



Influenza virus characterization

Summary report, Europe, January 2024

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Summary of the latest WHO Influenza Vaccine Composition meetings

Genetic and antigenic characterization data generated at the Worldwide Influenza Centre for viruses with collection dates after 31 January 2023 until 31 August 2023 informed the WHO influenza vaccine composition meeting (VCM) in September 2023 when recommendations were made for the southern hemisphere (SH) 2024 influenza season. At the September 2023 VCM it was recommended to change the A(H1N1)pdm09 and A(H3N2) vaccine components for the 2024 SH season. Previously, at the February 2023 VCM, which focused on data from viruses collected after 31 August 2022 until 31 January 2023, it was also recommended to change the A(H1N1)pdm09 vaccine component for the 2023-2024 northern hemisphere (NH) season.

It is recommended vaccines for use in the 2024 SH influenza season contain the following:

Trivalent: Egg-based Vaccines

- an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- an A/Thailand/8/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Trivalent: Cell- or recombinant-based Vaccines

- an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- an A/Massachusetts/18/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Quadrivalent (egg- or cell culture- or recombinant-based vaccines): Above 3 components; and a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Influenza B/Yamagata-lineage

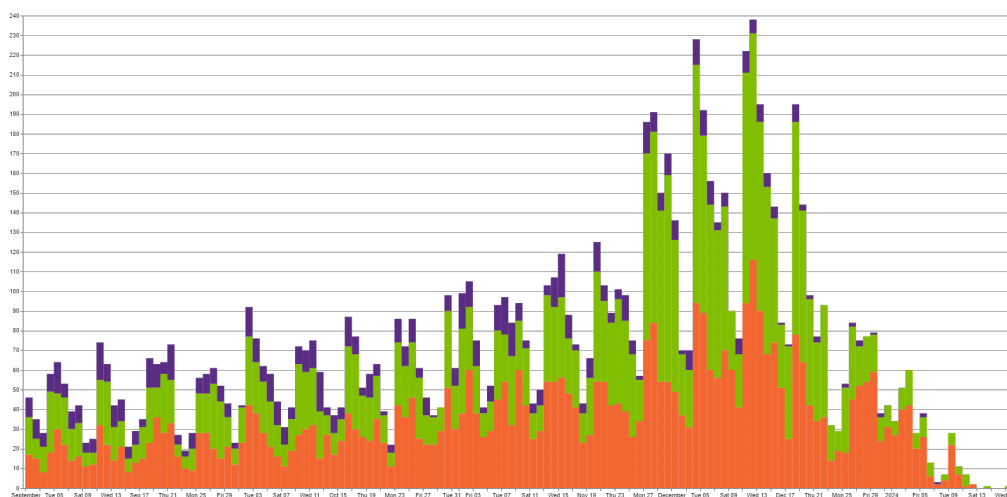
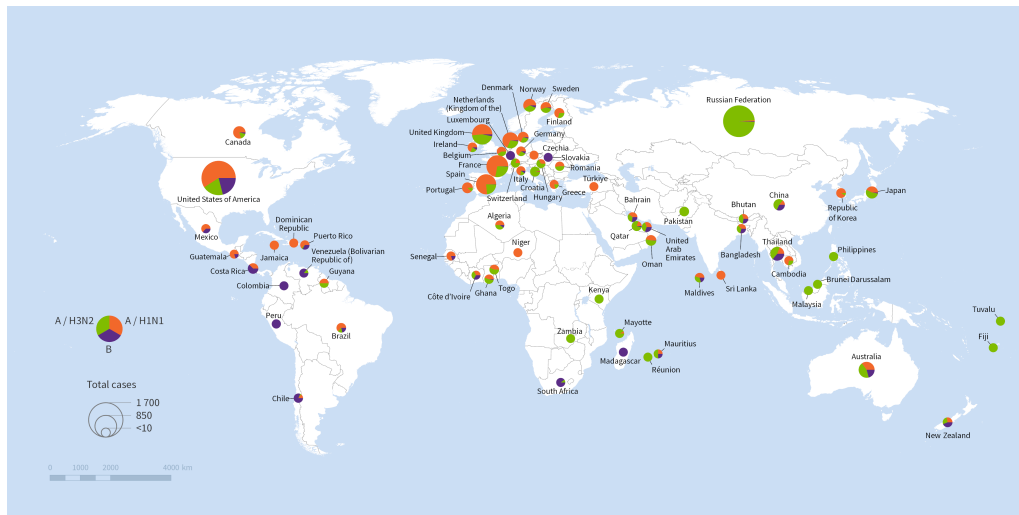
No B/Yamagata-lineage viruses with collection dates after March 2020 have been detected or sequences released in GISAID as of 23rd January 2024.

The absence of confirmed detection of naturally occurring B/Yamagata lineage viruses is indicative of very low risk of infection by B/Yamagata lineage viruses. Therefore, it is the opinion of the WHO influenza vaccine composition advisory committee that inclusion of a B/Yamagata lineage antigen in quadrivalent influenza vaccines is no longer warranted, and every effort should be made to exclude this component as soon as possible. A continued effort by all NICs of GISRS is required to identify B/Yamagata-lineage viruses for detailed characterization to determine if there are any in circulation.

