Not for public dissemination

February 2024

Influenza virus characterisation data reported by national influenza reference laboratories to The European Surveillance System (TESSy) for weeks 40/2023 to 3/2024

Summary

This report summarizes influenza virological surveillance data from 50 countries or territories of the WHO European Region, for weeks 40/2023 through 3/2024, as reported by National Influenza Centres and national influenza laboratories to The European Surveillance System (TESSy) at the European Centre for Disease Prevention and Control (ECDC).

Detections

Within the reporting period, 135 728 influenza virus detections (sentinel and non-sentinel combined) were reported from 50 countries and territories of the WHO European Region of which 98% (132 851) were type A and 2% (2 877) were type B virus.

Of the subtyped influenza A viruses, 20 747 (52%) were influenza A(H1)pdm09 and 18 783 (48%) were influenza A(H3). Of the 2 877 reported influenza type B viruses, the lineage for 283 (10%) was determined, with all viruses falling into the B/Victoria/2/87 lineage. No virus belonging to the B/Yamagata/16/88 lineage was reported.

Genetic characterisation

In the European Region, 3 567 (3% from sentinel and non-sentinel sources; 4% from sentinel sources) viruses from 16 countries were reported with genetic clade category. The majority (60%) of the 1 151 categorised A(H1N1)pdm09 viruses fell in clade 5a.2a, represented by A/Sydney/5/2021, the virus component for 2023 southern hemisphere (SH) vaccine, while 567 (38%) belonged to a subclade within clade 5a.2a.1, defined by T216A substitution and represented by A/Victoria/4897/2022, the virus component for 2023-24 northern hemisphere (NH) egg-based vaccine, and 32 (2%) to clade 5a.2a.1, represented by A/Wisconsin/67/2022, the cell culture-based 2023-2024 NH vaccine component. Some genetic diversification was observed in the 5a.2a viruses with branches having defined amino acid substitutions with a significant number of viruses such as T120A/K169Q in 5a.2a and S85P/R113K in 5a.2a.1.

The majority (n=1 231, 62%) of the 1 992 A(H3N2) viruses that were reported with genetic clade category belonged to clade 2a, represented by A/Darwin/9/2021, the recommended vaccine strain for egg-based vaccines for 2023-24 NH influenza season. Of genetically characterised A(H3N2) viruses, 38% (n=747) were reported in clade 2a.3a.1, represented by A/Thailand/8/2022 which has been recommended for the 2024 SH season vaccine. Based on sequence analysis, all A(H3N2) viruses fell into clade 2a.3 and the majority (99%) into 2a.3a.1. Most (78%) of A(H3N2) in 2a.3a.1 belonged to a subclade defined by the amino acid substitution K276E which was not represented by any reference virus. There were also two smaller subclades with I25V (10%) and I242M (6%) amino acid substitutions, respectively.

All 64 genetically characterised B/Victoria viruses belonged to clade V1A.3a.2, represented by B/Austria/1359417/2021, the recommended vaccine virus strain for the 2023/24 NH influenza season. However, 31% (n=17) of the viruses fell in a branch with an E128G substitution where no reference virus was present.

Antigenic characterisation

Antigenic characterisation was performed for 524 (<1% from combined sentinel and non-sentinel; 5% from sentinel sources) viruses (502 (96%) A and 22 (4%) B viruses). Of the 228 characterised A(H1N1)pdm09 viruses the majority (174, 76%%) were similar to the vaccine virus A/Victoria/4897/2022-like virus, 49 (21%) were A/Sydney/5/2021-like, and two were reported as A/Wisconsin/67/2022-like viruses. Three (1%) A(H1N1)pdm09 viruses were not attributed to any reporting category.

The majority of the 274 antigenically characterised A(H3N2) viruses (202, 74%) were reported as A/Thailand/8/2022-like, 69 (25%) were A/Darwin/9/2021-like, and three (1%) were not attributed to any of the reporting categories.

Among 22 (4%) antigenically characterised influenza B/Victoria viruses, the majority (20, 91%) were similar to the vaccine virus for the 2023/24 NH influenza season (B/Austria/1359417/2021). Two (9%) B/Victoria viruses were not attributed to any of the reporting categories.

Antiviral susceptibility

The majority of assessments for reduced susceptibility to neuraminidase inhibitors (oseltamivir and/or zanamivir) were based on genetic analysis of known mutations associated with a reduced susceptibility phenotype (n=2 076, 89%), while fewer viruses were assessed only or also phenotypically (n=258, 11%). Assessments of reduced susceptibility to baloxavir marboxil are solely based on genetic analyses.

Since the beginning of the season, 2 345 viruses were assessed for reduced susceptibility to neuraminidase inhibitors (oseltamivir and/or zanamivir) and/or to the polymerase acidic protein (PA) inhibitor baloxavir marboxil. In total, four viruses with reduced or highly reduced inhibition or susceptibility were detected based on genetic analyses while none were detected by phenotypic testing: three A(H1)pdm09 viruses exhibited genetic markers associated with either reduced or highly reduced inhibition by oseltamivir (all A(H1)pdm09); one A(H3) virus showed presence of amino acid substitutions associated with reduced susceptibility to baloxavir marboxil.

Contents

Background

Influenza vaccines are the principal measure for preventing influenza and reducing the impact of epidemics [1]. Influenza viruses frequently undergo genetic and antigenic changes. Therefore, based on global surveillance data, data on circulating influenza viruses are reviewed every year to inform recommendations on the vaccine composition. Since 1973, WHO publishes formal recommendations for the composition of influenza vaccines based on the information provided by the WHO Global Influenza Surveillance and Response System (GISRS) [2]. WHO updates its recommendations for the composition of the vaccine biannually to target the viruses expected to be the most frequently circulating in the coming influenza seasons in the northern (NH) and southern hemisphere (SH), respectively [3]. Twice per year, in February for the NH and in September for the SH, WHO convenes a consultation on the composition of influenza virus vaccines, also known as the vaccine composition meeting (VCM) [4,5]. This report summarizes virological surveillance data for influenza provided by 50 countries or territories from the WHO European Region for the NH VCM held by WHO in February 2024.

Surveillance system

The laboratory network responsible for the virological surveillance of influenza in the WHO European Region is part of GISRS and consists of national influenza laboratories in 50 countries across the WHO European Region and Kosovo; a WHO Collaborating Centre for Reference and Research on Influenza at the Francis Crick Institute Worldwide Influenza Centre, London, United Kingdom (WHO CC London); a WHO Collaborating Centre for Studies on Influenza at the Animal-human Interface at the State Research Center of Virology and Biotechnology "VECTOR", Koltsovo, the Russian Federation; a WHO Essential Regulatory Laboratory (ERL) at the Medicines and Healthcare products Regulatory Agency, Potters Bar, United Kingdom; and three WHO H5 reference laboratories in France, the Russian Federation and the WHO CC, United Kingdom [6-8]. National influenza laboratories in 47 countries in the WHO European Region are recognised by WHO as National Influenza Centres (NICs). Laboratories in 30 countries of the European Union/European Economic Area (EU/EEA) participate in the European Reference Laboratory Network for Human Influenza (ERLI-Net) coordinated by the European Centre for Disease Prevention and Control (ECDC). Most of the ERLI-Net laboratories are also NICs. [9]

NICs provide information on circulating influenza viruses by testing clinical specimens obtained from surveillance systems in their countries (outpatient and inpatient health care settings) for the presence of influenza virus by type (A and B) and subtype (A(H1)pdm09 or A(H1N1)pdm09 and A(H3) or A(H3N2) or lineage (B/Victoria or B/Yamagata), as well as by analysing data from diagnostic testing for influenza in other subnational laboratories. NICs also conduct preliminary antigenic characterisation of viruses, using strain-specific post-infection ferret antisera raised against vaccine viruses and reference viruses raised by the laboratories on their own, or from WHO CC Atlanta or provided by WHO CC London, and genetic characterisation through sequencing. Furthermore, susceptibility to neuraminidase inhibitor (NAI) antiviral agents and polymerase acidic protein (PA) inhibitor antiviral agents are assessed by phenotypic and/or genotypic tests. Influenza reference laboratories are encouraged to submit their characterisation results to The European Surveillance System (TESSy), managed by ECDC.

Following an email notification to the countries for a final update of their weekly data to TESSy, detection and virus characterisation data deposited by 25 January 2024 were accessed and summarized. The data for weeks 40/2023-3/2024 were included in this analysis.

Purpose

The purpose of this report is:

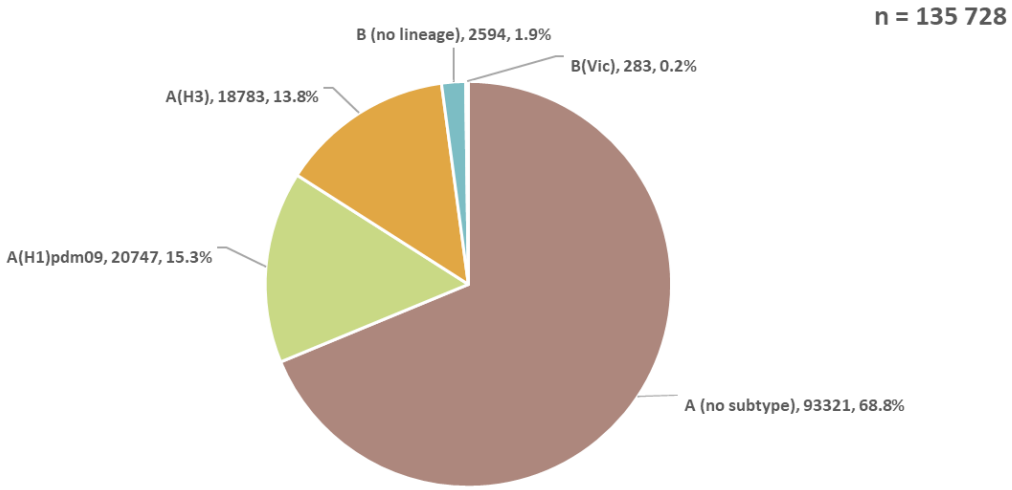
- to summarize reports on detections, antigenic and genetic data provided to TESSy by NICs in the WHO European Region during the 2023/24 influenza season from week 40/2023 to week 3/2024; in time for consideration by the WHO VCM;
- to monitor the diversity and circulation of viruses, their geographic occurrence and frequency;
- to provide feedback to NICs, through analysis of their antigenic and genetic characterisation results in the context of data from the WHO European Region;
- to monitor, maintain and enhance the quality of the characterisations data in TESSy through regular close review and analysis.

Results

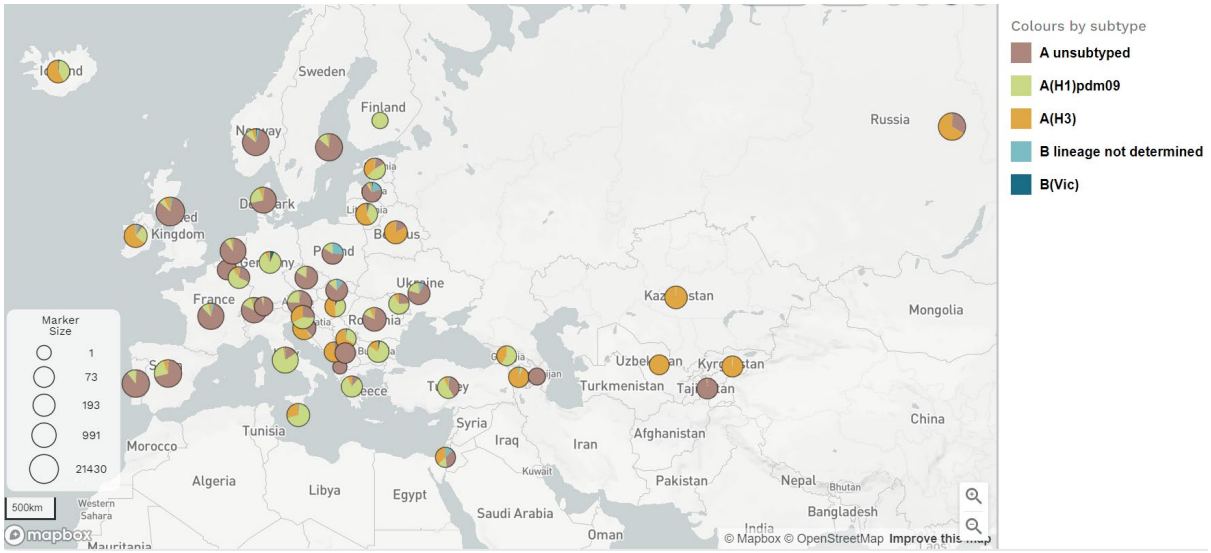
Weekly aggregate reports of detections

From week 40/2023 to week 3/2024, 135 728 influenza detections were reported from sentinel and non-sentinel surveillance sources in 50 countries and territories across the WHO European Region (Figures 1-6 and Map 1). Influenza type A viruses (132 851, 98%) dominated over type B (2 877, 2%). Of the 39 530 subtyped influenza A viruses, 20 747 (52%) were influenza A(H1)pdm09 and 18 783 (48%) were influenza A(H3). Of the A(H1)pdm09 viruses, 7 528 (19%) were subtyped based on the neuraminidase (NA). Of the A(H3) viruses, 5 077 (13%) were subtyped also based on NA gene. Eighteen countries carried out N-subtyping of the influenza A viruses, among which were Austria, Belarus, Switzerland, Germany, Denmark, Greece, Spain, Finland, France, Kyrgyzstan, Kazakhstan, Moldova, Malta, the Netherlands, the Russian Federation, Ukraine, the United Kingdom (Scotland and Wales). Lineage typing was performed for 283 (10%) influenza B viruses; all (100%) were B/Victoria viruses, with no evidence of B/Yamagata lineage circulation (Figures 1–6, Map 1).

Figure 1. Number and proportion of influenza virus detections in the sentinel and non-sentinel surveillance systems by subtype, WHO European Region, weeks 40/2023 through 3/2024.



Map 1. Proportions of influenza type/subtype, sentinel and nonsentinel surveillance systems, WHO European Region, weeks 40/2023 through 3/2024. An interactive map is available at: [Map 1. type/subtype (microreact.org)]



Sentinel detections

In the sentinel surveillance sources, influenza A (9 591, 97%) was the dominant type compared to influenza B (297, 3%; Figure 2 and 3). Of all 7 676 (sub)typed or lineage defined viruses, 66% were A(H1)pdm09, 33% A(H3) and 1% B/Victoria viruses. Of the 7 610 subtyped influenza A viruses, 5 107 (67%) were influenza A(H1)pdm09 and 2 503 (33%) were influenza A(H3). Of the A(H1)pdm09 viruses, 2 554 (26%) were subtyped based on the neuraminidase (NA). Of the A(H3) viruses, 948 (10%) were subtyped also based on NA gene. For 66 (22%) influenza B viruses lineage typing was carried out, all being B/Victoria lineage.

Figure 2. Number and proportion of influenza virus detections in the sentinel surveillance system by subtype, WHO European Region, weeks 40/2023 through 3/2024.

