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Influenza virus characterisation data reported by National Influenza Centres and national influenza laboratories to The European Surveillance System (TESSy) for weeks 40/2023 to 33/2024, WHO European Region

Summary

This report summarizes influenza virological surveillance data from 51 countries and territories of the WHO European Region, for weeks 40/2023 through 33/2024, as reported by National Influenza Centres (NICs) and National Influenza Laboratories (NILs) to The European Surveillance System (TESSy) at the European Centre for Disease Prevention and Control (ECDC).

Detections

Within the reporting period, 345 352 influenza virus detections (sentinel and non-sentinel combined) were reported of which 86% (298 516) were type A and 7% (23 454) were type B virus, while another 7% (23 382) were untyped.

Of the 79 321 subtyped influenza A viruses, 43 074 (54%) were subtype A(H1)pdm09 and 36 247 (46%) were subtype A(H3). Of the 23 454 reported influenza type B viruses, the lineage for 2 568 (11%) 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.

A(H1N1)pdm09

In the European Region, 5 513 A(H1N1)pdm09 viruses from 19 countries were reported with haemagglutinin (HA) sequence information. All of those fell in clade 5a.2a subclade C.1, represented by A/Sydney/5/2021, the virus strain recommended for 2023 southern hemisphere (SH) vaccine. Further genetic diversification was observed in the 5a.2a viruses with a significant number of viruses falling in subclade C.1.9 (39%, n=2 169) or subclade C.1.8 (18%, n=979). Only 80 viruses of all subclade C.1 viruses (2%) fell in subclade C.1.1, represented by A/Wisconsin/67/2022, NH 2023-24 vaccine strain for cell culture- or recombinant-based vaccines. Within 5a.2a, 24% (n=1 341) were further characterised as clade 5a.2a.1 subclade D, represented by A/Victoria/4897/2022, the NH 2023-24 vaccine strain for egg-based vaccines. Subclade D viruses evolved genetically even further and of

those 45% (n=599) had acquired R113K (subclade D.2), 32% (n=426) R45K (subclade D.1), and 13% (n=177) the T120A substitution (subclade D.3).

Of the 885 A(H1)pdm09 viruses characterised antigenically, the main reported categories were A/Sydney/5/2021-like, clade 5a.2a (subclade C.1) and A/Victoria/4897/2022-like, clade 5a.2a.1 (subclade D), representing 54% and 44%, respectively. Only 1% of the viruses were characterised as A/Wisconsin/67/2022-like, clade 5a.2a.1 (subclade C.1.1) and the remaining characterized viruses with less than 1% were the A/Victoria/2570/2019-like, clade 5a.2 (subclade C).

Fifty (1%) of 4 674 assessed A(H1N1)pdm09 viruses exhibited phenotypically reduced (n=33) or highly reduced inhibition (n=17) by oseltamivir or harboured genetic markers associated with such. Five (<1%) of 3 413 assessed A(H1N1)pdm09 viruses carried genetic markers associated to reduced susceptibility to baloxavir marboxil. No reduced inhibition to zanamivir was detected in analyses of A(H1N1)pdm09 viruses.

A(H3N2)

For A(H3N2) viruses, 19 countries reported 4 339 HA sequences. All A(H3) HA sequences fell into clade 2a.3, and the majority of those (n=4 325, 98%) to clade 2a.3a.1 (subclade J), represented by A/Thailand/8/2022, the vaccine strain recommended for the 2024 SH season vaccine. Based on sequence analysis, most (77%) of A(H3N2) in the 2a.3a.1 clade belonged to a branch with amino acid substitution N122D, constituting loss of a potential glycosylation site. In this branch, the vast majority of viruses (n=3 255, 75%) further diversified in subclade J.2 with substitution K276E. Eleven (<1%) A(H3N2) viruses fell in clade 2a.3a (subclade G.1.3.1) and another two (<1%) in 2a.3b (subclade G.1.3.2).

Among the 908 A(H3) viruses characterised antigenically, the main reported categories were A/Thailand/8/2022-like, clade 2a.3a.1 (subclade J) and A/Darwin/9/2021-like, clade 2a (subclade G1), representing 62% and 38%, respectively.

Four (<1%) of 2 987 assessed A(H3N2) viruses showed reduced susceptibility to neuraminidase inhibitors: two with phenotypically reduced or highly reduced inhibition by both oseltamivir and zanamivir and two which showed presence of amino acid substitutions associated with reduced or highly reduced inhibition by oseltamivir alone. No amino acid substitution associated with potentially reduced susceptibility to baloxavir marboxil was detected in genetic analyses of 1 957 A(H3N2) viruses.

B(Victoria)

Seventeen countries reported HA sequence data for 1 514 B/Victoria viruses. All reported viruses of B/Victoria carried HA genes that fell into genetic clade V1A.3a.2 (subclade C), represented by B/Austria/1359417/2021, the vaccine strain recommended for the 2023-24 NH influenza season. The majority (n=781, 52%) of viruses within 3a.2 fell in the C.5.7 subclade with E128G followed by 22% (n=336) in C.5.1 with E183K and 13% (n=194) in C.5.6 with the D129N amino acid substitution and <1% into C.5.5, C.3 and C.2, each.

Of the 292 antigenically characterised influenza B(Victoria) viruses, all viruses were B/Austria/1359417/2021-like, within clade V1A.3a.2 (subclade C).

Ten of 1 402 assessed B/Victoria viruses showed phenotypically reduced inhibition by oseltamivir or zanamivir or harboured genetic markers associated with such reduced or highly reduced inhibition. No reduced susceptibility to baloxavir marboxil was detected in genetic analyses of 885 B/Victoria viruses.

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, produced by European Centre for Disease Prevention and Control in collaboration with WHO Regional office for Europe, summarizes virological surveillance data for influenza provided by 51 countries and territories from the WHO European Region for the SH VCM to be held by WHO in September 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[1]; 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 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) [9]. Most of the ERLI-Net laboratories are also NICs.

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 obtained from the WHO Collaborating Centres within GISRS, 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 22 August 2024 were accessed and summarized. The data for weeks 40/2023 to 33/2024 were included in this analysis.

Purpose

The purpose of this report is:

[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

- to summarize reports on detections, antigenic and genetic data provided to TESSy by NICs and NILs in the WHO European Region during the 2023-24 influenza season from week 40/2023 to week 33/2024; 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 and NILs, 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

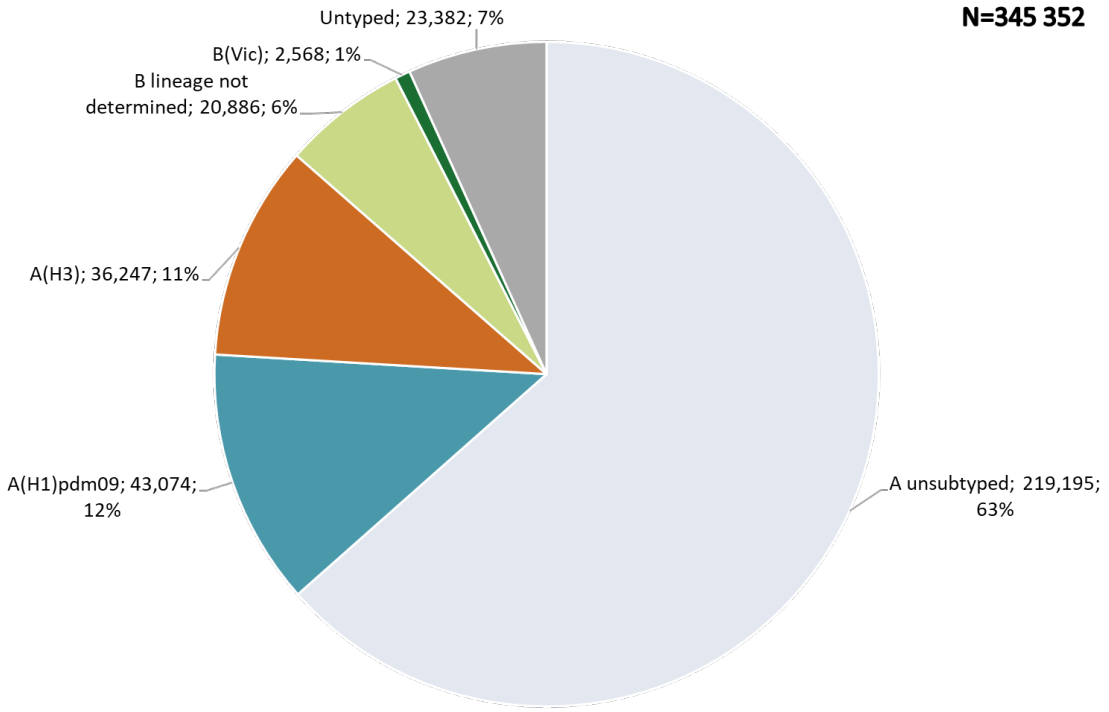
From week 40/2023 to week 33/2024, 345 352 influenza virus detections were reported from sentinel and non-sentinel surveillance sources in 51 countries and territories across the WHO European Region, including 298 516 (86%) as type A influenza viruses and 23 454 (7 %) as type B influenza viruses. The type was not reported for the 23 382 remaining viruses (Table 1, Figure 1). Out of the 79 321 type A viruses with a defined subtype (27% of type A viruses), 43 074 (54%) were A(H1)pdm09 and 36 247 (46%) were A(H3). For A(H1)pdm09, the neuraminidase subtype N1pdm09 was determined for 6 662 of the 11 829 sentinel detections (56%) and 11 890 of the 31 245 non sentinel detections (38%). For A(H3), the neuraminidase subtype N2 was determined for 1 921 of the 5 713 sentinel detections (34%) and 10 958 of the 30 534 non sentinel detections (36%). Out of the 2 568 type B viruses with a defined lineage (11% of type B viruses), all were assigned to the Victoria lineage.

Table 1. Number and proportion of detected influenza viruses, by type and subtype, reported to TESSy, WHO European Region, weeks 40/2023 through 33/2024.

		Sentinel		Non Sentinel		Total	
Type	Subtype	number	percent	number	percent	number	percent
A	A(H1)pdm09	11 829	46.5	31 245	9.8	43 074	12.47
	A(H3)	5 713	22.5	30 534	9.5	36 247	10.50
	A unsubtyped	4 657	18.3	214 538	67.1	219 195	63.47
B	B(Vic)	928	3.6	1 640	0.5	2 568	0.74
	B(Yam)	0	0.0	0	0.0	0	0.00
	B lineage not determined	2 213	8.7	18 673	5.8	20 886	6.05
Untyped	Untyped*	94	0.4	23 288	7.3	23 382	6.77
Total	-	25 434	100.0	319 918	100.0	345 352	100.00

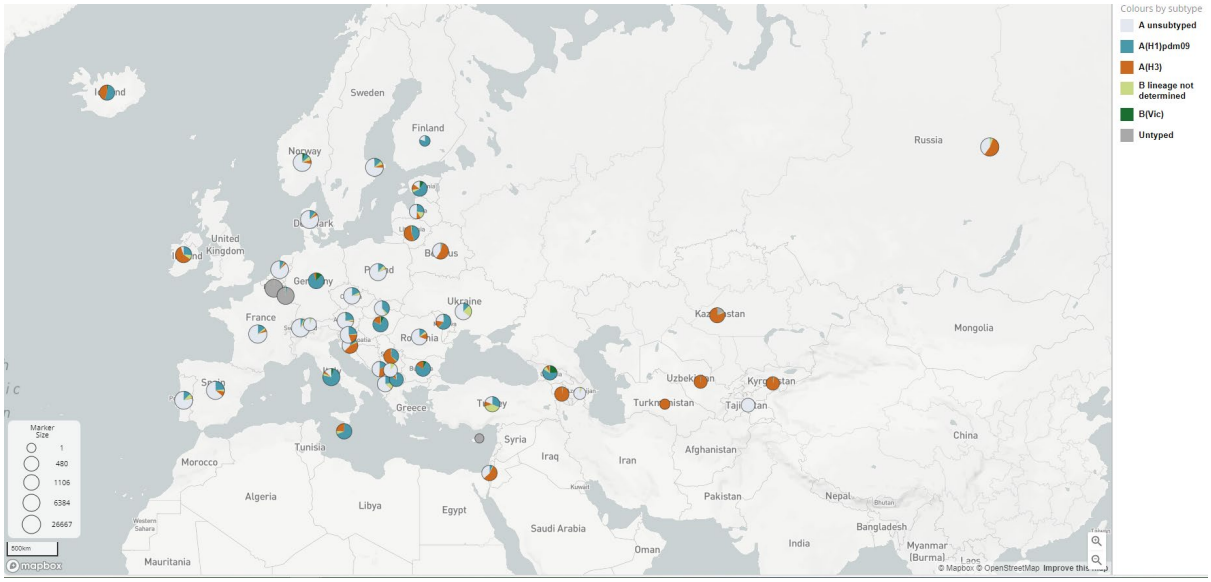
**Influenza untyped viruses are considered a reporting error and will be followed up with the reporting countries.*

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 33/2024.*



**Untyped influenza viruses are considered a reporting error and will be followed up with the reporting countries.*

Map 1. Proportions of influenza type/subtype, sentinel and nonsentinel surveillance systems together, WHO European Region, weeks 40/2023 through 33/2024. An interactive map is available at: Map 1 (microreact.org) *



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Sentinel detections

Among the 25 434 virus detections reported in the sentinel surveillance systems from week 40/2023 to week 33/2024, 22 199 (87%) were type A and 3 141 (12%) were type B. The type was not reported for the 94 remaining viruses (Table 1, Figure 2, Figure 3). Out of the 17 542 type A viruses with a defined subtype (79% of type A viruses), 11 829 (67%) were A(H1)pdm09 and 5 713 (33%) were A(H3). Out of the 928 type B viruses with a defined lineage (30% of type B viruses), all were assigned to the 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 33/2024.*

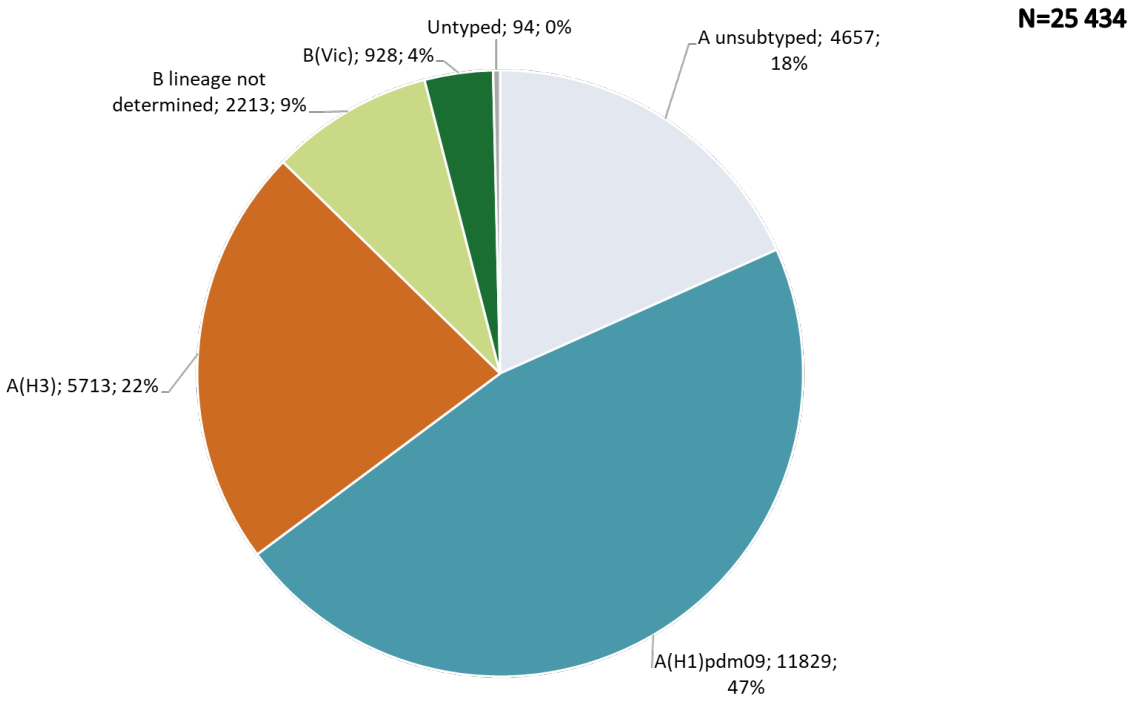

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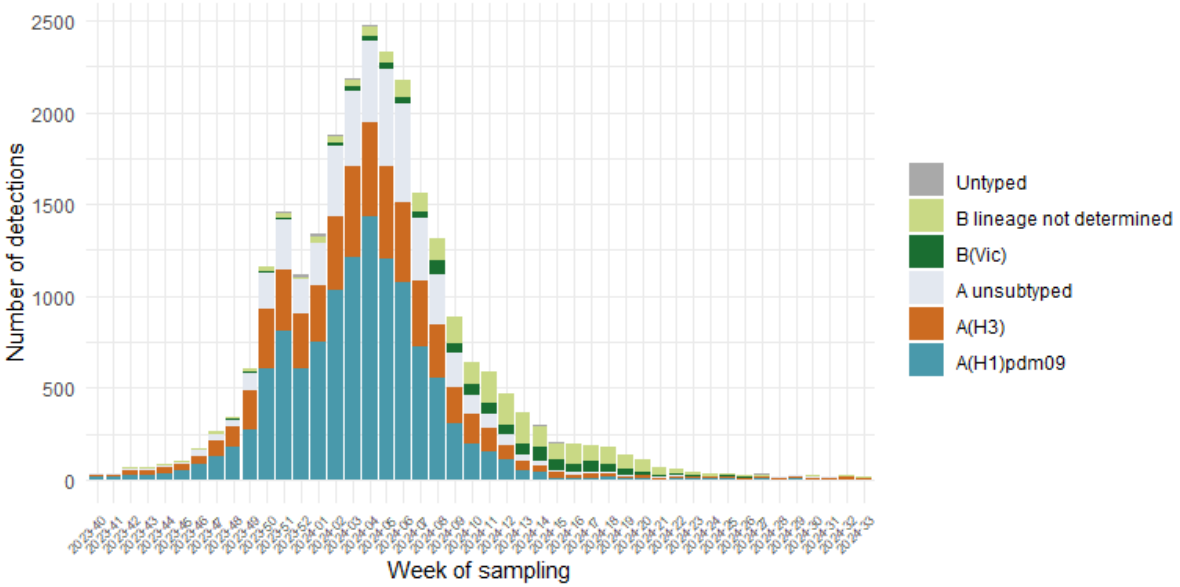
Figure 3. Distribution of detected influenza viruses in sentinel surveillance by week and by subtypes and lineages, WHO European Region, weeks 40/2023 through 33/2024.*