Influenza by type/subtype

Worldwide

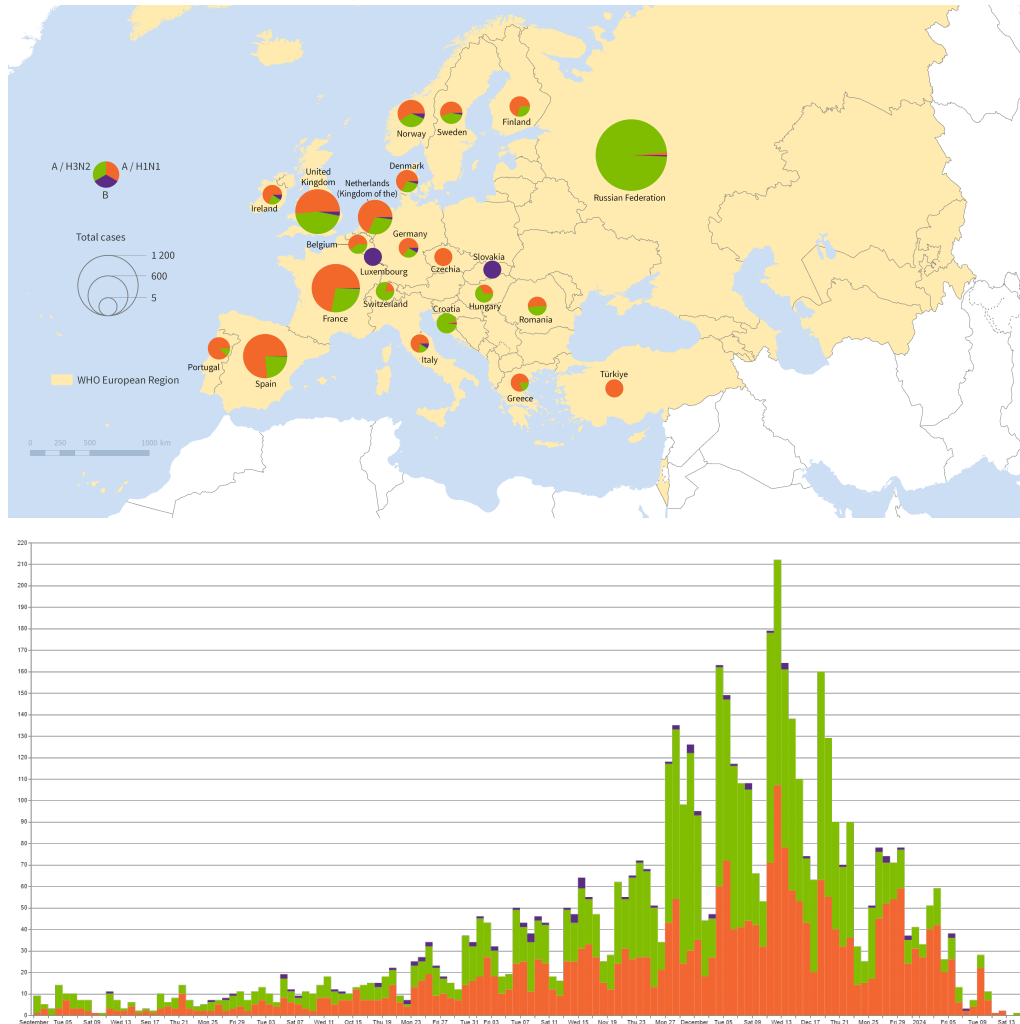
Geographical distribution of influenza viruses with collection dates from 1st September 2023 through to 23rd January 2024 as deposited in GISAID, coloured by Type/subtype. Geographic markers scaled to detection proportions. Full length HA. Map provided by [WHO GIS Centre for Health, DNA/DDI](#). Timeline obtained with [Microreact](#)



Globally, influenza detections remain elevated since the last report in December 2023. The relative proportions of A/H1N1, A/H3N2 and B/Victoria varied by geographic region with with cocirculation of A/H1N1 and A/H3N2 overall and some predominance of B/Victoria mostly in South America and South Africa, as indicated by the different colours in the pie charts by country.

European region

Geographical distribution in the European region of influenza viruses with collection dates from 1st September 2023 through to 23rd January 2024 as deposited in GISAID, coloured by Type/subtype. Geographic markers scaled to detection proportions. Full length HA.Map provided by [WHO GIS Centre for Health, DNA/DDI](#). Timeline obtained with [Microreact](#)



In the European region, influenza detections have increased since the last report in December 2023 and remained elevated for the past 4 weeks.

The majority of countries which reported detections showed co-circulation of A/H1N1 and A/H3N2 and sporadic detections of influenza B/Victoria, as indicated by the different colours in the pie charts.

Summary of influenza detections in the WHO European Region, week 35/2023 to 3/2024

Table 1 shows influenza virus detections in the WHO European Region reported to The European Surveillance System (TESSy) database from 1st September 2023 (weeks 35/2023 to 3/2024) compared with the same period in the previous season. For type-percentage calculations, the denominator is total detections; for subtype and lineage, it is the total influenza A subtyped and total influenza B lineage determined, respectively. As not all countries have a true non-sentinel testing denominator, no percentage calculations for total tested are shown (Data taken from [Flu News Europe](#) reports and from [ERVISS](#) (European Respiratory Virus Surveillance Summary)).

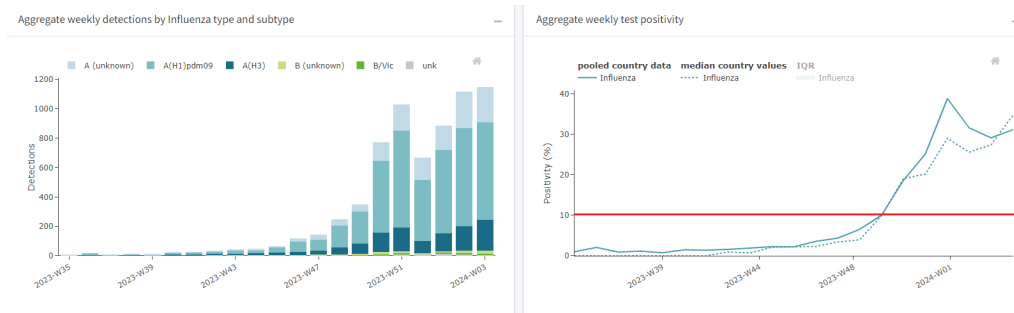
Virus type/subtype/lineage	Cumulative number of detections for weeks 35/2023 to 3/2024				Cumulative number of detections for weeks 35/2022 to 3/2023			
	Sentinel sources	Non-sentinel sources	Totals	%	Sentinel sources	Non-sentinel sources	Totals	%
Influenza A	6546	78347	84893	98	7399	84649	92048	91
A(H1N1)pdm09	4117	13384	17501	76	1528	15206	16734	57
A(H3N2)	1127	4384	5511	24	3870	8738	12608	43
A not subtyped	1302	60579	61881	NA	2001	60705	62706	NA
Influenza B	113	1585	1698	2	816	8511	9327	9
Victoria lineage	0	220	220	100	226	221	447	100
Yamagata lineage	0	0	0	NA	0	0	0	NA
Lineage not ascribed	113	1365	1478	NA	590	8290	8880	NA
Total detections	6659	79932	86591	NA	8215	93160	101375	NA
Total tested	51424	901210	952634	NA	45904	926809	972713	NA

Compared with the same period (weeks 35 to 3) in 2022-2023, for sentinel surveillance the number of specimens tested is slightly higher, whereas the number of influenza detections has slightly decreased. For non-sentinel surveillance, the number of tested specimens has decreased from last season to the current, as well as the number of detections. In both periods, the proportion of influenza A of unknown subtype was around 20% of sentinel cases and 70% of non-sentinel cases of the total influenza A detected.

Relative frequencies of type A vs B influenza viruses continue to show predominance of influenza A with a proportion of 98% compared with 91% in 2022-2023. Currently, in Europe there are sporadic detections of influenza B (2%), with most of the global detections circumscribed to the Americas. Relative frequencies of influenza A subtypes have also shifted, with A/H1N1 viruses increasing from 48% to 76% frequency, and a higher proportion of circulating A/H1N1 viruses (76% A/H1N1 vs 24% A/H3N2) compared to last season (57% A/H1N1 vs 43% A/H3N2).