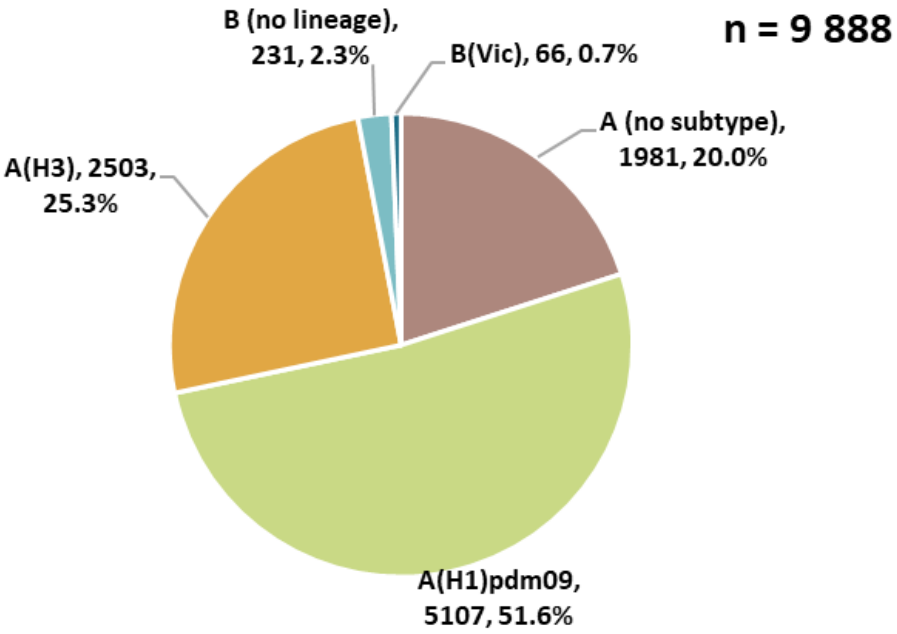
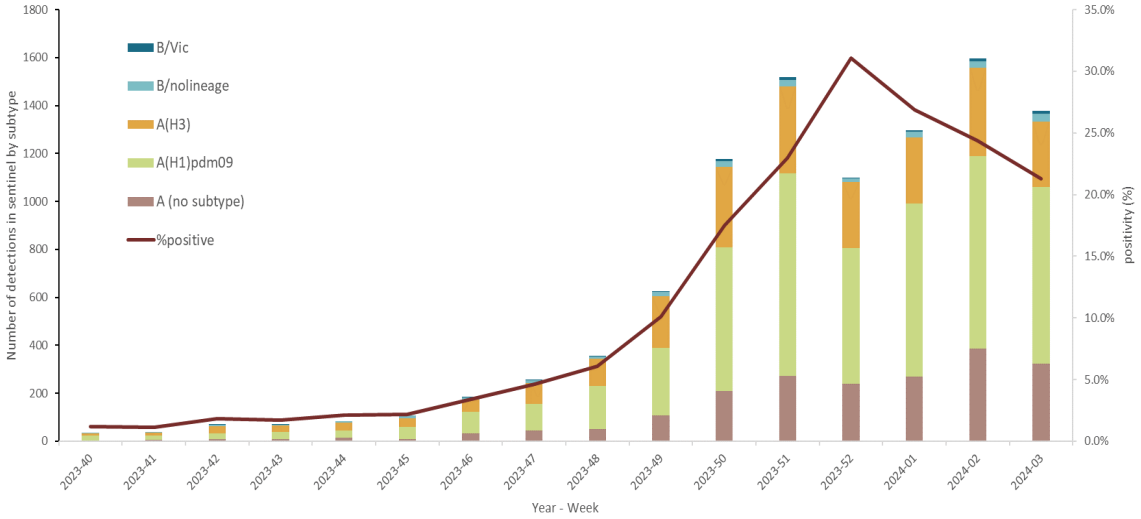


Figure 3. Number of detections in the sentinel surveillance system by subtype and proportion positive of all tested by week, WHO European Region, weeks 40/2023 through 3/2024.



Non-sentinel detections

Figure 4. Number and proportion of influenza virus detections in the non-sentinel surveillance system by subtype, WHO European Region, weeks 40/2023 through 3/2024.

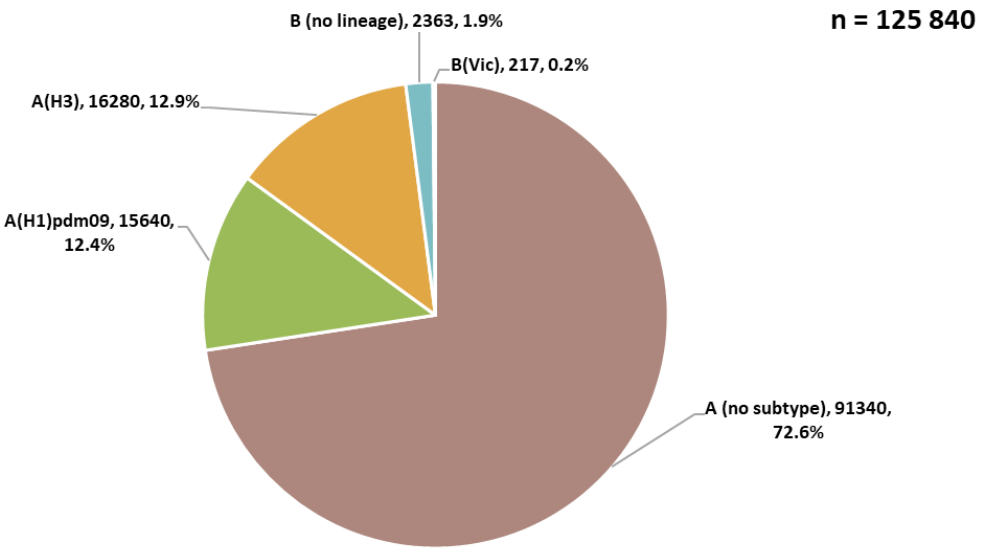


Figure 5. Number of detections in the non-sentinel surveillance system by subtype of all tested by week, WHO European Region weeks 40/2023 through 3/2024.

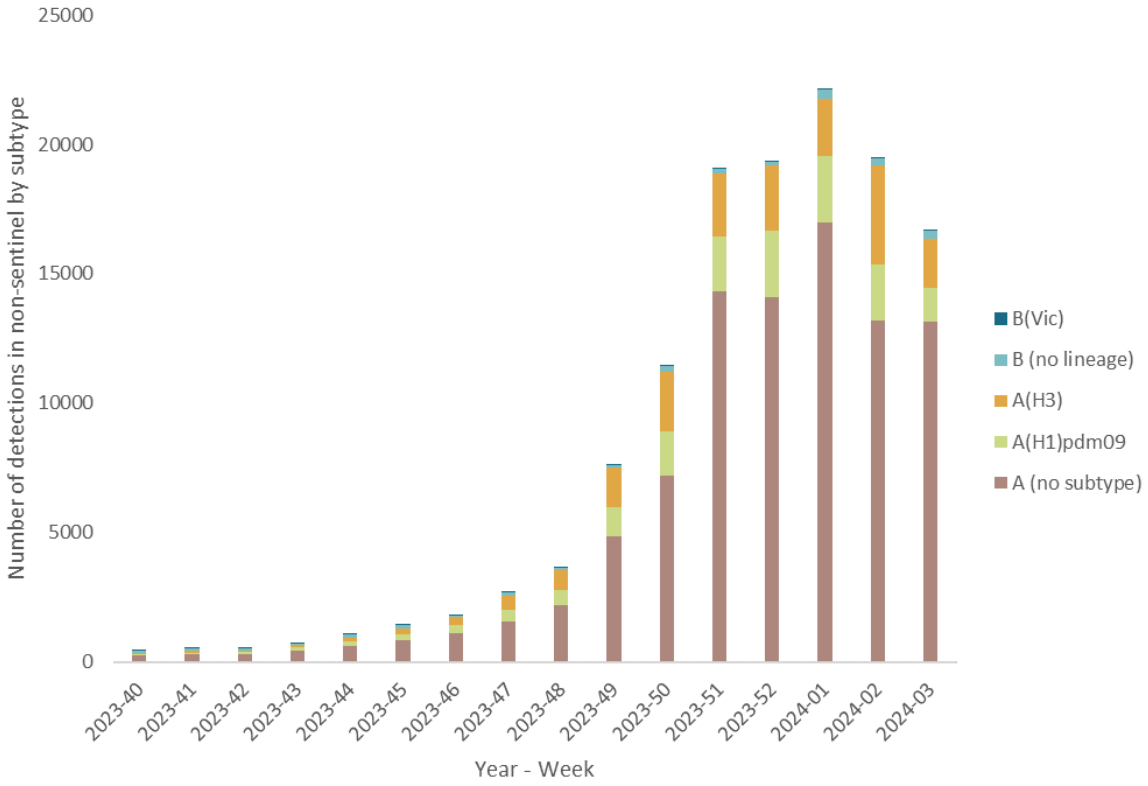
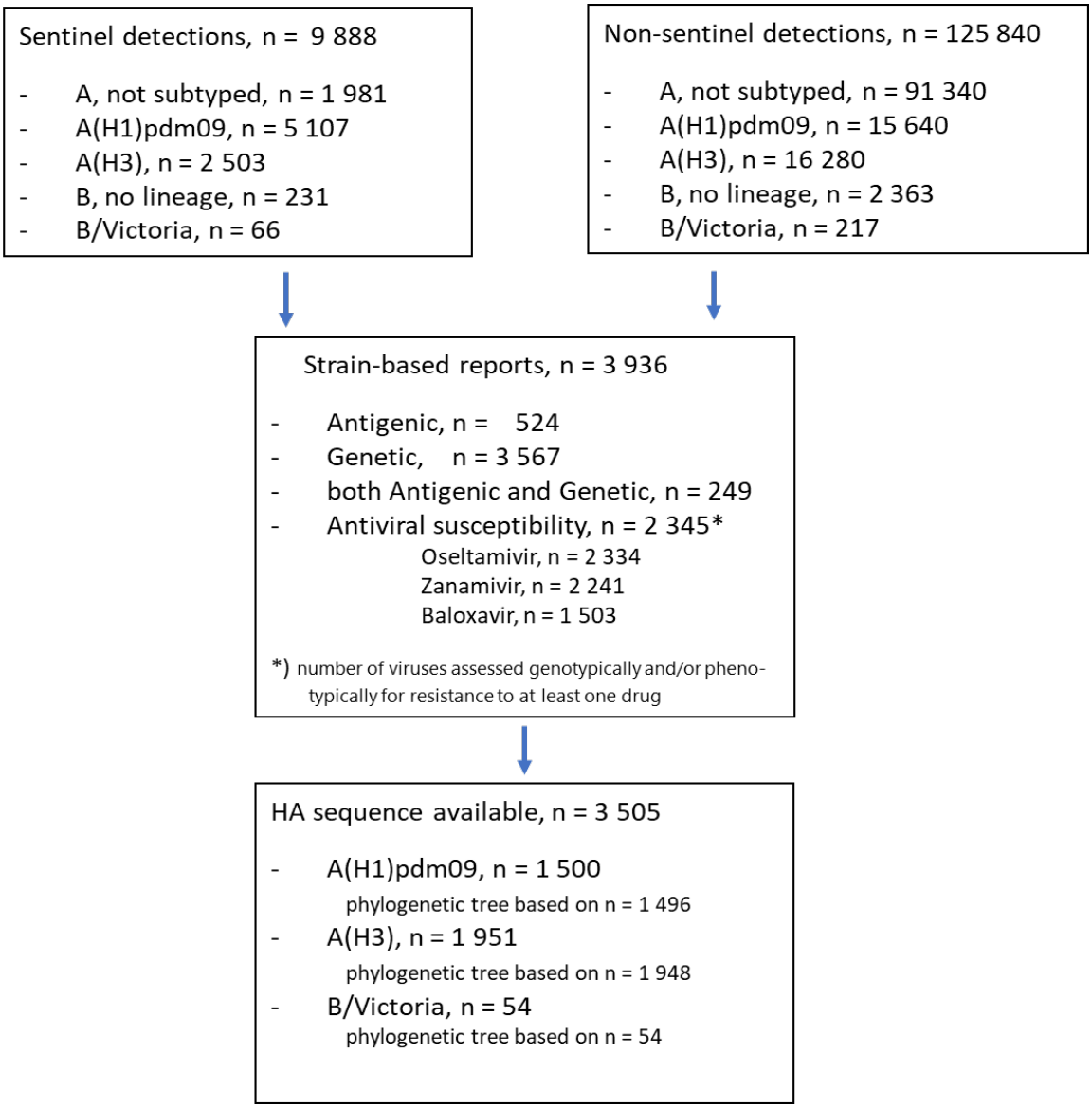


Figure 6. Flowchart presenting underlying number of specimens reported by country surveillance systems for detections, antigenic and genetic characterisation and antiviral susceptibility data as well as number of sequence data by subtype, used in the analysis of this report, WHO European Region, weeks 40/2023 through 3/2024.



Strain-based reports of detections

Strain-based reports were submitted to the record type INFLANTIVIR with further details on virus characteristics. Subtype data of these strain-based reports are summarised in this section to give a comparison to the overall detection data (see above). The data in this section describe how many viruses of each (sub)type were further characterised. From week 40/2023 to week 3/2024, 3 936 influenza strain-based reports were submitted from sentinel (620, 16%) and non-sentinel (2 104, 53%) surveillance sources in 19 countries across the WHO European Region (Map 2 and Figures 7 and 8). The remaining viruses (1 796, 46%) were reported with unknown surveillance system. In the strain-based reports, influenza type A viruses (3 856, 98%) dominated over type B (80, 2%). Of influenza type A viruses, the majority, 1 139 (65%) were N-subtyped as A(H1N1)pdm09, whereas 608 (35%) were A(H1)pdm09, and 1 517 (72%) were N-subtyped as A(H3N2), whereas 592 (28%) were A(H3) viruses.

Of influenza type B viruses 11 (<1%) were reported without lineage designation while the other 69 (2%) B viruses were reported as B/Victoria-lineage. The B viruses reported without lineage were confirmed as B/Victoria lineage by genetic clade information.