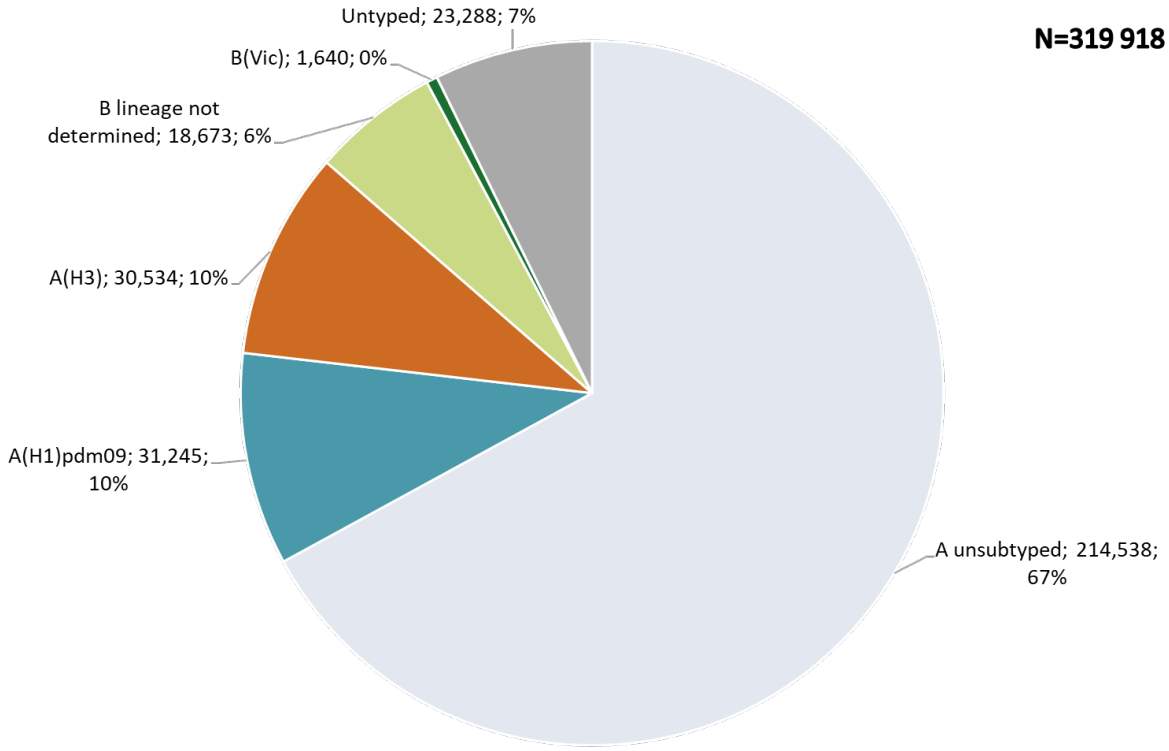
**Untyped influenza viruses are considered a reporting error and will be followed up with the reporting countries.*

Non-sentinel detections

Among the 319 918 virus detections reported in the non-sentinel surveillance systems from week 40/2023 to week 33/2024, 276 317 (86.4 %) were type A and 20 313 (6.3 %) were type B (Table 1, Figure 4, Figure 5). The type was not reported for the 23 288 remaining viruses. Out of the 61 779 type A viruses with a defined subtype (22.4

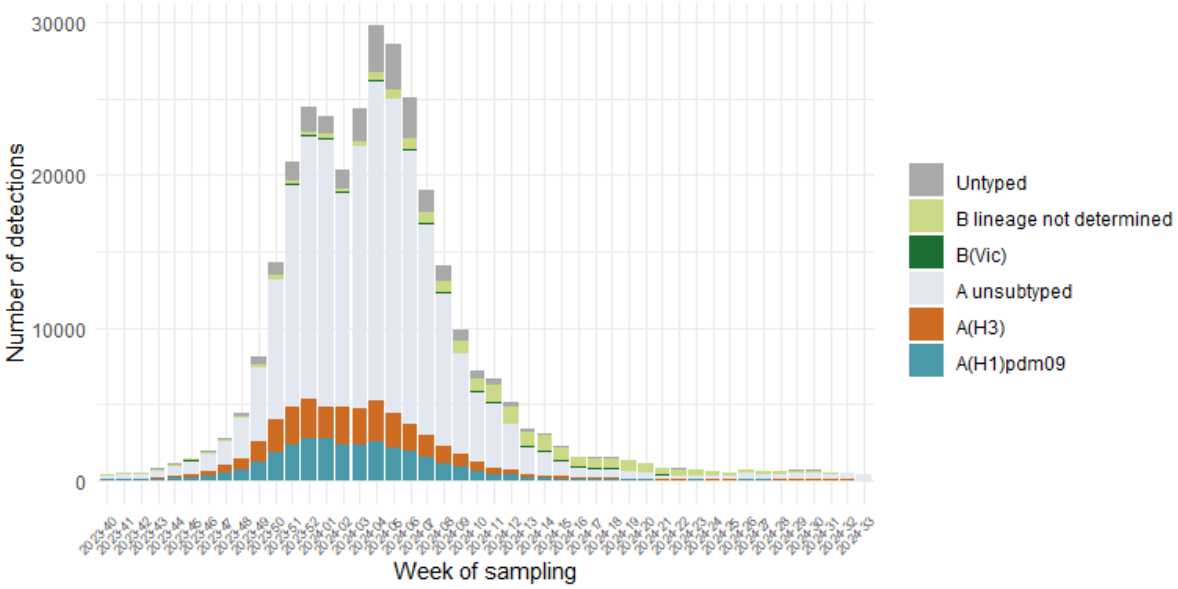
% of type A viruses), 31 245 (50.6 %) were A(H1)pdm09 and 30 534 (49.4) were A(H3). Out of the 1 640 type B viruses with a defined lineage (8.1 % of type B viruses), all were assigned to the Victoria lineage.

Figure 4. Number and proportion of influenza virus detections in the non-sentinel surveillance system by subtype, WHO European Region, weeks 40/2023 through 33/2024.*



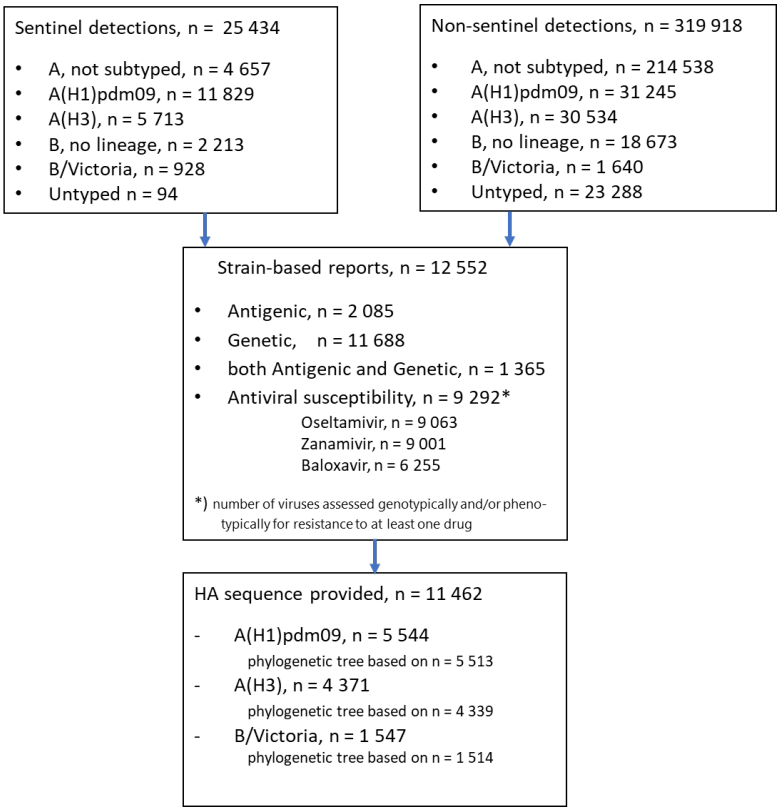
**Untyped influenza viruses are considered a reporting error and will be followed up with the reporting countries.*

Figure 5. Distribution of detected viruses in non sentinel surveillance by week and by subtypes and lineages, WHO European Region, weeks 40/2023 through 33/2024.*



**Untyped influenza viruses are considered a reporting error and will be followed up with the reporting countries.*

Figure 6. Flowchart presenting underlying number of specimens reported by country/territory 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 33/2024.*



**Untyped influenza viruses are considered a reporting error and will be followed up with the reporting countries.*

Virus characterisation

Using the INFLANTIVIR record type in TESSy, countries were invited to report strain-based characterization of influenza viruses detected and/or isolated during the season.

Overview of the reported data

From week 40/2023 to week 31/2024, 12 552 influenza strain-based reports from sentinel (5 443, 43.4%) and non-sentinel (5 551, 44.2%) surveillance sources were submitted by 21 countries across the WHO European Region (Table 2). Information about the surveillance system of origin was unknown or missing for the remaining viruses (1 558, 12.4%). At the time of the data extraction from TESSy, there was no characterisation reported for viruses detected after the week 31/2024.

Table 2. Number of reported viruses with virus characterisation data, WHO European Region, weeks 40/2023 through 33/2024.

		Surveillance system			
Type	Subtype	Sentinel	Non Sentinel	Unknown	Total
A	A(H1)pdm09	2 963	2 930	125	6 018
	A(H3)	1 440	2 007	1 353	4 800
B	B(Vic)	1 040	614	4	1 658
	B lineage not determined	0	0	76	76
Total	-	5 443	5 551	1 558	12 552

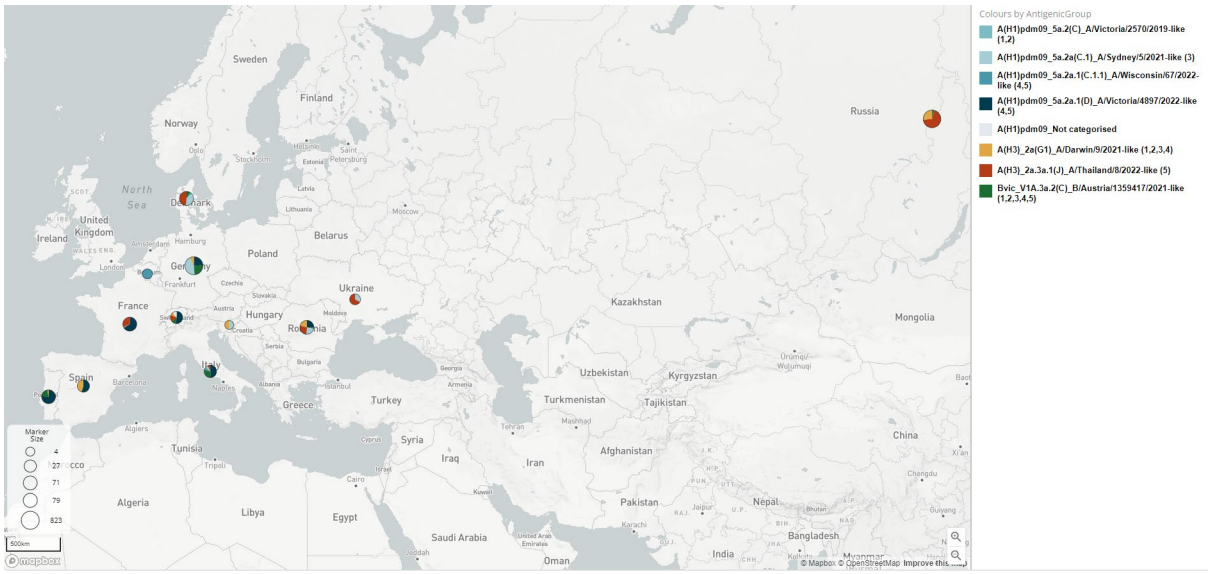
Out of the 10 818 type A influenza viruses, 6 018 (55.6%) were reported as subtype A(H1N1)pdm09 or A(H1)pdm09 and 4 800 (44.4%) as subtype A(H3N2) or A(H3). All 1 734 type B influenza viruses were assigned to the B/Victoria lineage.

Antigenic and genetic characterisations were reported to TESSy in weeks 40/2023 through 33/2024 (with last data being from week 31) by 20 countries: Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Romania, the Russian Federation, Slovenia, Spain, Sweden, Switzerland, Ukraine and the United Kingdom. Twelve countries (Belgium, Denmark, France, Germany, Greece, Italy, Portugal, Romania, the Russian Federation, Spain, Switzerland, Ukraine and the United Kingdom) reported both genetic and antigenic characterisation data, Slovenia provided only antigenic characterisation data and seven countries (Finland, Greece, Ireland, Luxembourg, the Netherlands, Norway, and Sweden) provided only genetic clade data during the reporting period (Table 3).

Table 3. Number of viruses characterised antigenically (AG) and genetically (GEN) as reported to TESSy by country (n=20) and week of sampling, WHO European Region, weeks 40/2023 through 33/2024. 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	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	Total	%
Belgium	AG																	3					2	2																								7	0.3
	GEN	2	1	4		4	4	11	5	5	2				3	4	4	20	12			1	6	7	7	1	2			1	1		1															108	0.9
Denmark	AG															1	4	1	3	12	12	2	2	17	10	6	5	1			1			2														79	3.8
	GEN	5	6	4	10	15	28	13							3	24	35	8	28	35	33	4	13	34	23	20	10	10	6	6	13	4	4	7														401	3.4
Finland	AG																																															0	0.0
	GEN	1	2	3	10	5	5	7	10	15	11	7	9	13	16	11			1	5	10	3	2	10	10	5				2	3	2	1	3	1					3	1	1	3	2				193	1.7
France	AG						3	4	3	4	8	15	15	7	8	7																																74	3.5
	GEN	2	4	7	7	7	6	17	3	18	40	54	14	1																																		180	1.5
Germany	AG		3	2	1	1	5	9	5	12	15	29	38	15	25	38	101	83	77	58	62	41	28	39	33	35	17	9	8	10	5	6	3	1	2		2			1	2			1	1			823	39.5
	GEN		2	3	1	2	5	10	6	6	17	49	41	16	25	37	90	77	112	100	79	63	44	34	15	23	13	8	5	6	6	9	4	2	1		1											912	7.8
Greece	AG												1																																			1	0.0
	GEN					4	1		1	1	1		2						2	2	3	5	4	2				1																				29	0.2
Ireland	AG																																															0	0.0
	GEN		1	4	2	3	4	6	14	22	24	24	9	12	12	16	12	21	14	18	7	14	10	4	1	3	3	2		1			1															264	2.3
Italy	AG								1	5	2						1		1	11	2	2	1				1		2																			29	1.4
	GEN						1	1	1	7	2	1	2	2	6		1		2	12	3	2	1				1	1	2		1																	49	0.4
Luxembourg	AG																																															0	0.0
	GEN						2	1	1	1	7	8	18	3	5	8	24	23	32	31	13	10	1	3																								191	1.6
Netherlands	AG																																															0	0.0
	GEN	9	9	9	14	11	10	16	16	30	52	61	21	25	47	59	47	71	56	53	48	44	39	43	34	26	21	15	13	8	9	5	7	7	13	3	6	11	5	2	1	6	6	3	4			995	8.5
Norway	AG																																															0	0.0
	GEN	4	8	3	25	39	11	11	39	26	7	5	3	28	33	19	38	35	8	5	35	26	24	37	21	9		15	22	34	2	27	19	11	3			14	9	13	4	2	13	13				700	6.0
Portugal	AG	1	1			1	2	2	1	3	2	12	2	6	8	2	6	2	1	1			6					1				1		1	3	2			2	2								71	3.4
	GEN	6	7	6	10	13	18	9	16	26	23	36	34	56	48	43	24	16	9	9	7	9	10	12	1	8	2	4		2	3	7	3	3	2	5	3	3										493	4.2
Romania	AG										2	4	1	1	6	10	5	8	8	8	7	5	4	1	1		1																					72	3.5
	GEN					1	1		1		3	12	9	14	19	17	26	27	27	30	11	7	9	2	2		1																					219	1.9
Russian Federation	AG	1	1		2	3	7	19	43	45	46	91	141	54	15	31	19	37	19	23	18	21	15	3	3	4		3	2						1	1												668	32.0
	GEN	1	2		4	5	14	37	145	309	264	266	283	111	15	46	51	45	53	55	42	37	26	14	8	8	3	7	3	4	9	16	15	9	4	5	2											1918	16.4
Slovenia	AG												1	2		1																																4	0.2
	GEN																																															0	0.0
Spain	AG			2	4		1	5	4	2	2	1	1	5	1	1																																29	1.4
	GEN	9	6	15	24	15	29	50	55	79	68	128	152	187	197	159	95	53	39	35	27	14	5	10	10	13	5	9	13	7	5	1	4	2	11	6	2	3	4	1								1547	13.2
Sweden	AG																																															0	0.0
	GEN	4	5	2	3	9	14	8	11	5	16	17	17	10	4	14	10	16	5	2	4		7	10	12	6	2	10	8	7	3	6	11	2														260	2.2
Switzerland	AG				2			3	6		5	3	1		5		2																															27	1.3
	GEN				2			2	1		10	12	8	9	3																																	47	0.4
Ukraine	AG															1	1	1	1	3			1		4																							12	0.6
	GEN															1	1	1	1	3			1		4																							12	0.1
United Kingdom	AG	1		1	4	6	10	10	8	11	18	28	32	14	9	10	12	3	4	5	2	1																										189	9.1
	GEN	8	8	13	8	19	27	43	37	86	190	264	321	199	171	124	112	178	169	140	128	92	92	111	146	89	56	81	44	32	41	41	31	17	9	8	8	9	10	5	3							3170	27.1
ALL	AG	3	5	5	13	11	28	52	71	82	100	183	233	104	77	102	151	138	114	121	103	72	59	62	51	45	24	14	12	10	6	7	3	4	6	3	2	0	2	3	2	0	0	1	1	0	0	2085	100.0
	GEN	51	61	73	120	152	180	242	362	636	737	944	943	686	607	582	570	591	570	535	450	331	294	333	294	211	119	163	116	110	96	118	101	63	44	27	22	40	28	24	9	9	22	18	4	0	0	11688	100.0

