21%), and were clustered into separate branches compared to the reference A/Thailand/8/2022 (J subclade).

No specific lineage or clade could be associated with oxygen supplementation (Fig. 3).

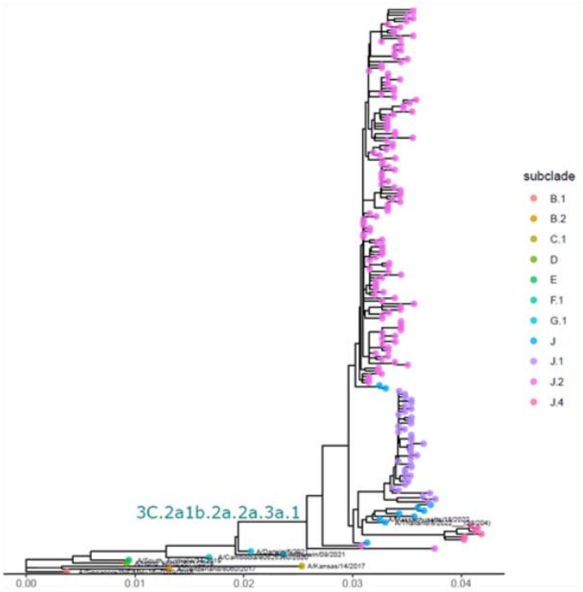

Fig 2a

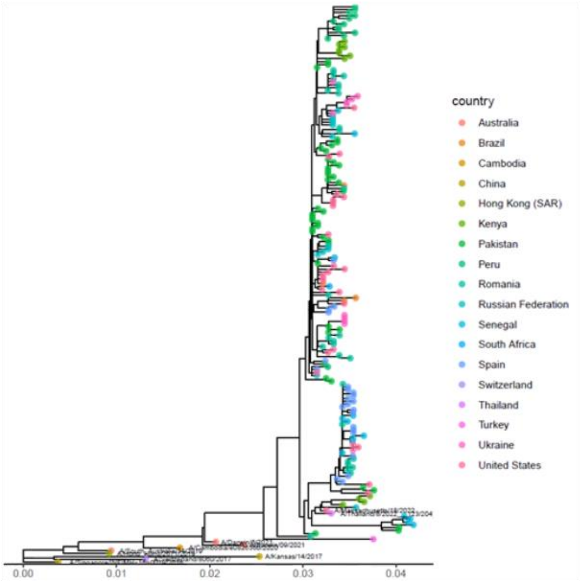

Fig 2b

Fig 2: Phylogenetic tree of the ***A(H3N2)*** *viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R.*

Fig 2a provide the phylogenetic tree with clade and sub clade distribution;

Fig 2b provide the geographic origin of the viruses sequenced by the laboratories of GIHSN, with countries given with color dots, vaccine reference strains are displayed in black.