Map 2. Proportions of influenza subtypes by **strain-based** reports by country, WHO European Region, weeks 40/2023 through 3/2024. An interactive map is available at: [Map 2 (microreact.org)]

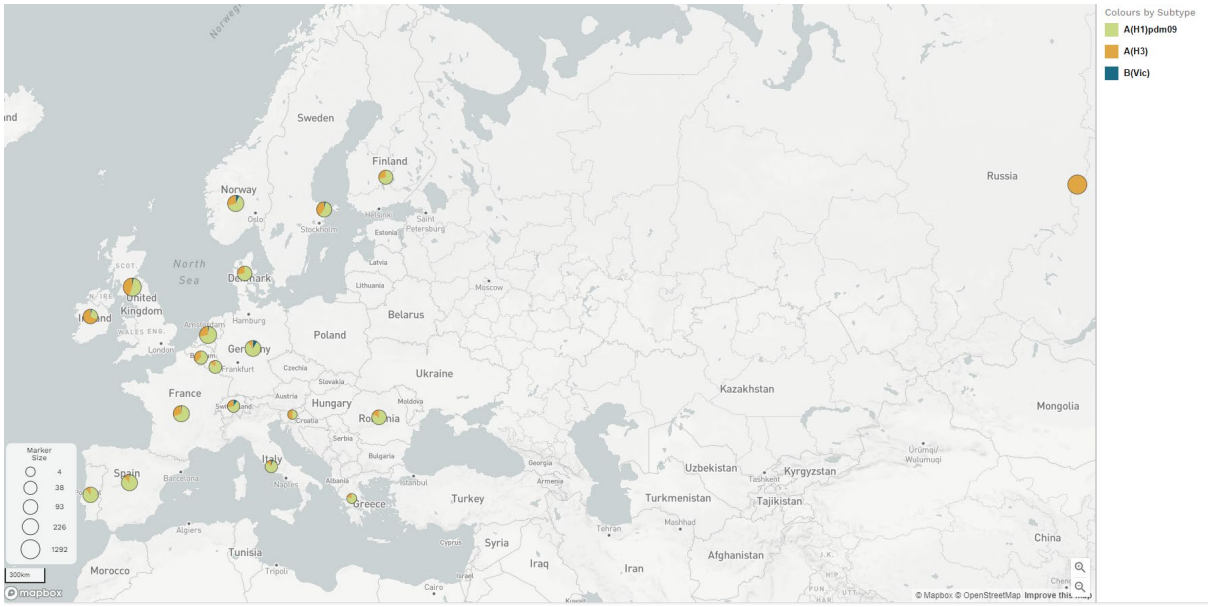


Figure 7. Number and proportion of influenza virus detections among the **strain-based reports** by subtype, WHO European Region, weeks 40/2023 through 3/2024.

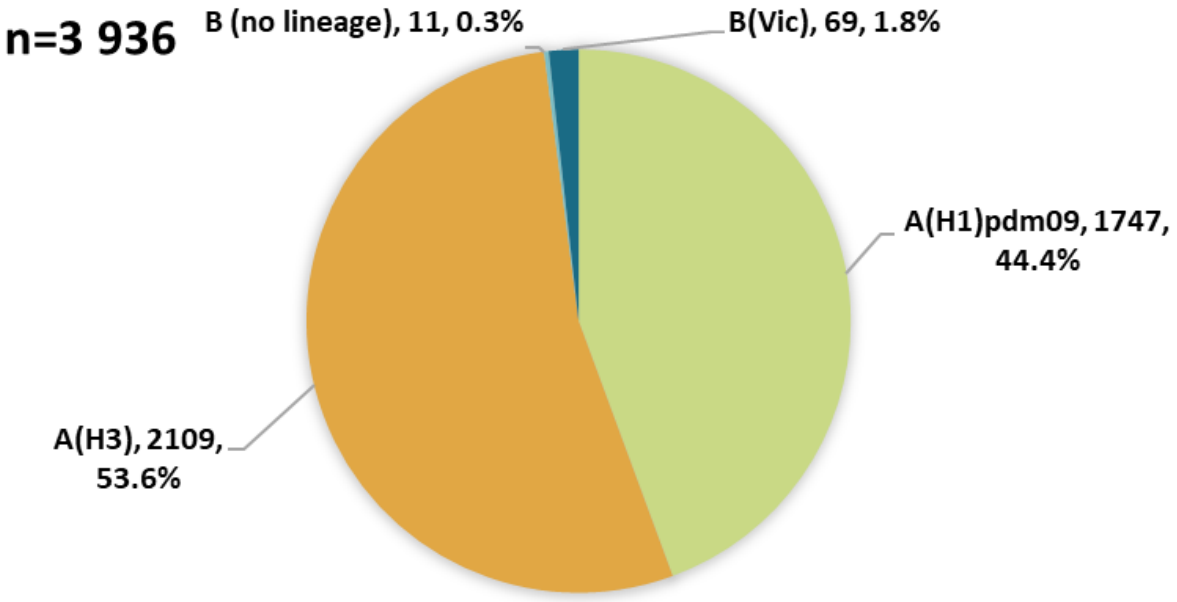
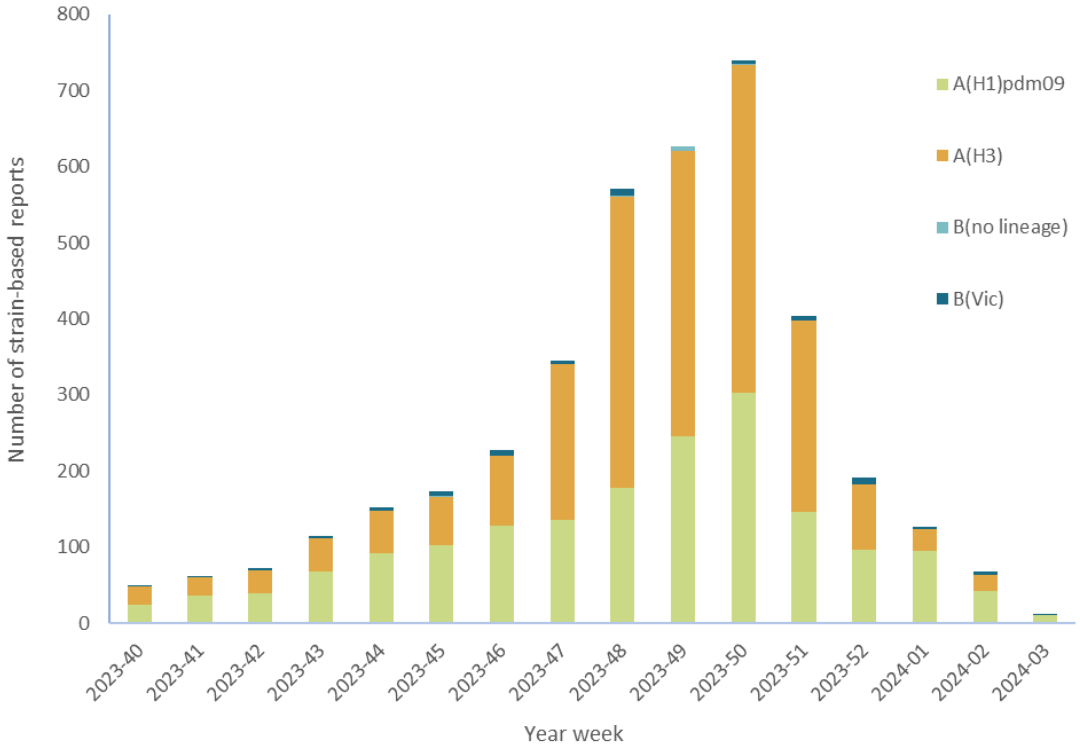


Figure 8. Number of viruses characterised (antigenically and/or genetically and/or tested for antiviral resistance) by subtype by week of specimen collection, **strain-based reports**, WHO European Region, weeks 40/2023 through 3/2024.



Overview of antigenic and genetic strain-based reports

Antigenic and genetic characterisations were reported to TESSy in weeks 40/2023 through 3/2024 (with last data being from week 3 and 2, respectively) by 18 countries: Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, the Russian Federation, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom. Seven countries (France, Germany, Greece, Italy, Portugal, the Russian Federation and the United Kingdom) reported both genetic and antigenic data, Slovenia and Switzerland provided only antigenic data and nine countries (Belgium, Denmark, Finland, Ireland, Luxembourg, the Netherlands, Norway, Spain and Sweden) provided only genetic clade data during the reporting period (Table 1).

Table 1. Number of viruses characterised antigenically (AG) and genetically (GEN) as reported to TESSy by country (n=18) and week of sampling, WHO European Region, weeks 40/2023 through 3/2024. Light blue indicates antigenic, light green indicates genetic characterisations.

	YEAR	2023													2024				
	WEEK	40	41	42	43	44	45	46	47	48	49	50	51	52	01	02	03	Total	%*
Belgium	AG																	0	0
	GEN	2	1	4		4	4	11	5	5	2							38	1.07
Denmark	AG																	0	0
	GEN	5	6	4	10	15	28	13										81	2.27
Finland	AG																	0	0
	GEN	1	2	3	10	5	5	7	10	14	8	4						69	1.93
France	AG	1		1	1		4	4	3	5	8	15	15	7	8	7		79	15.1
	GEN	2	4	7	7	7	6	17	3	18	40	54	14	1				180	5.05
Germany	AG		3	2	1	1	5	9	3	12	15	28	31	11	17	21	11	170	32.4
	GEN		2	3	1	2	5	10	6	4	5							38	1.07
Greece	AG												1					1	0.19
	GEN					2					1		2					5	0.14
Ireland	AG																	0	0
	GEN		2	4	2	4	4	6	11	16	13	9	1	5	6			83	2.33
Italy	AG								1	5	2							8	1.53
	GEN						1	1	1	7	2	1	2	2	6			23	0.64
Luxembourg	AG																	0	0
	GEN						2	1	1	1	7	8	10					30	0.84
Netherlands	AG																	0	0
	GEN	9	9	11	14	14	12	18	18	31	61	90	34	32	29	14		396	11.1
Norway	AG																	0	0
	GEN	4	8	3	25	39	11	11	39	26	7	5	3	27	26			234	6.56
Portugal	AG	1	1			1	2	2	1	2	2	9						21	4.01
	GEN	6	7	6	9	13	18	9	16	24	14	12	3	1				138	3.87
Russian Federation	AG	1	1		2	3	7	17	40	36	36	53	19					215	41
	GEN	1	2		4	5	13	35	141	296	253	244	175	56	4	4		1233	34.6
Slovenia	AG												1	2		1		4	0.76
	GEN																	0	0
Spain	AG																	0	0
	GEN	8	5	12	19	13	18	32	32	29	2	5	4	18	4			201	5.63
Sweden	AG																	0	0
	GEN	4	5	2	3	9	14	8	11	5	16	17	11	7	2			114	3.2
Switzerland	AG				2			3	5		5	3	1		2			21	4.01
	GEN																	0	0
United Kingdom	AG	1			2	1	1											5	0.95
	GEN	8	8	13	8	19	26	39	36	81	170	213	79	4				704	19.7
ALL	AG	4	5	3	8	6	19	35	53	60	68	108	68	20	27	29	11	524	100
	GEN	50	61	72	112	151	167	218	330	557	601	662	338	153	77	18	0	3567	100

**Percentage is calculated for antigenic and genetic characterisation data separately by country out of the total.*

Antigenic category reporting

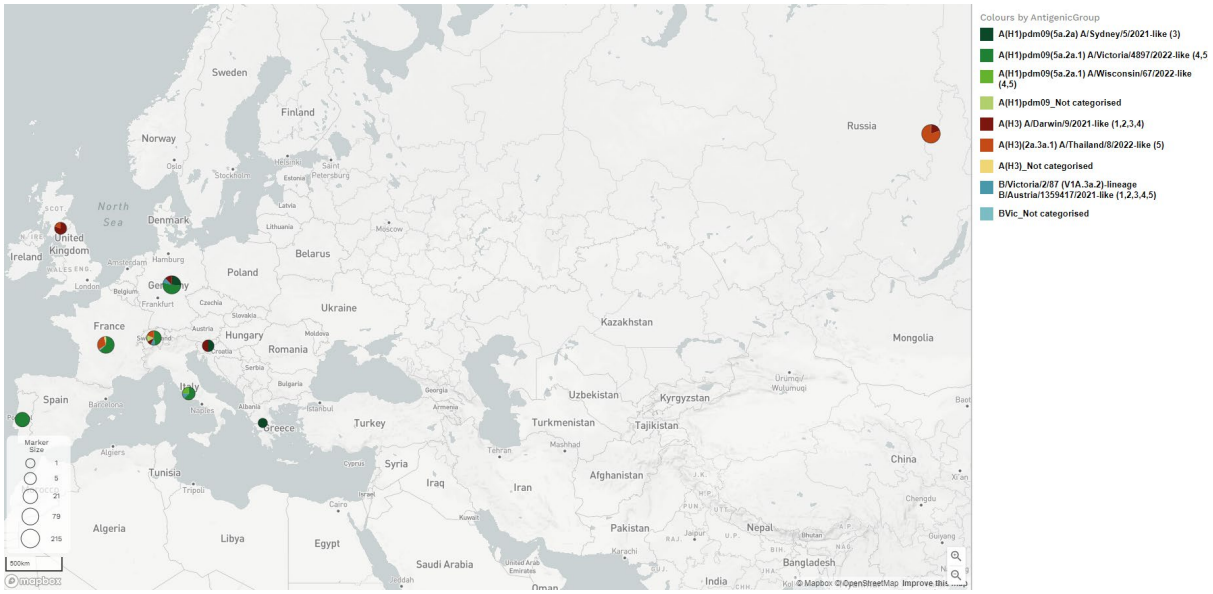
From weeks 40/2023 to 3/2024, with latest data reported for week 3/2024, nine countries reported antigenic characterisations to TESSy (Table 1, Map 3, Figures 9-11 and Table Annex 2.1). The Russian Federation and Germany reported the large majority of antigenic characterization data (41% and 32%, respectively), followed by France that reported 15% of viruses characterised antigenically. The viruses characterised antigenically fell within nine of the 12 available reporting categories (Table Annex 2.1).

Among the 524 antigenically characterised viruses, 502 (96%) were influenza A and 22 (4%) were influenza B (Table 1, Map 3, Figures 9-11 and Table Annex 2.1). Among the influenza A viruses antigenically characterised, 228 (44%) were A(H1)pdm09 viruses, and 274 (51%) were A(H3) viruses. Of the 228 (44% of all characterised influenza A viruses) antigenically characterised A(H1)pdm09 viruses, 174 (76%) were reported as A/Victoria/4897/2022-like, 49 (21%) reported as A/Sydney/5/2021-like, two (<1%) were reported as A/Wisconsin/67/2022-like. Three (1%) A(H1)pdm09 viruses were not attributed to any antigenic category, indicating antigenic difference using the current reference/vaccine virus antisera. Two of those were sent to WHO CC London for further characterisation and one was further genetically characterised.

Of the 274 antigenically characterised A(H3) viruses (52% of all characterised influenza A viruses), 202 (74%) viruses were A/Thailand/8/2022-like, 69 (25%) were A/Darwin/9/2021-like, and 3 (1%) viruses were not attributed to a category. Subsets of these viruses were sent to WHO CC London for further characterisation.

All 20 (4%) influenza B viruses that were antigenically characterised belonged to the B/Victoria lineage and all of these were characterised as B/Austria/1359417/2021-like and two viruses were not attributed to any predefined category.

