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Addendum to the Influenza virus surveillance in Switzerland for the season 2022-2023

(Week 17/2023 to week 39/2023)

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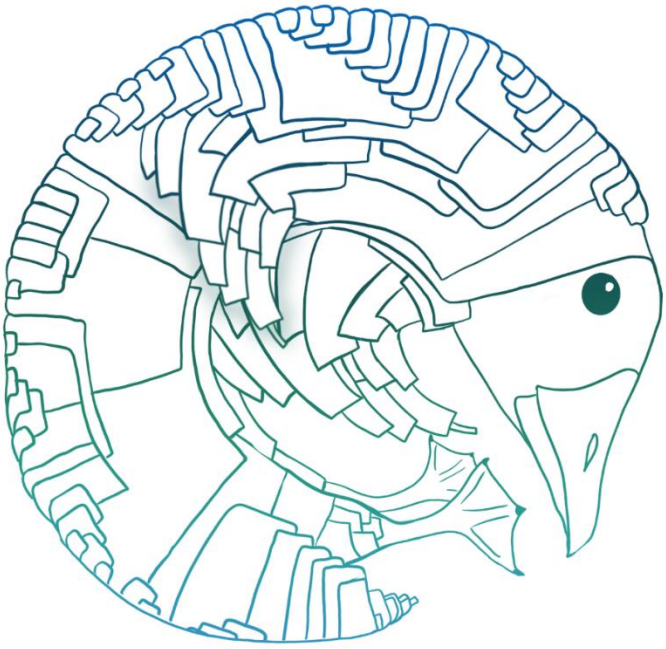

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Phylogenetic tree representing a wild goose.
Image definition: 2000x2000 pixels

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Abbreviations and Acronyms

GISAID	global initiative on sharing all influenza data
HAI	hemagglutinin inhibition
HAdV	human adenovirus
HBoV	human bocavirus
HCoV	human coronavirus
HPAI	high pathogenic avian influenza
HMPV	human metapneumovirus
HPIV	human parainfluenza virus
HRI	highly reduced inhibition
IA, IB	influenza A, B
NA	neuraminidase
NAI	neuraminidase inhibitor
NI	normal inhibition
NPS	nasopharyngeal sample/swab
NRCI	national reference centre of influenza
PA	acidic protein
RI	reduced inhibition
RV/EV	rhinovirus/enterovirus
RSV	respiratory syncytial virus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
rRT-PCR	real-time reverse-transcription polymerase chain reaction
Vic, Yam	victoria, yamagata

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Summary

A total of 639 nasopharyngeal swabs were tested in the context of the Swiss Sentinel surveillance network from week 17/2023 to week 39/2023.

Out of the 639 samples tested, 12 influenza viruses were detected, which represent 3.1 % of the positive samples. Of the 12 influenza viruses, 5 belonged to influenza A subtype A(H1N1)pdm09 and 2 to A(H3N2); 5 were influenza B viruses of B/Victoria/2/87 lineage. As could be expected, the influenza activity was low from week 17/2023 to 39/2023.

Five influenza isolates undergone antigenic characterization. Two A(H1N1)pdm09 viruses reacted well with the antiserum raised against the egg-propagated 2022/2023 vaccine strain A/Victoria/2570/2019 (subclade 5a.2). One A(H3N2) was well recognized by the antiserum raised against the egg-propagated 2023/2024 vaccine strain A/Darwin/9/2021 (subclade 3C.2a1b.2a.2). Two out of 5 influenza B viruses were characterized and reacted well with the antiserum raised against B/Austria/1359417/2021 virus (recommended vaccine strain for northern hemisphere 2023/2024, subclade V1A.3a.2).

During weeks 17/2023 to 39/2023, influenza viruses circulated at lower levels compared to the same period in 2022, where detection of influenza virus was observed almost every week. However, global influenza activity remained low.

No zoonotic influenza infections were observed in Switzerland during this period.

Other respiratory viruses detected during the reporting period comprised SARS-CoV-2, adenovirus, metapneumovirus, parainfluenza 1-4, rhinovirus/enterovirus, coronaviruses NL63/HKU1/E229/OC43, and bocavirus.

Rhinovirus/Enterovirus (RV/EV) and SARS-CoV-2 viruses were the most prevalent, retrieved in 170 (26.6%) and 129 (20.2%) specimens respectively.

1 Identification of influenza and other respiratory viruses

Data gathered in the present report correspond to sentinel samples received at the National Reference Centre of Influenza (NRCI) from April 22nd, 2023 (week 17/2023) to September 29th, 2023 (week 39/2023).

1.1 Detection of respiratory viruses in nasopharyngeal samples

From week 17/2023 to week 39/2023, 639 nasopharyngeal samples (NPS) were screened for influenza virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), respiratory syncytial virus (RSV), human coronaviruses (HCoV) NL63, HKU1, OC43, 229E, human parainfluenza viruses (HPIV1-4), human bocavirus (HBoV), human adenovirus (HAdV), rhinovirus/enterovirus (RV/EV) and human metapneumovirus (HMPV).

Three hundred and eighty-two samples (59.8%) were positive for at least one respiratory virus and 409 viruses were detected in total. Among these, the following pathogens were identified: RV/EV (n=170; 41.6%), SARS-CoV-2 (n=129; 31.5%), HPIV 1/3 (n=35; 8.6%), HAdV (n=21; 5.1%), HPIV 2/4 (n=21; 5.1%), HMPV (n=7; 1.7%), influenza A viruses (n=7; 1.7%), HCoV NL63 (n=6; 1.5%), influenza B viruses (n=5; 1.2%), HCoV HKU1 (n=4; 1%), HCoV OC43 (n=2; 0.5%), HCoV 229E (n=1; 0.2%), and HBoV (n=1; 0.2%) (Figure 1). No RSV was detected during this period.

A maximum positivity rate of 75% (n=33) during week 36/2023 and a minimum positivity rate of 38.5% (n=5) during week 29/2023 (median number of samples: 25, median positivity rate: 60.5%, range [38.5 to 75 %]; 95% CI (56.2-64.8 %)) were observed (Figure 2).

SARS-CoV-2 and RV/EV were regularly detected from week 17/2023 to week 39/2023. The prevalence of positive RV/EV samples was higher than that of positive SARS-CoV-2 during weeks 19/2023 to 31/2023 and in week 37/2023. Low numbers of HPIV1-4, HAdV and human coronaviruses (HKU1, NL63, OC43, 229E) positive samples were also regularly detected until week 39/2023. HMPV (weeks 17-18 and 22/2023) and HBoV (week 19/2023) were sporadically detected.

Co-detections were observed in 23 (7.4%) out of 382 positive samples (Annex 1). The highest number (n=4) was observed in week 38/2023. Not surprisingly, 14 concerned RV/EV (60.9%); which was often identified along with SARS-CoV-2 (64.3%), HPIV1/3 (21.4%), and others (21.4%).