Sentinel surveillance system dynamics, week 35/2023 to 49/2023

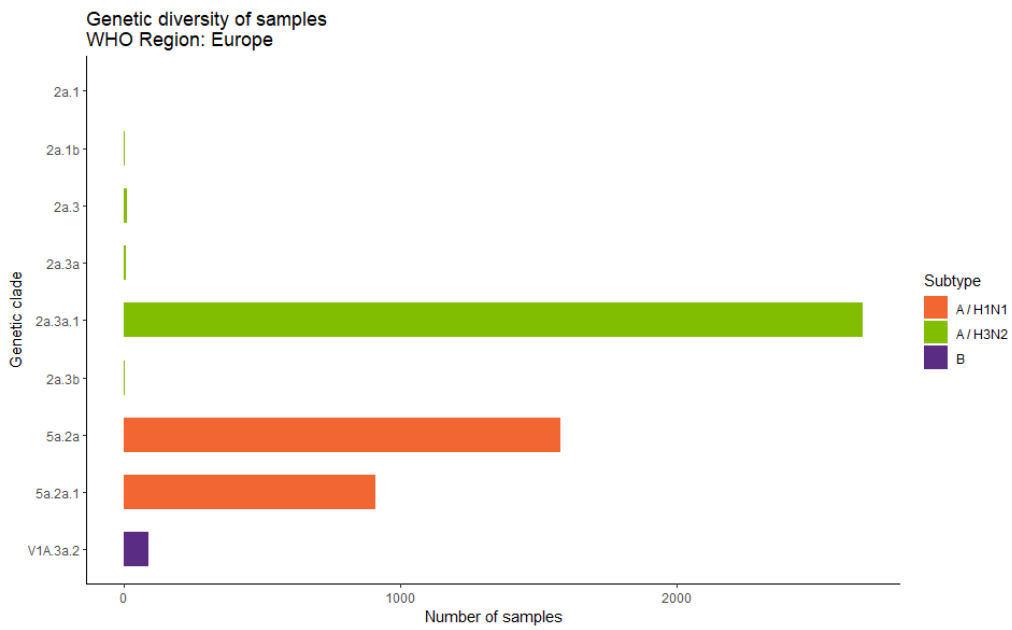
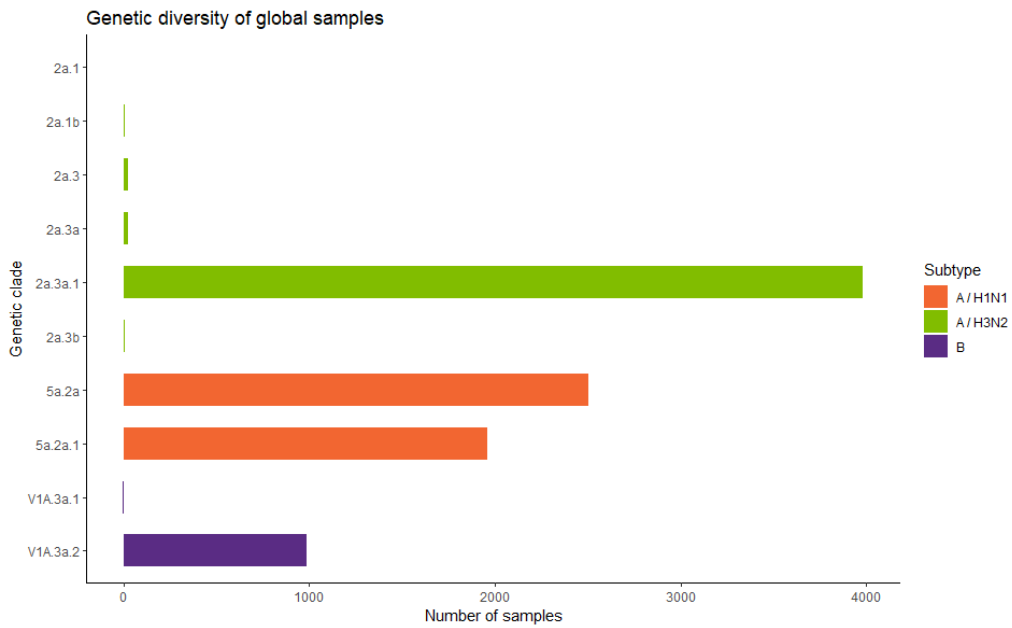
Figure adapted from [ERVISS](#)



During the period from week 35/2023 to week 3 of 2024, influenza activity remained at low levels through the reporting period until week 46 when it started to increase, crossing the epidemic threshold of 10% in week 50. This marks a late start of the influenza season when compared with the previous season where the epidemic threshold of 10% had been crossed by week 45.

Across sentinel surveillance, influenza A/H3N2 and A/H1N1 viruses cocirculated with predominance of A/H1N1 during most of this period, with overall frequencies of 78% for A/H1N1 and 22% for A/H3N2.

Genetic diversity by Type/Lineage and group



Influenza A/H1N1

Genetic analyses: A/H1N1

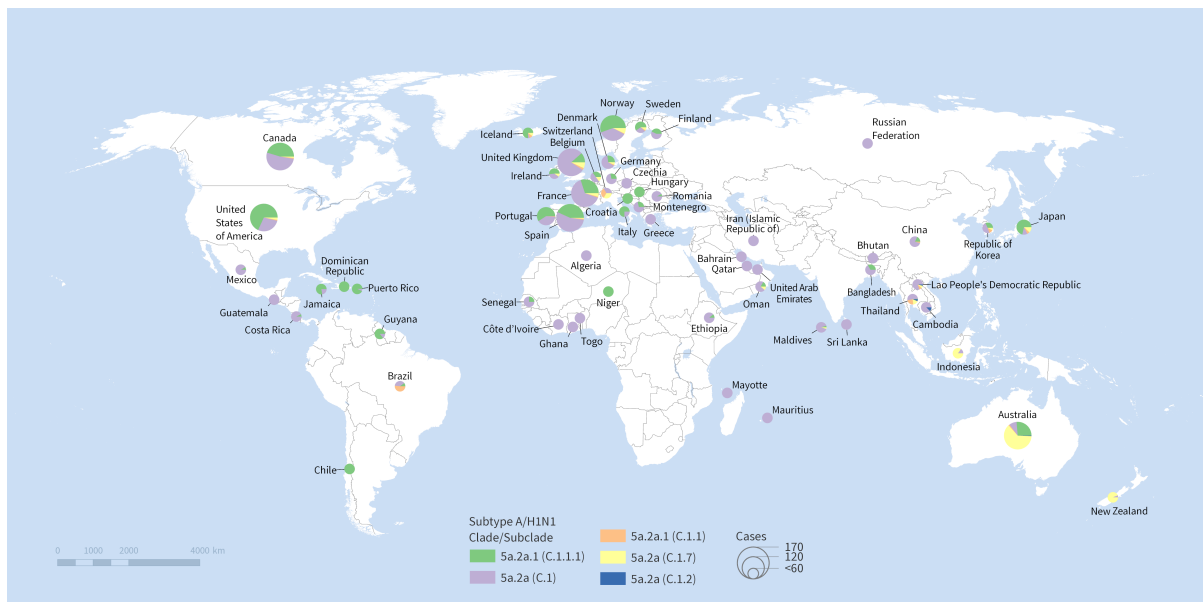
6B.1A.5a.2a and 6B.1A.5a.2a.1 clade viruses both continued to circulate with differing relative proportions depending on region, with a global predominance of 5a.2a viruses.

In Europe, both 5a.2a and 5a.2a.1 viruses were detected, with 5a.2a predominating in 2/3 of A/H1N1 sequenced viruses.

