GISHN report of activity prior to the WHO Consultation on the Composition of Influenza Virus Vaccines for use in the 2024-2025 Northern Hemisphere Influenza Season.

Report prepared the 14th of February 2024

1 - Description of the network

GIHSN is collecting clinical and virological information from hospitalized cases through a network of sites located in different regions of the world (figure1). 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 the next reports, a new indicator may be used to determine severe cases, based on a severity score that may be implemented in the next seasons. 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 are associated with more frequent severe presentation. It has been noted in the previous report of GIHSN (report of the 2022-2023 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.

For the 2023-2024 surveillance in GIHSN, influenza activity was detected earlier than usual, increasing rapidly in November in many Northern Hemisphere countries. Influenza A viruses predominated in most countries, with co-circulation of A/H1N1 and A/H3N2 in different relative proportions.

Regarding the Influenza B viruses, it has been reported 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 sequencing data from 8 sites collected on patients admitted in hospital from September 1st, 2023, until mid-January 2024: *Romania (25), Türkiye (4), Spain (24), South Africa (1), USA (36), Senegal (14), Pakistan (6), Ukraine (25).* All 135 sequences, from hospitalized cases only, have been uploaded in the GISAID database with a GIHSN tag.

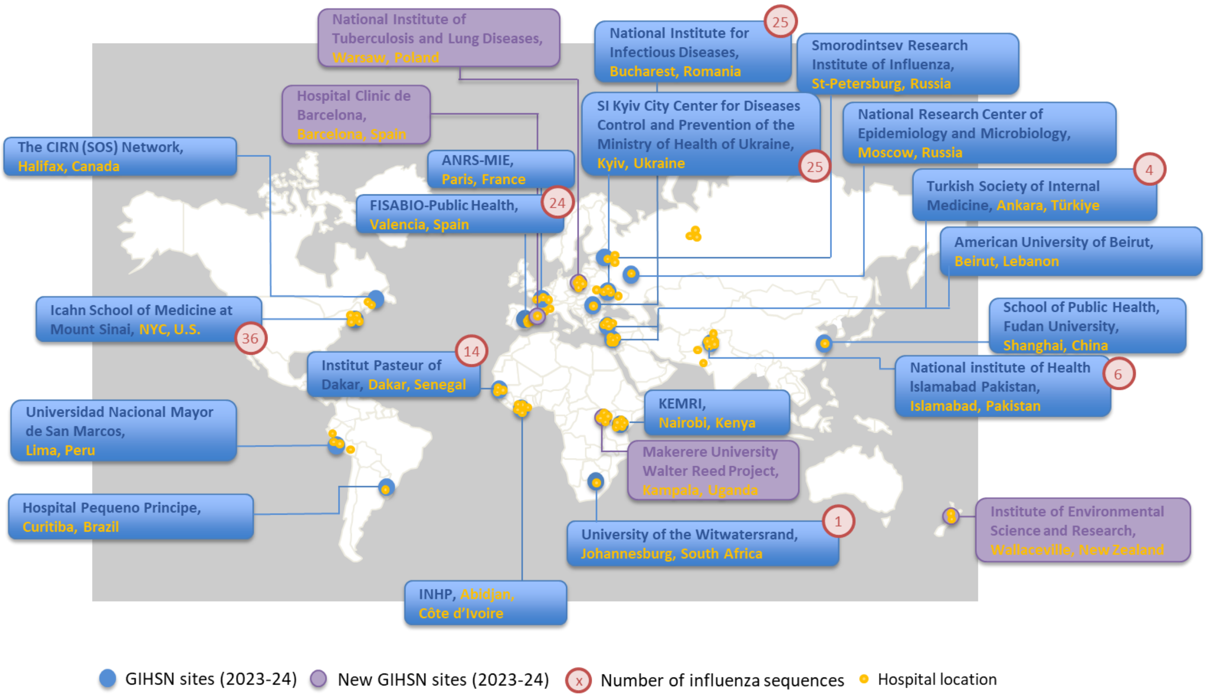

Fig. 1 Map showing the repartition of the participating countries, between September 2023 and January 2024. Four new participating sites are identified in purple. The number of sequences provided by the sites are indicated in the red circles.

2 - Description of the virus sequenced in the GIHSN

2.1 - Influenza A viruses

A(H1N1)pdm09 viruses

A(H1N1)pdm09 viruses were detected in most part of the world since September 2023. Sequencing results indicated that 30% 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 70% 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, all viruses but one belonged to C1 subclade, which can be further differentiated based on HA1 amino acid substitutions into different haplotypes including: C.1:197T; C1:137S; C.1:120A,169Q; C1:47I,96T,120A; C.1: 38D,120A,169Q. One virus belonged to C.1.7 subclade.

All viruses from clade 5a.2a.1 belonged to C.1.1.1 subclade. 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.