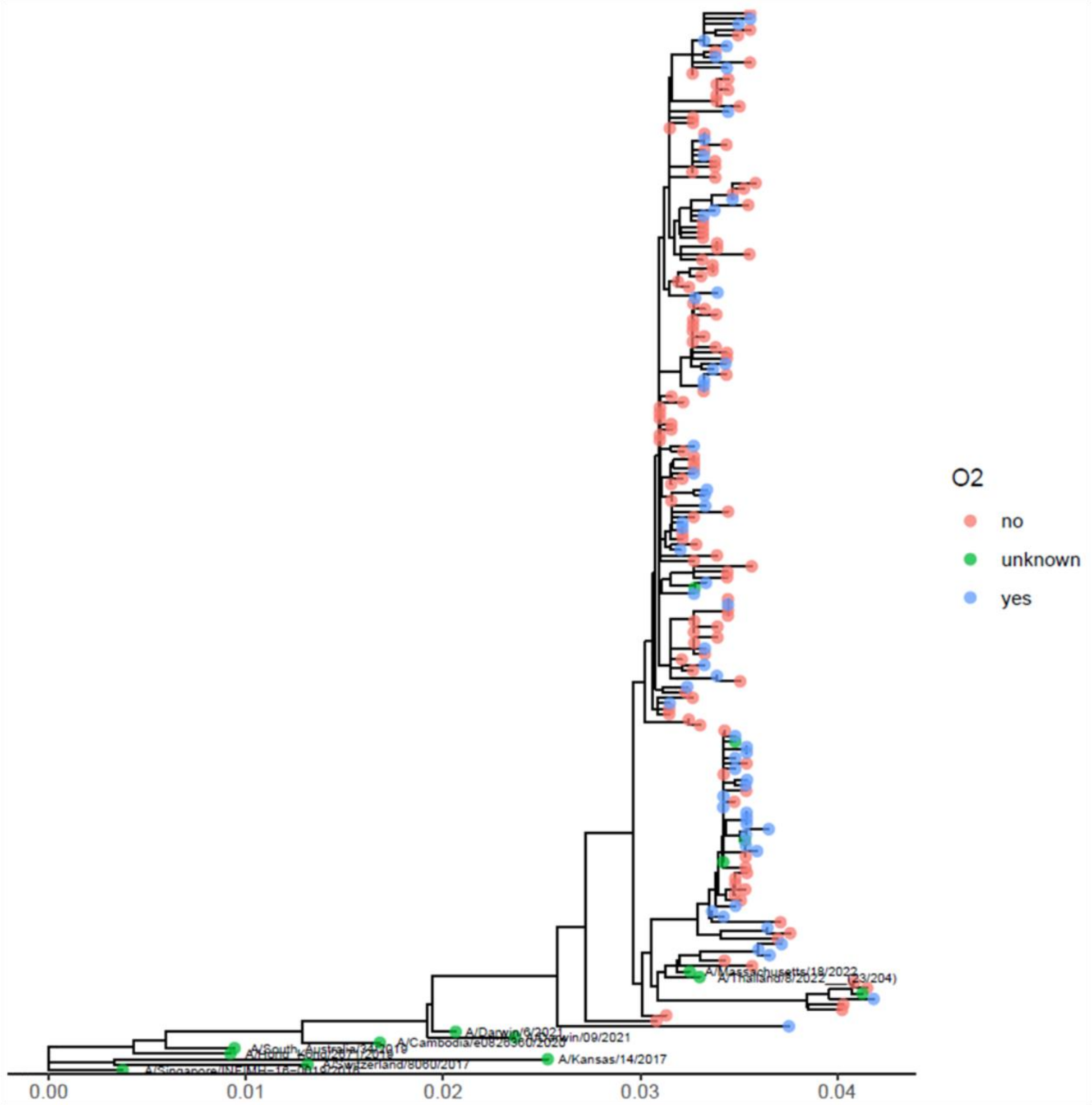

Fig 3c

*Fig 3c: Phylogenetic tree of the **A(H3N2)** viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red: no) with vaccine reference strains displayed in black.*

2.2 - Influenza B viruses

B/Victoria Lineage

During the surveillance in the GIHSN network, a minority of B viruses were detected. All belonged to the B/Victoria-lineage within V1A.3a clade. It is to note that for the 4th year, only B/Victoria-lineage viruses were detected by this network.

As reported by GISRS, all B viruses detected by the GIHSN network belong to the V1A.3a.2 clade. The most recent and the most frequently detected viruses are characterized by the additional substitution D197E, represented by B/Connecticut/01/2021 (subclade C.5). Subclades observed within V1A.3a.2 (C.5) are: C.5.1 with E183K (10% of the viruses), C.5.6 with D129N (20%) and C.5.7 with E183K and E128G (38%).

Due to the very limited data available, it is not possible to determine any possible or lack of specific association between any B/Victoria sub clade and O2 requirement