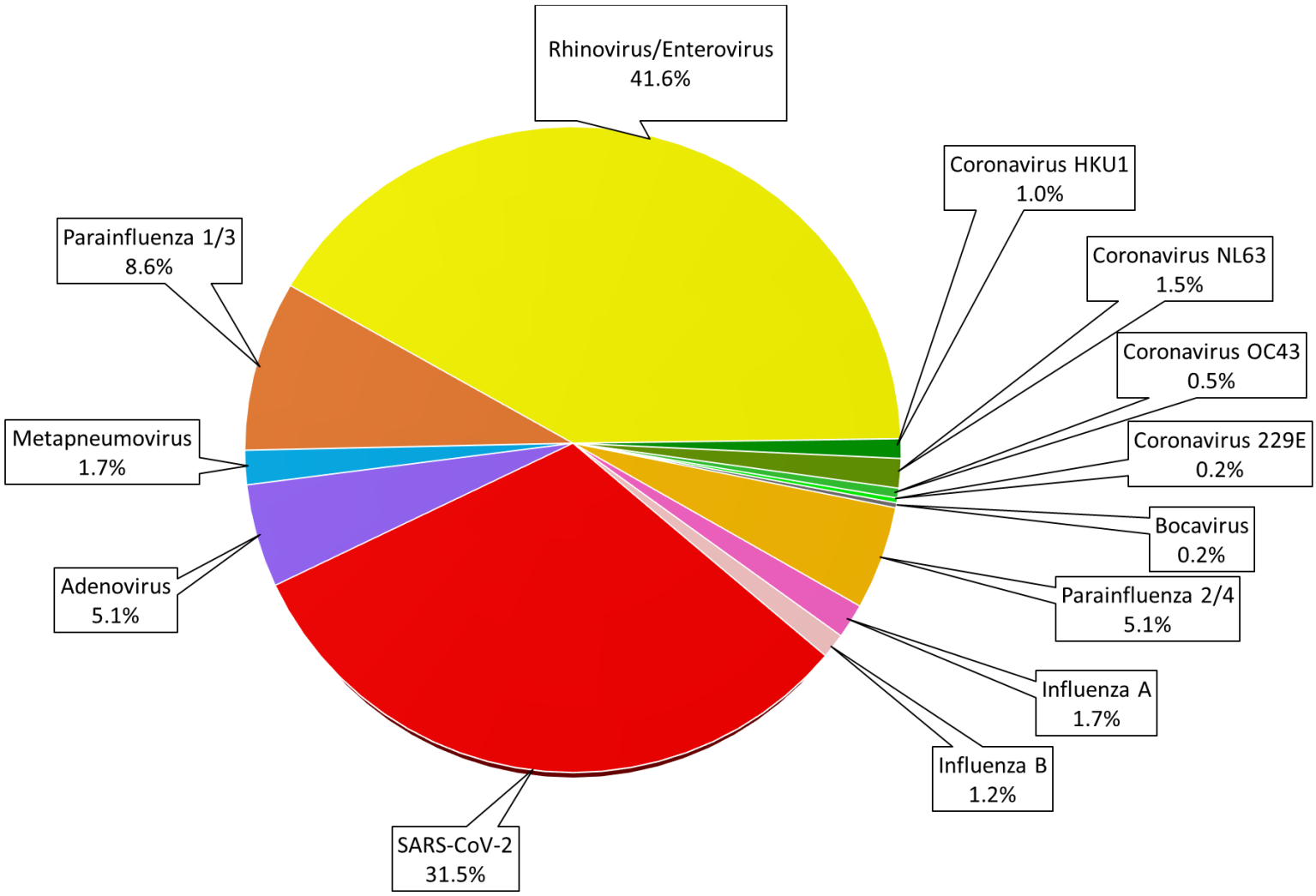


Figure 1. Percentage of the different respiratory viruses detected (n=409) in 639 NPS.