Although it appears on the phylogenetic tree that the frequency of report of Oxygen requirement seems to be more frequent in cases with the clade 6B.1A.5a.2a1 viruses, there is a bias due to the limited diversity of origin of these viruses (15 out of 23 sequenced viruses are coming from the New York site). With this preliminary data, it cannot be assessed that a specific lineage or clade could be associated with oxygen supplementation. However, this signal will be further investigated during the surveillance this year (Fig. 2).

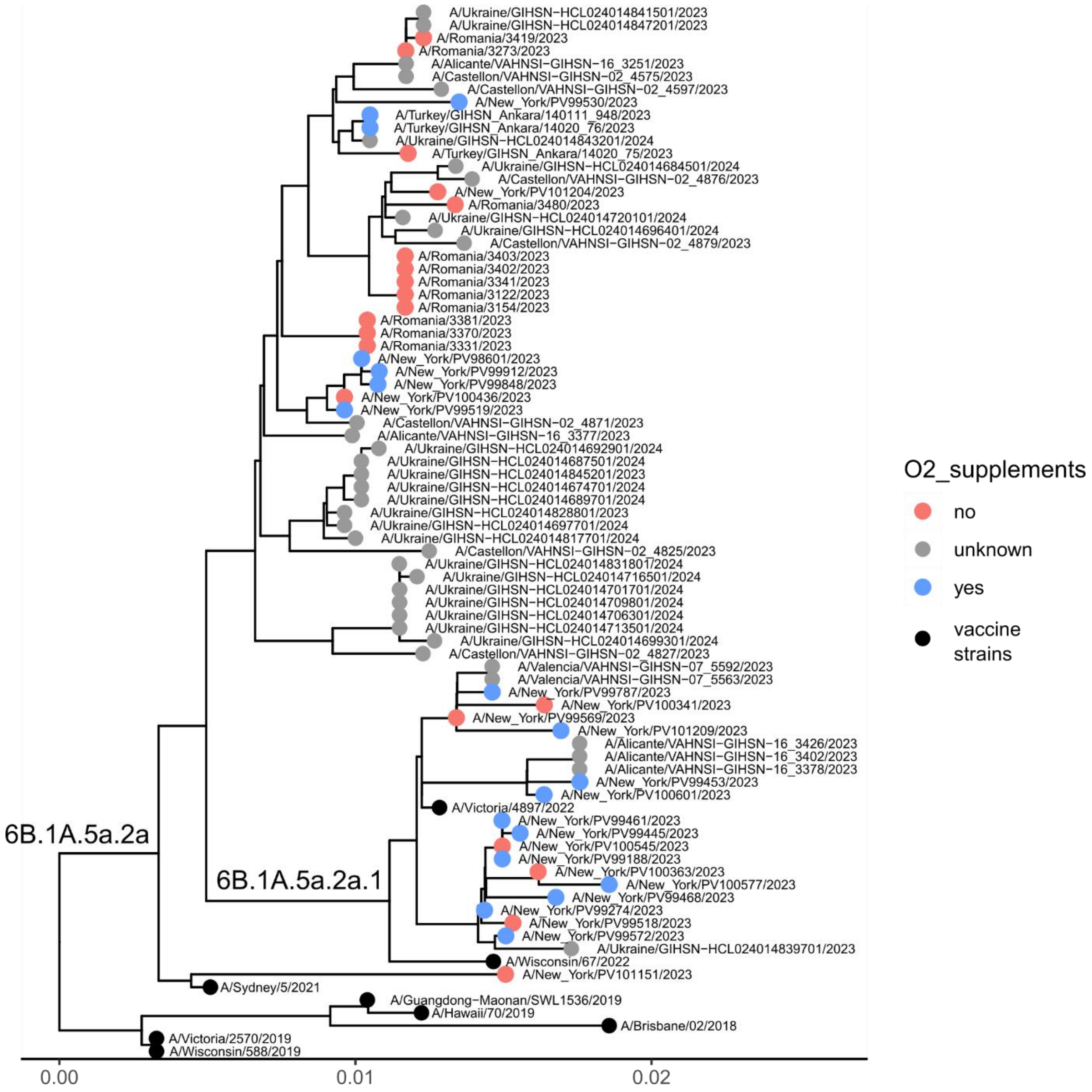

Fig 2: Phylogenetic tree of the A(H1N1pdm09) viruses analyzed between 1st of September 2023 and 1st of February 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red:no) with vaccine reference strains displayed in black.

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 (59%) H3N2 viruses belonged to H2 subclade defined by HA1:N122D and K276E substitutions (and bear a diversity of additional HA1 mutation but with no dominant cluster), while 37% belonged to H1 subclade defined by HA1:I25V, V347M, I418V and HA2:V18M substitutions. Finally, 2 viruses were classified as H subclade. Regional differences in H3N2 subclades have been previously reported in the GISRS report, with H1 subclade detected in Africa, Asia, Europe, North America and Oceania and H2 subclade detected in Asia, Europe, Oceania, North and South America.