Map 2. Proportions of antigenic categories reported by countries, WHO European Region, weeks 40/2023 through 33/2024. Numbers in brackets refer to footnotes below the map. An interactive map is available at [Map 2 (microreact.org)]



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

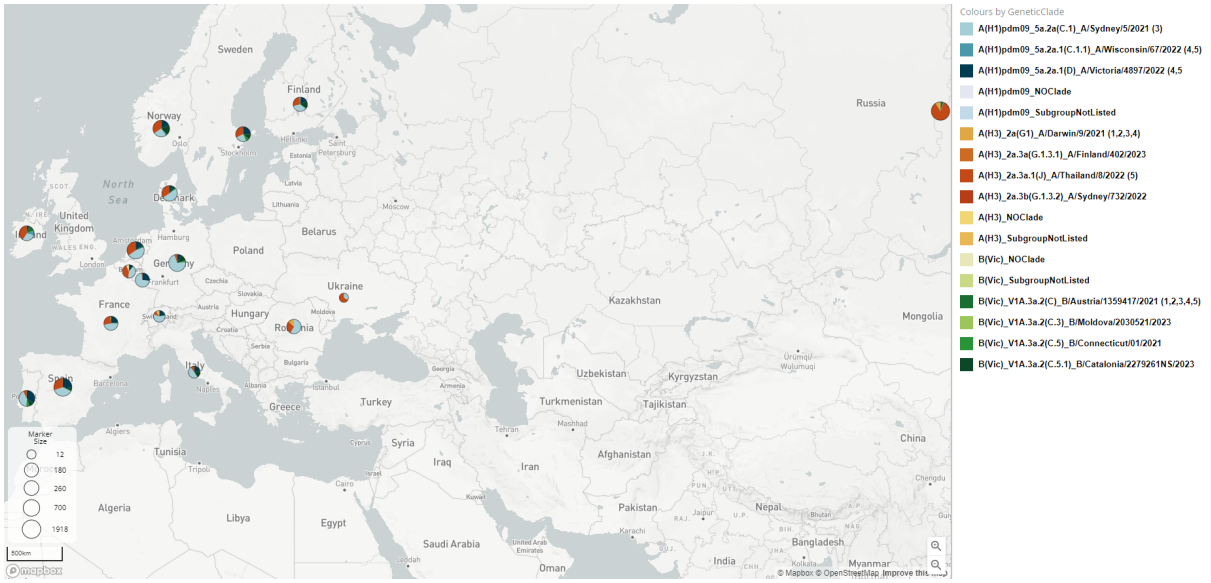
2 WHO recommended vaccine virus for the 2022-2023 northern hemisphere influenza season

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

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

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

Map 3. Proportions of genetic groups reported by countries, WHO European Region, weeks 40/2023 through 33/2024. Numbers in brackets refer to footnotes below the map. An interactive map is available: [Map 3 (microreact.org)]



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

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

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

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

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

A(H1N1)pdm09 viruses

Antigenic characterisation

Weeks 40/2023 through 33/2024, with latest data reported for collection week 23/2024, 14 countries reported antigenic characterization to TESSy for 885 A(H1N1)pdm09 influenza viruses. The three main countries that contributed were: Germany (62.9%), United Kingdom (9.7%) and Portugal (6.1%).

Countries were asked to report antigenic characterization results in TESSy according to the predefined categories described in Table 4. The option "not attributed to category", was available for each subtype and lineage.

Table 4. Predefined antigenic reporting categories for A(H1)pdm09 viruses.

TESSy category	Virus of reference	Clade long name	Clade short name [a]
agAH1/Victoria/2570/2019	A/Victoria/2570/2019-like	6B.1A.5a.2	5a.2(C)
agAH1/Sydney/5/2021	A/Sydney/5/2021-like	6B.1A.5a.2a	5a.2a(C.1)
agAH1/Wisconsin/67/2022	A/Wisconsin/67/2022-like	6B.1A.5a.2a.1	5a.2a.1(C.1.1)
agAH1/Victoria/4897/2022	A/Victoria/4897/2022-like	6B.1A.5a.2a.1	5a.2a.1(D)
agAH1NOCAT	none	Not attributed to category	Not attributed to category

[a] subclade in brackets

Among the 885 characterised A(H1)pdm09 viruses, the main reported categories were A/Sydney/5/2021-like, clade 5a.2a(C.1) and A/Victoria/4897/2022-like, clade 5a.2a.1(D), representing 54.2% and 43.8%, respectively (Table 5, Figure 7, Figure 8).

Table 5. Number of viruses by A(H1)pdm09 antigenic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
5a.2(C)	A/Victoria/2570/2019-like	2	0.2
5a.2a(C.1)	A/Sydney/5/2021-like	480	54.2
5a.2a.1(C.1.1)	A/Wisconsin/67/2022-like	12	1.4
5a.2a.1(D)	A/Victoria/4897/2022-like	388	43.8
Not attributed to category	none	3	0.3

Figure 7. A(H1)pdm09 clade weekly distribution based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.

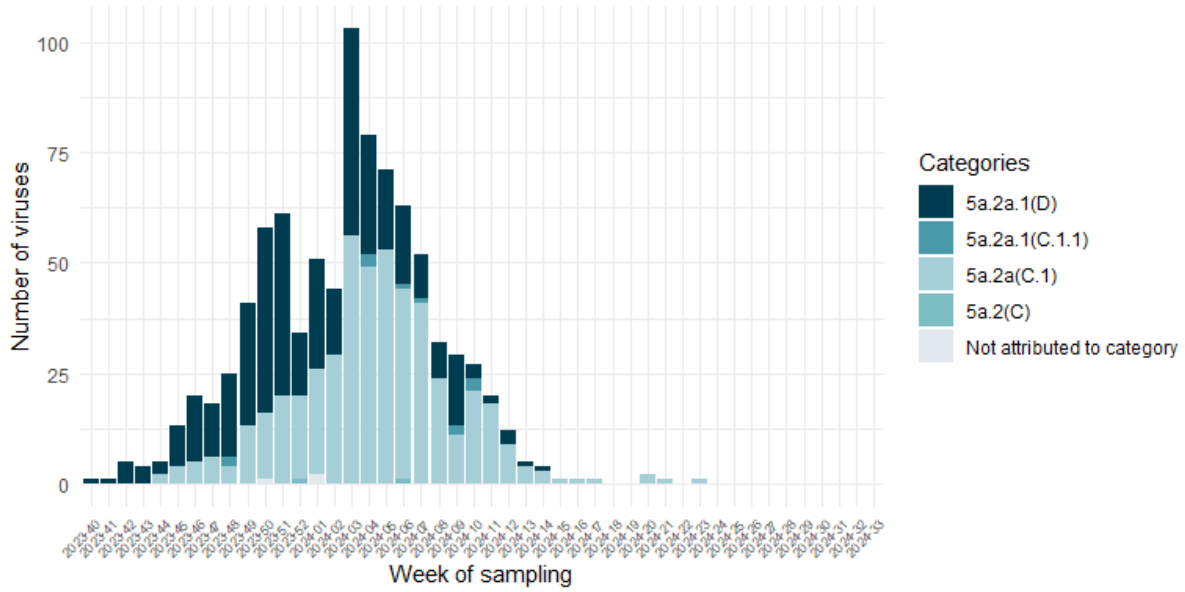
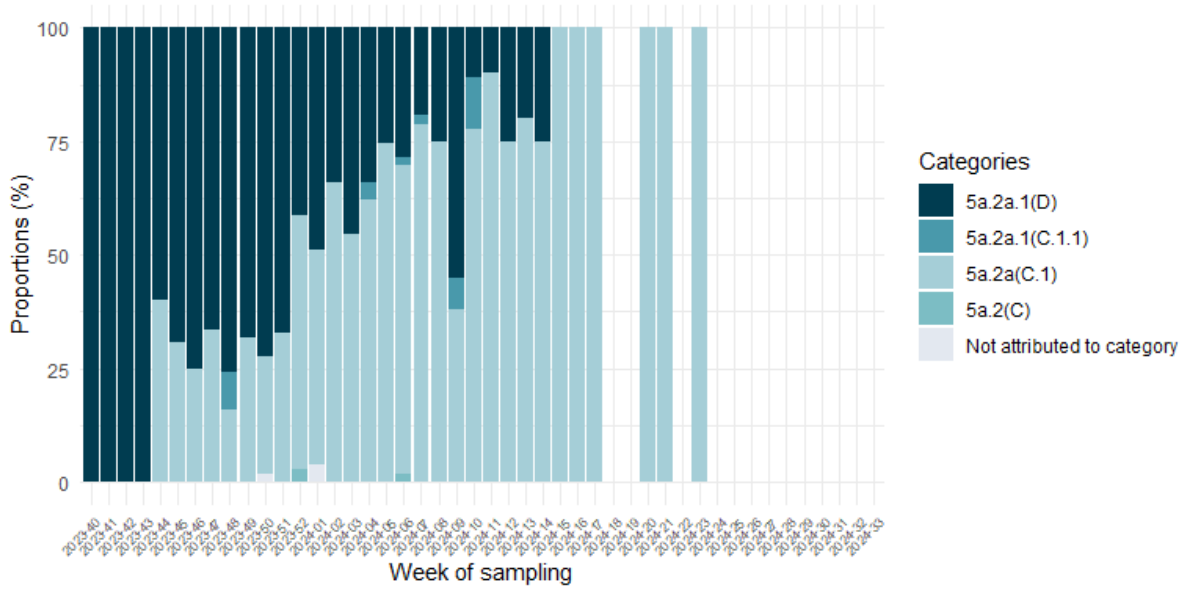


Figure 8. A(H1)pdm09 clade weekly proportion based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.



Genetic characterisation

From weeks 40/2023 to 31/2024, with latest data reported for week 30/2024, 19 countries reported genetic characterisation to TESSy for 5 547 A(H1N1)pdm09 influenza viruses. The three main countries that contributed A(H1N1)pdm09 data were: United Kingdom (24.9%), Spain (17.9%) and Germany (13%).

Countries were asked to report genetic characterisation results in TESSy according to the predefined categories described in Table 6. The options "not attributed to clade" and "attributed to recognised group in current guidance but not listed here", were available for each subtype and lineage.

Table 6. Predefined genetic reporting categories for A(H1)pdm09 viruses, WHO European Region, weeks 40/2023 through 33/2024.

TESSy category	Virus of reference	Clade long name	Clade short name [a]
genAH1/Victoria/2570/2019	A/Victoria/2570/2019	6B.1A.5a.2	5a.2(C)
genAH1/Sydney/5/2021	A/Sydney/5/2021	6B.1A.5a.2a	5a.2a(C.1)
genAH1/Wisconsin/67/2022	A/Wisconsin/67/2022	6B.1A.5a.2a.1	5a.2a.1(C.1.1)
genAH1/Victoria/4897/2022	A/Victoria/4897/2022	6B.1A.5a.2a.1	5a.2a.1(D)
genAH1NOClade	none	Not attributed to category	Not attributed to category
genAH1SubgroupNotListed	other	Subgroup not listed	Subgroup not listed

[a] subclade in brackets

Among the 5 547 characterised A(H1)pdm09 viruses, the main reported categories were A/Sydney/5/2021, clade 5a.2a(C.1) and A/Victoria/4897/2022, clade 5a.2a.1(D), representing 74.4% and 24.2% of the viruses, respectively (Table 7, Figure 9, Figure 10). For two of the three reports as 'Not attributed to category', the sequence was not available, however, one was clustering within 5a.2a.1 subclade D.3 in phylogenetic analysis. One of the four reports as 'Subgroup not listed' was reported with available sequence which clustered within 5a.2a subclade C.1.6, represented by A/South_Dakota/31/2023, which was not one of the reporting categories.

Table 7. Number of viruses by A(H1)pdm09 genetic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
5a.2a(C.1)	A/Sydney/5/2021	4 127	74.4
5a.2a.1(C.1.1)	A/Wisconsin/67/2022	71	1.3
5a.2a.1(D)	A/Victoria/4897/2022	1 342	24.2
Not attributed to category	none	3	0.1
Subgroup not listed	other	4	0.1

Figure 9. A(H1)pdm09 clade weekly distribution based on genetic characterisation, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.

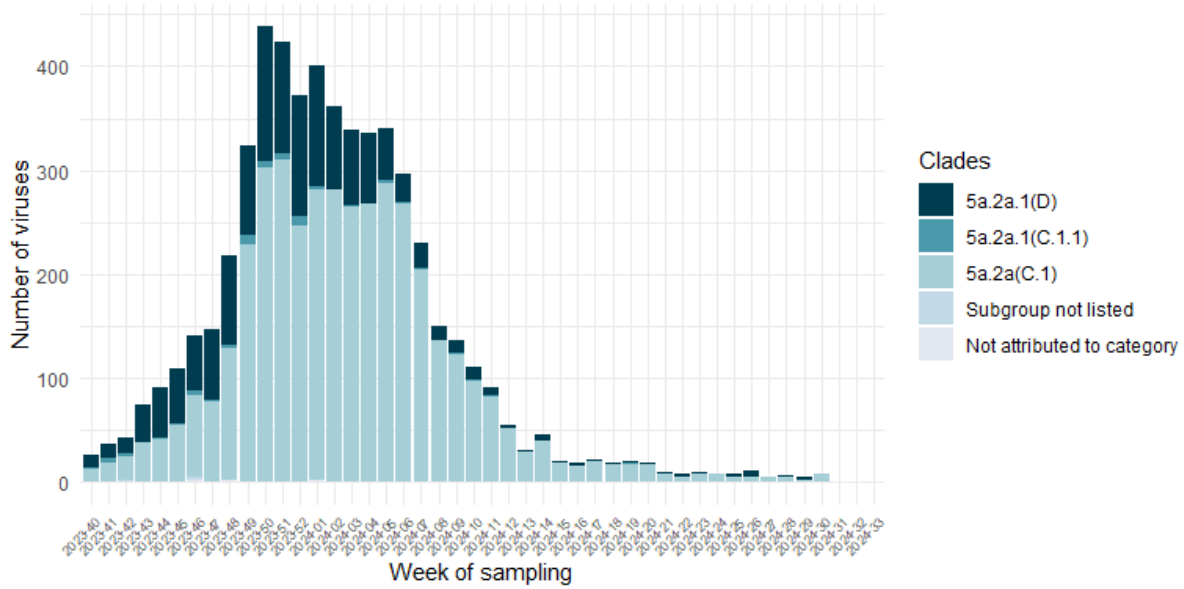
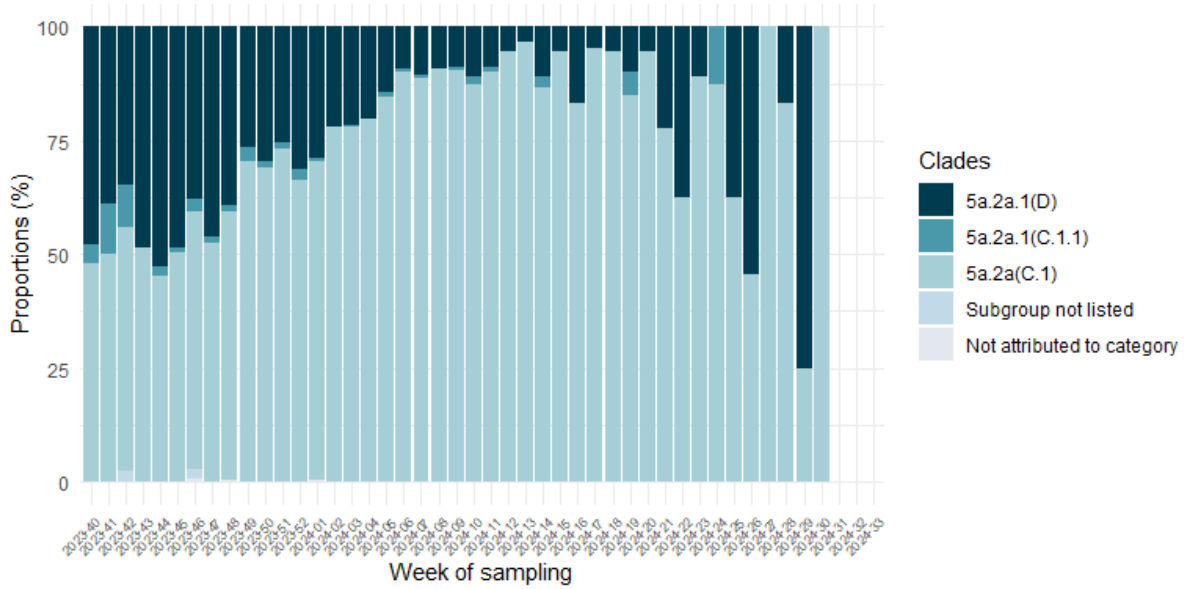


Figure 10. A(H1)pdm09 clade weekly proportion based on genetic characterisation, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.