Within the 5a.2a viruses, characterised by substitutions K54Q, A186T, E224A, R259K and K308R, some heterogeneity was observed: a recently emerged minor subclade with D94N and T216A (C.1.7, no reference assigned yet), with viruses predominating in Australia, New Zealand and Indonesia, and in minor proportions in Europe and Asia; a large subclade defined by substitution I418V (A/Sydney/5/2021, subclade C.1) which was predominating in the Middle East, Africa, South-East Asia, Central America and some countries in Europe, and circulated in significant proportions in other countries; this subclade included a cluster characterised by T120A with K169Q or V47I and another with P137S. Other subclades that were reported in previous weeks were not seen during this period, except for one with A48P (A/Maine/10/2022, subclade C.1.2) with viruses from Thailand and Vietnam.

Within the 5a.2a.1 viruses, characterised by substitutions P137S, K142R, D260E, T277A, E356D and N451H, there are two main groups of viruses: a major clade with T216A (A/Victoria/4897/2022, C.1.1.1) predominating in the US, the Caribbean, Japan and some countries in Europe, showing additional heterogeneity with a cluster with R45K; and a minor clade represented by A/Wisconsin/67/2022 (C.1.1) circulating in Brazil, Europe and South East Asia.

Global geographical distribution of influenza A/H1N1 genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using [Nextclade](#). Geographic markers scaled to detection proportions. Map provided by [WHO GIS Centre for Health, DNA/DDI](#)



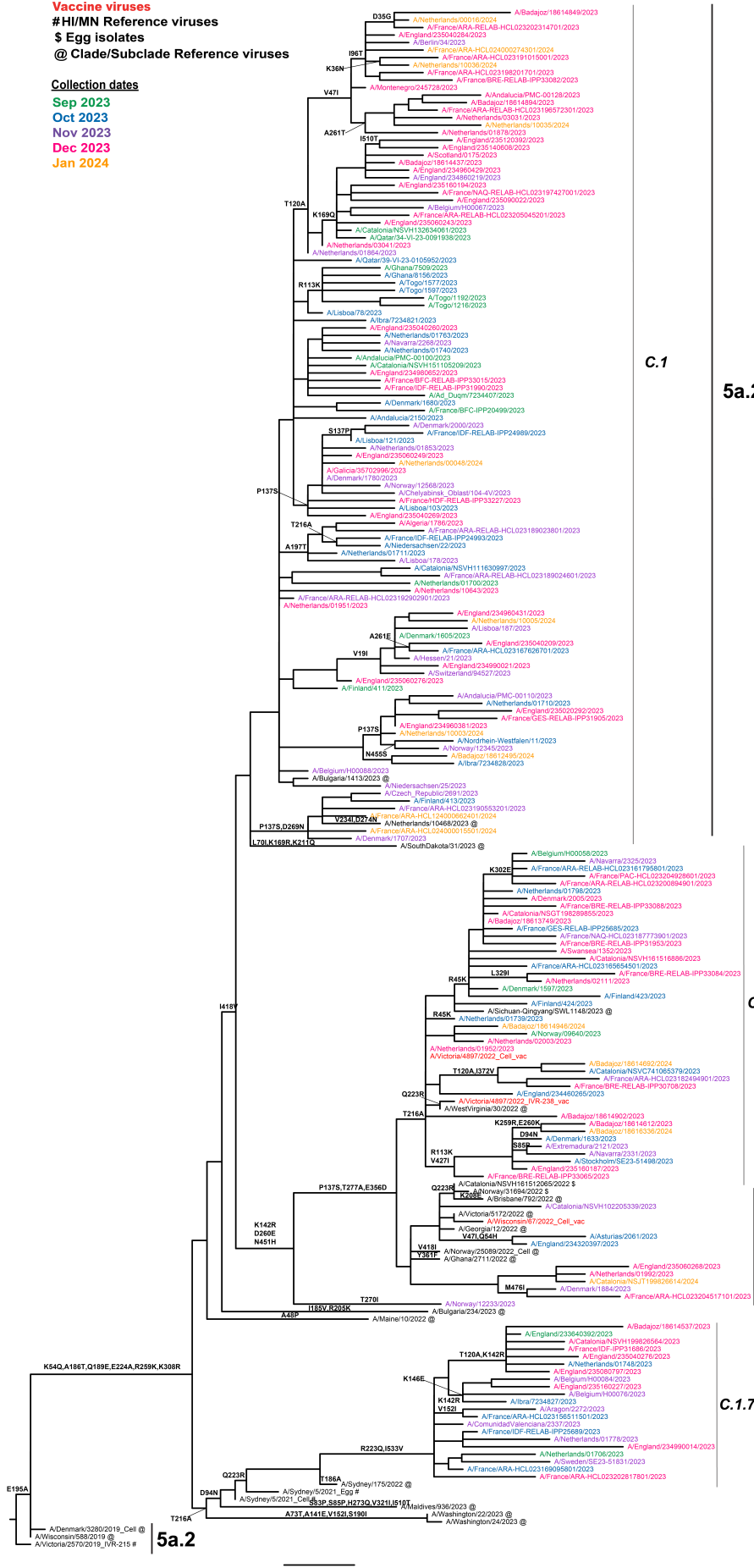
Maximum likelihood phylogenetic trees: A/H1N1

Maximum likelihood phylogenetic tree inferred using Iqtree2 from HA sequence data obtained from GISAID from 1st September onwards. Trees were manually curated and, if sequence numbers were > 200, downsampled using Treemer to retain a representative tree topology of 200 sequences with emphasis on viruses from the European region. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction. References and CVVs are marked as Cell or Egg.

Vaccine viruses
HI/MN Reference viruses
\$ Egg isolates
@ Clade/Subclade Reference viruses

Collection dates

Sep 2023
Oct 2023
Nov 2023
Dec 2023
Jan 2024



Summary of the antigenic properties of A/H1N1 viruses circulating in the reporting period

Both cell- and egg-based NH 2023-24 strain A/Victoria/4897/2022 recognises both 5a.2a and 5a.2a.1 test viruses well.

For an overall picture of the past season, see the Annex.