Map 3. Proportions of antigenic categories within countries, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the map. An interactive map is available at [Map 3. Antigenic categories (microreact.org)]



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

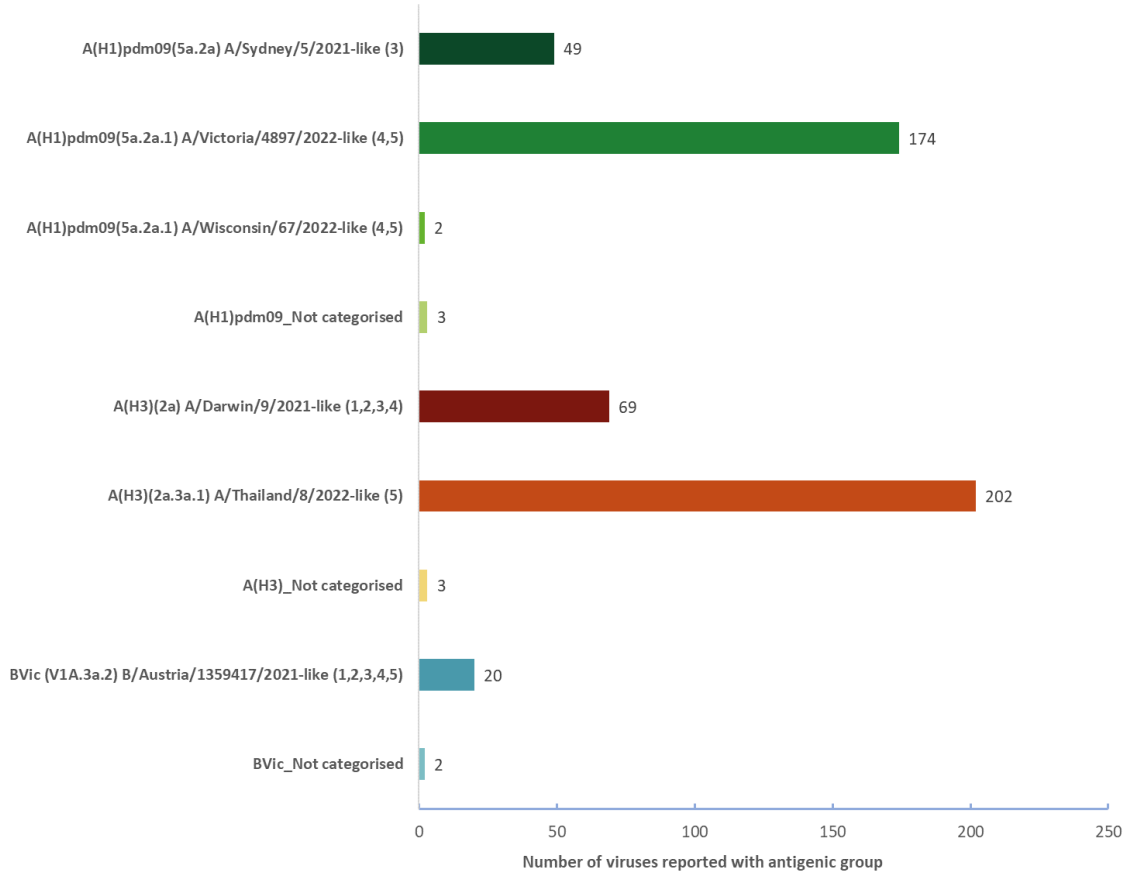
2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

Figure 9. Antigenic characterisation data by reporting category, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the figure.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

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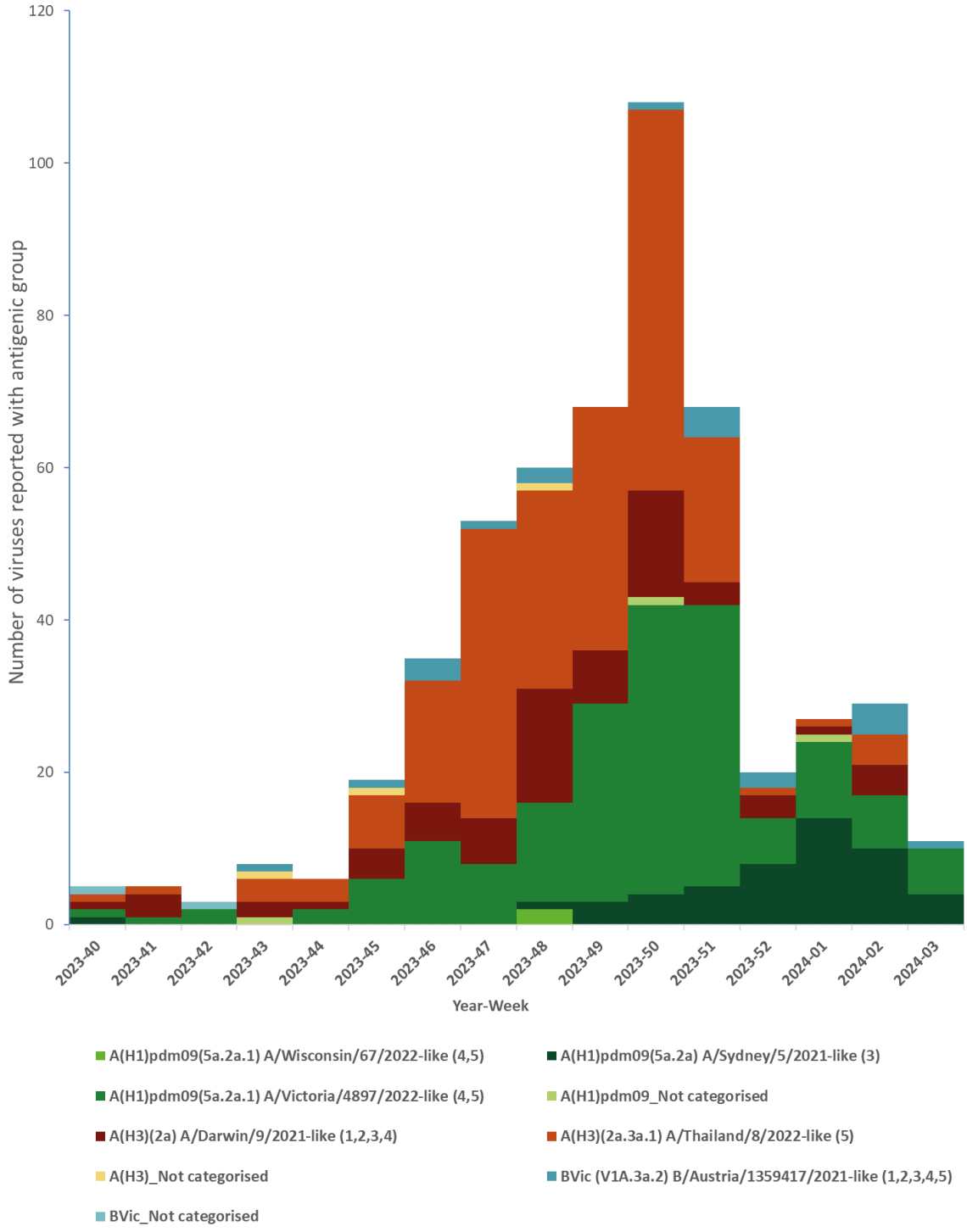
3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

Figure 10. Antigenic category reports by week, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the figure.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

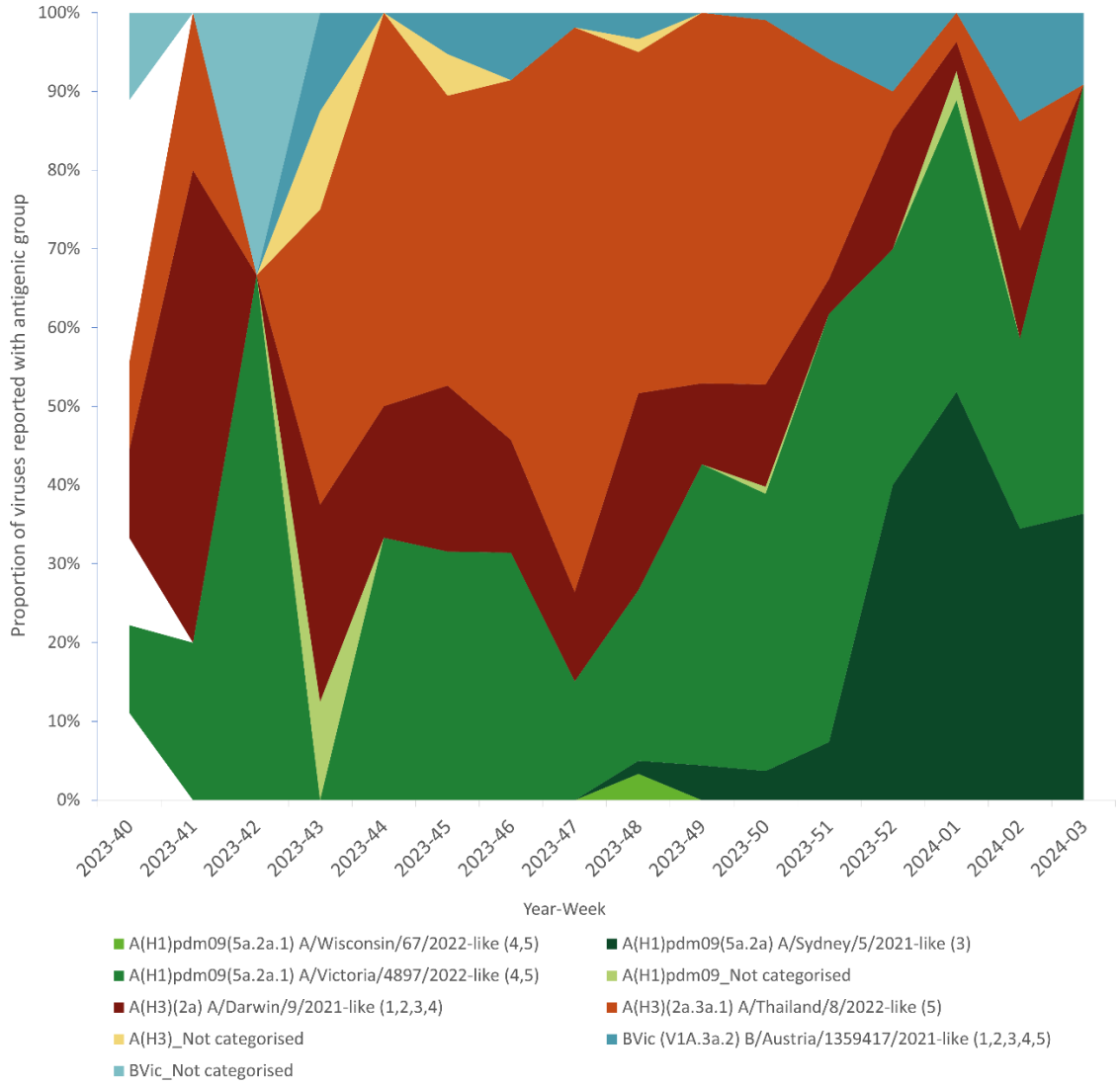
2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

Figure 11. Proportion of antigenic group categories by week, WHO European Region, weeks 40/2023 through 3/2024. It is of note that in the last six weeks, only a few specimens have been reported. Numbers in brackets refer to footnotes below the figure.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

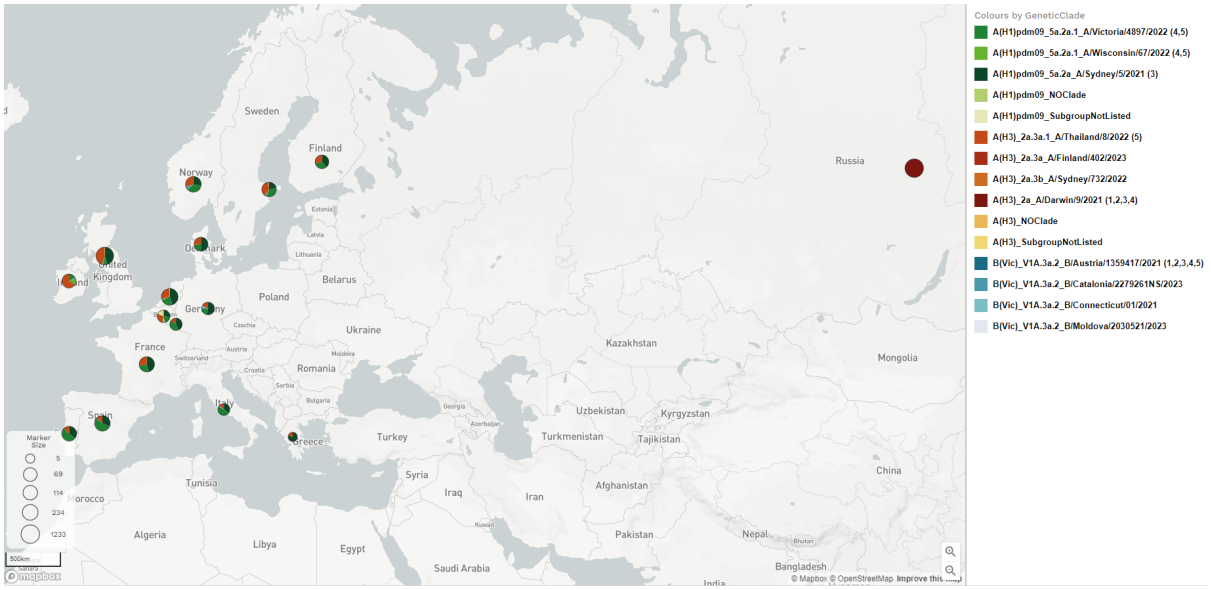
4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

Genetic group reporting

For specimens collected since week 40/2023, with latest data reported for week 2/2024, genetic characterisation data of 3 567 viruses were reported to TESSy by 16 countries (Map 4, Table Annex 2.2). The largest contributors of the genetic data were the Russian Federation (35%), the United Kingdom (20%) and the Netherlands (11%) followed by other countries contributing with less than 10%. The viruses characterised genetically fell within 11 of the 16 available reporting categories (Figures 12-14, Table Annex 2.2). In addition, the option "not attributed to clade" and "attributed to recognised group in current guidance but not listed here" was available for each subtype and lineage. Among the genetically characterised viruses, 3 503 (98%) were influenza type A, with 1 511 (42%) A(H1)pdm09 and 1 992 (56%) A(H3) viruses, and 64 (2%) influenza type B viruses.