Phylogenetic analysis

During the reporting period of weeks 40/2023 to 33/2024, a total of 11 366 HA sequences from 20 countries were reported, retrieved and included in the analyses. Countries that reported HA sequences are shown in Table Annex 4.1. None of the retrieved sequences were falling below the sequence length threshold (900 bp).

By week 33/2024, 5 513 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 (Annex Table 4).

All A(H1)pdm09 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 (NH 2022/23) vaccine strain A/Victoria/2570/2019 and it is represented by A/Sydney/5/2021 (SH 2023 vaccine strain).

Most viruses within 5a.2a (subclade C.1) carried T120A and combined either with K169Q (39%, n=2 169, subclade C.1.9) or V47I (18%, n= 979, subclade C.1.8) and none of these were represented by a reference virus. On two independent branches, P137S was present, constituting 7% (n=389) of the 5a.2a viruses.

A proportion of 24% (n=1 341) within 5a.2a were further characterised into clade 5a.2a.1 subclade D that has the additional T216A amino acid substitution and is represented by A/Victoria/4897/2022, the NH 2023-24 vaccine strain for egg-based vaccines. Subclade D viruses had evolved genetically even further and of those 45% (n=599) had acquired R113K (subclade D.2), 32% (n=426) R45K (subclade D.1), and 13% (n=177) the T120A substitution (subclade D.3). Few viruses (n=80, 2%) of all subclade C.1 viruses fell into subclade C.1.1, represented by A/Wisconsin/67/2022, NH 2023-24 vaccine strain for cell culture- or recombinant-based vaccines.

For the comparison of reported versus assigned clades, we grouped assigned subclades to the reporting categories. The phylogenetic results aligned well with the categorical reporting of genetic clade by the countries with only up to 0.2% differences in the proportion of different (sub)clades, when comparing assigned subclades of C.1, C.1.1 and D (Table Annex 4.2).

Figure 11. 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).

Match between antigenic and genetic characterisations

Of the 493 A(H1N1)pdm09 viruses that had both genetic and antigenic data reported, half (n=245, 50%) were reported antigenically as 5a.2a.1 A/Victoria/4897/2022-like (Table Annex 2.4), which is the A(H1N1)pmd09 vaccine strain recommended for egg-based NH vaccines for the 2023-24 and 2024-25 seasons. Of those, the majority (n=162, 66%) were reported as genetic subgroup 5a.2a subclade C.1 represented by A/Sydney/5/2021, while 81 viruses (33%) were assigned to the genetic clade 5a.2a.1 subclade C.1.1 represented by A/Wisconsin/67/2022 (the A(H1N1)pmd09 vaccine strain recommended for cell-based NH vaccines for 2023-24 and 2024-25 seasons). The remaining two viruses were assigned to homologous genetic subgroup 5a.2a.1 subclade D represented by A/Victoria/4897/2022.

The other half (n=232, 47%) of the A(H1N1)pdm09 viruses with both genetic and antigenic data reported, were reported antigenically as A/Sydney/5/2021-like. Of those, the majority (n=223, 96%) fell also genetically to homologous clade 5a.2a subclade C.1, represented by A/Sydney/5/2021. Also, the two A(H1N1)pdm09 viruses that were indicated as antigenically distinct from vaccine or reference viruses were genetically assigned in the same C.1 subclade. Further two viruses were reported antigenically as A/Victoria/2570/2019-like (clade 5a.2) but genetically still assigned to clade 5a.2a subclade C.1.

Only 12 A(H1N1)pdm09 viruses were antigenically reported similar to A/Wisconsin/67/2022, the NH 2023-24 vaccine strain for cell culture- or recombinant-based vaccines, and genetically those viruses were distributed across the subclades 5a.2a and 5a.2a.1.

Antiviral susceptibility

Weeks 40/2023 through 33/2024, with latest data reported for collection week 30/2024, 4 920 A(H1N1)pdm09 influenza viruses were assessed genotypically and/or phenotypically for susceptibility to at least one drug (oseltamivir, zanamivir or baloxavir marboxil) by 18 countries. The three main countries that contributed were: United Kingdom (28%), Spain (19%) and Netherlands (12%).

Regarding the susceptibility to neuraminidase inhibitors, 9 countries performed a phenotypic assessment, with the three main contributors being Germany (44%), Poland (16%) and Spain (15%). Reduced or highly reduced inhibition by oseltamivir was observed for 10 (2%) and 3 (0.7 %) of the 439 tested A(H1N1)pdm09 viruses, respectively (Table 8). The susceptibility of the remaining 4 235 viruses was assessed genetically based on the presence of amino acid substitutions in the neuraminidase protein known to confer reduced or highly reduced inhibition. Substitutions associated with reduced or highly reduced inhibition by oseltamivir were observed for 23 (0.5 %) and 14 (0.3 %) viruses, respectively. Most viruses carried amino acid substitutions NA:I223V+NA:S247N (n=30) or NA:H275Y (n=17) (Annex 3). For zanamivir, no substitutions associated with reduced or highly reduced inhibition were observed for the 4 210 assessed viruses.

Table 8. Number of A(H1N1)pdm09 viruses by reporting categories for neuraminidase inhibitor susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Phenotypic			Genotypic		
Antiviral	NI [a]	RI	HRI	AANI	AARI	AAHRI
Oseltamivir	426	10	3	4 198	23	14
Zanamivir	436	0	0	4 210	0	0

[a] reporting categories: NI / AANI, normal inhibition; RI / AARI, reduced inhibition; HRI / AAHRI, highly reduced inhibition

The susceptibility to polymerase inhibitors was assessed genetically based on the presence of amino acid substitutions in the PA polymerase acidic protein that are known to confer reduced susceptibility. Sequencing data of the PA gene were reported by 13 countries, with the three main contributors being United Kingdom (30%), Spain (21%) and Netherlands (12%). Out of the 3 413 assessed A(H1N1)pdm09 viruses, substitutions associated with reduced susceptibility were observed for 5 (0.1 %) viruses (Table 9). Amino acid substitutions detected were PA:E23K (n=2), PA:E199G (n=2) and PA:I38L (n=1) (Annex 3).

Table 9. Number of A(H1N1)pdm09 viruses by reporting categories for baloxavir marboxil susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Genotypic	
Antiviral	AANS [a]	AARS
Baloxavir marboxil	3 408	5

[a] reporting categories: AANS, normal susceptibility; AARS, reduced susceptibility

A(H3N2) viruses

Antigenic characterisation

Weeks 40/2023 through 31/2024, with latest data reported for collection week 31/2024, 12 countries reported antigenic characterization to TESSy for 908 A(H3N2) influenza viruses. The three main countries that contributed were: Russian Federation (70.3%), United Kingdom (8.5%) and Germany (6.8%).

Countries were asked to report antigenic characterization results in TESSy according to the predefined categories described in Table 10.

Table 10. Predefined antigenic reporting categories for A(H3) viruses, WHO European Region, weeks 40/2023 through 33/2024.

TESSy category	Virus of reference	Clade long name	Clade short name [a]
agAH3/Darwin/9/2021	A/Darwin/9/2021-like	3C.2a1b.2a.2a	2a(G1)
agAH3/Catalonia/NSVH161512067/2022	A/Catalonia/NSVH161512067/2022-like	3C.2a1b.2a.2a.1b	2a.1b(G.1.1.2)
agAH3/Thailand/8/2022	A/Thailand/8/2022-like	3C.2a1b.2a.2a.3a.1	2a.3a.1(J)
agAH3/Thuringen/10/2022	A/Thuringen/10/2022-like	3C.2a1b.2a.2b	2b(G.2.2)
agAH3NOCAT	none	Not attributed to category	Not attributed to category

[a] subclade in brackets

Among the 908 characterised A(H3) viruses, the main reported categories were A/Thailand/8/2022-like, clade 2a.3a.1(J) and A/Darwin/9/2021-like, clade 2a(G1), representing 61.8% and 38.2%, respectively (Table 11, Figure 11, Figure 12).

Table 11. Number of viruses by A(H3) antigenic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
2a(G1)	A/Darwin/9/2021-like	347	38.2
2a.3a.1(J)	A/Thailand/8/2022-like	561	61.8

Figure 11. A(H3N2) clade weekly distribution based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.

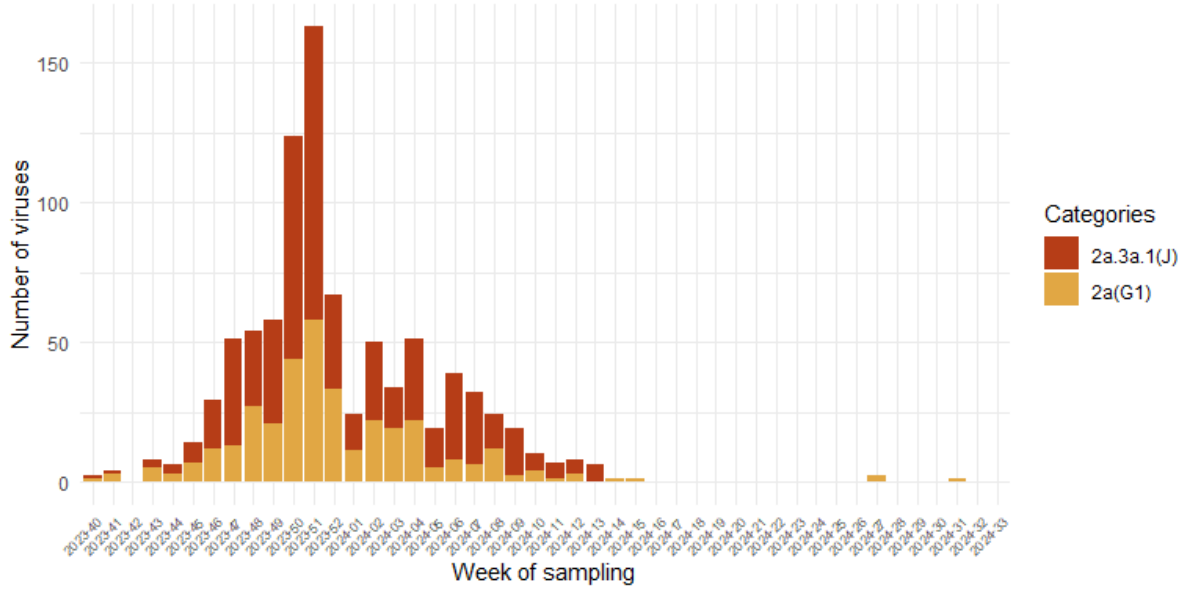
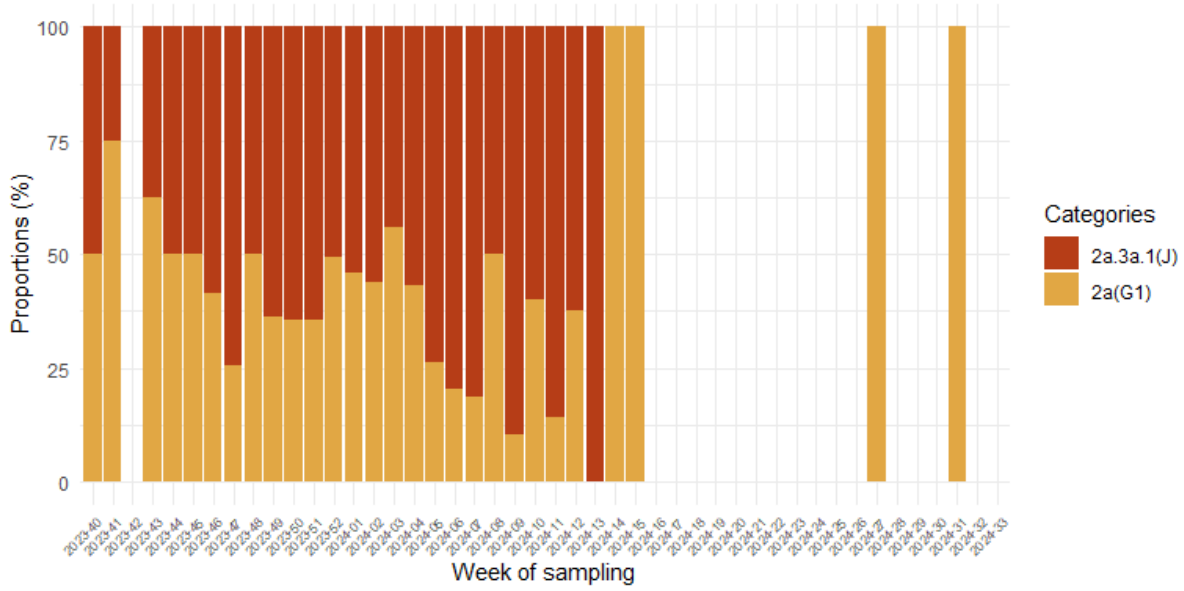


Figure 12. A(H3) clade weekly proportion based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.



Genetic characterisation

Weeks 40/2023 through 31/2024, with latest data reported for collection week 31/2024, 19 countries reported genetic characterization to TESSy for 4 527 A(H3N2) influenza viruses. The three main countries that contributed A(H3N2) data were: Russian Federation (40%), United Kingdom (21.4%) and Spain (10%).

Countries were asked to report genetic characterization results in TESSy according to the predefined categories described in Table 12.

Table 12. Predefined genetic reporting categories for A(H3) viruses.

TESSy category	Virus of reference	Clade long name	Clade short name [a]
genAH3/Darwin/9/2021	A/Darwin/9/2021	3C.2a1b.2a.2a	2a(G1)
genAH3/Catalonia/NSVH161512067/2022	A/Catalonia/NSVH161512067/2022	3C.2a1b.2a.2a.1b	2a.1b(G.1.1.2)
genAH3/Finland/402/2023	A/Finland/402/2023	3C.2a1b.2a.2a.3a	2a.3a(G.1.3.1)
genAH3/Thailand/8/2022	A/Thailand/8/2022	3C.2a1b.2a.2a.3a.1	2a.3a.1(J)
genAH3/Sydney/732/2022	A/Sydney/732/2022	3C.2a1b.2a.2a.3b	2a.3b(G.1.3.2)
genAH3/Thuringen/10/2022	A/Thuringen/10/2022	3C.2a1b.2a.2b	2b(G.2.2)
genAH3NOClade	none	Not attributed to category	Not attributed to category
genAH3SubgroupNotListed	other	Subgroup not listed	Subgroup not listed

[a] subclade in brackets

Among the 4 527 characterised A(H3) viruses, the main reported categories were A/Thailand/8/2022, clade 2a.3a.1(J) and A/Darwin/9/2021, clade 2a(G1), representing 95.1% and 4.5%, respectively (Table 13, Figure 13, Figure 14). For the one virus reported as 'Not attributed to category', no sequence was available. For three out of five viruses reported as 'Subgroup not listed', sequence information was availablegiand one of those viruses clustered within subclade G.1.3.1 and two within subclade J.

Table 13. Number of viruses by A(H3) genetic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
2a(G1)	A/Darwin/9/2021	204	4.5
2a.3a(G.1.3.1)	A/Finland/402/2023	11	0.2
2a.3a.1(J)	A/Thailand/8/2022	4 304	95.1
2a.3b(G.1.3.2)	A/Sydney/732/2022	2	0.0
Not attributed to category	none	1	0.0
Subgroup not listed	other	5	0.1

Figure 13. A(H3) clade weekly distribution based on genetic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.