A/H1N1: References

Virus	Genetic group	Virus passage	Ferret ID
IVR-215 (A/Victoria/2570/2019)	5a.2	E4/D7/E3	F37/21
A/Sydney/5/2021	5a.2a	MDCK3/MDCK3	F46/22
A/Sydney/5/2021	5a.2a	E3/E3	F04/22
A/Victoria/4897/2022	5a.2a.1	SIAT2/MDCK2	F05/23
IVR-238 (A/Victoria/4897/2022)	5a.2a.1	E3/D6/E1	F07/23
A/Wisconsin/67/2022	5a.2a.1	MDCK2	F17/23

Influenza A/H3N2

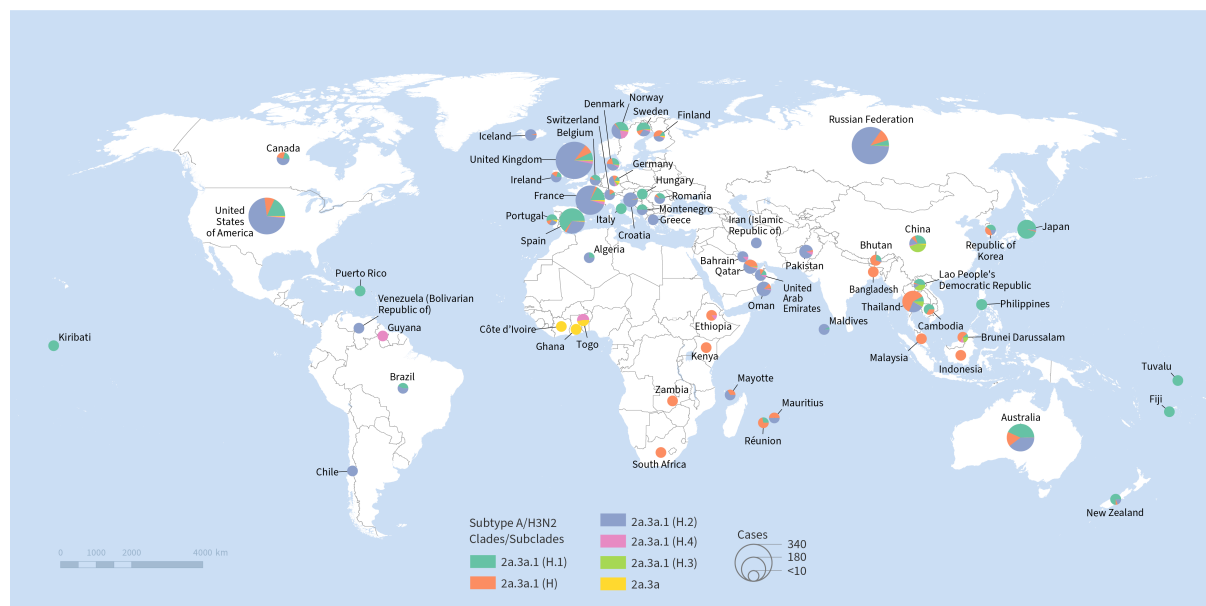
Genetic analyses: A/H3N2

Clade 3C.2a1b.2a.2 (renamed as **2** since February 2023) predominated since 1st February in all geographic regions where A/H3N2 circulated.

During this reporting period, the great majority of H3 viruses detected belong to clade 2a.3a.1, which share substitution E50K with clade 2a.3a and present additional substitutions I140K and I223V (A/Thailand/8/2022, subclade H). Within clade 2a.3a.1, viruses with I25V, V347M and some with I418V (subclade H.1) represented by new reference A/Sydney/856/2023 were seen in Europe, South-East Asia and Australia, whereas viruses with N122D and K276E (subclade H.2) represented by new reference A/Sydney/878/2023 were predominating in Europe, the US and the Middle East. Clade 2a.3a.1 included a subclade with N122D and V347M viruses from US, Australia and Qatar (the latter characterised by V112I and S145N) whereas the rest of clade 2a.3a.1 was detected in Africa, South East Asia and a minority in Europe and the US, with no subclade-specific amino acids. Minor subclade H.4 (no reference assigned yet) was seen in Norway, West Africa and Central America.

A few viruses predominating in West Africa with substitutions K276E and V347M form a cluster within clade 2a.3a (A/Finland/402/2023).

Global geographical distribution of influenza A/H3N2 genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using [Nextclade](#). Geographic markers scaled to detection proportions. Map provided by [WHO GIS Centre for Health, DNA/DDI](#)



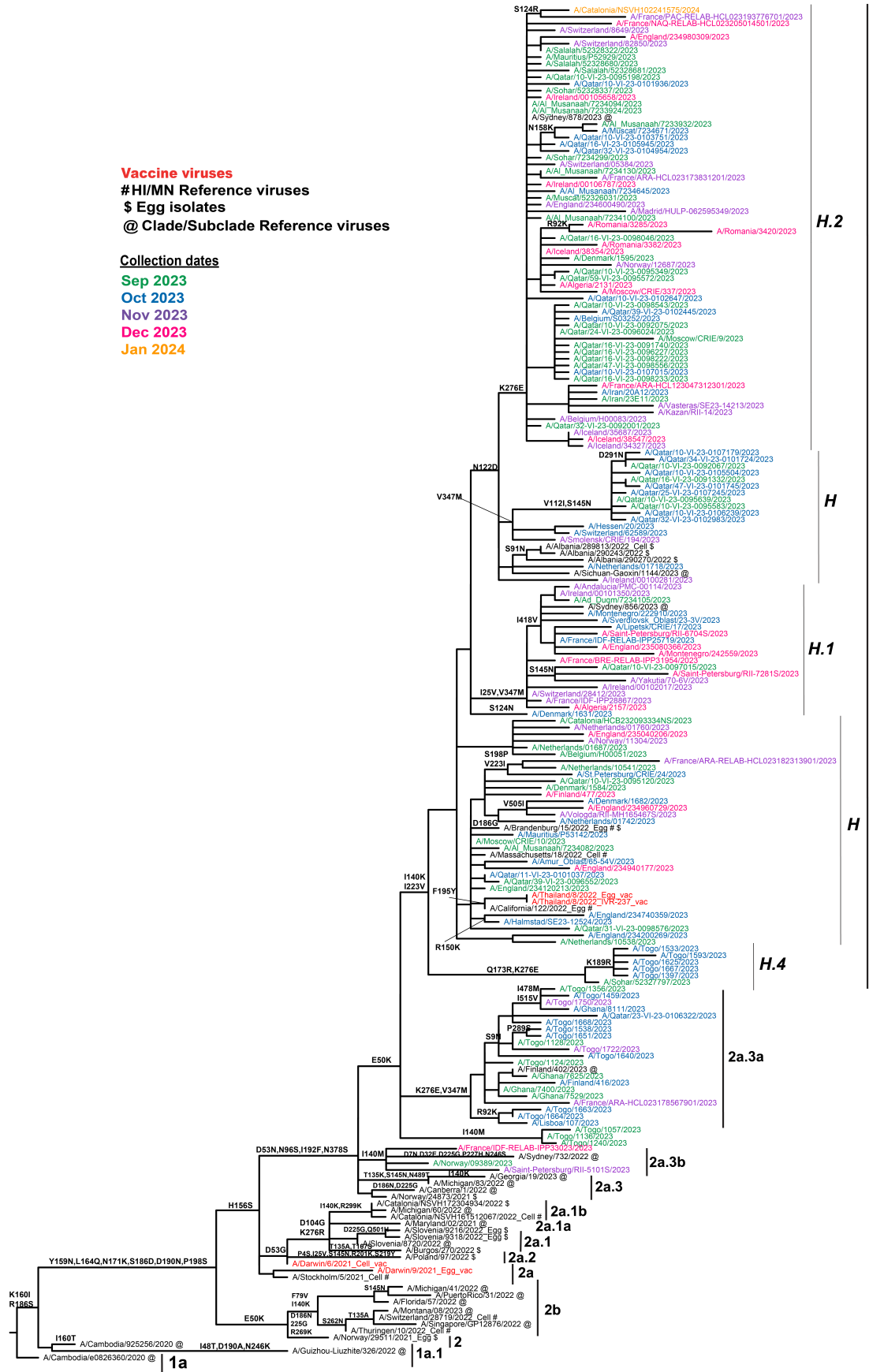
Maximum likelihood phylogenetic tree: A/H3N2

Maximum likelihood phylogenetic tree inferred using Iqtree2 from HA sequence data obtained from GISAID from 1st September onwards. Trees were manually curated and, if sequence numbers were > 200, downsampled using Treemer to retain a representative tree topology of 200 sequences with emphasis on viruses from the European region. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction. References and CVVs are marked as Cell or Egg.