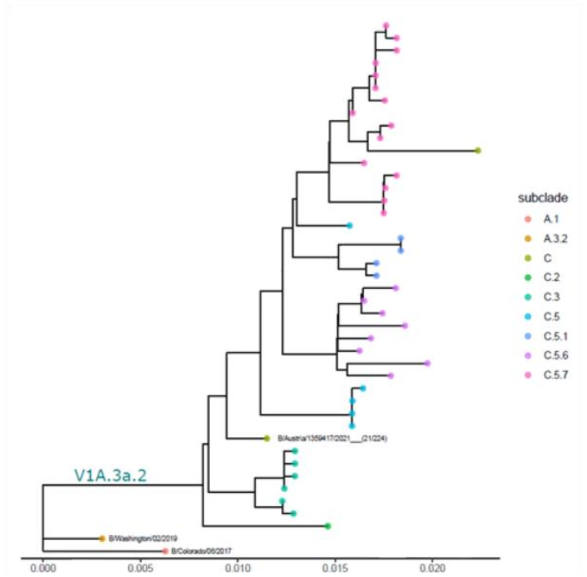

Fig 3a

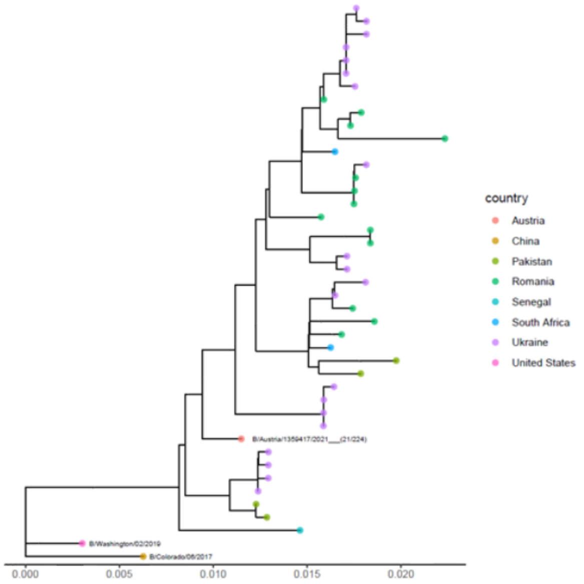

Fig 3b

*Fig 3: Phylogenetic tree of the **B/Victoria** viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R.*

Fig 3a provide the phylogenetic tree with clade and sub clade distribution;

Fig 3b provide the geographic origin of the viruses sequenced by the laboratories of GIHSN, with countries given with color dots, most recent vaccine reference strains are displayed in black.