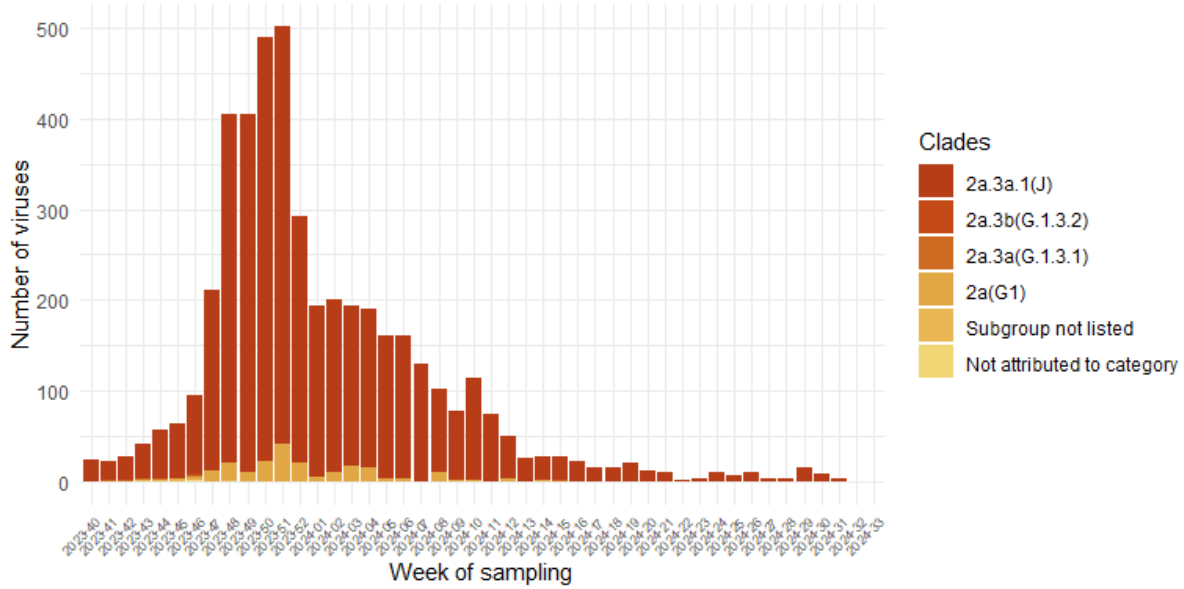
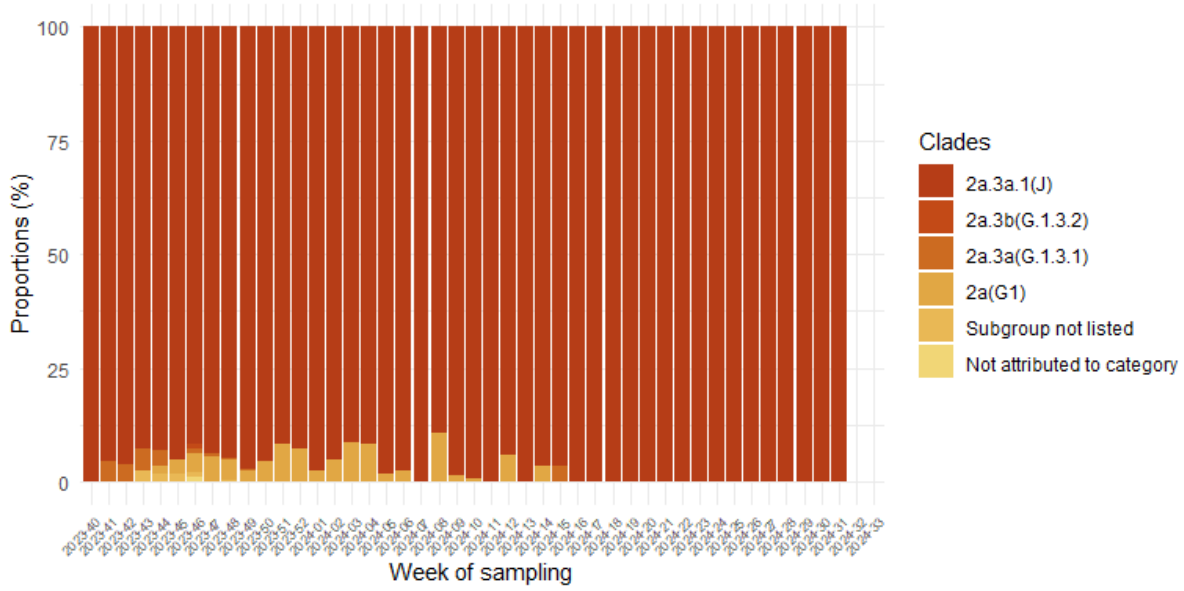


Figure 14. A(H3) clade weekly proportion based on genetic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.



Phylogenetic analysis

By week 33/2024, 4 339 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.

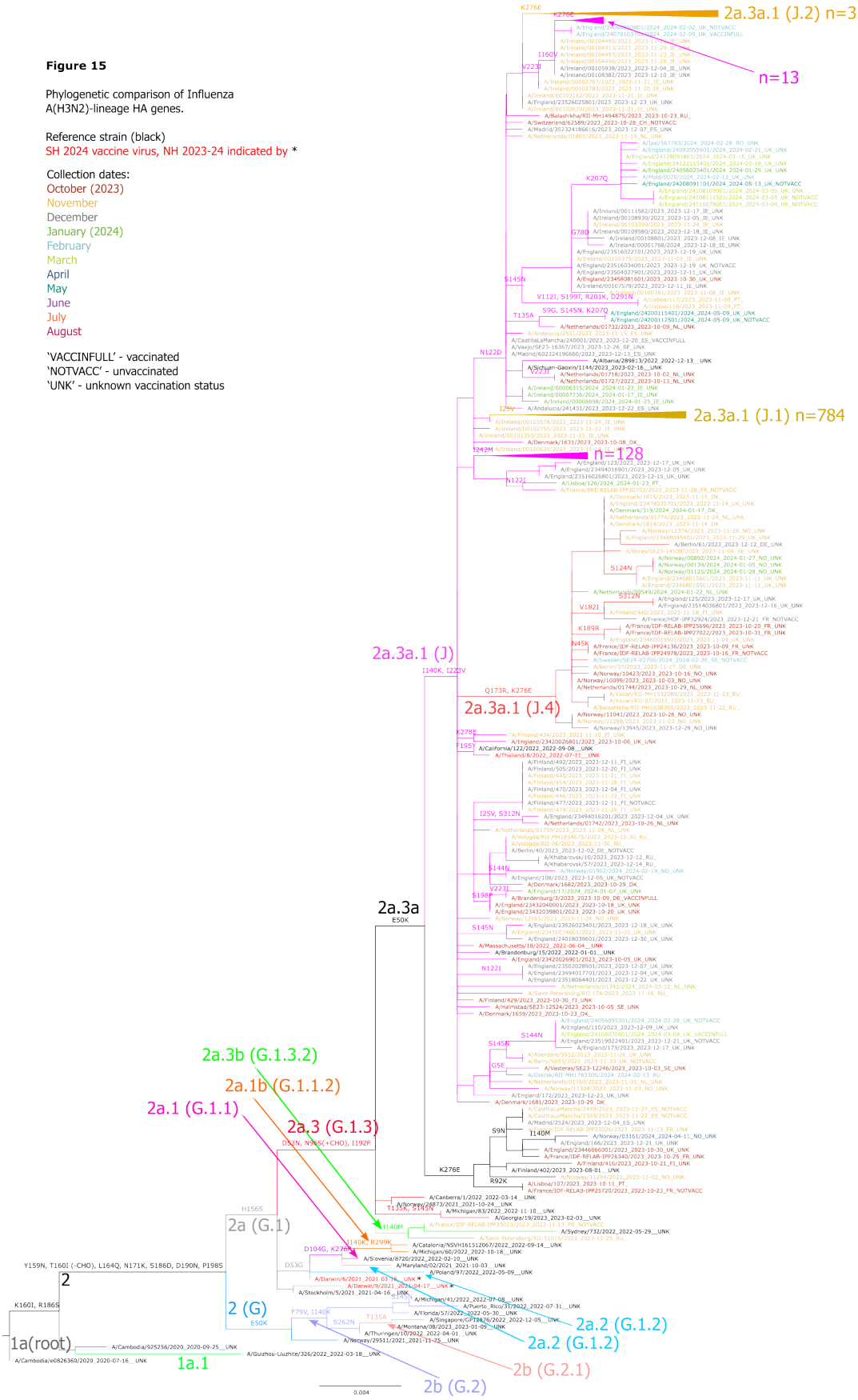
All A(H3) HA sequences fell into clade 2a.3, which is defined by D53N, N96S (addition of potential N-glycosylation site) and I192F amino acid substitutions compared to 2023-24 NH influenza season vaccine strain A/Darwin/9/2021. Within 2a.3, >99% (n=4 337) fell into 2a.3a defined by E50K compared to 2a.3 representative virus A/Norway/24873/2021 and out of these a majority of >99% (n=4 325) fell into 2a.3a.1 subclade J characterised by I140K and I223V and represented by SH 2024 egg-based vaccine strain A/Thailand/8/2022.

Within clade 2a.3a.1, 77% (n=3 317) fell into a branch with N122D compared with 2024 SH cell culture- or recombinant-based vaccine strain A/Massachusetts/18/2022 and represented by A/Albania/289813/2022. This branch further diversified with 98% (n=3 255) of its viruses in subclade J.2 characterised by amino acid substitution K276E which is not represented by any reference virus. Furthermore, 24% (n=784) of the viruses within 2a.3a.1 belonged to a subclade J.1 with I25V and 4% (n=128) to a branch defined by I242M where no reference strains were present. Less than 1% (n=35) within 2a.3a.1 fell into subclade J.4.

Two viruses belonged to 2a.3b subclade G.1.3.2, represented by A/Sydney/732/2022.

For the comparison of reported versus assigned clades, we grouped assigned subclades to the reporting categories. The phylogenetic results aligned well with the categorical reporting of genetic clade by the countries with only up to 5% differences in the proportion of different (sub)clades, when comparing assigned subclades of G.1.3.1, G.1.3.2 and J (Table Annex 4.3). Based on the phylogenetic analysis, almost all viruses (>99%) were assigned to 2a.3a.1 subclade J, while based on categorical genetic clade reports, 95% fell in this subclade.

Figure 15. 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).



Match between antigenic and genetic characterisations

Of the 695 A(H3N2) viruses that had both genetic and antigenic data reported, 378 (54%) were reported antigenically and genetically as A/Thailand/8/2022-like, representing NH vaccine strain for season 2024-25 (Table Annex 2.4). The other 317 (46%) A(H3N2) viruses were reported as A/Darwin/9/2021-like, which is the vaccine strain for NH 2023-24 season. The majority of those (n=83, 58%) were reported genetically to the homologous 2a clade represented by A/Darwin/9/2021, while 131 (41%) were assigned to the genetic clade 2a.3a.1 represented by A/Thailand/8/2022. Of the antigenically characterised viruses overall, the majority (62%) were A/Thailand/8/2022-like, the NH 2024-25 vaccine strain. Two A(H3N2) viruses that were genetically not assigned to any current reporting categories, were antigenically characterised as A/Darwin/9/2021-like and one virus that was antigenically A/Darwin/9/2021-like, was assigned genetically to subgroup 2a.3b (subclade G.1.3.2) _A/Sydney/732/2022.

Antiviral susceptibility

Weeks 40/2023 through 33/2024, with latest data reported for collection week 31/2024, 2 997 A(H3N2) influenza viruses were assessed genotypically and/or phenotypically for susceptibility to at least one drug (oseltamivir, zanamivir or baloxavir marboxil) by 18 countries. The three main countries that contributed were: United Kingdom (32%), Russian Federation (18%) and Spain (15%).

Regarding the susceptibility to neuraminidase inhibitors, 9 countries performed a phenotypic assessment, with the three main contributors being Russian Federation (82%), Germany (8%) and Spain (3.5%). Reduced or highly reduced inhibition was observed for 1 (0.2 %) and 1 (0.2 %) of the 663 A(H3N2) viruses tested for susceptibility to oseltamivir, respectively, and for 1 (0.2 %) and 1 (0.2 %) of the 652 viruses tested for susceptibility to zanamivir, respectively (Table 14). The susceptibility of the remaining viruses was assessed genetically based on the presence of amino acid substitutions in the neuraminidase protein known to confer reduced or highly reduced inhibition. Substitutions associated with reduced or highly reduced inhibition by oseltamivir were observed for 1 (0 %) and 1 (0 %) of the 2 318 viruses that could be assessed, respectively. Amino acid substitutions detected were NA:E119V (n=1) and NA:N329R (n=1) (Annex 3). No amino acid substitutions associated with reduced or highly-reduced inhibition by zanamivir were observed among the 2 312 viruses that could be assessed.

Table 14. Number of A(H3N2) viruses by reporting categories for neuraminidase inhibitor susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Phenotypic			Genotypic			
Antiviral	NI [a]	RI	HRI	AANI	AARI	AAHRI	AAINP
Oseltamivir	661	1	1	2 316	1	1	6
Zanamivir	650	1	1	2 312	0	0	1

[a] reporting categories: NI / AANI, normal inhibition; RI / AARI, reduced inhibition, HRI / AAHRI, highly reduced inhibition, AAINP, interpretation not possible

The susceptibility to polymerase inhibitors was assessed genetically based on the presence of amino acid substitutions in the PA polymerase acidic protein known to confer reduced susceptibility. Sequencing data were reported by 13 countries, with the three main contributors being United Kingdom, Netherlands and Spain. Out of the 1 957 assessed A(H3N2) viruses, no substitutions associated with reduced susceptibility were observed (Table 15).

Table 15. Number of A(H3N2) viruses by reporting categories for baloxavir marboxil susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Genotypic
Antiviral	AANS [a]
Baloxavir marboxil	1 957

[a] reporting category: AANS, normal susceptibility

B/Victoria lineage viruses

Antigenic characterisation

Weeks 40/2023 through 31/2024, with latest data reported for collection week 30/2024, 8 countries reported antigenic characterization to TESSy for 292 B(Victoria) influenza viruses. The three main countries that contributed were: Germany (69.9%), Russian Federation (8.9%) and United Kingdom (8.9%).

Countries were asked to report antigenic characterization results in TESSy according to the predefined categories described in Table 16.

Table 16. Predefined antigenic reporting categories for B(Victoria) viruses

TESSy category	Virus of reference	Clade long name	Clade short name [a]
agBVicB/Washington/02/2019	B/Washington/02/2019-like	V1A.3	V1A.3(A.3.2)
agBVicB/Austria/1359417/2021	B/Austria/1359417/2021-like	V1A.3a.2	V1A.3a.2(C)
agBVicB/Stockholm/3/2022	B/Stockholm/3/2022-like	V1A.3a.2	V1A.3a.2(C.5)
agBVicNOCAT	none	Not attributed to category	Not attributed to category

[a] subclade in brackets

Among the 292 characterised B(Victoria) viruses, all viruses were B/Austria/1359417/2021-like, clade V1A.3a.2(C) (Table 17, Figure 15, Figure 16).

Table 17. Number of viruses by B(Victoria) antigenic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
V1A.3a.2(C)	B/Austria/1359417/2021-like	292	100

Figure 15. B(Victoria) clade weekly distribution based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.