Vaccine viruses
HI/MN Reference viruses
\$ Egg isolates
@ Clade/Subclade Reference viruses

Collection dates

- Sep 2023
- Oct 2023
- Nov 2023
- Dec 2023
- Jan 2024



Summary of the antigenic properties of A/H3N2 viruses circulating in the reporting period

We note variable recognition by current 2a.3a.1 reference and vaccine antisera for a number of 2a.3a.1 viruses that have been analysed since September.

For an overall picture of the past season, see the Annex.

A/H3N2: HI reagents and references

Virus	Genetic group	Virus passage	Ferret ID
A/Thuringen/10/2022	2b	P1/SIAT2	F36/22
A/Stockholm/5/2021	2a	SIAT0/SIAT3	F35/21
A/Darwin/9/2021	2a	E3/E4	F39/21
A/Norway/24873/2021	2a.3	SIAT2	F10/22
A/Norway/24873/2021	2a.3	E3 (Am2A1)	F11/22
A/Poland/97/2022	2a.2	S2	F39/22
A/Slovenia/8720/2022	2a.1	SIAT1/MDCK1/SIAT2	F24/22
A/Lille/50053/2022	2a.1	MDCK1/SIAT3	F02/23
A/Catalonia/NSVH161512067/2022	2a.1b	SIAT1/SIAT3	F41/22
A/Albania/289813/2022	2a.3a.1	MDCK1	F21/23
A/Brandenburg/15/2022	2a.3a.1	E5(Am1A12)	F18/23
A/Switzerland/28719/2022	2b	SIAT1	F29/23
A/Massachusetts/18/2022	2a.3a.1	SIAT3/SIAT1	F36/23
A/California/122/2022	2a.3a.1	E1/E1	F33/23
A/Thailand/08/2022	2a.3a.1	E3/E1	F34/23
IVR-237(A/Thailand/08/2022)	2a.3a.1	E3/D7/E1	F35/23

Influenza B

Genetic analyses: B/Victoria

Clade V1A.3a.2 viruses characterised by substitutions A127T, P144L, N150K, G184E, N197D (-CHO), K203R and R279K (B/Austria/1359417/2021, subclade C) predominated since 1st February 2023 in geographic regions where B/Victoria-lineage viruses were detected.

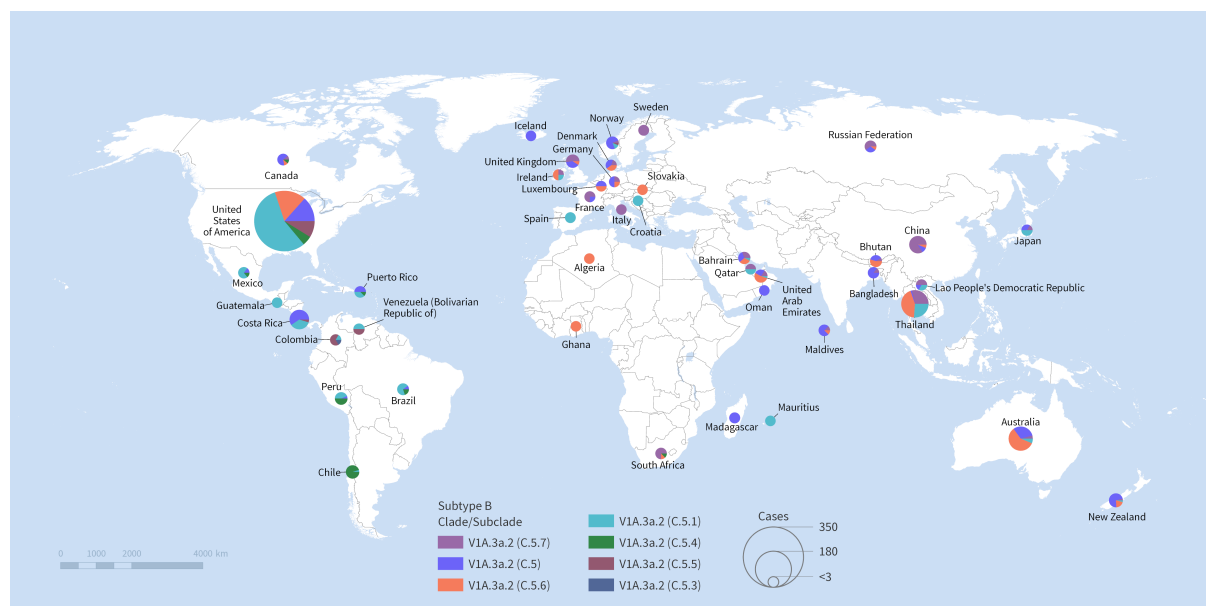
During this reporting period, only a minority of B/Victoria viruses were detected and characterised in Europe. Within V1A.3a.2, the most recent viruses are characterised by additional substitution D197E, represented by B/Connecticut/01/2021 (subclade C.5). Subclades observed within V1A.3a.2 (C.5) are: C.5.1 with E183K represented by B/Catalonia/2279261NS/2023, detected in Central America, Brazil, the US and Europe; C.5.4 (B/Slovenia/924/2023) with V117I, E128K, A154T and K326R detected in the Americas; C.5.5 (B/Paraguay/2102/2023) with R80G, E184K detected in US and Central/South America; C.5.6 (B/Norway/08717/2023) with D129N predominating in Australia, South East Asia, Middle East and Africa; C.5.7 (no reference assigned yet) with E183K and E128G seen in China, Thailand, Europe, Middle East and South Africa.

Other C.5 viruses were detected in variable proportions across the globe.

No Clade V1A.3 viruses were detected since 1st February 2023.

No B/Yamagata lineage viruses have been detected since March 2020.