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

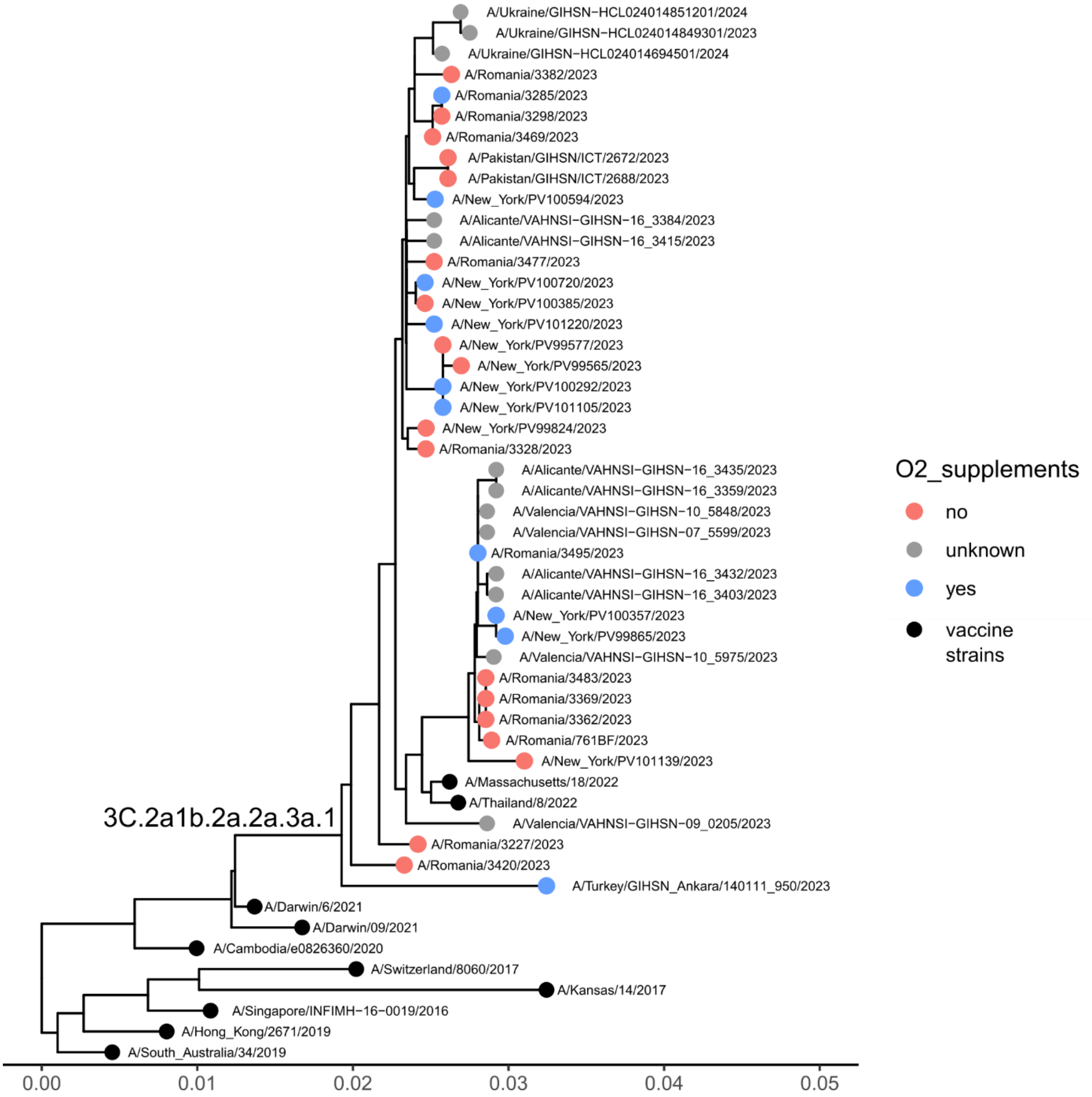

Fig 3: Phylogenetic tree of the A(H3N2) viruses analyzed between 1st of September 2023 and 1st of February 2024. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: blue; red:no) with vaccine reference strains displayed in black.

2.2 - Influenza B viruses

B/Victoria Lineage

Only one influenza virus from B/Victoria/2/87 lineage virus was sequenced into the GIHSN network since September 2023 (A/Senegal/1637/2023). This virus belonged to V1A.3a.2 clade, subclade C with a rare pattern of substitution in HA1 (including T182A and G184E).

B/Yamagata viruses

No B/Yamagata/16/88 viruses have been detected.

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