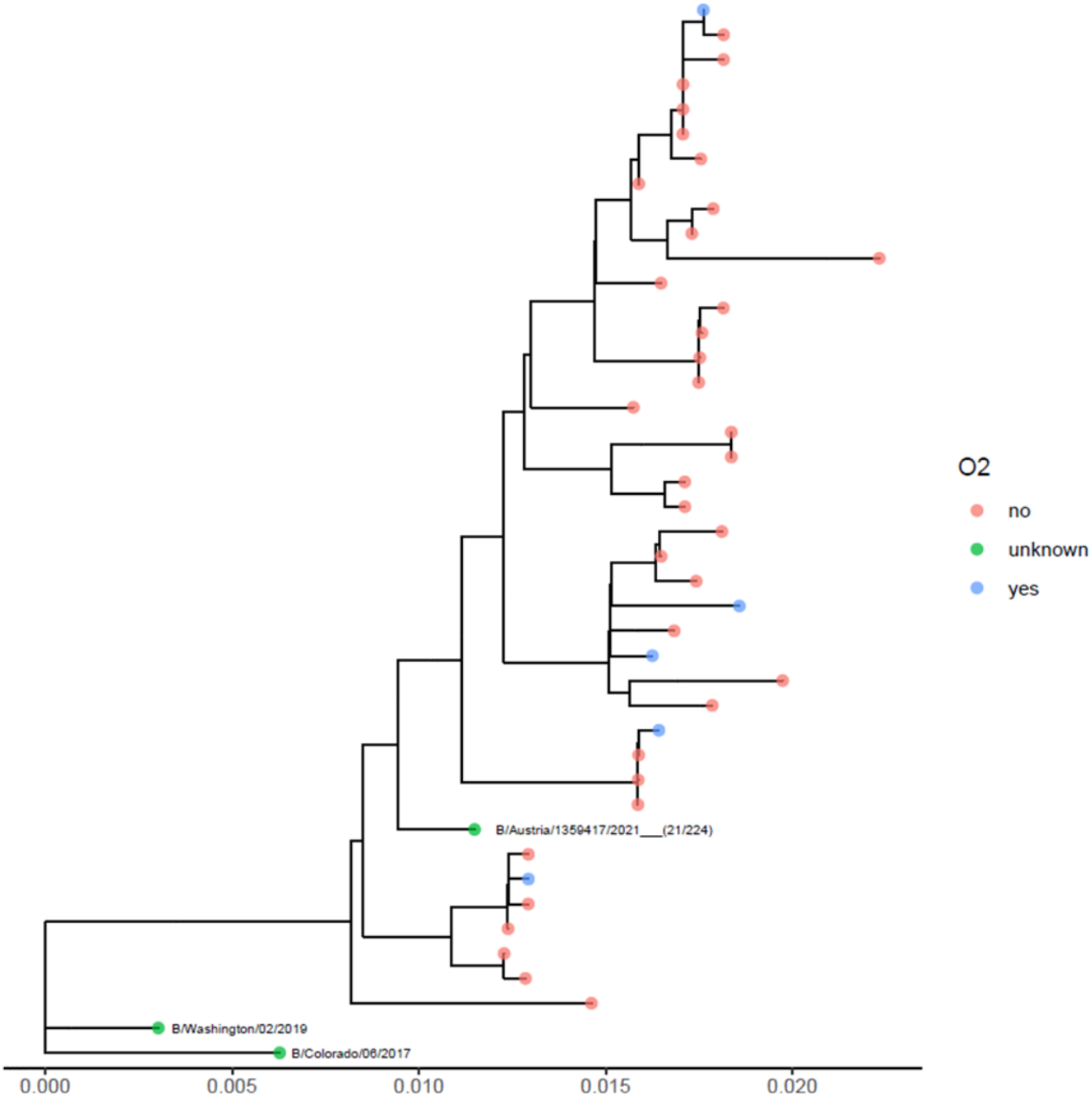

Fig 3c

*Fig 3c: Phylogenetic tree of the **B/Victoria** viruses analyzed between February 1st, 2024 and August 31st, 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red:no) with vaccine reference strains displayed in black.*

B/Yamagata viruses

No B/Yamagata viruses have been detected.

This report was prepared by the **National Influenza Center in Lyon, France:** Bruno Lina, Laurence Josset, Antonin Bal, Nathalie Bergaud, Gwendolyne Burfin, Gregory Queromes, Hadrien Regue, Quentin Semanas, and the GENEPII platform.

Acknowledgments to sites which contributed sequences: Pakistan: National Institute of Health, Islamabad, Pakistan, (Muhammad Salman, MD; Nazish Badar); Romania: National Institute for Infectious Diseases "Prof. Dr. Matei Bals", Bucharest (Anca Cristina Draganescu, MD, PhD; Oana Sandulescu); Senegal: Institut Pasteur of Dakar (IPD), Dakar (Ndongo Dia, MD); South Africa: Vaccines and Infectious Diseases Analytics Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg (Vicky Baillie); Spain: Fisabio-Public Health, Valencia (Ainara Mira Iglesias; Alejandro Orrico Sanchez); Türkiye: Turkish Society of Internal Medicine, Ankara (Serhat Unal, MD; Mine Durusu Tanriover); Ukraine: SI Kyiv City Center for Diseases Control and Prevention of the Ministry of Health of Ukraine (Alla Mironenko; Nataliia Teteriiuk); USA: Icahn School of Medicine at Mount Sinai, NYC (Viviana Simon, MD, Harm van Bakel, PhD); Kenya: Kenya Medical Research Institute (KEMRI), Nairobi (Nancy A. Otieno); Brazil: Hospital Pequeno Principe, Curitiba (Sonia Mara Raboni and Heloisa Isle Giamberardino); Peru: Clínica internacional, Instituto de Medicina Tropical Universidad Nacional Mayor de San Marcos, Lima (Dr Victor Alberto Laguna-Torres); Russia Moscow: FSBI "N.F. Gamaleya NRCEM" Ministry of Health of the Russian Federation (Federal Research Budgetary Institute "National Research Center of Epidemiology and Microbiology named after honorary academician N.F. Gamaleya), Moscow (Dr Elena Burtseva).