Map 4. Proportions of genetic groups within countries, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the map. An interactive map is available: [Map 4. Genetic clades (microreact.org)]



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

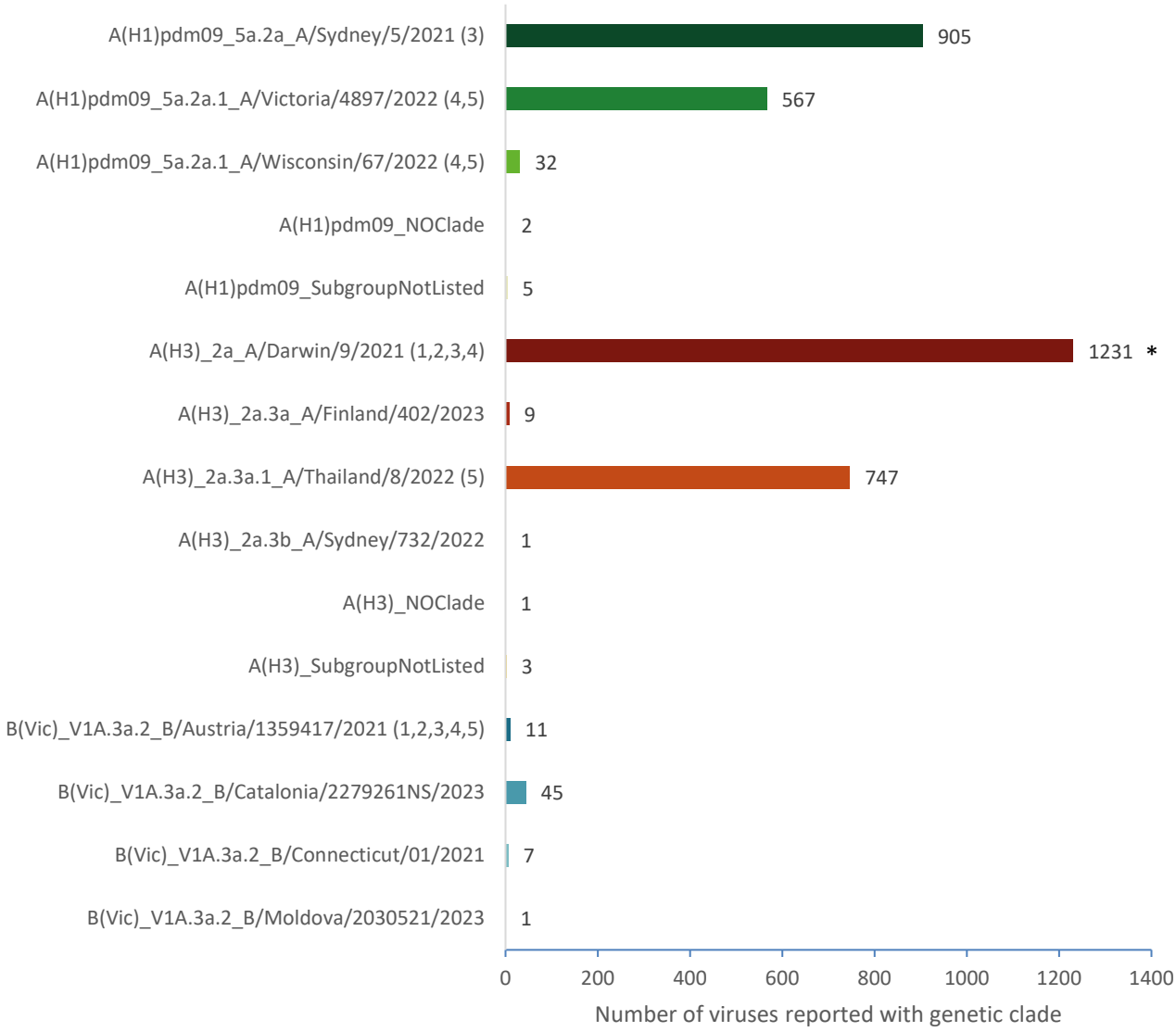
3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.

Figure 12. Genetic group data by reporting category, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the figure.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

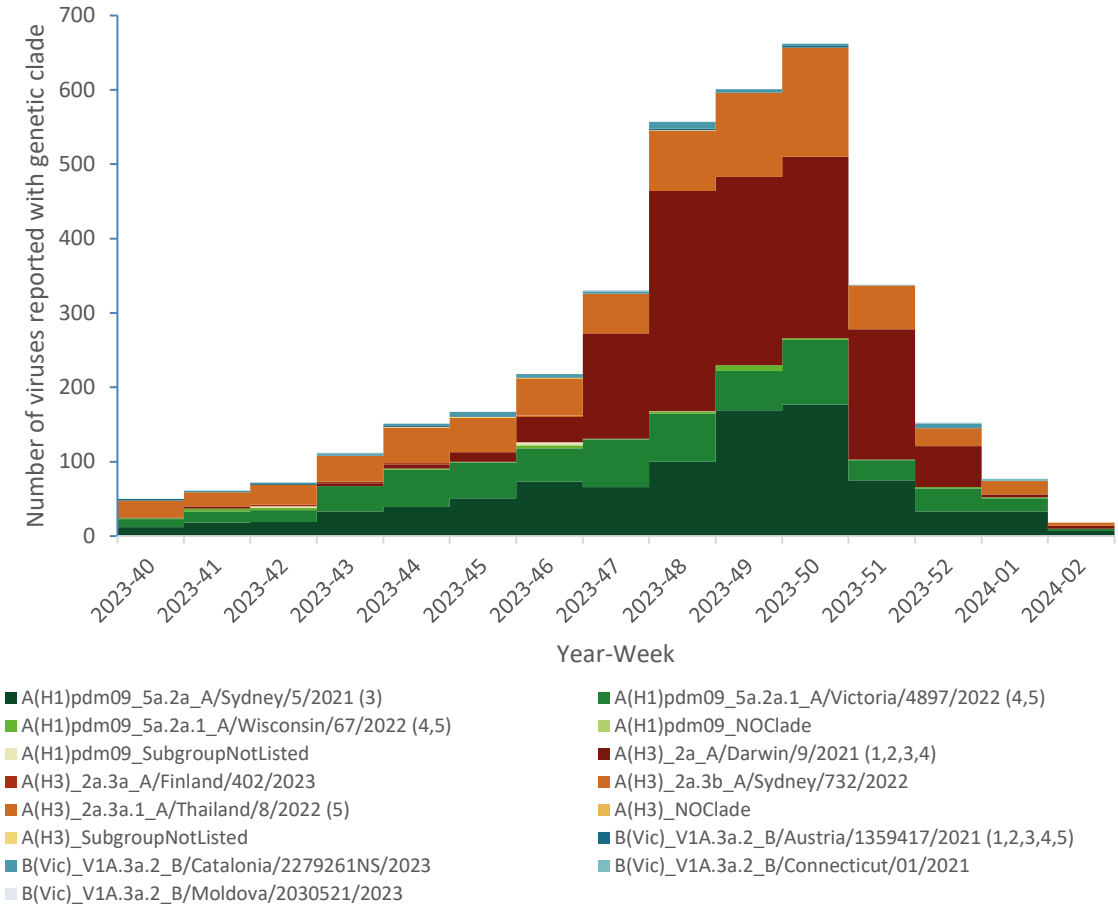
3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

**All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.*

Figure 13. Genetic group reports by week, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the figure.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

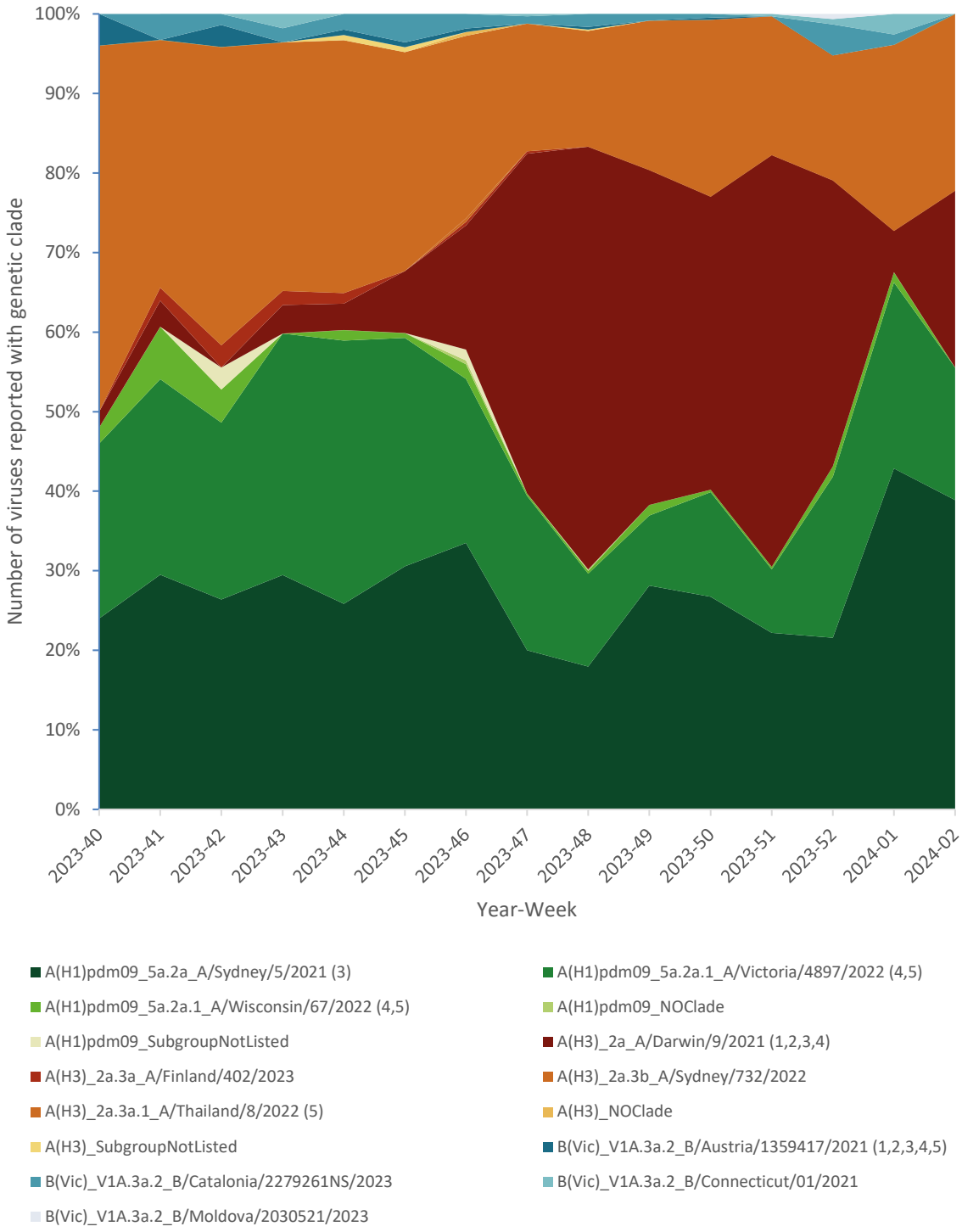
All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.

The genetic clade was reported for 1 511 characterised A(H1)pdm09 viruses (43% of all influenza type A viruses genetically characterised). Of those, 905 (60%) fell in clade 5a.2a, represented by A/Sydney/5/2021, the virus component for 2023 SH vaccine, while 567 (38%) belonged to a subclade of the 5a.2a.1 clade represented by A/Victoria/4897/2022, the virus component for 2023-2024 NH egg-based vaccine, and 32 (2%) belonged to another subclade of the 5a.2a.1 clade, represented by A/Wisconsin/67/2022, the cell-based 2023-24 NH vaccine component. For all five A(H1)pdm09 viruses (0.3% of A(H1N1)pdm09 viruses) reported as "attributed to recognised group in current guidance but not listed here" the HA sequence was provided and for four viruses the sequence quality was poor and they were left out from the phylogenetic analysis and the remaining one fell in subgroup 5a.2a. Only one of these viruses was provided with the required comment field and assessed as "6B.1A.5a.2a". Further information is provided in section "Genetic and phylogenetic analysis of HA sequences".

The genetic clade was reported for 1 992 characterised A(H3) viruses (56% of influenza type A viruses genetically characterised). The majority (1 231, 62%), belonged to clade 2a, represented by A/Darwin/9/2021, the recommended vaccine strain for egg-based vaccines for 2023-24 NH influenza season. These viruses were all reported by the Russian Federation and following phylogenetic analysis they belonged to the 2a.3a.1 group (represented by A/Thailand/8/2022; noted as a footnote in Map 4 and Figures 12-14). The second largest number (n=747, 38%) of A(H3) viruses were reported in subgroup 2a.3a.1, represented by A/Thailand/8/2022. Further nine (0.5%) viruses were assigned to subgroup 2a.3a represented by A/Finland/402/2023, one of which clustered with 2a.3a.1 in the phylogenetic tree. Only one virus (0.1%) belonged to the subgroup 2a.3b, represented by A/Sydney/732/2022. One virus (0.1%) that was not attributed to any predefined genetic clade, the HA sequence had low sequence quality and is subject for further analysis at WHO CC London. Three A(H3) viruses (0.2% of all A(H3) viruses genetically characterised) were reported to a subgroup not listed in the current guidance. The corresponding HA sequences were reported, and one virus fell in clade 2a.3a and the other virus sequences could not be included in the phylogenetic analysis due to bad sequence quality. Further information is provided in section "Genetic and phylogenetic analysis of HA sequences".

For the B/Victoria lineage, 64 viruses were reported with genetic clade information (100% of all genetically characterised influenza type B viruses). All belonged to clade V1A.3a.2, represented by B/Austria/1359417/2021, the recommended vaccine virus strain for the 2023-24 NH influenza season. Within that genetic clade, there were some further subclades defined and out of the reported viruses 45 (70%) had similar amino acid substitutions to B/Catalonia/2279261NS/2023, seven to B/Connecticut/01/2021 and one to B/Moldova/2030521/2023 reference viruses. Further information can be found in the section "Genetic and phylogenetic analysis of HA sequences".

Figure 14. Proportion of genetic groups by week, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the figure. NB. For week 2/2024 less than 10 viruses have been reported and therefore data in proportions is unreliable.



1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.

Descriptive analysis of antigenic and genetic characterisation data

Seven countries, namely France, Germany, Greece, Italy, Portugal, the Russian Federation and the United Kingdom reported **both** genetic and antigenic data for the same viruses during the reporting period (Table Annex 3.3).

For strain-based reporting, it is possible to compare antigenic and genetic information for the same virus and combine it with information from sequence data if sequence identifier was shared. Overall, 249 viruses had both antigenic and genetic characterisations reported (67 (27%) A(H1)pdm09, 176 (71%) A(H3) and 6 (2%) B/Victoria viruses; Table Annex 2.4).

Of the 67 A(H1)pdm09 viruses that had both genetic and antigenic data reported, the majority (n=64) were reported antigenically as 5a.2a.1 A/Victoria/4897/2022-like (Table Annex 2.4), which is the recommended A(H1)pmd09 component for egg-based NH vaccines for the 2023-24 season. Of those, the majority (n=40) were reported as genetic subgroup 5a.2a represented by A/Sydney/5/2021, while the remaining were assigned to the genetic 5a.2a.1 represented by A/Victoria/4897/2022 (n=24). Another two viruses were reported antigenically as 5a.2a.1 A/Wisconsin/67/2022-like (the recommended A(H1N1)pmd09 component for cell-based NH vaccines for 2023-24 season) while assigned to the genetic subgroup 5a.2a.1 represented by A/Victoria/4897/2022 and one virus was reported antigenically as 5a.2a A/Sydney/5/2021-like antigenically and assigned to the same genetic subgroup A/Sydney/5/2021. Antigenic group results reported by the Member States to TESSy therefore support that ferret antisera raised against A/Wisconsin/67/2022 and A/Victoria/4897/2022 from the 5a.2a.1 subgroup recognise viruses in both 5a.2a and 5a.2a.1 subclades well. Similarly, ferret antisera against A/Sydney/5/2021-like (5a.2a) recognised well viruses in subclades 5a.2a and 5a.2a.1 [10]. It might be noted that the characterisations guidance advises to categorise preferentially to the current vaccine strain in cases where titre-differences against a vaccine strain and another reference strain are the same. Furthermore, while ferret antisera distinguishes poorly between clade 5a.2a and 5a.2a.1 viruses, human sera indicate that they are distinguishable for humoral immunity in humans [10].