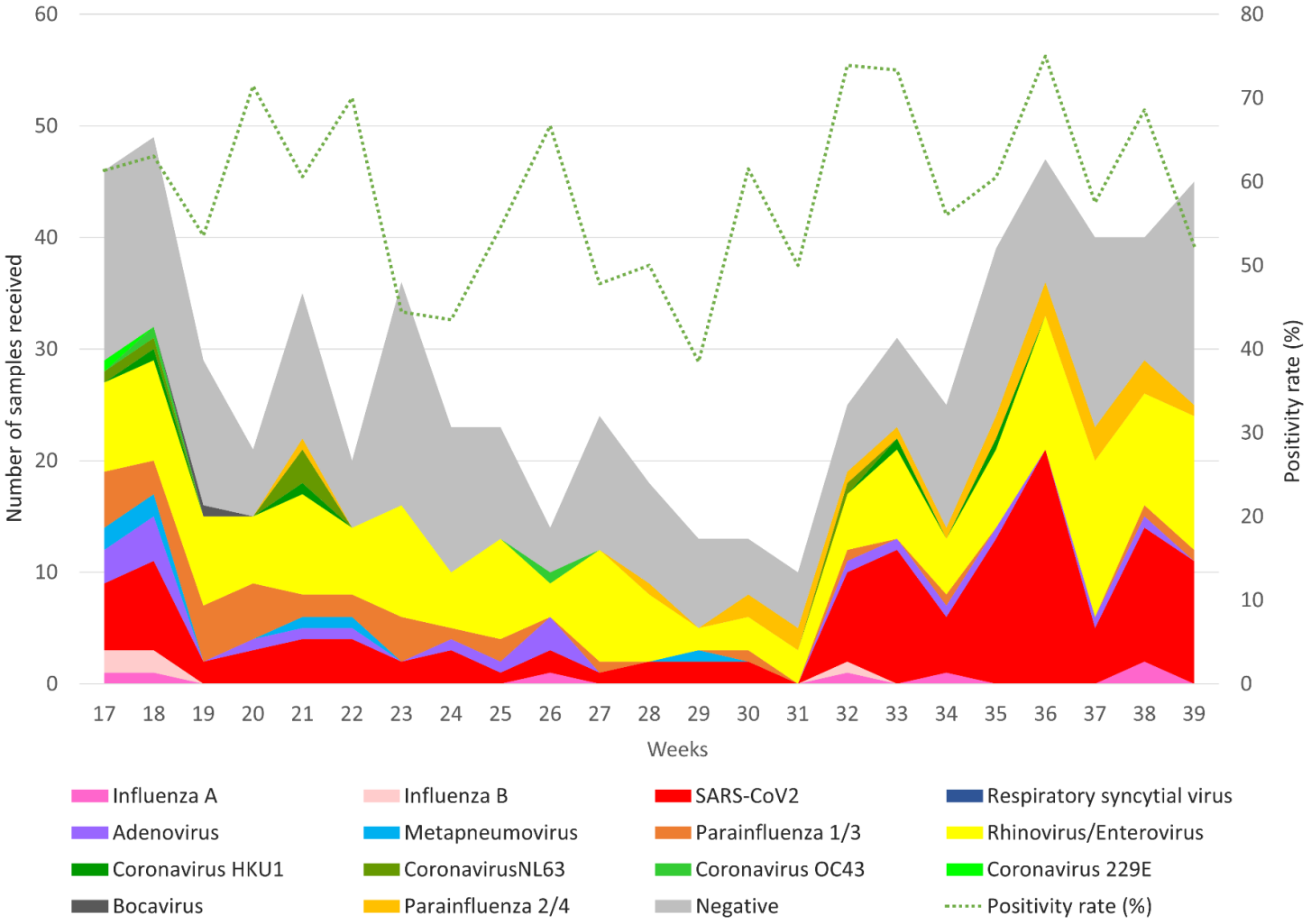
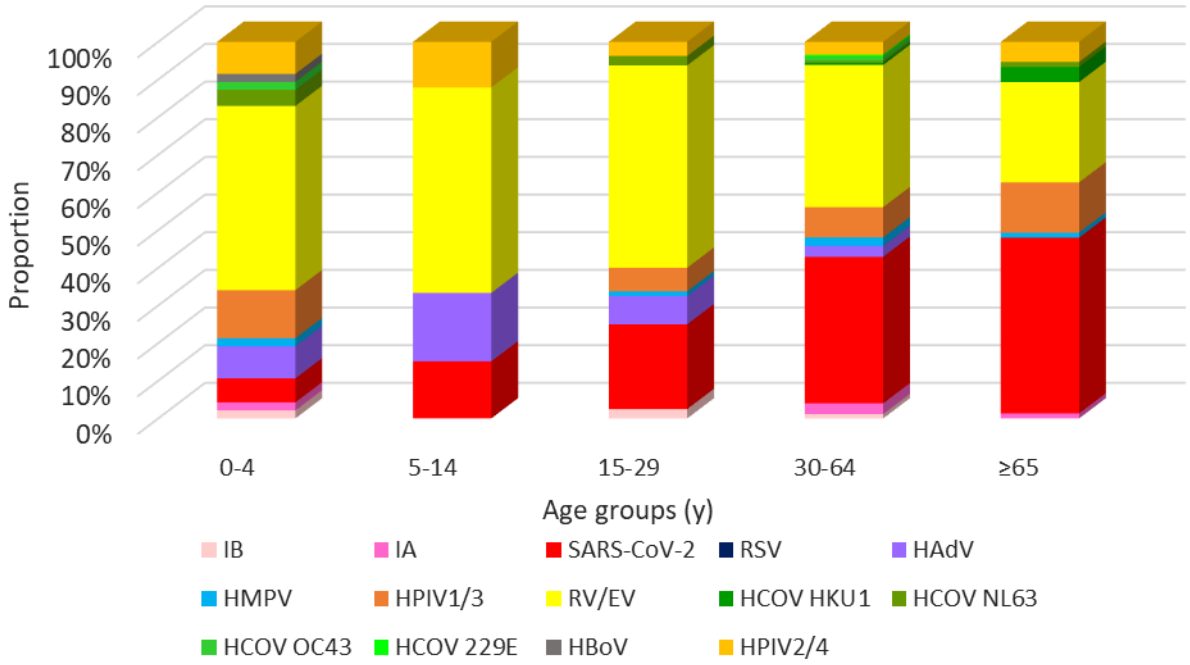


Figure 2. Distribution of the samples tested and the detected pathogens throughout the surveillance period. Positivity rate is based on the number of positive samples per total number of samples received each week**.**

When stratifying the detected pathogens by age groups, RV/EV viruses were observed at a high prevalence in all age groups (Figure 3 a,b). HPIV1/3 (12.5%), HPIV2/4 (8.5%) and HAdV (8.5%) were the most prevalent viruses in infants (0-4 year-old group). The only HBoV positive sample identified during this period was also found in the 0-4 year-old group (2.1%). In toddlers (5-14 year-old group), HAdV (18.2%) virus was the most prevalent after RV/EV. Not surprisingly, in elderly (≥65 year-old group), the prevalence of SARS-CoV-2 (46.7%) virus was the highest observed following with RV/EV (26.7%), and HPIV1/3 (13.3%). Of note, SARS-CoV-2 virus was present in all age groups, as RV/EV (Figure 3 a,b).

a.



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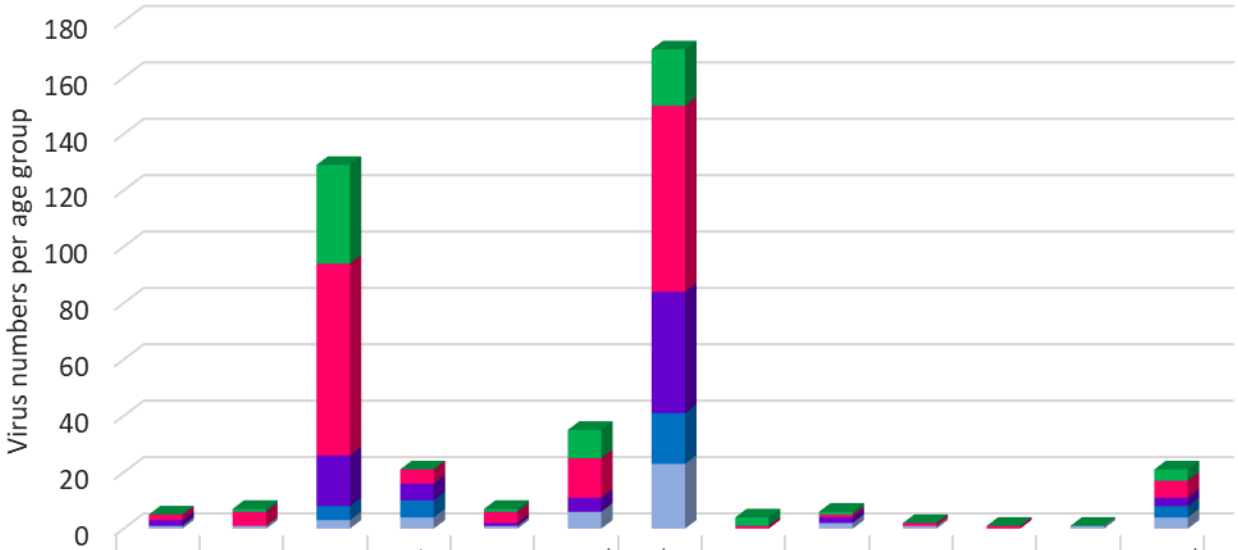


	IB	IA	SARS-CoV-2	HAdV	HMPV	HPIV1/3	RV/EV	HCOV HKU1	HCOV NL63	HCOV OC43	HCOV 229E	HBoV	HPIV2/4
≥65	0	1	35	0	1	10	20	3	1	0	0	0	4
30-64	2	5	68	5	4	14	66	1	1	1	1	0	6
15-29	2	0	18	6	1	5	43	0	2	0	0	0	3
5-14	0	0	5	6	0	0	18	0	0	0	0	0	4
0-4	1	1	3	4	1	6	23	0	2	1	0	1	4

Figure 3. Respiratory viruses' distribution: a. per age group in percent; **b.** in absolute numbers of positive samples.