Global geographical distribution of influenza B/Victoria genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using [Nextclade](#). Geographic markers scaled to detection proportions. Map provided by [WHO GIS Centre for Health, DNA/DDI](#)



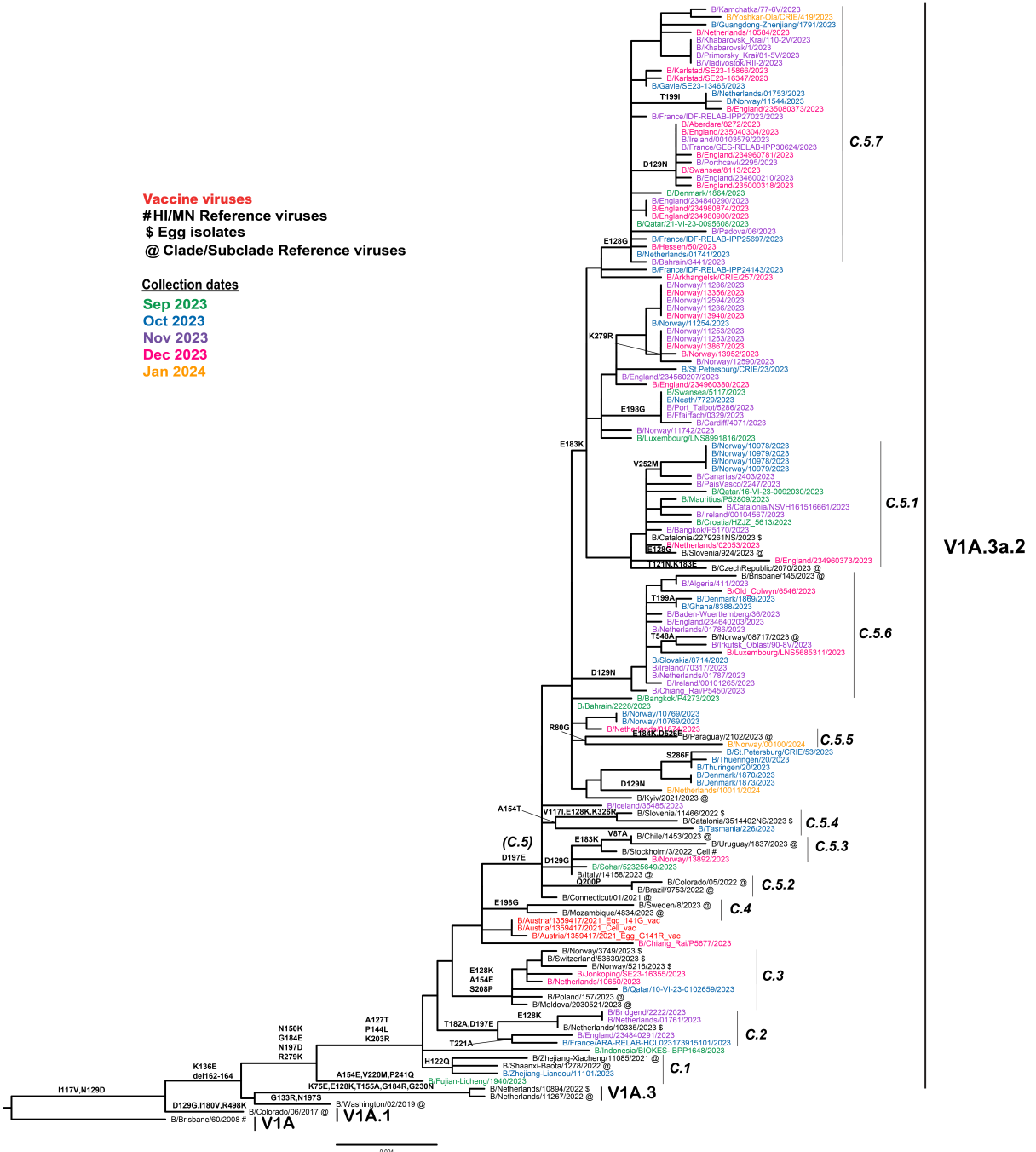
Maximum likelihood phylogenetic tree: B/Victoria

Maximum likelihood phylogenetic tree inferred using Iqtree2 from HA sequence data obtained from GISAID from 1st September onwards. Trees were manually curated and, if sequence numbers were > 200, downsampled using Treemer to retain a representative tree topology of 200 sequences with emphasis on viruses from the European region. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction. References and CVVs are marked as Cell or Egg.

Vaccine viruses
HI/MN Reference viruses
\$ Egg isolates
@ Clade/Subclade Reference viruses

Collection dates

Sep 2023
Oct 2023
Nov 2023
Dec 2023
Jan 2024



Summary of the antigenic properties of B/Victoria lineage viruses circulating in the reporting period

Very few B/Victoria viruses collected since 1st September have been phenotypically characterized by haemagglutination inhibition (HI). All V1A.3a.2 viruses tested were well-recognised by antisera raised against B/Austria/1359417/2021 and -like viruses.

For an overall picture of the past season, see the Annex.

B/Victoria: Reagents and references

Virus	Genetic group	Virus passage	Ferret ID
B/Brisbane/60/2008	V1A	E4/E4	sheep pool
B/Stockholm/3/2022	V1A.3a.2	SIAT1/MDCK3	F28/22
B/Austria/1359417/2021	V1A.3a.2	SIAT1/MDCK4	NIB F01/21
B/Austria/1359417/2021 G141	V1A.3a.2	E3/E5	F15/21
B/Austria/1359417/2021 G141R	V1A.3a.2	E3/E5	F44/21

Antiviral susceptibility testing

At the WIC, influenza viruses detected within the WHO EURO Region since 1st September 2023 (weeks 35/2023 to 3/2024) were assessed for phenotypic and/or genotypic susceptibility to antivirals. Of these, 31 A/H1N1, 29 A/H3N2 and 14 B/Victoria viruses were phenotypically assessed against oseltamivir and zanamivir. All viruses showed Normal Inhibition (NI) by both NAIs.

Phenotypic testing for susceptibility to baloxavir marboxil was performed for 9 A/H1N1, 8 A/H3N2 viruses and 14 B/Victoria viruses, with all of them showing Normal Inhibition.

Genotypic assessment of 79 A/H1N1, 81 A/H3N2 NA AND 10 B/Victoria gene sequences from influenza viruses detected within the WHO EURO Region since 1st September 2023 and received at the WIC did not find any marker associated with reduced susceptibility to NAI.

For 55 A/H1N1, 74 A/H3N2 and 8 B/Victoria viruses where PA gene sequencing was successful, no markers associated with reduced inhibition by baloxavir marboxil were identified.

Summaries of data submitted to TESSy

Genetic characterization

(According to the guidance produced for TESSy reporting at the beginning of the 2023-2024 influenza season)

Overall, 1,424 viruses detected from week 35/2023 to 3/2024 were genetically characterized:

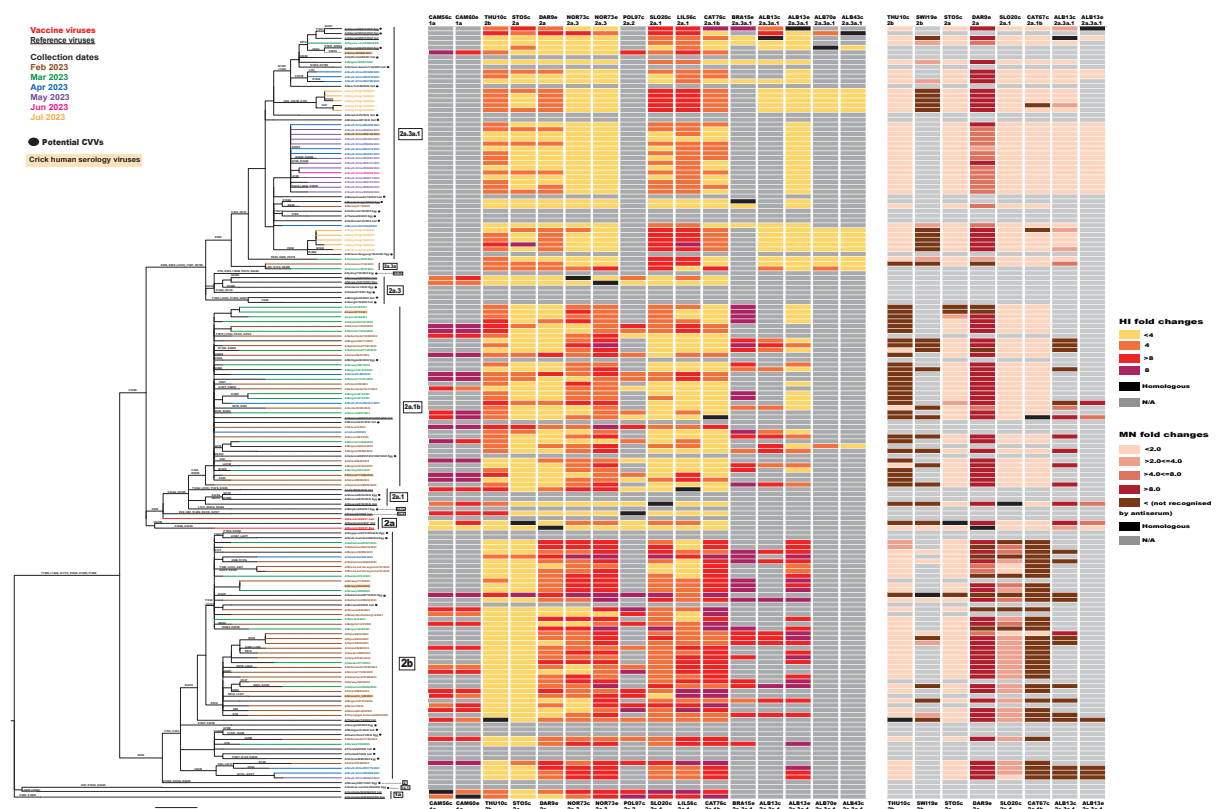
- Of 990 A/H1N1 viruses, all belonged to clade 6B.1A.5a.2 (clade **5a.2**) with 490 (49%) represented by A/Sydney/5/2021 (5a.2a), 469 (47%) by A/Victoria/4897/2022 (5a.2a.1) and 24 (2%) by A/Wisconsin/67/2022 (5a.2a.1), while two viruses were unclassified and five (1%) were allocated to the 'Subgroup Not Listed' category.
- Of 395 A/H3N2 viruses, all belonged to clade (3C.2a1b.2a.2, renamed as **2**) with 387 (98%) represented by A/Thailand/8/2022 (clade 2a.3a.1) and five (2%) represented by A/Finland/402/2023 (clade 2a.3a). One H3 virus was unclassified and two (1%) were allocated to the 'Subgroup Not Listed' category.
- Of 39 B/Victoria-lineage viruses, all belonged to clade V1A.3a.2, with 27 (69%) represented by B/Catalonia/2279261NS/2023 (subclade C.5.1), seven (18%) represented by B/Connecticut/01/2021 (subclade C.5) and four (10%) represented by B/Austria/1359417/2021 (subclade C). No viruses were allocated to the 'Subgroup Not Listed' category.

Susceptibility to antivirals

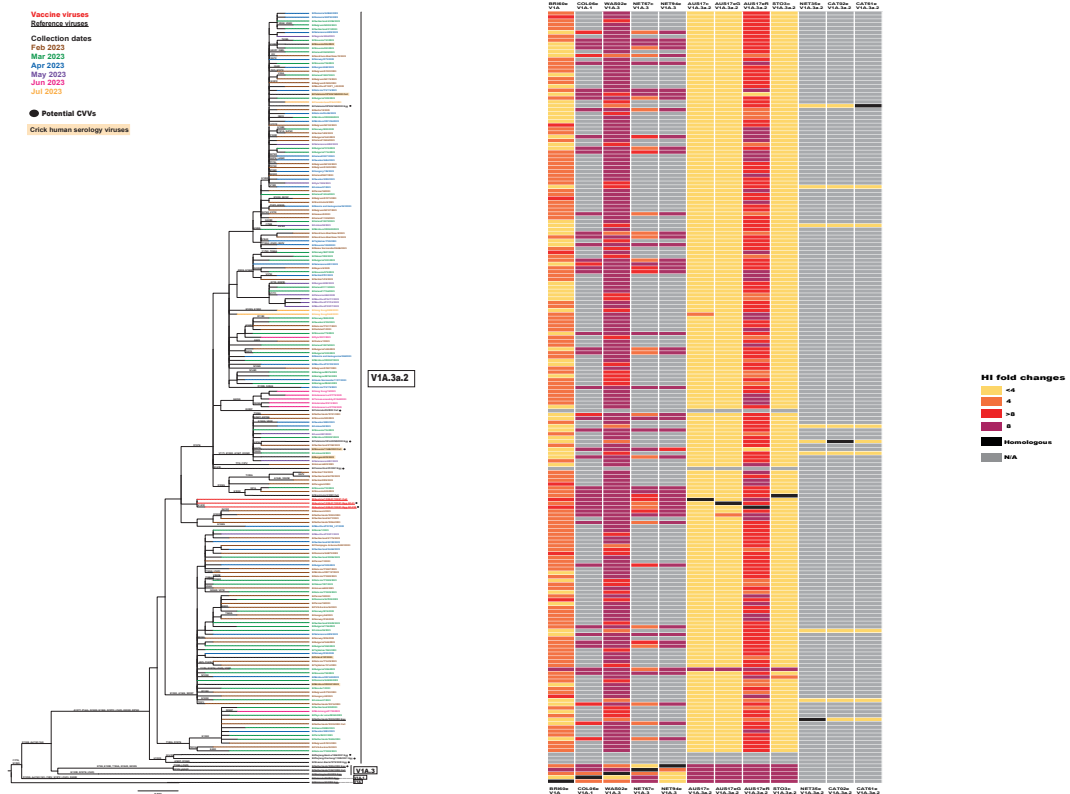
Between weeks 35 and 39/2023, 8 viruses were assessed for susceptibility to neuraminidase inhibitors and 7 were assessed for susceptibility to baloxavir marboxil. Phenotypically and/or genotypically, no markers associated with reduced susceptibility were identified.

No antiviral susceptibility data was available so far for weeks 40/2023 to 3/2024 of season 2023-2024.

A/H3N2



B/Victoria



WHO Collaborating Centre reports

A full description of results generated by the London WHO Collaborating Centre at the WIC and used at the September 2023 WHO VCM, and previous ones, can be found at <https://www.crick.ac.uk/partnerships/world-wide-influenza-centre/annual-and-interim-reports>



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