Of the 176 A(H3N2) viruses that had both genetic and antigenic data reported, 129 (73%) were reported antigenically as 2a.3a.1 A/Thailand/8/2022-like (Table Annex 2.4). The majority of those (n=120) were reported genetically as clade 2a represented A/Darwin/9/2021 (all from the Russian Federation and later clarified through phylogenetic analysis to belong to genetic clade 2a.3a.1), while nine were assigned to the genetic clade 2a.3a.1 represented by A/Thailand/8/2022. Thirty-five viruses were reported antigenically as 2a A/Darwin/9/2021-like and genetically assigned to the homologous 2a clade, which supports that ferret antisera raised against A/Darwin/9/2021, representing the vaccine viruses for the 2023-24 NH influenza season, recognise circulating clade 2a viruses well. A further eleven viruses that were antigenically A/Darwin/9/2021-like, were assigned genetically to subgroup 2a.3a.1 A/Thailand/8/2022. One virus that was genetically assigned to 2a.3a.1 A/Thailand/8/2022 was reported as not categorised antigenically. The above support that antisera raised against 2a.3a.1-like viruses (like A/Thailand/8/2022) recognise many (all but one in our study material, however, very few antigenic reports available) circulating viruses well. This one virus that was reported as not being able to be characterised antigenically (pending confirmation from the laboratory) was a 2a.3a.1 subclade virus similar to A/Sichuan-Gaoxin/1144/2023 with additional amino acid substitution K276E.

All genetically and antigenically characterised type B viruses belonged to the B/Victoria lineage viruses in line with the overall reported type B virus lineage detections. Of the six B/Victoria viruses that had genetic and antigenic data reported, four were reported antigenically as V1A.3a.2 B/Austria/1359417/2021-like, while two were reported as not categorised (Table Annex 2.4). HA sequences that were reported for B/Victoria viruses fell in three reporting categories within V1A.3a.2: one virus as B/Austria/1359417/2021, two as B/Catalonia/2279261NS/2023 and one as B/Connecticut/01/2021. The two viruses that were not categorised (pending confirmation from the laboratory) were genetically similar to B/Slovenia/924/2023 with K182E and additional amino acid substitution E128G. Antigenic group results reported by the Member States to TESSy therefore support that circulating viruses in subclade V1A.3a.2 are well inhibited by ferret antisera raised against B/Austria/1359417/2021-like viruses, representing the vaccine viruses for the 2023-24 NH influenza season [10], even if only a small number of B/Victoria-lineage viruses were available for analysis.

Genetic and phylogenetic analysis of HA sequences

During the reporting period of weeks 40/2023 to 3/2024, a total of 3 498 HA sequences from 17 countries were reported, retrieved and included in the analyses. Countries that reported HA sequences are shown in Table 2.

There were 1 496 A(H1)pdm09, 1 948 A(H3) and 54 B/Victoria viruses with reported sequencing results that were retrieved and included in the phylogenetic analyses (Table 2). HA sequences provided in TESSy and in the EpiFlu database of GISAID, were excluded either when they were not present or released in GISAID EpiFlu or having inconsistency between virus name and provided accession number, or a clearly discrepant HA sequence (such as belonging to a different subtype than reported). None were falling below the sequence length threshold (900 bp). Four A(H1)pdm09 and three A(H3) viruses were excluded based on low sequence quality. This was deemed to have no impact on the overall results.

Table 2. Number of influenza virus haemagglutinin (HA) gene sequences retrieved with GISAID EpiFlu database accession number and analysed in this report by subtype/lineage and country, WHO European Region, weeks 40/2023 through 3/2024.

Country/HA sequences	A(H1N1)pdm09	A(H3N2)	B/Victoria	Total	% of total sequences
Belgium	18	11		29	0.8%
Denmark	59	22		81	2.3%
Finland	49	20		69	2.0%
France	125	50	4	179	5.1%
Germany	28	7	3	38	1.1%
Greece	1			1	0.0%
Ireland	23	55	3	81	2.3%
Italy	19	3	1	23	0.7%
Luxembourg	26	4		30	0.9%
Netherlands	272	112	9	393	11.2%
Norway	147	69	17	233	6.7%
Poland			1	1	0.0%
Portugal	121	16		137	3.9%
Russian Federation	1	1196	1	1198	34.2%
Spain	173	25	2	200	5.7%
Sweden	65	45	4	114	3.3%
United Kingdom	369	313	9	691	19.8%
Total number of HA sequences	**1496**	**1948**	**54**	**3498**	

Influenza A viruses

A(H1)pdm09

By week 3/2024, 1 496 HA gene sequences from A(H1)pdm09 viruses deposited in the EpiFlu database of GISAID and also referenced to TESSy were included in the genetic analysis.

All viruses fell into clade 5a.2a, which is defined by the amino acid substitutions K54Q, A186T, Q189E, E224A, R259K and K308R compared with 5a.2 former vaccine strain A/Victoria/2570/2019 and it is represented by A/Sydney/5/2021 (SH 2023 vaccine component). A proportion of 40% (n=592) within 5a.2a were further characterised in clade 5a.2a.1 that has the additional P137S and T277A amino acid substitutions and is represented by A/Wisconsin/67/2022.

Most viruses within 5a.2a carried either T120A and K169Q (47%, n=421) or T120A and V47I (19%, n=173) which is a profile not represented by any reference virus. In clade 5a.2a.1, 41% (n=245) formed a major branch in the T216A subclade defined by R113K when compared with A/Victoria/4897/2022 (NH 2023/24 vaccine strain) and 51% (n=127) of these also carried S85P. No reference virus was present in this branch, neither in second largest branch defined by R45K including 37% (n=218) of 5a.2a.1.

Figure 15. Phylogenetic comparison of influenza A(H1N1)pdm09 HA genes. The vaccine strains are red, reference strains black and sequences reported to TESSy coloured according to the virus collection date by month (file attached).

A(H3)

By week 3/2024, 1 948 HA gene sequences from A(H3) viruses deposited in the EpiFlu database of GISAID and also referenced to TESSy were included in the genetic analysis.

All A(H3) HA sequences fell into clade 2a.3, hereby referred to as 2a.3, which is defined by D53N, N96S (addition of N-glycosylation potential site) and I192F compared to vaccine strain A/Darwin/9/2021. Within 2a.3, >99% (n=1946) fell into 2a.3a defined by E50K compared to 2a.3 representative virus A/Norway/24873/2021 and out of these a majority of >99% (n=1937) fell into 2a.3a.1 characterised by I140K and I223V and represented by vaccine virus A/Thailand/8/2022. Two viruses belonged to 2a.3b represented by A/Sydney/732/2022. No viruses fell into clade 2a.2 as observed in previous seasons.

Within clade 2a.3a.1, 79% (n=1 545) fell into a subclade defined by N122D compared with vaccine strain for the 2024 SH A/Massachusetts/18/2022 and represented by A/Sichuan-Gaoxin/1144/2023. This subclade further diversified with amino acid substitution K276E which is not represented by any reference virus and included 78% (n=1 527) of all 2a.3a.1. Furthermore, 10% (n=197) of the viruses within 2a.3a.1 belonged to a branch with I25V and 6% (n=123) to a branch defined by I242M where no reference strains were present.

The two 2a.3b viruses shared the amino acid profile of reference virus A/Sydney/732/2022.

Figure 16. Phylogenetic comparison of influenza A(H3N2) HA genes. The vaccine strains are red, reference strains black and sequences reported to TESSy coloured according to the virus collection date by month (file attached).

Influenza B viruses

B/Victoria-lineage

By week 3/2024, 54 HA gene sequences from B/Victoria viruses deposited in the EpiFlu database of GISAID were reported to TESSy and were included in the genetic analysis.

All reported viruses of B/Victoria carried HA genes that fell into genetic clade V1A.3a.2 with characteristic amino acid substitutions A127T, P144L, N150K, G184E, N197D (loss of N-glycosylation potential site), K203R and R279K compared to vaccine strain B/Washington/02/2019 and represented by vaccine virus B/Austria/1359417/2021.

Within 3a.2, there were several subclades-branches characterised by specific amino acid substitutions represented by groups with defined reference viruses. However, 31% (n=17) of the viruses fell in a branch with E128G where no reference virus was present.

No viruses fell in clades V1A.1 (e.g. B/Colorado/06/2017) or V1A.3 (e.g. former vaccine strain B/Washington/02/2019).

Figure 17. Phylogenetic comparison of influenza B/Victoria-lineage HA genes. The vaccine strains are red, reference strains black and sequences reported to TESSy coloured according to the virus collection date by month (file attached).

B/Yamagata-lineage

By week 3/2024, no HA gene sequence from B/Yamagata viruses was either deposited in the EpiFlu database of GISAID or reported to TESSy. No phylogenetic analysis for B/Yamagata was performed.

Antiviral susceptibility

From week 40/2023 through week 3/2024, a total of 2 345 influenza viruses were assessed genotypically and/or phenotypically for resistance to at least one drug (oseltamivir, zanamivir or baloxavir marboxil) by 15 countries (Belgium, Denmark, Estonia Finland, Germany, Italy, Luxembourg, the Netherlands, Norway, Portugal, Romania, the Russian Federation, Spain, Sweden, and the United Kingdom). Phenotypic antiviral resistance testing data were reported from Germany, Italy, the Netherlands, and the Russian Federation. Inhibition by oseltamivir was assessed genotypically and/or phenotypically for 2 334 viruses (1 476 A(H1)pdm09, 800 A(H3), and 58 B/Victoria viruses) and for 2 241 viruses to zanamivir (1 401 A(H1)pdm09, 782 A(H3), and 58 B/Victoria viruses). Susceptibility to baloxavir marboxil was assessed genotypically for 1 503 viruses in the reporting period (935 A(H1)pdm09, 539 A(H3), and 29 B/Victoria viruses). The neuraminidase subtype is known for most viruses tested, but not for all, therefore viruses are designated without neuraminidase subtype in this section.

In total, four viruses with reduced or highly reduced inhibition or susceptibility were detected. Three A(H1)pdm09 viruses exhibited either genotypic reduced or highly reduced inhibition by oseltamivir. One A(H3) virus showed genotypically reduced susceptibility to baloxavir marboxil.

Susceptibility to oseltamivir

In total, three viruses carried amino acid substitutions associated with highly reduced or reduced inhibition to oseltamivir (all A(H1N1)pdm09) (out of 1 476 tested, <1%).
Sequence analysis showed presence of amino acid substitution NA:H275Y resulting in assessment of highly reduced inhibition for two of the three viruses. The third virus carried amino acid substitution NA:D199E, associated with reduced inhibition (Table 3, Table Annex 4.1).

Table 3. Influenza subtypes and lineages with and without reduced inhibition following antiviral susceptibility testing to oseltamivir reported to TESSy, weeks 40/2023 through 3/2024, WHO European Region. HRI: Highly reduced inhibition; RI: Reduced inhibition; NI: Normal inhibition; prefix 'AA': Amino acid, refers to genotypic testing result. Phenotypic testing results are highlighted in light green colour.

	Oseltamivir				
	NI n (%)	AANI n (%)	AAHRI n (%)	AARI n (%)	Total
A(H1)pdm09	99 (6.7%)	1374 (93.1%)	2 (0.1%)	1 (0.1%)	1 476
A(H3)	150 (18.8%)	650 (81.3%)	0 (0%)	0 (0%)	800
B/Vic	9 (15.5%)	49 (84.5%)	0 (0%)	0 (0%)	58
Total	258 (11.1%)	2073 (88.8%)	2 (0.1%)	1 (0%)	2 334

Susceptibility to zanamivir

No virus with reduced inhibition to zanamivir was detected in the reporting period (Table 4, Table Annex 4.1).

Table 4. Influenza subtypes and lineages with and without reduced inhibition following antiviral susceptibility testing to zanamivir reported to TESSy, weeks 40/2023 through week 3/2024, WHO European Region. HRI: Highly reduced inhibition; RI: Reduced inhibition; NI: Normal inhibition; INP: Interpretation not possible; prefix 'AA': Amino acid, refers to genotypic testing result. Phenotypic testing results are highlighted in light green colour.

	Zanamivir		
	NI n (%)	AANI n (%)	Total
A(H1)pdm09	99 (7.1%)	1302 (92.9%)	1 401
A(H3)	150 (19.2%)	632 (80.8%)	782
B/Vic	9 (15.5%)	49 (84.5%)	58
Total	258 (11.5%)	1983 (88.5%)	2 241

Susceptibility to baloxavir marboxil

One A(H3N2) virus (out of 539 tested, <1%) carrying amino acid substitution PA:P28L which is associated with reduced susceptibility to baloxavir marboxil was detected in the reporting period (Table 5, Table Annex 4.1).

Table 5. Influenza subtypes and lineages with and without reduced susceptibility following antiviral susceptibility testing to baloxavir marboxil reported to TESSy, weeks 40/2023 through week 3/2024, WHO European Region. NS: Normal susceptibility; RS: Reduced susceptibility; prefix 'AA': Amino acid, refers to genotypic testing result.

	Baloxavir marboxil		
	AANS n (%)	AARS n (%)	Total
A(H1)pdm09	935 (100%)	0 (0%)	935
A(H3)	538 (100%)	1 (0.2%)	539
B/Vic	29 (100%)	0 (0%)	29
Total	1 503 (100%)	1 (0.1%)	1 503

Conclusions

From the WHO European Region, for the period covering weeks 40/2023 through 3/2024, 135 728 influenza virus detections, 524 antigenic and 3 567 genetic characterisations were reported to TESSy. Among the 39 813 (sub)typed or lineage defined viruses, A(H1)pdm09 (52%), A(H3) (47%) and B/Victoria (0.7%) were reported from sentinel and/or non-sentinel surveillance specimens. No wildtype, inactivated vaccine contamination nor live-attenuated vaccine derived B/Yamagata-lineage viruses have been recorded in TESSy during this influenza season. Taken together, this influenza season is characterised by co-circulation of different influenza (sub)types at the same time. Please see further surveillance data, maps and country-specific tables at www.erviss.org.

The distribution of type A and B viruses that had antigenic analyses reflected the overall virus distribution by sentinel and non-sentinel surveillance systems (98% influenza A and 2% influenza B detected viruses vs 96% and 4% antigenically characterised, respectively). Among the A viruses, the share of A(H3) viruses that were antigenically characterised was higher (55%) when comparing to the A(H1)pdm09 viruses (45%). A(H1)pdm09 viruses were slightly underrepresented in antigenic characterisations (52% detected, 45% characterised) and A(H3) viruses were antigenically characterised more frequently (48% detected, 55% characterised). Also, for the genetic clade reports, A(H1)pdm09 were underrepresented in comparison to the detections (43% characterised

among the subtyped A viruses vs 52% detected) and A(H3) viruses were overrepresented among the genetically characterised viruses (57% characterised vs 48% detected). However, sequencing strategies for influenza should not necessarily be strictly proportional. Minority subtypes/types are more likely to be epidemic next year than the majority virus and should be selectively sampled for sequencing. In total, only 16% (620 of 9 888 sentinel detections) have so far been entered as characterised into TESSy. This is disappointing as NICs have been encouraged to characterise as many as possible of their sentinel influenza viruses and asked to sequence all sentinel influenza viruses [11]. Overall, the HA sequence identifier provision in TESSy in connection to the genetic clade variable reporting is high with 3505 out of 3936, 89% reports including this information.