When stratifying the positive cases by age group and gender, no significant differences could be observed between female and male (Figure 4).

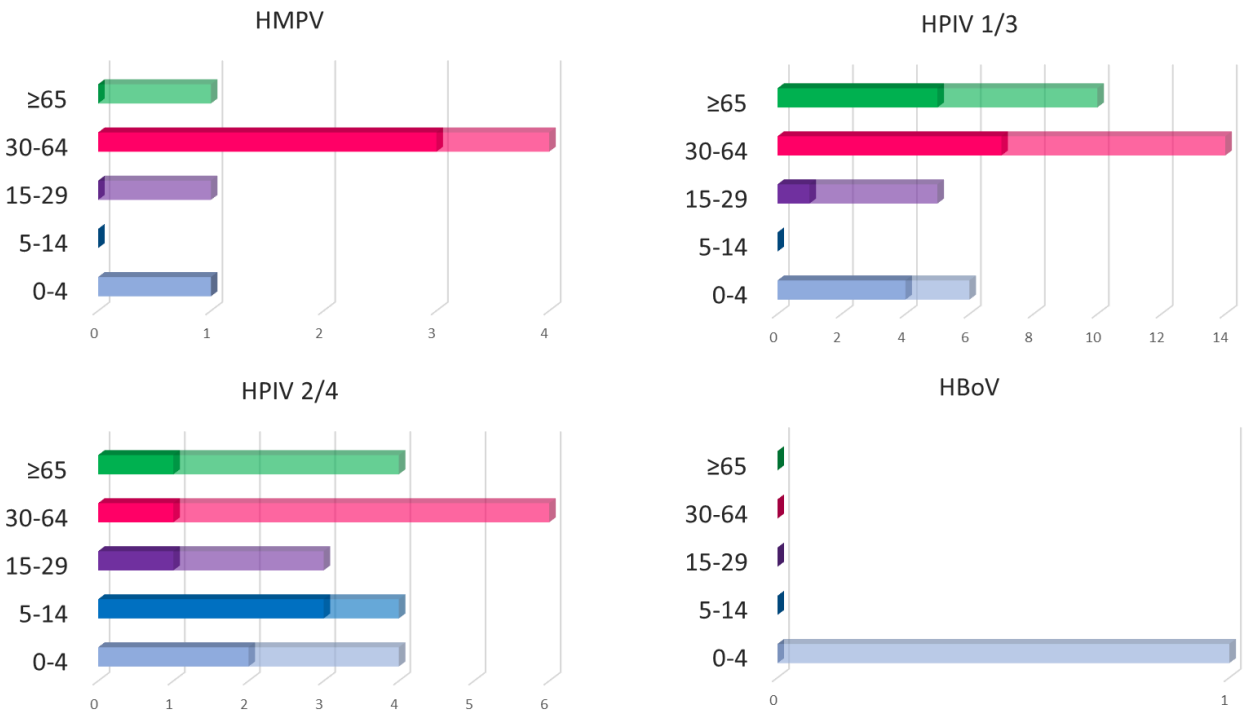
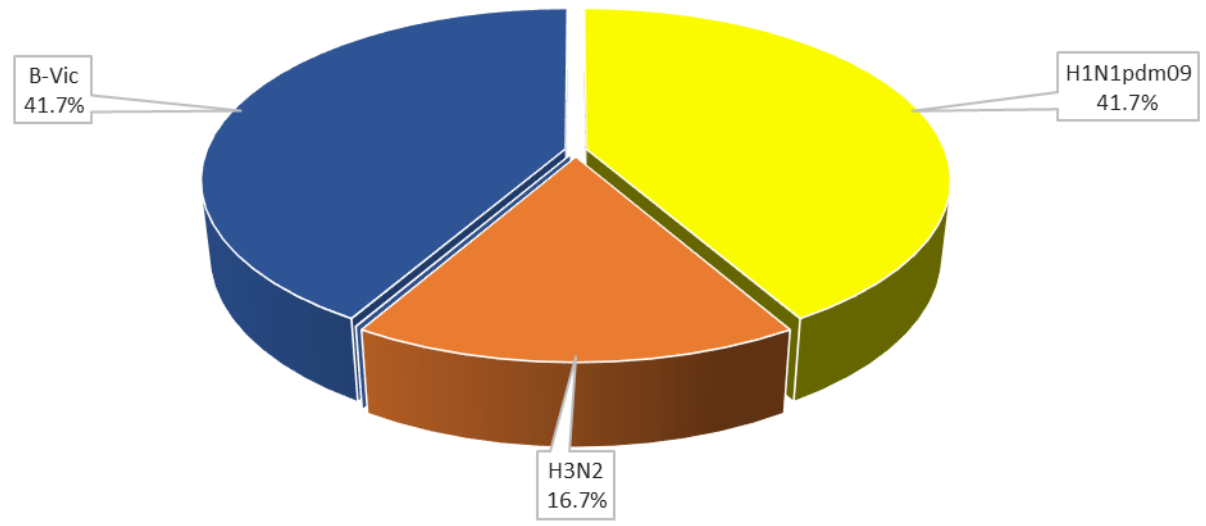


Figure 4. Respiratory viruses' distribution by gender and age groups in absolute number. Dark and light shades represent the female and male sex respectively. Age group is showed on the y axis and the number of viruses detected on the x axis.

1.2 Detection of influenza viruses

Among the 12 influenza viruses detected, 7 influenza A and 5 influenza B were identified (Figures 5a, b). Two influenza A were subtyped as A(H3N2) (16.7%) and five as A(H1N1)pdm09 (41.7%). Of the five influenza B viruses, all belonged to B-Victoria lineage (41.7%) (Figure 5a). The median positivity rate for influenza was zero (range [0 to 8.7%]; 95% CI (0-1.3%)) with a peak of positivity at 8.7% (n= 2) during week 32/2023 (Figure 5b).

a.



b.