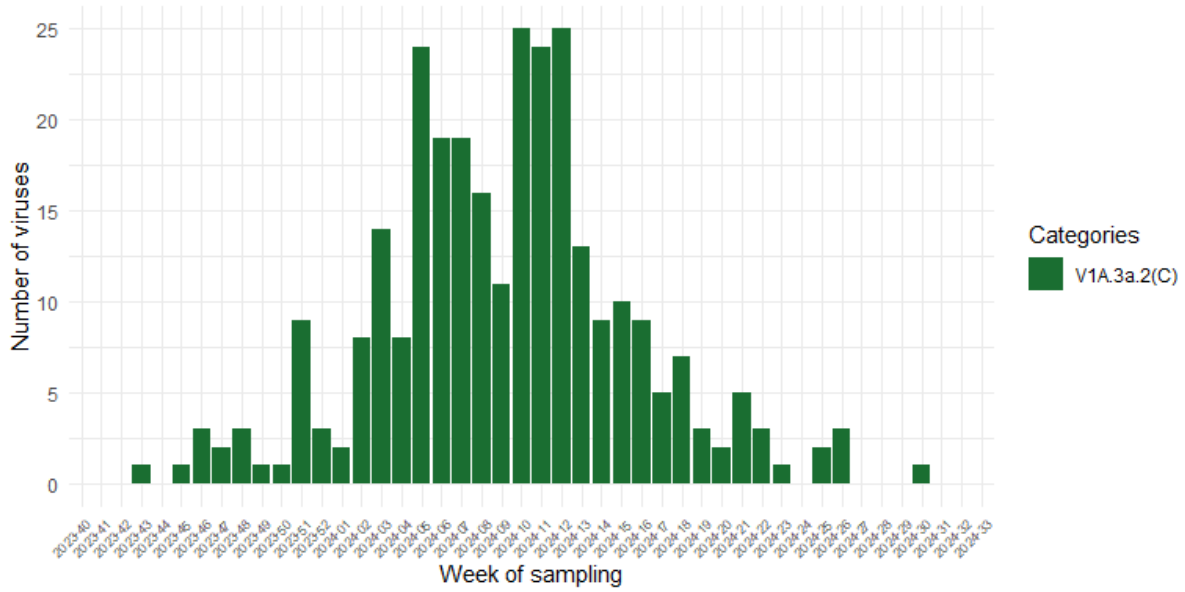
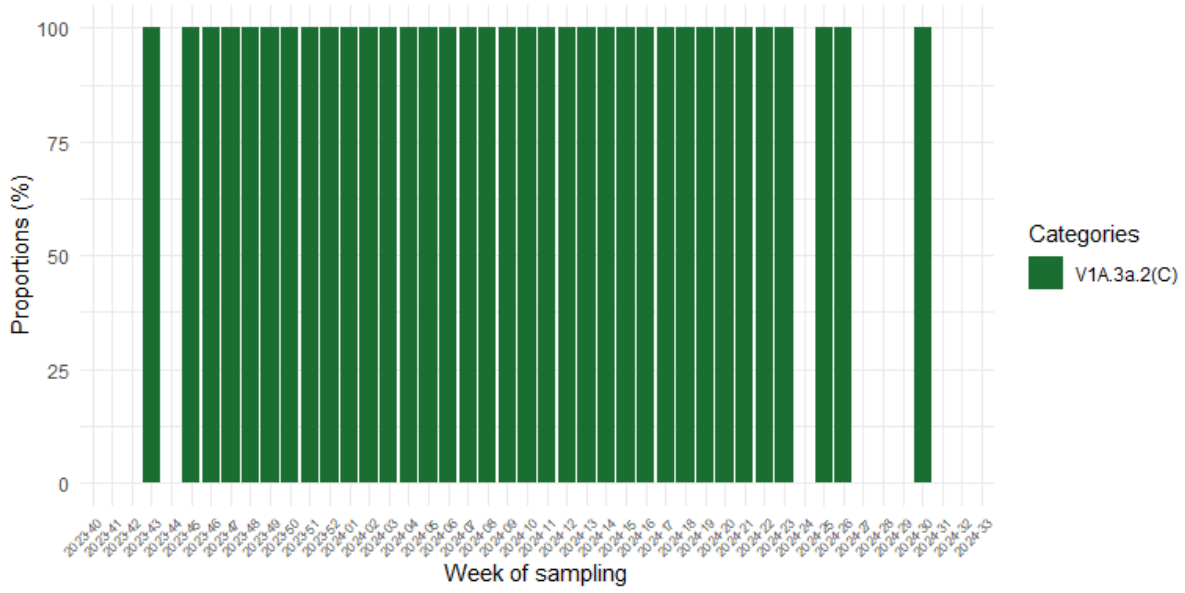


Figure 16. B(Victoria) clade weekly proportion based on antigenic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the short clade name is given with the subclade in brackets.



Genetic characterisation

From weeks 40/2023 to 31/2024, with latest data reported for week 31/2024, 16 countries reported genetic characterisation to TESSy for 1 614 B(Victoria) influenza viruses. The three main countries that contributed B/Victoria data were: United Kingdom (50.9%), Norway (9.4%) and Germany (9%).

Countries were asked to report genetic characterisation results in TESSy according to the predefined categories described in Table 18.

Table 18. Predefined genetic reporting categories for B(Victoria) viruses.

TESSy category	Virus of reference	Clade short name [a]
genBVicB/Washington/02/2019	B/Washington/02/2019	V1A.3(A.3.2)
genBVicB/Austria/1359417/2021	B/Austria/1359417/2021	V1A.3a.2(C)
genBVicB/Moldova/2030521/2023	B/Moldova/2030521/2023	V1A.3a.2(C.3)
genBVicB/Connecticut/01/2021	B/Connecticut/01/2021	V1A.3a.2(C.5)
genBVicB/Catalonia/2279261NS/2023	B/Catalonia/2279261NS/2023	V1A.3a.2(C.5.1)
genBVicNOClade	none	Not attributed to category
genBVicSubgroupNotListed	other	Subgroup not listed

[a] subclade in brackets

Among the 1 614 characterised B(Victoria) viruses, the main reported categories were B/Austria/1359417/2021, clade V1A.3a.2(C), B/Catalonia/2279261NS/2023, clade V1A.3a.2(C.5.1), and B/Connecticut/01/2021, clade V1A.3a.2(C.5), representing 56.5%, 34.6% and 8.4%, respectively (Table 19, Figure 17, Figure 18). The four viruses reported as 'Subgroup not listed' belonged all to V1A.3a.2 subclade C.5.7. One virus was reported as 'Not attributed to category', however, turned out to belong to subclade C.5.1.

Table 19. Number of viruses by B(Victoria) genetic reporting categories, WHO European Region, weeks 40/2023 through 33/2024.

Clade	Virus of reference	number	percent
V1A.3a.2(C)	B/Austria/1359417/2021	912	56.5
V1A.3a.2(C.3)	B/Moldova/2030521/2023	3	0.2
V1A.3a.2(C.5)	B/Connecticut/01/2021	136	8.4
V1A.3a.2(C.5.1)	B/Catalonia/2279261NS/2023	558	34.6
Not attributed to category	none	1	0.1
Subgroup not listed	other	4	0.2

Figure 17. B(Victoria) clade weekly distribution based on genetic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the clade name is given with the subclade in brackets.

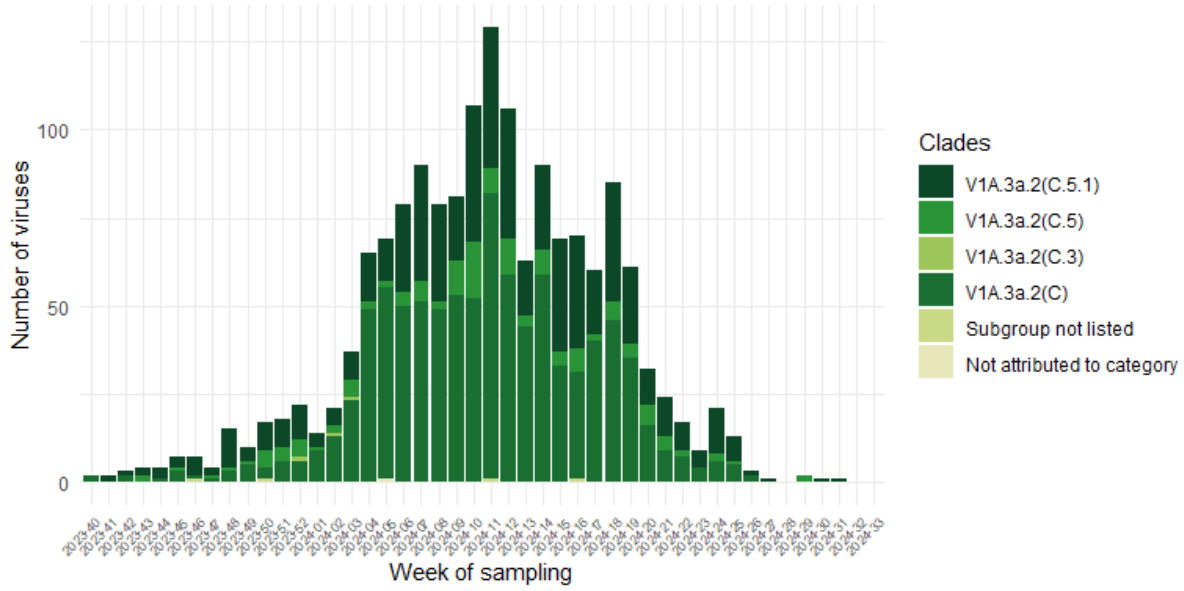
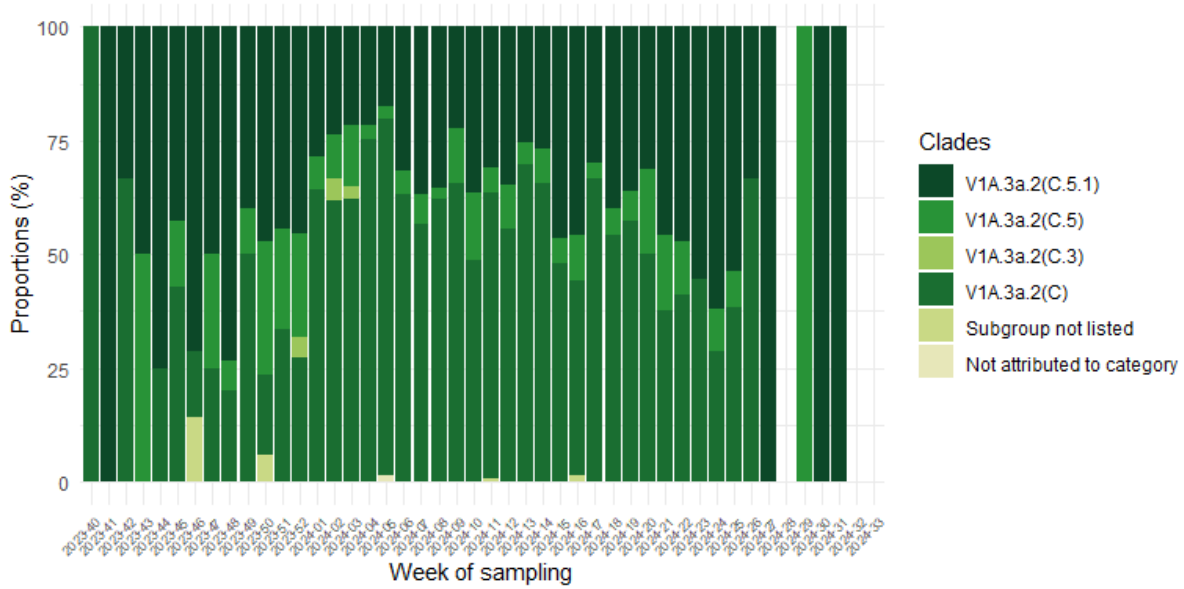


Figure 18. B(Victoria) clade weekly proportion based on genetic characterization, WHO European Region, weeks 40/2023 through 33/2024. In the categories, the clade name is given with the subclade in brackets.



Phylogenetic analysis

By week 33/2024, 1 514 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.

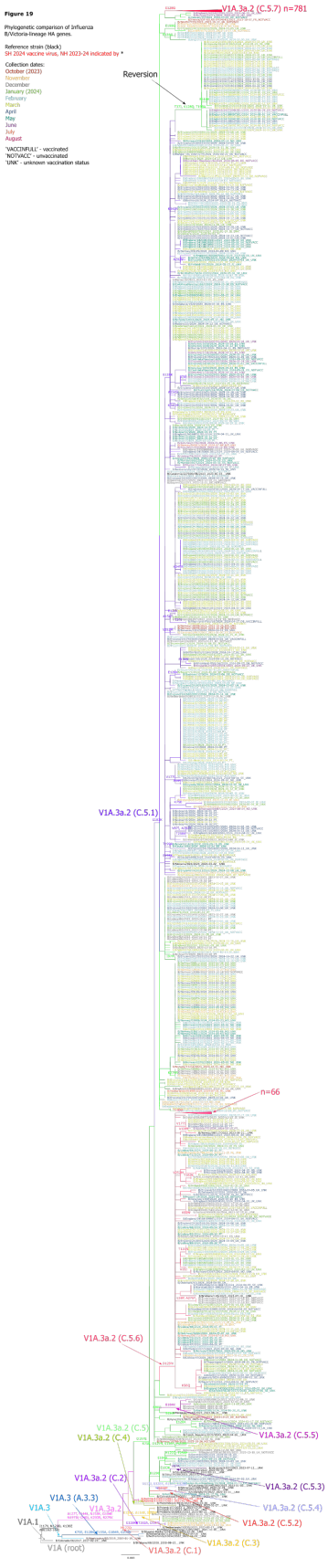
All reported viruses of B/Victoria carried HA genes that fell into genetic clade V1A.3a.2 subclade C with characteristic amino acid substitutions A127T, P144L, N150K, G184E, N197D (loss of potential N-glycosylation site), K203R and R279K compared to previous vaccine strain B/Washington/02/2019 and represented by NH 2023-24 vaccine strain B/Austria/1359417/2021.

The majority of 52% (n=781) of viruses within 3a.2 fell in the C.5.7 subclade with E128G followed by 22% (n=336) in C.5.1 with E183K and 13% (n=194) in C.5.6 with the D129N amino acid substitution. A few viruses also represented the subclades C.5.5 (n=6), C.3 (n=5) and C.2 (n=2) respectively characterised by the amino acid substitution E184K, the combination of E128K, A154E and S208P similar to reference strain B/Poland/157/2023, and the combination of E128K, T182A and D197E similar to the B/Netherlands/10335/2023 reference strain.

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).

For the comparison of reported versus assigned clades, we grouped assigned subclades to the reporting categories. The phylogenetic results aligned rather well with the categorical reporting of genetic clade by the countries with up to 12% differences in the proportion of different (sub)clades, when comparing assigned subclades of C, C.3, C.5 and C.5.1 (Table Annex 4.4). Based on the phylogenetic analysis, we had a larger proportion (65%) of viruses assigned to V1A.3a.2 (subclade C) represented by vaccine strain B/Austria/1359417/2021 than based on categorical reporting of genetic clade (57%), while the opposite was the case for V1A.3a.2 subclade C.5.1 viruses represented by B/Catalonia/2279261NS/2023, where 35% of genetic clades were reported and only 22% assigned in phylogenetic analysis.

Figure 19. 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).



Match between antigenic and genetic characterisations

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 177 B/Victoria viruses that had genetic and antigenic data reported, all were reported antigenically as V1A.3a.2 B/Austria/1359417/2021-like (Table Annex 2.4). HA sequences that were reported for B/Victoria viruses fell in three reporting categories within V1A.3a.2: 49 (28%) viruses as B/Austria/1359417/2021, 105 (59%) as B/Connecticut/01/2021 and 21 (12%) as B/Catalonia/2279261NS/2023. The two viruses that were genetically not categorised were antigenically similar to B/Austria/1359417/2021.

Antiviral susceptibility

Weeks 40/2023 through 33/2024, with latest data reported for collection week 31/2024, 1408 B/Victoria influenza viruses were assessed genotypically and/or phenotypically for susceptibility to at least one drug (oseltamivir, zanamivir or baloxavir marboxil), by 15 countries. The three main countries that contributed were: United Kingdom (58%), Norway (9%) and Germany (7%).

Regarding the susceptibility to neuraminidase inhibitors, 6 countries performed a phenotypic assessment, with the three main contributors being Germany (74%), Portugal (10%) and Italy (6.4%). Reduced inhibition by oseltamivir and zanamivir was observed for 1 of the 125 (0.8 %) tested B(Victoria) viruses (Table 20). The susceptibility of the remaining viruses was assessed genetically based on the presence of amino acid substitutions in the neuraminidase protein known to confer resistance. Amino acid substitutions associated with reduced inhibition by oseltamivir were observed for 6 (0.5 %) of the 1 274 viruses that could be assessed. Viruses carried amino acid substitutions NA:H273Y (n=3), NA:D197N (n=2), or NA:I221T (n=1) (Annex 3). For zanamivir, amino acid substitutions associated with reduced or highly-reduced inhibition were observed for 4 (0.3 %) and 1 (0.1 %) of the 1 265 assessed viruses, respectively. These were NA:N151S (n=2), NA:D197N (n=2) or NA:A245T (n=1) (Annex3).

Table 20. Number of B(Victoria) viruses by reporting categories for neuraminidase inhibitor susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Phenotypic		Genotypic			
Antiviral	NI [a]	RI	AANI	AARI	AAHRI	AAINP
Oseltamivir	124	1	1 268	6	0	3
Zanamivir	124	1	1 260	4	1	0

[a] reporting categories: NI / AANI, normal inhibition; RI / AARI, reduced inhibition, HRI / AAHRI, highly reduced inhibition, AAINP, interpretation not possible

The susceptibility to polymerase inhibitor were assessed genetically based on the presence of amino acid substitutions in the PA polymerase acidic protein that are known to confer reduced susceptibility. Sequencing data were reported by 8 countries, with the three main contributors being United Kingdom, Spain and Sweden. No substitutions associated with reduced susceptibility were observed for the 885 assessed B(Victoria) viruses (Table 21).

Table 21. Number of B(Victoria) viruses by reporting categories for baloxavir marboxil susceptibility, WHO European Region, weeks 40/2023 through 33/2024.

	Genotypic
Antiviral	AANS [a]
Baloxavir marboxil	885

[a] reporting category: AANS, normal susceptibility

B/Yamagata lineage viruses

No influenza B viruses of the Yamagata lineage were detected during the 2023-24 season.

Conclusions

From the WHO European Region, for the period covering weeks 40/2023 through 33/2024, 345 352 influenza virus detections, 2 085 antigenic and 11 688 genetic characterisations were reported to TESSy. Among the 81 889 (sub)typed or lineage defined viruses, 43 074 A(H1)pdm09 (53 %), 36 247 A(H3) (44 %) and 2 568 B/Victoria (3%) 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 reported in TESSy during this influenza season. Taken together, this influenza season was characterised by co-circulation of different influenza (sub)types. Please see further surveillance data, maps and country-specific tables at www.erviss.org.