Regarding the antigenic similarity of circulating A(H1)pdm09 viruses to the 2023/24 NH vaccine components, the European picture appears uniform with respect to the viruses that circulated, with exclusively 5a.2a clade viruses circulating (100%). The circulating viruses appear to be antigenically similar to the vaccine virus components recommended for the 2023-24 NH season A/Victoria/4897/2022 (egg-based) and A/Wisconsin/67/2022 (cell culture- or recombinant-based vaccines), when characterised with ferret antisera. However, genetically, 40% of 5a.2a A(H1)pdm09 viruses fell to the 5a.2a.1 subgroup represented by A/Victoria/4897/2022, the virus component for 2023-2024 NH egg-based vaccine. Most 5a.2a viruses (66%) additionally carried T120A and V47I or K169Q. There was some genetic diversification also observed in the 5a.2a.1 viruses, with 41% carrying R113K with or without S85P or 37% carrying R45K. Susceptibility to oseltamivir, zanamivir, and baloxavir marboxil was assessed genetic or phenotypic analyses for 1 486 A(H1)pdm09 viruses. In total, three A(H1)pdm09 viruses (<1%) showed reduced or highly reduced inhibition by oseltamivir as indicated by presence of amino acid substitutions NA:D199E and NA:H275Y, respectively. No A(H1)pdm09 viruses with reduced inhibition by zanamivir or reduced susceptibility to baloxavir marboxil were detected.

For A(H3), almost all circulating viruses fell in clade 2a.3a.1 represented by A/Thailand/8/2022; the limited available antigenic data supported the antigenic similarity of many of those viruses with the vaccine strain A/Darwin/9/2021 for the 2023/24 NH influenza season. However, it should be noted that in our data set, for A(H3N2) viruses, only 274 antigenic reports were available in comparison to 1 992 genetic data and that the NICs did not have many types of ferret antisera available to test for more detailed antigenic characteristics. One of the clade 2a.3a.1 A(H3N2) viruses was reported as antigenically discrepant from the vaccine strain which could indicate that reduced reactivity was seen against some recent viruses expressing HA genes from subclade 2a.3a.1. Noteworthy, 79% of A(H3N2) viruses belonged genetically to the clade 2a.3a.1 (SH 2024 vaccine group with additional amino acid substitution K276E, while there were also two other smaller subgroups with I25V (10%) and I242M (6%) respectively. For this report, susceptibility to oseltamivir, zanamivir, and baloxavir marboxil was assessed by genetic or phenotypic analyses for 801 A(H3) viruses. One A(H3) virus (<1%) showed reduced susceptibility to baloxavir marboxil as indicated by amino acid substitution PA:P28L. This mutation is associated with a small reduction in susceptibility of 1-3 fold [12]. No A(H3) viruses with reduced inhibition by oseltamivir or zanamivir were detected.

For the B/Victoria lineage, all antigenically characterised viruses were V1A.3a.2 B/Austria/1359417/2021-like, which is the current vaccine component in tri- and quadrivalent vaccines in the NH 2023/24. The B/Victoria lineage viruses have genetically diversified and, within the V1A.3a.2, the following four subclades were detected: 1) 70% of the B/Victoria viruses fell into a subgroup with amino acid substitutions A221T or E183K similar to B/Catalonia/2279261NS/2023, 2) 17% of the viruses were genetically similar to the vaccine component B/Austria/1359417/2021 subgroup, 3) 11% of the viruses were characterised by D197E substitution similar to B/Connecticut/01/2021, and 4) approximately 2% of the viruses carried E128K, A154E, S208P similar to B/Moldova/2030521/2023. Interestingly, there was a branch of viruses within 3a.2 that carried E128G (31%) and was not represented by any defined reference virus. Susceptibility to oseltamivir and zanamivir was assessed by genetic or phenotypic analyses for 58 B/Victoria viruses and 29 B/Victoria viruses were analysed for genetic markers conferring reduced susceptibility to baloxavir marboxil. No B/Victoria viruses showed reduced inhibition or highly reduced inhibition by oseltamivir or zanamivir or reduced susceptibility tobaloxavir marboxil.

Early influenza VE results from Canada against infection showed 61% (95% CI: 58-64) against influenza A(H1N1), 49% (95% CI: 28-63) against influenza A(H3N2) and 75% (95% CI: 58-85) against influenza B [13].

Due to the question of whether B/Yamagata lineage viruses have become extinct, all B viruses that NICs receive should ideally be lineage-determined as only 2% of detected influenza viruses were B viruses. Among the A viruses, antigenic and genetic characterisations were performed more among A(H3N2) than would have been expected from the number of detections in sentinel and non-sentinel surveillance systems. Overall, these differences between

proportion of detected and characterised viruses could be due to many reasons such as selection bias of viruses to characterisation or different success rate of virus isolation by (sub)type.

Only 19 out of 50 countries reported virus characterisation data along with influenza detection data, and to varying extent. Antigenic and genetic characterisations were reported by nine and 16 countries, respectively. This is an increase since February 2023, when six and 15 countries reported antigenic and genetic data, respectively. However, the number of antigenic reports has fallen almost to half from last year's 1 050 reports at this time of the year. The genetic reports have stayed on the same level (3 301 reports last year). Understanding the reason behind the decline in antigenic reports, despite three additional countries providing data, poses a challenge. Only one more country has contributed to the genetic reports, resulting in data volumes closely resembling those of the previous year.

There are limitations to these data. The specimen sources (sentinel GPs, hospital, ICU, outbreak investigations) and selection processes for the viruses that undergo characterisation vary from country to country. Only a small percentage (0.4% antigenically and 2.6% genetically; 0.6 and 4.4% from the sentinel source viruses, respectively) of detected viruses were characterised overall, even from the sentinel source. ECDC and WHO Regional Office for Europe have previously recommended to sequence all influenza viruses detected from sentinel sources and this is clearly not yet implemented [11]. Furthermore, for the antigenic data reported to TESSy only the laboratory interpretations are considered, and no direct analysis of antigenic properties is possible. Therefore, the antigenic characterisation results from the different laboratories may not be directly comparable. Also, for the antiviral susceptibility analysis, the laboratories' interpretation of their antiviral test results about the drug resistance rather than reported test values were used for the analysis. For the genetic clades, the reporting system does not consider emerging amino acid substitutions or additional nucleotide mutations that cause genetic diversity that is not reflected in a distant root clade designation. Therefore, the countries have a reason to report "attributed to recognised group in current guidance but not listed here". The reporting guidance specifies that "subgroup not listed in the current reporting categories" applies to previously defined groups that are no longer available for reporting, not to new emerging subgroups that have not become designated in the reporting guidance yet. The guidance advises that emerging substitutions deemed significant is entered in the comment field for genetic characterisations, however, only one of the eleven viruses was provided with a comment. However, this time, we saw much fewer reports of the category "subgroup not listed in the current reporting categories" and this indicates that the reporting categories were better matched to the circulating viruses than last year, and that the NICs' phylogenetic analyses agreed with the categories provided.

Despite the indicated limitations of influenza surveillance data collection, influenza virus detection and virus characterisation data from the WHO European Region remain crucial for the selection of viruses to be sent to a WHO CC for detailed analyses that inform the decision-making process of recommending influenza viruses for inclusion in vaccines at biannual WHO vaccine composition meetings.

Contributors and acknowledgements

The report was prepared on behalf of the European Influenza Surveillance Network and WHO European Region Influenza Surveillance Network by Eeva Broberg, Angeliki Melidou, Maximilian Riess, Olov Svartstrom and Maja Vukovikj (ECDC), Iris Hasibra (WHO Regional Office for Europe). The report was reviewed by Olav Hungnes (Norway), Katarina Prosenc (Slovenia), Edoardo Colzani and Ole Heuer (ECDC), Karen Nahapetyan and Marc-Alain Widdowson (WHO Regional Office for Europe), Dmitriy Pereyaslov (WHO headquarters), Monica Galiano and Nicola Lewis (WHO CC London).

We gratefully acknowledge the work of the country representatives that have reported their data to TESSy and the authors, originating and submitting laboratories of the data and the sequences in the EpiFlu database of GISAID that were downloaded for use in the preparation of this report (all submitters of data may be contacted directly via the GISAID website). We acknowledge Marius Valentin Valcu (ECDC) for his support in TESSy data management and Erik Alm (ECDC) for the in-house genetic analysis tool.

Disclaimer

The detection data were extracted 25 January 2024 from the TESSy database. Any error in the database at this time will have affected the analysis. All countries with unclear reports have been contacted in order to correct the data retrospectively for future reports.

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Contacts

European Centre for Disease Prevention and Control (ECDC) ECDC.Influenza@ecdc.europa.eu Tel. +46 858 60 10 00 Fax +46 858 60 10 01 www.ecdc.europa.eu	**WHO Regional Office for Europe** euinfluenza@who.int Tel. +45 45 33 70 00 Fax +45 45 33 70 01 www.euro.who.int

Annexes

Annex 1 – Methods

Data sources

NICs receive clinical specimens and data from sentinel and non-sentinel surveillance sources for virological analysis. Fifty of the 53 countries or territories of the WHO European Region, including EU/EEA countries, regularly report epidemiological and virological influenza surveillance data to ECDC and the WHO Regional Office for Europe from primary care sentinel sites and other sources (e.g., hospitals, non-sentinel primary care, outbreak investigations) reported as non-sentinel data. A detailed overview of country-specific surveillance systems can be found on the Flu News Europe | About Us and WHO website [14].

The detection of influenza A and B viruses, subtyping of influenza A(H1N1)pdm09 and A(H3N2) viruses, and in some instances, type B lineage determination was performed with real-time RT-PCR techniques. Weekly detection data by country were reported to TESSy in aggregate format through INFLVIRWAGGR and RESPIAGGR record types. For the virus characterisation data from INFLANTIVIR record type, majority of the A(H1) and A(H3) viruses were reported with N-subtype (1 139, 65% and 1 517, 72%, respectively). The remainder of the type A viruses were reported without N-subtype to TESSy, and therefore we are using A(H1)pdm09 and A(H3) nomenclature for all type A viruses throughout the characterisation parts of the report.

NICs cultured influenza viruses, from a subset of influenza-positive clinical specimens, in MDCK, MDCK-SIAT or other cell lines and, in some instances, embryonated chicken eggs [15,16]. Virus recovery was commonly assessed by agglutination of red blood cells (RBCs), most commonly from turkey, guinea pig or humans. A haemagglutination inhibition (HI) assay was used for antigenic characterisation of recovered influenza viruses using post-infection ferret antisera raised against vaccine/reference influenza viruses (supplied by WHO CC London or WHO CC Atlanta or laboratories' own generated) [16] to inhibit virus-induced agglutination of RBCs. A virus isolate was considered antigenically similar to a reference virus, if the HI titre with the respective post-infection ferret antiserum differed by no more than 4-fold (usually a decrease), in a 2-fold dilution series, from the HI titre of the antiserum with the reference virus itself. To consider an isolate antigenically different from a reference virus, the HI titre had to show a decrease of 8-fold or more. For antigenic characterisation of A(H3N2) viruses, some NICs conducted HI assays in the presence of oseltamivir, to prevent haemagglutination by the N2 neuraminidase, and/or performed virus neutralization assays. Antigenic characterisations are reported to TESSy under the different representative influenza virus categories in strain-based format. In addition, "not attributed to category" was available for each subtype and lineage to accommodate viruses that either did not match one of the pre-set major antigenic groups or did not yield a conclusive HI assay result. Viruses that did not match reporting categories were included in total counts of characterised viruses but were explained further in the text upon consultation with the reporting country.

NICs also conducted genetic characterisation of viruses through sequencing, often directly on clinical specimens. To report a virus as belonging to a specific genetic group, the phylogenetic and amino acid sequence analyses must meet the following criteria: a) in phylogenetic analysis of the HA gene, the virus should cluster within the clade represented by the indicated vaccine/reference virus, and b) it should neither contain many nor critical amino acid substitutions when compared to viruses recognised as belonging to the specific group with which it associates. WHO CC London provided the list of reference viruses to be used for the purpose of genetic analysis in October 2023 together with reporting categories for influenza virus characterisation related to the HA gene (genetic) and the encoded glycoprotein product (antigenic) (ECDC/WHO Europe, TESSy influenza virus characterisation guidelines for the northern hemisphere influenza season 2023/24, November 2023, available upon request). GISAID accession numbers were reported; sequences were either obtained through sequencing at the influenza reference laboratories or at the WHO Collaborating Centres. Weekly virus characterisation data were reported to ECDC in strain-based format by date of sampling (or in some cases by date of onset if date of sampling was not available). Viruses that were reported as 'subgroup not listed' or which did not match reporting categories were included in total counts of characterised viruses but were explained further in the text upon phylogenetic analysis if sequence was available or upon consultation with the reporting country.

Data on susceptibility to NAI antiviral agents were produced by the NICs using genotypic (limited SNP detection by RT-PCR or pyrosequencing, or partial or full NA gene sequence analysis) and/or phenotypic analysis (drug-

specific IC50 determination), and results were reported to TESSy. For genotypic analysis, susceptibility was determined by the reported amino acid substitutions associated with reduced/highly reduced inhibition (RI/HRI) by NAIs oseltamivir or zanamivir [17]. Phenotypic susceptibility was assessed by determining IC50 values representing the concentration of oseltamivir or zanamivir needed to inhibit viral neuraminidase activity by 50%. For influenza A viruses, inhibition was classified as normal inhibition (NI) if a reported value was a <10-fold increase above the median IC50 value after removal of obvious outliers. Reduced inhibition (RI) required a 10 to 100-fold increase above the median IC50 and highly reduced inhibition (HRI) >100-fold above the median IC50. For influenza B viruses the corresponding values were: <5-fold increase above median (NI); 5 to 50-fold increase above median (RI) and >50-fold increase above median (HRI) [18]. Median values and fold-changes were calculated by virus (sub)type, antiviral drug and IC50 assay method. The submitting laboratories reported their own interpretation of the genotypic and phenotypic assessments as NI, RI or HRI to TESSy, and the same with the prefix 'AA' for genotypic assessments. Reported values for interpretation of baloxavir marboxil susceptibility are described below. If no assessment was done, 'not applicable' (NA) was reported, and if genotypic interpretation was not possible that was reported separately as 'amino acid interpretation not possible' (AAINP). These assessments of the submitting laboratories were used for the calculations in this report.