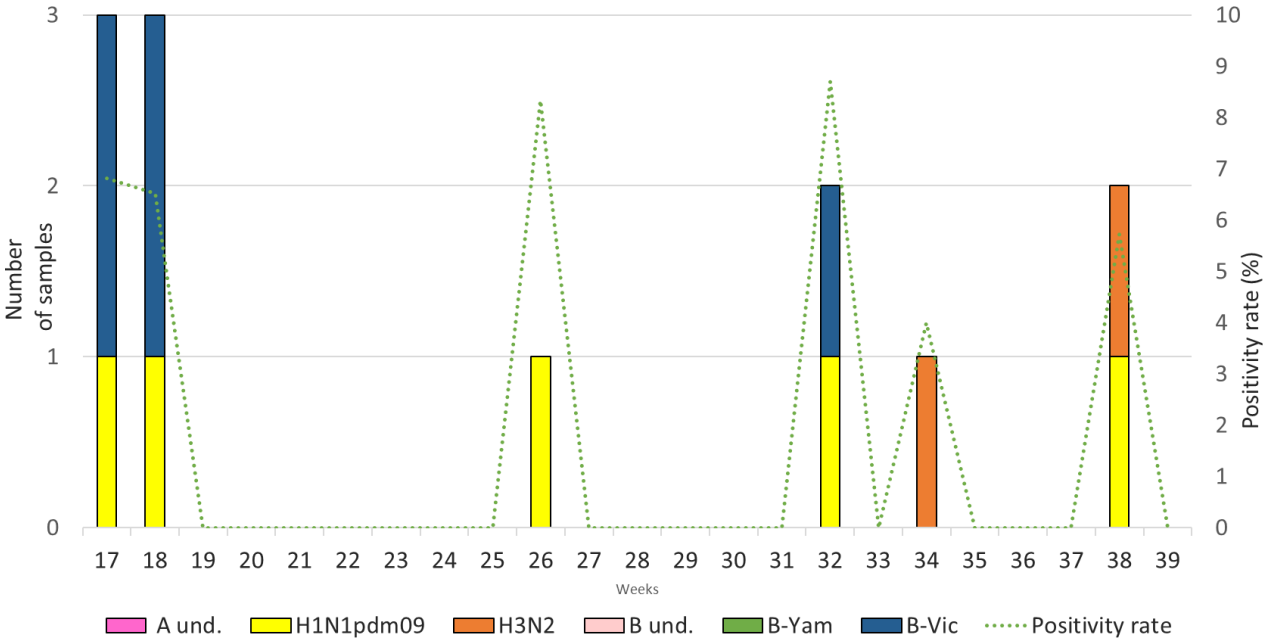


Figure 5. Percentage and temporal distribution of Influenza viruses detected in NPS collected from week 17/2023 to week 39/2023. a. Percentage of influenza viruses, subtypes (FluA) and lineages (FluB). N=12 influenza viruses. **b.** Distribution of the detected influenza viruses throughout the surveillance period. Influenza viruses typing and subtyping done by real-time rRT-PCR. A und. and B und.: influenza A and B viruses that could not be further subtyped. H1N1pdm09 and H3N2 refer to influenza A(H1N1)pdm09 and influenza A(H3N2), respectively. B-Yam: influenza B virus of Yamagata lineage. B-Vic: influenza B virus of Victoria lineage. Positivity rate is based on the number of weekly positive influenza samples per the number of samples received each week.

1.3 SARS-CoV-2 and influenza viruses' characterization

1.3.1 SARS-CoV-2 genetic analysis and variants identification

Among the 129 SARS-CoV-2 positive samples identified from week 17/2023 to week 39/2023, 90 had Ct values lower than 32 and were further characterized by whole genome sequencing. Eighty two sequences were submitted to the global initiative on sharing all influenza data (GISAID) database and fell into 34 distinct Pangolin[1, 2] lineages[3] (Table 1). All sequences were XBB derived sublineages of Omicron, and in particular the EG.5.1 sublineage (n= 10; 12.3%). Those results are in line with what has been observed within the national SARS-CoV-2 genomic and surveillance program (https://www.hug.ch/centre-maladies-virales-emergentes/programme-sequencage-national-du-sars-cov-2).

Table 1. List of the different SARS-CoV-2 Pangolin lineages within which Sentinel isolates were distributed

Pangolin[1] sub-lineages	Number of isolates	Pangolin sub-lineages	Number of isolates
DV.7.1	1	XBB.1.16	3
EG.1	5	XBB.1.16.11	3
EG.1.4	2	XBB.1.16.15	1
EG.5.1	10	XBB.1.16.21	1
EG.5.1.1	6	XBB.1.16.3	1
EG.5.1.3	4	XBB.1.16.6	4
EG.5.1.4	2	XBB.1.42	1
EG.5.1.5	1	XBB.1.5	3
EG.6.1	1	XBB.1.5.13	1
EG.7	1	XBB.1.5.5	1
FL.11	1	XBB.1.5.7	1
GE.1	3	XBB.1.5.94	1
GF.1	1	XBB.1.9.1	4
GJ.1	2	XBB.1.9.2	6
GJ.1.2	2	XBB.2.3.10	1
GK.1.3	1	XBB.2.3.11	3
HK.3	2	XBB.2.3.3	2
N	82		

[1] Web-based lineage assessment: https://cov-lineages.org/lineage_list.html

1.4 Antigenic and genetic characterization of influenza viruses

Hundred and nine SARS-CoV-2 negative samples were submitted to cell culture. Among them, 8 were known to be influenza positive by PCR.

1.4.1 Characterization of influenza A (H3N2) viruses

One A(H3N2) was antigenically characterized. The virus was well recognized by the antiserum raised against the egg-propagated northern hemisphere 2023/2024 vaccine strain A/Darwin/9/2021 (subclade 3C.2a1b.2a.2). No genetic analysis for this sample was performed.

1.4.2 Characterization of influenza A(H1N1pdm09) viruses

Two A(H1N1)pdm09 were antigenically characterized. Both were well recognized by the antiserum raised against the egg-propagated northern hemisphere vaccine strain 2022/2023 A/Victoria/2570/2019.

Genetic analysis was performed for both (A/Switzerland/85043/2023 and A/Switzerland/77731/2023) samples, which were already described in the annual report of “the Influenza virus surveillance in Switzerland-Season 2022–2023” (Annex 2).

1.4.3 Characterization of influenza B/Victoria viruses

Two influenza B isolates reacted well with the antiserum raised against B/Austria/1359417/2021 virus (recommended northern hemisphere 2023/2024 vaccine strain).

One influenza B (B/Switzerland/07551/2023) (Annex 2) genetic analysis was carried out and was also described in the annual report.

1.5 Antiviral resistance

No phenotypic tests for antiviral assessment were performed during the weeks 17/2023 to 39/2023. Sequencing analysis did not show any mutations associated with reduced susceptibility to antivirals.