In total, 21% (5 443 of 25 434 sentinel detections) of detected viruses have so far been entered as characterised into TESSy. This is an increase from February 2024 when 16% of sentinel specimens were characterised. NICs have been encouraged to characterise as many as possible of their sentinel influenza viruses and asked to sequence all sentinel influenza viruses [10], which is clearly not yet happening. However, based on the results, clear efforts towards characterisation of influenza viruses have been made across Europe. Twenty-one out of 50 countries reported virus characterisation data along with influenza detection data, and to varying extent. Antigenic and genetic characterisations were reported by 14 and 19 countries, respectively. It means that three more countries reported antigenic data in comparison to August 2023, which is a major improvement as in general the trend for antigenic reports has been decreasing. Keeping with this decreasing trend, we had now 2 085 reports in comparison to 2 604 reports last year at this time of the year. In contrast, the genetic reports have further increased with the same number of countries reporting (9 544 reports last year, now 11 688), probably also due to increased influenza activity. Understanding the reason behind the decline in antigenic reports, despite three additional countries providing data, poses a challenge, but could be due to sequencing first approach, i.e. selecting viruses to antigenic characterisation based on sequence screening first.

The distribution of type A and B viruses that had antigenic analyses reflected the overall virus distribution by sentinel and non-sentinel surveillance systems for type A and the double for type B (86% influenza A and 7% influenza B detected viruses vs 86% and 14% antigenically characterised, respectively). Among the A viruses, the share of A(H3) viruses that were antigenically characterised was almost the same (51%) when comparing to the A(H1)pdm09 viruses (49%). A(H1)pdm09 viruses were slightly underrepresented in antigenic characterisations (54% detected, 49% characterised) and A(H3) viruses were antigenically characterised more frequently (46% detected, 51% characterised). For the genetic clade reports, A(H1N1)pdm09 and A(H3) viruses were characterised in line with the detected viruses (among the subtyped A viruses, for A(H1N1)pdm09: 54% detected, 55% genetically characterised; and for A(H3N2): 46% detected and 44% genetically characterised). B viruses were detected at 7% of all influenza viruses and out of the characterised viruses 13% were B viruses, which would be in line with the attempt to characterise as many B viruses as possible during a non-B dominated influenza season. Minority subtypes/types are more likely to be epidemic next year than the majority virus and should be selectively sampled for sequencing, and therefore, sequencing strategies for influenza should not necessarily be strictly proportional. Overall, the HA sequence identifier provision in TESSy in connection to the genetic clade variable reporting is high with 98% (11 501 out of 11 688) reports including this information. Furthermore, the country-reported genetic clade categories aligned well with our phylogenetic analysis and assignment of clades.

Regarding the antigenic similarity of circulating A(H1)pdm09 viruses to the 2023-24 NH vaccine strains, 44% of circulating viruses were similar to the NH 2023-24 vaccine strain A/Victoria/4897/2022, when characterised with ferret antisera. However, the majority (54%) of A(H1N1)pdm09 viruses circulating in Europe were similar to A/Sydney/5/2021, which was the SH 2023 vaccine strain. Furthermore, genetically, 74% of A(H1)pdm09 viruses fell to the 5a.2a subgroup represented by A/Sydney/5/2021. Based on sequence analysis, most 5a.2a viruses (77%) carried additionally T120A and V47I or K169Q substitutions. There was some genetic diversification also observed in the 5a.2a.1 viruses, with 42% carrying R113K with or without S85P or 30% carrying R45K, similar to the Canadian report [11]. Antigenic group results reported by the Member States , however, supported that ferret antisera raised against A/Victoria/4897/2022 from the 5a.2a.1 subgroup recognised viruses in both 5a.2a and 5a.2a.1 subclades well as presented also earlier [4]. 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.

In total, fifty (1.1%) A(H1N1)pdm09 viruses of all tested showed reduced or highly reduced inhibition by oseltamivir by phenotypic testing or carried associated amino acid substitution markers. Several (n=17) viruses carried amino acid substitution NA:H275Y, which is a well-known oseltamivir highly reduced inhibited conferring amino acid substitution [12]. However, the highest number of oseltamivir reduced inhibited isolates (n=30) carried a double substitution of NA:I223V+NA:S247N, which was first notified to the network in the previous NH VCM and is not yet included in the WHO table [12] but is phenotypically confirmed to confer reduced inhibition by oseltamivir [13,14]. Of note, of the 30 viruses carrying these mutations, ten have also been tested for phenotypic oseltamivir susceptibility and were assessed as reduced inhibited. One A(H1N1)pdm09 virus carried the double mutation but was assessed as normal inhibited by phenotypic testing and was therefore considered normal inhibited in the analysis. No reduced susceptibility to zanamivir was detected in analyses of A(H1N1)pdm09 viruses. Five A(H1N1)pdm09 viruses carried genetic markers for reduced susceptibility to baloxavir marboxil with a mixed set of underlying amino acid substitutions.

For A(H3N2), based on genetic clade reporting, almost all (95%) circulating viruses fell in clade 2a.3a.1 represented by NH 2024-25 vaccine strain A/Thailand/8/2022. The available antigenic data supported the antigenic similarity of majority (62%) of those viruses with the A/Thailand/8/2022, while only 5% were similar to A/Darwin/9/2021, the current 2023-24 NH influenza season vaccine strain. The above supported that antisera raised against 2a.3a.1-like viruses (like A/Thailand/8/2022) recognised many circulating viruses well. However, it should be noted that the NICs did not have many types of ferret antisera available to test for more detailed antigenic characteristics. Noteworthy, within clade 2a.3a.1, 77% (n=3 317) of viruses fell into a branch with N122D, which confers loss of a potential glycosylation site which may influence antigenicity [15] and the vast majority in this branch further diversified in subclade J.2 characterised amino acid substitution K276E, while there were also two other smaller subgroups within 2a.3a.1 either with I25V or I242M.

Only four A(H3N2) viruses (<1%) showed reduced susceptibility to antivirals: two A(H3N2) viruses exhibited phenotypically reduced or highly reduced inhibition by both oseltamivir and zanamivir) and two A(H3N2) viruses, which showed presence of amino acid substitutions associated with reduced or highly reduced inhibition by oseltamivir alone. No reduced susceptibility to baloxavir marboxil was detected in genetic analyses of A(H3N2) viruses. Of note, one virus considered AARS in the NH VCM of this season is now considered AANS in this analysis instead because the updated WHO table listing PA mutations associated with baloxavir marboxil reduced susceptibility from 8 July 2024 [16] no longer indicates PA:L28P as resistance conferring mutation in A(H3N2) viruses. For the B/Victoria lineage, all antigenically characterised viruses were V1A.3a.2 B/Austria/1359417/2021-like, which is the current vaccine strain in tri- and quadrivalent vaccines in the NH 2023-24. Based on these data, circulating viruses in subclade V1A.3a.2 are well inhibited by ferret antisera raised against B/Austria/1359417/2021-like viruses, representing the vaccine strains for the 2023-24 [17] and 2024-25 [4] NH influenza seasons. However, the B/Victoria lineage viruses have genetically diversified and, within the V1A.3a.2 (C.5), 52% fell into subclade C.5.7, 22% into C.5.1, 13% into C.5.6 and <1% into C.5.5.

Ten B/Victoria viruses (<1%) showed phenotypically reduced inhibition by oseltamivir or zanamivir or harboured mixed sets of amino acid substitutions associated with such reduced or highly reduced inhibition without clear trend. No potentially reduced susceptibility to baloxavir marboxil was detected in PA amino acid substitution analyses of B/Victoria viruses.

Interim European vaccine effectiveness data showed 53% (95% CI: 41 to 63) protection against influenza A(H1N1)pdm09 in all ages in the primary care and 44% (95% CI: 30 to 55) for hospitalised patients [15]. The same study showed reduced protection for currently circulating A(H3N2) viruses of 30% (95% CI: −3 to 54) in primary care and, in hospital studies, 14% (95% CI: −32 to 43). This indicated that many of the currently circulating A(H3N2) 2a.3a.1 subclade strains in the EU/EEA had diversified antigenically from the NH 2023-24 vaccine strain A/Darwin/9/2021 [17]. Early influenza VE results from Alberta/Canada against infection showed 61% (95% CI: 58-64) against influenza A(H1N1)pdm09, 49% (95% CI: 28-63) against influenza A(H3N2) and 75% (95% CI: 58-85) against influenza B [18]. Another Canadian study found similar results with 63% (95% CI: 51-72) vaccine effectiveness against influenza A(H1N1)pdm09 overall but 56% (95% CI: 33-71) against clade 5a.2a.1, and 40% (95% CI: 5-61) against influenza A(H3N2) in sentinel practitioner surveillance [11].

Due to the question of whether B/Yamagata lineage viruses have become extinct, all B viruses that NICs and NILs receive should ideally be lineage-determined especially in non-B virus predominating seasons. At the moment, in the sentinel source data, about a third of the B viruses are lineage determined. In the virus characterisation data, though, the majority (96%) of the B viruses were reported with lineage.

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 (0.2% antigenically and 1.5% genetically from total influenza detections; 3.3% and 21% from the sentinel source viruses, respectively) of detected viruses were characterised overall, which is low 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 [10]. However, a large increase in sequencing has occurred during 2023-24 season, especially on sentinel source specimens. Furthermore, for the antigenic data reported to TESSy only the laboratory interpretations are considered, and no direct analysis of HI-assay data is possible. Therefore, the antigenic characterisation results from the different laboratories may not be directly comparable. For the antiviral susceptibility analysis, the laboratories' interpretation of their antiviral test results about the drug susceptibility rather than reported IC50 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, none of the thirteen 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 season, 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 Cyril Barbezange, Eeva Broberg, Maximilian Riess and Olov Svartström (ECDC), Iris Hasibra (WHO Regional Office for Europe). The report was reviewed by Olav Hungnes (Norway), Adam Meijer (The Netherlands), Katarina Prosenc (Slovenia), 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).

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Disclaimer

The data were extracted on 23 August 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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Annexes

Annex 1 – Methods

Data sources

In the WHO European Region, 51 countries and territories, including EU/EEA countries are regularly reporting influenza surveillance data. Out of 54 countries, 47 countries have National Influenza Centres (NICs), three countries have national influenza laboratories (NILs; Azerbaijan, Bosnia and Herzegovina, Uzbekistan) and Kosovo[2] is considered a territory. NICs and NILs receive clinical specimens and data from sentinel and non-sentinel surveillance sources for virological analysis. They 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 WHO website [19].

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 or sequencing. 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, a majority of the A(H1) and A(H3) viruses were reported with N-subtype (5 303, 88% and 4 332, 90%, 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 and NILs 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 [20,21]. 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 strains (supplied by WHO CC London or WHO CC Atlanta or generated by the laboratories in-house) [21] 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 and NILs 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 strain, 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

[2]All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

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 TESSy 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 [12]. In addition, the double substitution NA:I223V+NA:S247N in A(H1)pdm09 viruses was considered associated with reduced inhibition (AARI). 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) [22]. 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 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 [16,23]. 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, IRINA) 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 [24]. For reporting purposes, amino acid substitutions associated with up to 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) [16]. 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 2023-24 season (3 October 2023 – 22 August 2024) 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, or a clearly discrepant HA sequence (such as belonging to a different subtype than reported). 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 (https://github.com/tamuri/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 and a subset of additional viruses by querying their HA sequences on Nextclade tool of Nextstrain [25]. The clades of the sequences were determined by comparison with the references in the phylogenetic tree. The subclade classification was based on Nextstrain. 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=14), WHO European Region, weeks 40/2023 through 33/2024. 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	Belgium	Denmark	France	Germany	Greece	Italy	Portugal	Romania	Russian Federation	Slovenia	Spain	Switzerland	Ukraine	United Kingdom	Total	%
A(H1)pdm09_5a.2a(C.1)_A/Sydney/5/2021-like (3)		31	1	359	1	2		17		2			4	63	**480**	**23.0**
A(H1)pdm09_5a.2(C)_A/Victoria/2570/2019-like (1,2)									2						**2**	**0.1**
A(H1)pdm09_5a.2a.1(D)_A/Victoria/4897/2022-like (4,5)			49	198		14	54	18	2		16	14		23	**388**	**18.6**
A(H1)pdm09_5a.2a.1(C.1.1)_A/Wisconsin/67/2022-like (4,5)	7	3				2									**12**	**0.6**
A(H1)pdm09_Not categorised												3			**3**	**0.1**
A(H3)_2a(G1)_A/Darwin/9/2021-like (1,2,3,4)				62			2	15	177	2	13	2		74	**347**	**16.6**
A(H3)_2a.3a.1(J)_A/Thailand/8/2022-like (5)		38	24			2		20	461			5	8	3	**561**	**26.9**
Bvic_V1A.3a.2(C)_B/Austria/1359417/2021-like (1,2,3,4,5)		7		204		9	15	2	26			3		26	**292**	**14.0**
Total	**7**	**79**	**74**	**823**	**1**	**29**	**71**	**72**	**668**	**4**	**29**	**27**	**12**	**189**	**2085**	**100**

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

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

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

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

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

Table Annex 2.2. Genetic characterisation data by category as reported to TESSy, by country, WHO European Region, weeks 40/2023 through 33/2024. 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	Romania	Russian Federation	Spain	Sweden	Switzerland	Ukraine	United Kingdom	Total by clade	%
A(H1)pdm09_5a.2a(C.1)_A/Sydney/5/2021 (3)	40	201	68	84	651	8	78	24	136	455	172	202	127	5	579	60	27	4	1206	**4127**	**35.3**
A(H1)pdm09_5a.2a.1(C.1.1)_A/Wisconsin/67/2022 (4,5)		3					25			7	7	1			2	2	1		23	**71**	**0.6**
A(H1)pdm09_5a.2a.1(D)_A/Victoria/4897/2022 (4,	12	27	34	41	68	1	12	11	51	145	130	172		2	410	65	10		151	**1342**	**11.5**
A(H1)pdm09_NOClade	2		1																	**3**	**0.0**
A(H1)pdm09_SubgroupNotListed	4																			**4**	**0.0**
A(H3)_2a(G1)_A/Darwin/9/2021 (1,2,3,4)						1							29	174						**204**	**1.7**
A(H3)_2a.3a(G.1.3.1)_A/Finland/402/2023			1	3							2	1			3				1	**11**	**0.1**
A(H3)_2a.3b(G.1.3.2)_A/Sydney/732/2022				1															1	**2**	**0.0**
A(H3)_2a.3a.1(J)_A/Thailand/8/2022 (5)	44	137	54	47	47	11	108	5	4	347	238	36	63	1638	463	84	5	8	965	**4304**	**36.8**
A(H3)_NOClade	1																			**1**	**0.0**
A(H3)_SubgroupNotListed	2																2		1	**5**	**0.0**
B(Vic)_V1A.3a.2(C)_B/Austria/1359417/2021 (1,2,3,4,5)				4			30			3				99					776	**912**	**7.8**
B(Vic)_V1A.3a.2(C.5.1)_B/Catalonia/2279261NS/2023		25	34		116	1	6	9		32	134	49			83	30			39	**558**	**4.8**
B(Vic)_V1A.3a.2(C.5)_B/Connecticut/01/2021		8	1		30	7	5			6	17	32			7	16			7	**136**	**1.2**
B(Vic)_V1A.3a.2(C.3)_B/Moldova/2030521/2023																3				**3**	**0.0**
B(Vic)_NOClade	1																			**1**	**0.0**
B(Vic)_SubgroupNotListed	2																2			**4**	**0.0**
Total	**108**	**401**	**193**	**180**	**912**	**29**	**264**	**49**	**191**	**995**	**700**	**493**	**219**	**1918**	**1547**	**260**	**47**	**12**	**3170**	**11688**	**100.0**