Baloxavir marboxil susceptibility data have been reported based on the amino acid substitutions present in the polymerase acidic protein (PA). The PA amino acid substitutions that have been detected in viruses from respiratory specimens and associated with reduced susceptibility are listed in the WHO guidance [12,19]. Provisionally and for reporting purposes, the IC50 fold-change threshold for identifying a reduced susceptible virus was set at 3, but further evaluation of data from different implementations of IC50 determination is still needed for setting a definitive threshold fold-change value. The WHO table includes all of the studied amino acid positions for all virus subtypes and their observed values so far, not only those that are considered reduced susceptible (amino acid – reduced susceptible viruses, AARS). Currently, different non-standardised assays (focus, plaque, or yield reduction assay, high-content imaging neutralization, ViroDot assay) are mainly used by WHO CCs for the phenotypic analyses and monitoring of reduced baloxavir marboxil susceptibility and therefore the indicated fold changes in the WHO list are not necessarily comparable [20]. For reporting purposes, amino acid substitutions associated with below 3-fold change in phenotypic assays are considered as normal (amino acid – normally susceptible viruses, AANS), while those associated with a value of ≥3 are considered reduced susceptible (AARS; Amino acid substitution in PA previously associated with reduced susceptibility) [19]. When there is no amino acid substitution in PA previously associated with reduced susceptibility, the virus is reported as AANS, when there is an amino acid substitution in PA previously associated with reduced susceptibility it is reported as AARS, and when interpretation is not possible, it is reported as 'Genotypic interpretation not possible' (AAINP).

All virus characterisation data were reported in strain-based manner through INFLANTIVIR TESSy record type. If a virus was reported with 'not applicable' result in TESSy, data were excluded from the analysis.

Phylogenetic analysis

All seasonal influenza HA sequences for A(H1N1)pdm09, A(H3N2) and B/Victoria from 2022/23 were downloaded from the EpiFlu database of GISAID. An ECDC in-house programme was used to process the sequence data for each subtype separately as follows: all entries in TESSy, reported with a HA sequences and available on GISAID, were matched with the downloaded GISAID data, keeping entries in TESSy with a matching GISAID Isolate ID or sequence accession (complemented with a few cases of Isolate name matches) number and extracting the sequences of those matches into a separate file. HA sequences were excluded in cases of unreleased sequences, errors in the accession number or a mismatch between the name of the virus in the TESSy report and GISAID. An HA sequence length limit of at least 900 bp was also required. Alignment was performed using mafft v7, first aligning the reference sequences and then adding the available test sequences, and the alignment was trimmed to include only the HA1 coding region. RAxML v8.2.7 was used to construct a phylogenetic tree using 10 bootstraps and a maximum likelihood search. The tree was rooted on the oldest reference sequence using treesub () and PAML baseml v4.9f was used to perform ancestral reconstruction of the HA1 sequences for all internal nodes of the tree. Treesub was used to annotate the tree branches with amino acid substitutions, based on the root sequence. The nodes were coloured according to month and the tree was exported in nexus format. Clades were retrieved for the references by querying their HA sequences on Nextclade. The clades of the sequences were determined by comparison with the references in the phylogenetic tree. SVG trees were edited and annotated using FigTree and Inkscape. HA amino acid sequence alignments were used to inspect amino acid substitutions in Bioedit, Flusurver and Nextclade.

Annex 2 – Antigenic group and genetic clade category reports

Table Annex 2.1. Antigenic characterisation data by reporting category as reported to TESSy, by country (n=9), WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the table. To denote a virus isolate as being like a vaccine/reference virus its HI titre with post-infection ferret antiserum raised against the vaccine/reference virus should differ by no more than 4-fold (usually a decrease), in a 2-fold dilution series, compared to the HI titre (homologous) with the vaccine/reference virus itself. A virus isolate is considered antigenically different ('Not categorised) from a vaccine/reference virus if the HI titre with post-infection ferret antiserum raised against the vaccine/reference virus differs by 8-fold or more (a decrease), in a 2-fold dilution series, compared to the HI titre (homologous) with the vaccine/reference virus itself.

Countries/Antigenic group	France	Germany	Greece	Italy	Portugal	Russian Federation	Slovenia	Switzerland	United Kingdom	Grand Total	%
A(H1)pdm09(5a.2a) A/Sydney/5/2021-like (3)	1	45	1				2			49	9.4
A(H1)pdm09(5a.2a.1) A/Victoria/4897/2022-like (4,5)	49	89		5	21			10		174	33.2
A(H1)pdm09(5a.2a.1) A/Wisconsin/67/2022-like (4,5)				2						2	0.4
A(H1)pdm09_Not categorised								3		3	0.6
A(H3)(2a) A/Darwin/9/2021-like (1,2,3,4)		21				40	2	2	4	69	13.2
A(H3)(2a.3a.1) A/Thailand/8/2022-like (5)	24					173		4	1	202	38.5
A(H3)_Not categorised	3									3	0.6
BVic (V1A.3a.2) B/Austria/1359417/2021-like (1,2,3,4,5)		15		1		2		2		20	3.8
BVic_Not categorised	2									2	0.4
Total	**79**	**170**	**1**	**8**	**21**	**215**	**4**	**21**	**5**	**524**	**100.0**

1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

Table Annex 2.2. Genetic characterisation data by category as reported to TESSy, by country, WHO European Region, weeks 40/2023 through 3/2024. Numbers in brackets refer to footnotes below the table. To report a virus as belonging to a specific genetic group, the phylogenetic and amino-acid sequence analyses should meet the following criteria: 1) In phylogenetic analysis of the HA gene, it should cluster within the clade represented by the indicated vaccine/reference virus. 2) It should neither contain many nor critical (i.e. those that significantly affect antigenicity) amino acid substitutions when compared to viruses recognised as belonging to the specific group with which it associates. Viruses with sequences that fall well outside all recognised groups are entered in the 'not attributed to clade' category – this is also be done for viruses not falling within a designated group and with evidence of antigenic drift.

Countries/Genetic clades	Belgium	Denmark	Finland	France	Germany	Greece	Ireland	Italy	Luxembourg	Netherlands	Norway	Portugal	Russian Federation	Spain	Sweden	United Kingdom	Total by clade	%
A(H1)pdm09_5a.2a_A/Sydney/5/2021 (3)	10	41	27	84	20	4	1	8	13	179	65	49	1	62	24	317	**905**	**25.4**
A(H1)pdm09_5a.2a.1_A/Victoria/4897/2022 (4,5)	8	18	22	41	8		12	11	13	87	81	72		111	39	44	**567**	**15.9**
A(H1)pdm09_5a.2a.1_A/Wisconsin/67/2022 (4,5)							12			7	1	1		1	2	8	**32**	**0.9**
A(H1)pdm09_NOClade	2																**2**	**0.1**
A(H1)pdm09_SubgroupNotListed	4									1							**5**	**0.1**
A(H3)_2a_A/Darwin/9/2021 (1,2,3,4)													1231				**1231**	**34.5**
A(H3)_2a.3a_A/Finland/402/2023			1	3						1	1	1		1		1	**9**	**0.3**
A(H3)_2a.3b_A/Sydney/732/2022				1													**1**	**0**
A(H3)_2a.3a.1_A/Thailand/8/2022 (5)	11	22	19	47	7	1	55	3	4	112	69	15		24	45	313	**747**	**20.9**
A(H3)_NOClade	1																**1**	**0**
A(H3)_SubgroupNotListed	2															1	**3**	**0.1**
B(Vic)_V1A.3a.2_B/Austria/1359417/2021 (1,2,3,4,5)				4						4			1			2	**11**	**0.3**
B(Vic)_V1A.3a.2_B/Catalonia/2279261NS/2023					1		3	1		3	14			2	3	18	**45**	**1.3**
B(Vic)_V1A.3a.2_B/Connecticut/01/2021					2					2	3						**7**	**0.2**
B(Vic)_V1A.3a.2_B/Moldova/2030521/2023															1		**1**	**0**
Total	**38**	**81**	**69**	**180**	**38**	**5**	**83**	**23**	**30**	**396**	**234**	**138**	**1233**	**201**	**114**	**704**	**3567**	**100**

1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.

Table Annex 2.3. Antigenic and genetic characterisation data as reported to TESSy by week of sampling, WHO European Region, weeks 40/2023 through 3/2024. Light blue indicates antigenic, light green indicates genetic characterisations. Numbers in brackets refer to footnotes below the table.

		ANTIGENIC										GENETIC														
YEAR	WEEK	A(H1)pdm09(5a.2a) A/Sydney/5/2021-like (3)	A(H1)pdm09(5a.2a.1) A/Victoria/4897/2022-like (4,5)	A(H1)pdm09(5a.2a.1) A/Wisconsin/67/2022-like (4,5)	A(H1)pdm09_Not categorised	A(H3) A/Darwin/9/2021-like (1,2,3,4)	A(H3)(2a.3a.1) A/Thailand/8/2022-like (5)	A(H3)_Not categorised	BVic (V1A.3a.2) B/Austria/1359417/2021-like (1,2,3,4,5)	BVic_Not categorised	TOTAL ANTIGENIC	A(H1)pdm09_5a.2a.1_A/Victoria/4897/2022 (4,5)	A(H1)pdm09_5a.2a.1_A/Wisconsin/67/2022 (4,5)	A(H1)pdm09_5a.2a_A/Sydney/5/2021 (3)	A(H1)pdm09_NOClade	A(H1)pdm09_SubgroupNotListed	A(H3)_2a.1b_A/Catalonia/NSVH161512067/2022	A(H3)_2a.3a.1_A/Thailand/8/2022 (5)	A(H3)_2a.3a_A/Finland/402/2023	A(H3)_2a.3b_A/Sydney/732/2022	A(H3)_2a_A/Darwin/9/2021 (1,2,3,4)	A(H3)_NOClade	A(H3)_SubgroupNotListed	B(Vic)_V1A.3a.2_B/Austria/1359417/2021 (1,2,3,4,5)	B(Vic)_V1A.3a.2_B/Connecticut/01/2021	B(Vic)_V1A.3a.2_B/Moldova/20305521/2023	TOTAL GENETIC
2023	40		1			1	1			1	4	11	1	12				23			1			2			50
	41		1			3	1				5	15	4	18			2	19	1		2						61
	42		2							1	3	16	3	19		2	1	27	2					2			72
	43				1	2	3	1	1		8	34		33			2	35	2		4				2		112
	44		2			1	3				6	50	2	39			3	48	2		5		1	1			151
	45		6			4	7	1	1		19	48	1	51			6	46			13		1	1			167
	46		11			5	16		3		35	45	4	73	1	3	4	50	1	1	34	1		1			218
	47		8			6	38		1		53	64	1	66			3	53	1		141				1		330
	48	1	13	2		15	26	1	2		60	65	2	100	1		9	81			296		1	2			557
	49	3	26			7	32				68	53	8	169			5	113			253						601
	50	4	38		1	14	50		1		108	87	2	177			3	147			244			2			662
	51	5	37			3	19		4		68	27	1	75				59			175				1		338
	52	8	6			3	1		2		20	31	2	33			6	24			55				1	1	153
2024	1	14	10		1	1	1				27	18	1	33			1	18			4				2		77
	2	10	7			4	4		4		29	3		7				4			4						18
	3	4	6						1		11																0
	4										0																0
	ALL	49	174	2	3	69	202	3	20	2	524	567	32	905	2	5	45	747	9	1	1231	1	3	11	7	1	3567

1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

All 1 231 viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.

Table Annex 2.4. Antigenic and genetic characterisation data where both type of data were available in TESSy by categories of reporting, WHO European Region, weeks 40/2023 through 3/2024. Columns marked in light blue indicate antigenic categories, lines in green indicate genetic characterisation categories. Numbers in brackets refer to footnotes below the table.

	Antigenic group								
Genetic clade	**A(H1)pdm09(5a.2a) A/Sydney/5/2021-like (3)**	**A(H1)pdm09(5a.2a.1) A/Victoria/4897/2022-like (4,5)**	**A(H1)pdm09(5a.2a.1) A/Wisconsin/67/2022-like (4,5)**	**A(H3) A/Darwin/9/2021-like (1,2,3,4)**	**A(H3)(2a.3a.1) A/Thailand/8/2022-like (5)**	**A(H3)_Not categorised**	**BVic (V1A.3a.2) B/Austria/1359417/2021-like (1,2,3,4,5)**	**BVic_Not categorised**	**Total**
A(H1)pdm09_5a.2a_A/Sydney/5/2021 (3)	1	40							**41**
A(H1)pdm09_5a.2a.1_A/Victoria/4897/2022 (4,5)		24	2						**26**
A(H3)_2a_A/Darwin/9/2021 (1,2,3,4)#				35	120				**155**
A(H3)_2a.3a.1_A/Thailand/8/2022 (5)				11	9	1*			**21**
B(Vic)_V1A.3a.2_B/Austria/1359417/2021 (1,2,3,4,5)							1	2*	**3**
B(Vic)_V1A.3a.2_B/Catalonia/2279261NS/2023							2		**2**
B(Vic)_V1A.3a.2_B/Connecticut/01/2021							1		**1**
Total	**1**	**64**	**2**	**46**	**129**	**1**	**4**	**2**	**249**

1 WHO recommended vaccine virus for the 2022 southern hemisphere influenza season (Trivalent vaccine)

2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season (Trivalent vaccine)

3 WHO recommended vaccine virus for the 2023 southern hemisphere influenza season (Trivalent vaccine)

4 WHO recommended vaccine virus for the 2023-2024 northern hemisphere influenza season (Trivalent vaccine)

5 WHO recommended vaccine virus for the 2024 southern hemisphere influenza season (Trivalent vaccine)

**Asked further clarification by the country, the virus names are A/France/IDF-IPP29542/2023; B/France/IDF-RELAB-IPP24143/2023; B/France/IDF-RELAB-IPP25697/2023; # All viruses reported in A(H3)_2a_A/Darwing/92021 genetic clade category were confirmed retrospectively through phylogenetic analysis to belong to 2a.3a.1 clade (A/Thailand/8/2022-like), see phylogenetic analysis and tree.*

Annex 3 – Antiviral susceptibility testing

Table Annex 3.1. List of viruses reported with reduced inhibition or susceptibility by antiviral, subtypes and lineages, phenotypic or genotypic testing as well as corresponding GISAID id and interpretation defining mutation. TESSy, weeks 40/2023 through 3/2024, WHO Euro Region. AST: Antiviral susceptibility testing; HRI: Highly reduced inhibition; RI: Reduced inhibition; RS: Reduced susceptibility; prefix 'AA': Amino acid, refers to genotypic testing result. N/A: Not available.

Oseltamivir					
GISAID ID	**Virus**	**AST**	**Interpretation**	**NAISD**	**NAAAMutations**
A/England/235040260/2023	A(H1)pdm09	Genotypic	AAHRI	EPI2935562	H275Y
A/England/235040261/2023	A(H1)pdm09	Genotypic	AAHRI	EPI2935564	H275Y
A/England/234980678/2023	A(H1)pdm09	Genotypic	AARI	EPI2875938	D199E
Zanamivir					
GISAID ID	**Virus**	**AST**	**Interpretation**	**NAISD**	**NAAAMutations**
N/A	N/A	N/A	N/A	N/A	N/A
Baloxavir marboxil					
GISAID ID	**Virus**	**AST**	**Interpretation**	**NAISD**	**NAAAMutations**
A/Boras/SE23-15976/2023	A(H3)	Genotypic	AARS	EPI2933899	P28L