2 Worldwide influenza activity

In the southern hemisphere, influenza viruses' detection raised up from week 4/2023 to week 22/2023, resulting in a return to a normal influenza activity compared to the 2022 period, where there was an extended influenza activity. Influenza A of subtype A(H1N1)pdm09 was dominant overall compared to A(H3N2), except in some regions of Tropical South America where influenza B virus of B-Victoria lineage from subclade 1A.3 dominated.[4] In the northern hemisphere and since week 13/2023, influenza activity remained below the epidemic threshold (10%) and at inter-seasonal levels in most European countries.[5,6]

Globally the number of influenza detection from weeks 17/2023 to 39/2023 was comparable to the same period in 2022, with influenza A of subtype A(H1N1)pdm09 dominant since February 2023.[4,6]

A(H1N1)pdm09 viruses were mostly attributed to the subclade 6B.1A.5a.2, which was mainly observed in Asia, Africa, Europe and Oceania. Viruses from subclade 5a.1 predominated in North America and some regions of the Central and South America. The HAI assays showed that most of the viruses of subclade 5a.2 were well recognised by ferret antisera raised against the southern hemisphere and northern hemisphere 2023 vaccine strains (egg- and cell culture-based A/Sydney/5/2021, cell culture-based A/Wisconsin/67/2022 and egg-propagated A/Victoria/4897/2022), while viruses from subclade 5a.1 were poorly recognised. [4]

Viruses from subtype A(H3N2) were dominant in few geographic regions, particularly in the temperate zones of the northern hemisphere. Most of the A(H3N2) viruses circulating during this monitoring period belonged to the clade 3C.2a1b.2a.2, with three predominant subclades, namely 2a.1b, 2b, and 2a.3a. While those two latter were present globally, 2a.1b viruses were mainly detected in North America and Europe. HAI assays showed that antisera raised against the 2023 vaccine strains (cell culture-based A/Darwin/6/2021-like and egg-based A/Darwin/9/2021-like 2a viruses) recognised the viruses from the subclade 2a well.[4]

One-third of the influenza viruses detected globally during the period of interest was of type B and all belonged to B/Victoria/2/87 lineage; clade 1A.3. which further diversified into the subclade 1A.3a with two main subgroups, 3a.1 and 3a.2. The subgroup 3a.2 was dominant worldwide, while few detections were observed for the 3a.1 viruses. Antigenic characterization demonstrated that post-infection ferret antisera raised

against the 2023 vaccine B/Austria/1359417/2021 virus recognised well the viruses from the dominant subgroup 1A.3a.2.[4]

According to the ECDC/WHO report[7] and up to week 35/2023 more than 6600 and 4200 viruses were tested for phenotypic and genotypic susceptibility to neuraminidase inhibitors (NAIs) and PA inhibitor (Baloxavir marboxil), respectively. Five A(H1N1)pdm09 viruses were identified to carry the mutation H275Y in the NA gene as a marker of highly reduced inhibition (HRI).[7]

3 Zoonotic influenza infections in humans

From week 17/2023 to week 39/2023, no samples were sent to the NRCI for suspicion of zoonotic influenza.

In 2023, two cases of A(H1N1)v were reported in Brazil and Netherland, both had history exposure to swines.[4] Three cases of A(H1N2)v were reported in Taiwan, one in China and 2 in the United States of America. One A(H3)v case was recorded in the United States of America.[8]

At the global scale and from 31st February 2023 to 22nd September 2023, four human cases of A(H5N6), one case of A(H3N8) and five cases of A(H9N2) were reported in China after exposure to infected birds.[4]

In 2023, 6 human cases of A(H5N1), including one death were reported in Cambodia.[9] The last two human confirmed cases were infected with a virus belonging to the 2.3.2.1c clade, which is the clade that has been circulating in Cambodia and Southeast Asia since 2013-2014. Two cases were detected in Chile and China. Four A(H5N1) cases were reported in Great Britain and Northern Ireland.[10] Phylogenetic analysis showed that the virus from those cases in Chile, China, and great Britain fell in the recent highly pathogenic avian influenza (HPAI) clade 2.3.4.4.b.[11-13]

To date, no human infection related to an A(H5N1) of mammalian origin has been identified.

Human infections with avian influenza remain generally seldom and the risk of infection with currently circulating avian A(H5Nx) influenza viruses of clade 2.3.4.4b in Europe remains low for the general population and low to moderate for the population exposed to infected bird or mammals. In Switzerland, no human cases have been reported to date.[14,15]

4 Avian influenza A[16] in animals

Avian influenza circulation remained high but constant since 2021 in animals. From 24th June to 1st September 2023, highly pathogenic avian influenza (HPAI) A(H5) viruses have been reported in wild (n=482) and domestic (n=25) birds among 21 countries in Europe. These outbreaks were most often detected along the coastlines than inland. In poultry and domestic birds, although at a lower level than the previous epidemiological year 2022, HPAI infections were widely distributed across many European countries and appear to be linked to seabirds' transmission. Regarding the outbreaks in wild birds, rookery-breeding seabirds are still the most impacted but the number of HPAI infections in other seabirds such as the waterfowl is increasing. The total number of HPAI detection in wild birds has already overpassed (n= 4'116) the one of the previous epidemiological year 2021-2022 (n=3'936).[16,17]

A(H5N1) transmission to mammals, continues to be reported, especially among American mink, red and arctic fox, and common raccoon dog bred in fur farms; most likely upon contact with gulls in Finland.[16]

At a global scale, wild mammals also continued to be affected, mostly red foxes and seal species. The risk of extinction for many species of cetacean and some of pinniped in Antarctica is increasing as spring migration includes wild birds from South America to breeding sites in Antarctic.

In Switzerland and since September 2020, several cases of HPAI A(H5) have been detected in wild (n =135) and domestics birds (n= 4).[18]

5 Ongoing project

The NRCI continues to collaborate with the Health 2030 Genome Centre DNA Sequencing and Data Analytics and Interpretation Platforms' team in order to evaluate Illumina's "Respiratory Virus Oligo Panel" kit performance. Preliminary tests including clinical samples positive for SARS-CoV-2, RSV, influenza A/B, coronaviruses-OC43/229E/NL63/HKU1, parainfluenza 1 to 4, human metapneumovirus and/or human bocavirus shown a good proportion of reads corresponding to the expected viruses and that we could obtain 80% to 100% genome coverage. Good consensus sequences were obtained for different viruses and in particular for Influenza A.

Currently, analyses including 192 clinical samples are in progress to further evaluate the sensitivity and specificity of this assay. Positive samples have Ct values ranging from 11 to 37.7, and consist in 100 influenza A, 50 RSV A/B, 7 OC43, 10 NL63, 4 229E and 1 HKU1 virus. Twenty-one samples negative for SARS-CoV-2, RSV, HCoV NL63, HKU1, OC43, 229E, HPIV1-4, HBoV, HAdV, RV/EV and HMPV were also included in this evaluation.