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

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

Table Annex 2.3. Antigenic and genetic characterisation data as reported to TESSy by week of sampling, WHO European Region, weeks 40/2023 through 33/2024. 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.2[C]_A/Victoria/2570/2019-like (1,2)	A(H1)pdm09_5a.2a[C.1]_A/Sydney/5/2021-like (3)	A(H1)pdm09_5a.2a.1[C.1.1]_A/Wisconsin/67/2022-like (4,5)	A(H1)pdm09_5a.2a.1[D]_A/Victoria/4897/2022-like (4,5)	A(H1)pdm09_Not categorised	A(H3)_2a[G1]_A/Darwin/9/2021-like (1,2,3,4)	A(H3)_2a.3a.1[J]_A/Thailand/8/2022-like (5)	Bvic_V1A.3a.2[C]_B/Austria/1359417/2021-like (1,2,3,4,5)	TOTAL ANTIGENIC	A(H1)pdm09_5a.2a[C.1]_A/Sydney/5/2021 (3)	A(H1)pdm09_5a.2a.1[C.1.1]_A/Wisconsin/67/2022 (4,5)	A(H1)pdm09_5a.2a.1[D]_A/Victoria/4897/2022 (4,5	A(H1)pdm09_NOClade	A(H1)pdm09_SubgroupNotListed	A(H3)_2a[G1]_A/Darwin/9/2021 (1,2,3,4)	A(H3)_2a.3a[G.1.3.1]_A/Finland/402/2023	A(H3)_2a.3b[G.1.3.2]_A/Sydney/732/2022	A(H3)_2a.3a.1[J]_A/Thailand/8/2022 (5)	A(H3)_NOClade	A(H3)_SubgroupNotListed	B(Vic)_V1A.3a.2[C]_B/Austria/1359417/2021 (1,2,3,4,5)	B(Vic)_V1A.3a.2[C.3]_B/Moldova/2020521/2023	B(Vic)_V1A.3a.2[C.5]_B/Connecticut/01/2021	B(Vic)_V1A.3a.2[C.5.1]_B/Catalonia/2279261NS/2023	B(Vic)_NOClade	B(Vic)_SubgroupNotListed	TOTAL GENETIC
2023	40				1		1	1		3	12	1	12						24			2						51
	41				1		3	1		5	18	4	14				1		22						2			61
	42				5					5	23	4	15		1		1		26			2			1			73
	43				4		5	3	1	13	38		36				2		39		1			2	2			120
	44		2		3		3	3		11	41	2	48			1	2		53		1	1			3			152
	45		4		9		7	7	1	28	55	1	53			2			61		1	3		1	3			180
	46		5		15		12	17	3	52	79	4	53	1	3	4	1	1	87	1	1	1			5		1	242
	47		6		12		13	38	2	71	77	2	68			12	1		198			1		1	2			362
	48		4	2	19		27	27	3	82	128	3	85	1		19	1		383		1	3		1	11			636
	49		13		28		21	37	1	100	228	10	85			10	1		393			5		1	4			737
	50		15		42	1	44	80	1	183	302	7	129			22			467			3		5	8		1	944
	51		20		41		58	105	9	233	310	6	108			41		1	459			6		4	8			943
	52	1	19		14		33	34	3	104	247	9	116			21			271			6	1	5	10			686
2024	1		24		25	2	11	13	2	77	280	3	116	1		5			188			9		1	4			607
	2		29		15		22	28	8	102	281		80			10			190			13	1	2	5			582
	3		56		47		19	15	14	151	265	1	73			17			177			23	1	5	8			570
	4		49	3	27		22	29	8	138	267		68			16			175			49		2	14			591
	5		53		18		5	14	24	114	288	3	49			3			158			54		2	12	1		570
	6	1	43	1	18		8	31	19	121	267	2	27			4			156			50		4	25			535
	7		41	1	10		6	26	19	103	204	2	24						130			51		6	33			450
	8		24		8		12	12	16	72	136		14			11			91			49		2	28			331
	9		11	2	16		2	17	11	59	123	1	12			1			76			53		10	18			294
	10		21	3	3		4	6	25	62	97	2	12			1			114			52		16	39			333
	11		18		2		1	6	24	51	82	1	8						74			81		7	40		1	294
	12		9		3		3	5	25	45	52		3			3			47			59		10	37			211
	13		4		1			6	13	24	29		1						26			44		3	16			119
	14		3		1		1		9	14	39	1	5			1			27			59		7	24			163
	15		1				1		10	12	18		1				1		27			33		4	32			116
	16		1						9	10	15		3						22			30		7	32		1	110
	17		1						5	6	20		1						15			40		2	18			96
	18								7	7	17		1						15			46		5	34			118
	19								3	3	17	1	2						20			35		4	22			101
	20		2						2	4	17		1						13			16		6	10			63
	21		1						5	6	7		2						11			9		4	11			44
	22								3	3	5		3						2			7		2	8			27
	23		1						1	2	8		1						4			4			5			22
	24								2	2	7	1							11			6		2	13			40
	25								3	3	5		3						7			5		1	7			28
	26						2			2	5		6						10			2			1			24
	27								1	1	4								4						1			9
	28						1			1	5		1						3									9
	29									0	1		3						16					2				22
	30									0	8								9						1			18
	31									0									3						1			4
	32									0																		0
	33									0																		0
	ALL	2	480	12	388	3	347	561	292	2085	4127	71	1342	3	4	204	11	2	4304	1	5	912	3	136	558	1	4	11688

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

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

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

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

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

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 33/2024. Categories listed vertically are antigenic reporting categories, categories listed horizontally indicate genetic clade reporting categories. Numbers in brackets refer to footnotes below the table.

	ANTIGENIC								
GENETIC	A(H1)pdm09_5a.2a(C.1)_A/Sydney/5/2021-like (3)	A(H1)pdm09_5a.2(C)_A/Victoria/2570/2019-like (1,2)	A(H1)pdm09_5a.2a.1(D)_A/Victoria/4897/2022-like (4,5)	A(H1)pdm09_5a.2a.1(C.1.1)_A/Wisconsin/67/2022-like (4,5)	A(H1)pdm09_Not categorised	A(H3)_2a(G1)_A/Darwin/9/2021-like (1,2,3,4)	A(H3)_2a.3a.1(J)_A/Thailand/8/2022-like (5)	agBVicB/Austria/1359417/2021	**Total**
A(H1)pdm09_5a.2a(C.1)_A/Sydney/5/2021 (3)	223	2	162	7	2	0	0	0	**396**
A(H1)pdm09_5a.2a.1(C.1.1)_A/Wisconsin/67/2022 (4,5)	9	0	81	2	0	0	0	0	**92**
A(H1)pdm09_5a.2a.1(D)_A/Victoria/4897/2022 (4,5)	0	0	2	3	0	0	0	0	**5**
A(H3)_2a(G1)_A/Darwin/9/2021 (1,2,3,4)	0	0	0	0	0	183	0	0	**183**
A(H3)_2a.3b(G.1.3.2)_A/Sydney/732/2022	0	0	0	0	0	1	0	0	**1**
A(H3)_2a.3a.1(J)_A/Thailand/8/2022 (5)	0	0	0	0	0	131	378	0	**509**
A(H3)_SubgroupNotListed	0	0	0	0	0	2	0	0	**2**
B(Vic)_V1A.3a.2(C)_B/Austria/1359417/2021 (1,2,3,4,5)	0	0	0	0	0	0	0	49	**49**
B(Vic)_V1A.3a.2(C.5)_B/Connecticut/01/2021	0	0	0	0	0	0	0	105	**105**
B(Vic)_V1A.3a.2(C.5.1)_B/Catalonia/2279261NS/2023	0	0	0	0	0	0	0	21	**21**
B(Vic)_SubgroupNotListed	0	0	0	0	0	0	0	2	**2**
Total	**232**	**2**	**245**	**12**	**2**	**317**	**378**	**177**	**1365**

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

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

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

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

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

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 sequence number (ID) and interpretation defining mutation. TESSy, weeks 40/2023 through 33/2024, WHO Euro Region. P: phenotypic susceptibility testing; G: genotypic 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.

Subtype/ lineage	Virus	Antiviral	Assessment	Interpretation	GISAID	Associated mutations
A(H1)pdm09	A/Torino/295/2024	Oseltamivir	P, G	HRI	EPI3488120	H275Y
	A/Torino/294/2024	Oseltamivir	P, G	HRI	EPI3488118	H275Y
	A/Torino/262/2024	Oseltamivir	P, G	HRI	EPI3488122	H275Y
	A/Netherlands/01137/2024	Oseltamivir	P, G	RI	EPI3099165	I223V + S247N
	A/Netherlands/00988/2024	Oseltamivir	P, G	RI	EPI3099083	I223V + S247N
	A/Netherlands/00901/2024	Oseltamivir	P, G	RI	EPI3079937	I223V + S247N
	A/Netherlands/10463/2024	Oseltamivir	P, G	RI	EPI3072712	I223V + S247N
	A/Netherlands/00507/2024	Oseltamivir	P, G	RI	EPI2977737	I223V + S247N
	A/Netherlands/10231/2024	Oseltamivir	P, G	RI	EPI3008606	I223V + S247N
	A/Netherlands/10144/2024	Oseltamivir	P, G	RI	EPI3008473	I223V + S247N
	A/Netherlands/02111/2023	Oseltamivir	P, G	RI	EPI2904642	I223V + S247N
	A/Norway/10938/2023	Oseltamivir	P, G	RI	EPI2808196	I223V + S247N
	A/Netherlands/00257/2024	Oseltamivir	P, G	RI	EPI2977684	I223V + S247N
	A/Jonkoping/SE24-03869/2024	Oseltamivir	G	AAHRI	EPI3229309	H275Y
	A/Murcia/899/2024	Oseltamivir	G	AAHRI	EPI3219975	H275Y
	A/Mountain_Ash/2439/2024	Oseltamivir	G	AAHRI	EPI3441668	H275Y
	A/England/53/2024	Oseltamivir	G	AAHRI	EPI3100643	H275Y
	A/Netherlands/01992/2023	Oseltamivir	G	AAHRI	EPI2887056	H275Y
	A/PaisVasco/2470/2023	Oseltamivir	G	AAHRI	EPI3013913	H275Y
	A/Stockholm/SE24-05340/2024	Oseltamivir	G	AAHRI	EPI3280641	H275Y
	A/Denmark/558/2024	Oseltamivir	G	AAHRI	EPI3111602	H275Y
	A/Athens.GR/ILI P113/2024	Oseltamivir	G	AAHRI	EPI3493105	H275Y
	A/England/24106036701/2024	Oseltamivir	G	AAHRI	EPI3208028	H275Y
	A/Gelligaer/9270/2024	Oseltamivir	G	AAHRI	EPI3440982	H275Y
	A/England/23518027101/2023	Oseltamivir	G	AAHRI	EPI3142553	H275Y
	A/England/23504026001/2023	Oseltamivir	G	AAHRI	EPI2935562	H275Y
	A/England/23504026101/2023	Oseltamivir	G	AAHRI	EPI2935564	H275Y
	A/Netherlands/02060/2023	Oseltamivir	G	AARI	EPI2904617	I223T
	A/England/23498067801/2023	Oseltamivir	G	AARI	EPI2875938	D199E
	A/Milano/114/2024	Oseltamivir	G	AARI	EPI3490508	I223K
	A/Netherlands/00474/2024	Oseltamivir	G	AARI	EPI3005691	I223V + S247N
	A/Netherlands/00088/2024	Oseltamivir	G	AARI	EPI2933211	I223V + S247N
	A/Netherlands/00101/2024	Oseltamivir	G	AARI	EPI2933240	I223V + S247N
	A/Netherlands/03127/2023	Oseltamivir	G	AARI	EPI2933217	I223V + S247N
	A/Netherlands/01188/2024	Oseltamivir	G	AARI	EPI3112840	I223V + S247N
	A/Netherlands/00707/2024	Oseltamivir	G	AARI	EPI3054265	I223V + S247N

	A/Netherlands/00315/2024	Oseltamivir	G	AARI	EPI3005489	I223V + S247N
	A/Netherlands/00393/2024	Oseltamivir	G	AARI	EPI3005590	I223V + S247N
	A/Netherlands/00330/2024	Oseltamivir	G	AARI	EPI3005506	I223V + S247N
	A/Netherlands/10264/2024	Oseltamivir	G	AARI	EPI3026811	I223V + S247N
	A/Belgium/G00173/2024	Oseltamivir	G	AARI	EPI3471952	I223V + S247N
	A/Melilla/241383/2023	Oseltamivir	G	AARI	EPI3326493	I223V + S247N
	A/England/24060097801/2024	Oseltamivir	G	AARI	EPI3100763	I223V + S247N
	A/England/24022054701/2024	Oseltamivir	G	AARI	EPI3005759	I223V + S247N
	A/England/129/2023	Oseltamivir	G	AARI	EPI3005203	I223V + S247N
	A/England/23474085501/2023	Oseltamivir	G	AARI	EPI3030705	I223V + S247N
	A/England/23472023601/2023	Oseltamivir	G	AARI	EPI3030694	I223V + S247N
	A/England/23468015401/2023	Oseltamivir	G	AARI	EPI3030684	I223V + S247N
	A/Cardiff/1245/2024	Oseltamivir	G	AARI	EPI3083896	I223V + S247N
	A/Luxembourg/LNS3718055/2024	Oseltamivir	G	AARI	EPI3445929	I223V + S247N
	A/Denmark/1662/2023	Baloxavir marboxil	G	AARS	EPI2809184	E23K
	A/Denmark/1934/2024	Baloxavir marboxil	G	AARS	EPI3319927	E23K
	A/Andalucia/240585/2023	Baloxavir marboxil	G	AARS	EPI3153307	I38L
	A/England/31/2024	Baloxavir marboxil	G	AARS	EPI3029431	E199G
	A/England/23514032901/2023	Baloxavir marboxil	G	AARS	EPI2936515	E199G
A(H3)	A/Moscow/3/2024	Oseltamivir, Zanamivir	P	HRI	N/A	N/A
	A/Moscow/26/2023	Oseltamivir, Zanamivir	P	RI	N/A	N/A
	A/England/24236015601/2024	Oseltamivir	G	AAHRI	EPI3466154	E119V
	A/England/24240029501/2024	Oseltamivir	G	AARI	EPI3466186	N329R
B(Vic)	B/Poland/09/2024	Oseltamivir	P	RI	N/A	N/A
	B/England/24184036201/2024	Oseltamivir	G	AARI	EPI3465410	D197N
	B/England/24166026201/2024	Oseltamivir	G	AARI	EPI3464940	D197N
	B/England/24074033501/2024	Oseltamivir	G	AARI	EPI3141797	I221T
	B/Norway/03286/2024	Oseltamivir	G	AARI	EPI3284303	H273Y
	B/Norway/02993/2024	Oseltamivir	G	AARI	EPI3292727	H273Y
	B/Norway/02992/2024	Oseltamivir	G	AARI	EPI3292725	A245T; H273Y
	B/Thueringen/14/2024	Zanamivir	P	RI	N/A	N/A
	B/Norway/02992/2024	Zanamivir	G	AAHRI	EPI3292725	A245T
	B/Andalucia/1585/2024	Zanamivir	G	AARI	EPI3382419	N151S
	B/Andalucia/1520/2024	Zanamivir	G	AARI	EPI3382358	N151S
	B/England/24184036201/2024	Zanamivir	G	AARI	EPI3465410	D197N
	B/England/24166026201/2024	Zanamivir	G	AARI	EPI3464940	D197N

Annex 4 – Phylogenetic analysis

Table Annex 4.1 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 33/2024.

Country/HA sequences	A(H1N1)pdm09	A(H3N2)	B/Victoria	Total	% of total sequences
Belgium	54	44	3	101	0.9%
Denmark	218	130	25	373	3.3%
Finland	103	54	35	192	1.7%
France	125	51	4	180	1.6%
Germany	719	47	145	911	8.0%
Greece	6	11	8	25	0.2%
Ireland	115	108	41	264	2.3%
Italy	35	5	9	49	0.4%
Luxembourg	187	4	-	191	1.7%
Netherlands	607	346	41	994	8.7%
Norway	309	239	151	699	6.1%
Poland			1	1	0.0%
Portugal	375	37	81	493	4.3%
Romania	124	86	-	210	1.8%
Russian Federation	5	1646	10	1661	14.6%
Spain	991	466	90	1547	13.6%
Sweden	127	84	49	260	2.3%
Switzerland	38	7	2	47	0.4%
Ukraine	4	8	-	12	0.1%
United Kingdom	1371	966	819	3156	27.8%
Total number of HA sequences	**5513**	**4339**	**1514**	**11366**	

Table Annex 4.2. Number and proportion of A(H1N1)pdm09 reported genetic clades by countries and assigned clades based on phylogenetic analysis, weeks 40/2023 through 33/2024, WHO Euro Region.

Clade	**Virus of reference**	**Reported clade**	**Percent**	**Assigned clade**	**Percent**
5a.2a(C.1)	A/Sydney/5/2021	4127	74.4	4092*	74.2
5a.2a.1(C.1.1)	A/Wisconsin/67/2022	71	1.3	80	1.5
5a.2a.1(D)	A/Victoria/4897/2022	1342	24.2	1341#	24.3
Not attributed to category	none	3	0.1		0.0
Subgroup not listed	other	4	0.1		0.0
Total		**5547**		**5513**	

*Sum of 5a.2a (C.1) and other C clades except for C.1.1; #Sum of all D subclades

Table Annex 4.3. Number and proportion of A(H3N2) reported genetic clades by countries and assigned clades based on phylogenetic analysis, weeks 40/2023 through 33/2024, WHO Euro Region

Clade	Virus of reference	Reported clade	Percent	Assigned clade	Percent
2a(G.1)	A/Darwin/9/2021	204	4.5		0.0
2a.3a(G.1.3.1)	A/Finland/402/2023	11	0.2	12	0.3
2a.3a.1(J)	A/Thailand/8/2022	4304	95.1	4325*	99.7
2a.3b(G.1.3.2)	A/Sydney/732/2022	2	0.0	2	0.0
Not attributed to category	none	1	0.0		0.0
Subgroup not listed	other	5	0.1		0.0
Total		**4527**		**4339**	

*Sum of all J subclades

Table Annex 4.4. Number and proportion of B/Victoria reported genetic clades by countries and assigned clades based on phylogenetic analysis, weeks 40/2023 through 33/2024, WHO Euro Region

Clade	Virus of reference	Reported clade	Percent	Assigned clade	Percent
V1A.3a.2(C)	B/Austria/1359417/2021	912	56.5	983*	64.9
V1A.3a.2(C.3)	B/Moldova/2030521/2023	3	0.2	5	0.3
V1A.3a.2(C.5)	B/Connecticut/01/2021	136	8.4	190	12.5
V1A.3a.2(C.5.1)	B/Catalonia/2279261NS/2023	558	34.6	336	22.2
Not attributed to category	none	1	0.1		0.0
Subgroup not listed	other	4	0.2		0.0
Total		**1614**		**1514**	

*Sum of all remaining C subclades