6 External quality controls

In order to assess our analytical performance, we participate yearly to different external quality assessment programs for the detection of Influenza, SARS-CoV-2 and other respiratory viruses.

The tables 2 to 6 below summarise the results of our external quality control assessments for the season 2022-2023.

Table 2. External Quality Assessment Programme panel 22 (2023) for influenza viruses/SARS-CoV-2 by RT-PCR (full score achieved)

Sample	Intended result	Your result
V01-2023	Influenza A(H1)pdm09	Influenza A(H1)pdm09
V02-2023	Influenza B	Influenza B (Victoria lineage)
V03-2023	Negative	Negative
V04-2023	SARS-CoV-2	SARS-CoV-2
V05-2023	SARS-CoV-2	SARS-CoV-2
V06-2023	Influenza A(H3)	Influenza A(H3)
V07-2023	Influenza A(H7)	Influenza A(H7)
V08-2023	SARS-CoV-2	SARS-CoV-2
V09-2023	Negative+	RSV
V10-2023	Influenza A(H5)	Influenza A(H5N1)
V11-2023	Influenza A(H9)	Influenza A(H9)
V12-2023	SARS-CoV-2	SARS-CoV-2
V13-2023	Influenza B	Influenza B (Yamagata lineage)
V14-2023	Influenza A(H5)	Influenza A(H5N1)
V15-2023	Influenza A(H1)pdm09	Influenza A(H1)pdm09

+ Sample contains respiratory syncytial virus (RSV). Only results for influenza viruses and SARS-CoV-2 are scored.

Table 3. External Quality Assessment Programme panel 22 (2023) for influenza viruses antiviral susceptibility testing (full score achieved)

Sample	Results	Genotypic testing		Phenotypic testing	
		Amino acid substitution* (Nucleotide change detected)	Associated with (highly) reduced susceptibility	Oseltamivir	Zanamivir
A(H1N1)pdm09 NAI01P-2023 NAI01G-2023	Intended	H275Y (823T)	Yes	(Highly) reduced inhibition	Normal inhibition
	Submitted	H275Y (C823T)	Yes (Oseltamivir)	Highly reduced inhibition	Normal inhibition
A(H1N1)pdm09 NAI02P-2023 NAI02G-2023	Intended	Wild type^	No	Normal inhibition	Normal inhibition
	Submitted	NA- no mutation, PA- I38T (T113C)	Yes (Baloxavir)	Normal inhibition	Normal inhibition
A(H1N1)pdm09 NAI03P-2023 NAI03G-2023	Intended	Mixture of wild type and H275Y (C823T)	Yes	(Highly) reduced inhibition	Normal inhibition
	Submitted	H275Y (C823T)	Yes (Oseltamivir)	Highly reduced inhibition	Normal inhibition
B(Victoria) NAI04P-2023 NAI04G-2023	Intended	Wild type	No	Normal inhibition	Normal inhibition
	Submitted	Wild type	No	Normal inhibition	Normal inhibition

* Residue position in N1 neuraminidase numbering

^ Sample contains PA-I38T substitution associated with reduced susceptibility to baloxavir (for educational purpose)

Table 4. Quality Control for Molecular Diagnostics (QCMD) 2023 Respiratory I/II Program (QAV164188_89, full score achieved)

Sample No.	Intended results	Obtained results	Sample No.	Intended results	Obtained results
RESPI23C1-01	Negative	Negative	RESPII23C1-01	HMPV	HMPV
RESPI23C1-02	RSV	RSV	RESPII23C1-02	RV	RV
RESPI23C1-03	IB	IB	RESPII23C1-03	Negative	Negative
RESPI23C1-04	IB	IB	RESPII23C1-04	HPIV1	HPIV1/3
RESPI23C1-05	IA	IA	RESPII23C1-05	ADV	ADV
RESPI23C2-01	IA	IA	RESPII23C2-01	OC43	OC43
RESPI23C2-02	IA; RSV	IA; RSV	RESPII23C2-02	RV	RV
RESPI23C2-03	IA	IA	RESPII23C2-03	ADV	ADV
RESPI23C2-04	IB	IB	RESPII23C2-04	HCoV NL63	HCoV NL63
RESPI23C2-05	VRS	VRS	RESPII23C2-05	HPIV1	HPIV1/3

Table 5. Panel EEQIAP 2023 molecular detection, antigenic and genetic characterization

Sample No.	Subtype/Lineage	Antigenic Category	Genetic Category *
EISN_INF23-01	A(H1N1)pdm09	NA	6B.1A.5a.2a.1 (5a.2a.1) representative A/Norway/25089/2022
EISN_INF23-02	A(H3N2)	NA	3C.2a1b.2a.2b (2b) representative A/Bangladesh/4005/2020
EISN_INF23-03	B/Victoria	NA	NA
EISN_INF23-04	A(H3N2)	NA	3C.2a1b.2a.2a.3 (2a.3) representative A/Darwin/9/2021
EISN_INF23-05	NA	No characterisation	No characterisation
EISN_INF23-06	A(H1N1)pdm09	NA	6B.1A.5a.1 (5a.1) representative A/GuangdongMaonan/SWL1536/2019
EISN_INF23-07	B/Victoria	NA	NA
EISN_INF23-08	A(H3N2)	NA	3C.2a1b.1a representative A/Denmark/3264/2019

*reference Tessy, NA = not applicable

Reference Tessy: https://www.ecdc.europa.eu/sites/default/files/documents/respiratory-virus-surveillance-reporting-protocol-version-1-2.pdf

Table 6. Panel EEQIAP 2023 phenotypic and genotypic antiviral susceptibility

Sample No.	Phenotypic testing		Genotypic testing		
	Oseltamivir	*Zanamivir*	*Oseltamivir*	*Zanamivir*	*Baloxavir Marboxil*
EISN_INF23-01	Not tested		AANI	AANI	NA
EISN_INF23-02	Not tested		AANI	AANI	NA
EISN_INF23-03	Not tested		AANI	AANI	Not tested
EISN_INF23-04	Not tested		AANI	AANI	NA
EISN_INF23-05	Not tested		Not tested	Not tested	Not tested
EISN_INF23-06	Not tested		AANI	AANI	NA
EISN_INF23-07	Not tested		AANI	AANI	NA
EISN_INF23-08	Not tested		AANI	AANI	NA
EISN_AV23-01 (H275Y)	HRI	NI	AAHRI	AANI	NA
EISN_AV23-02	NI	NI	AANI	AANI	NA
EISN_AV23-03 (del245-248)	HRI	NI	AAHRI	AARI	NA

NI= normal inhibition (fold-change IC50; A<10; B<5)

RI = reduced inhibition (fold-change IC50; A≥10 and ≤100; B≥5 and ≤ 50)

HRI = highly reduced inhibition (fold-change IC50; A≥100 ; B≥50)

AANI = no amino acid substitutions previously associated with RI

AARI_ amino acid substitutions previously associated with RI

AAHRI_ amino acid substitutions previously associated with HRI

NA= not applicable

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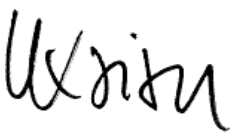

Annex 1: Description of the observed co-detections, n=23 (17/2023-39/2023)

Weeks	Co-detections				
17	RV-EV/IB	HPIV1-3/RV-EV			2
18	HMPV/HAdV	HPIV1-3/HAdV			2
19	HPIV1-3/HBoV				1
21	HPIV1-3/RV-EV/ HCoVNL63				1
26	SARS-CoV2/ HAdV	HCoVOC43/RV-EV			2
27	RV-EV/SARS-CoV2				1
32	HPIV2-4/ SARS-CoV2	HPIV1-3/RV-EV			2
33	RV-EV/HAdV				1
35	HPIV2-4/ SARS-CoV2				2
36	RV-EV/HPIV2-4/ SARS-CoV2	RV-EV/SARS-CoV2			2
38	RV-EV/SARS-CoV2	SARS-CoV2/ HAdV	HPIV1-3/SARS-CoV2	RV-EV/SARS-CoV2	4
39	RV-EV/SARS-CoV2	RV-EV/SARS-CoV2	RV-EV/SARS-CoV2		3
Total					23

Annex 2: Lists of Influenza isolates submitted to GISAID (2023)

Collection date	Isolate-ID	Isolate name
2023-Jan-09	EPI_ISL_18101352	A/Switzerland/90292/2023
2023-Jan-09	EPI_ISL_18101353	A/Switzerland/02256/2023
2023-Jan-10	EPI_ISL_18101354	A/Switzerland/02543/2023
2023-Jan-11	EPI_ISL_18102595	B/Switzerland/81294/2023
2023-Jan-12	EPI_ISL_18101355	A/Switzerland/37489/2023
2023-Jan-16	EPI_ISL_18101356	A/Switzerland/57488/2023
2023-Jan-17	EPI_ISL_18101357	A/Switzerland/70155/2023
2023-Jan-16	EPI_ISL_18101358	A/Switzerland/70240/2023
2023-Jan-19	EPI_ISL_18101359	A/Switzerland/92881/2023
2023-Jan-20	EPI_ISL_18101360	A/Switzerland/24098/2023
2023-Jan-23	EPI_ISL_18101361	A/Switzerland/35896/2023
2023-Jan-23	EPI_ISL_18101387	B/Switzerland/23779/2023
2023-Jan-23	EPI_ISL_18101388	B/Switzerland/24096/2023
2023-Jan-24	EPI_ISL_18101389	B/Switzerland/35829/2023
2023-Jan-24	EPI_ISL_18101390	B/Switzerland/57816/2023
2023-Jan-25	EPI_ISL_18101362	A/Switzerland/57971/2023
2023-Jan-26	EPI_ISL_18101391	B/Switzerland/57873/2023
2023-Jan-30	EPI_ISL_18101392	B/Switzerland/02574/2023
2023-Feb-01	EPI_ISL_18101363	A/Switzerland/13142/2023
2023-Feb-01	EPI_ISL_18101364	A/Switzerland/13356/2023
2023-Feb-03	EPI_ISL_18101365	A/Switzerland/45434/2023
2023-Feb-03	EPI_ISL_18101397	B/Switzerland/58676/2023
2023-Feb-06	EPI_ISL_18101393	B/Switzerland/44993/2023
2023-Feb-06	EPI_ISL_18101394	B/Switzerland/45225/2023
2023-Feb-06	EPI_ISL_18101395	B/Switzerland/45344/2023
2023-Feb-06	EPI_ISL_18101396	B/Switzerland/58634/2023
2023-Feb-06	EPI_ISL_18101366	A/Switzerland/58518/2023
2023-Feb-07	EPI_ISL_18101398	B/Switzerland/83630/2023
2023-Feb-08	EPI_ISL_18101367	A/Switzerland/83341/2023
2023-Feb-08	EPI_ISL_18101369	A/Switzerland/95050/2023
2023-Feb-09	EPI_ISL_18101368	A/Switzerland/94869/2023
2023-Feb-16	EPI_ISL_18101372	A/Switzerland/85635/2023
2023-Feb-17	EPI_ISL_18101370	A/Switzerland/28184/2023
2023-Feb-17	EPI_ISL_18101399	B/Switzerland/06471/2023
2023-Feb-17	EPI_ISL_18101400	B/Switzerland/28151/2023
2023-Feb-17	EPI_ISL_18101401	B/Switzerland/39981/2023
2023-Feb-17	EPI_ISL_18101402	B/Switzerland/40332/2023
2023-Feb-17	EPI_ISL_18101403	B/Switzerland/51739/2023
2023-Feb-17	EPI_ISL_18101404	B/Switzerland/51768/2023

Collection date	Isolate-ID	Isolate name
2023-Feb-17	EPI_ISL_18101405	B/Switzerland/51774/2023
2023-Feb-22	EPI_ISL_18101406	B/Switzerland/20984/2023
2023-Feb-22	EPI_ISL_18101371	A/Switzerland/40234/2023
2023-Feb-22	EPI_ISL_18101373	A/Switzerland/32897/2023
2023-Feb-24	EPI_ISL_18101375	A/Switzerland/76199/2023
2023-Feb-25	EPI_ISL_18101374	A/Switzerland/64417/2023
2023-Feb-27	EPI_ISL_18101407	B/Switzerland/64623/2023
2023-Feb-27	EPI_ISL_18101408	B/Switzerland/64703/2023
2023-Feb-27	EPI_ISL_18101377	A/Switzerland/76467/2023
2023-Feb-28	EPI_ISL_18101409	B/Switzerland/76130/2023
2023-Feb-28	EPI_ISL_18101376	A/Switzerland/76424/2023
2023-Mar-07	EPI_ISL_18101378	A/Switzerland/43530/2023
2023-Mar-07	EPI_ISL_18101379	A/Switzerland/66700/2023
2023-Mar-03	EPI_ISL_18101410	B/Switzerland/19819/2023
2023-Mar-03	EPI_ISL_18101411	B/Switzerland/20084/2023
2023-Mar-06	EPI_ISL_18101412	B/Switzerland/43256/2023
2023-Mar-10	EPI_ISL_18101380	A/Switzerland/87207/2023
2023-Mar-13	EPI_ISL_18101413	B/Switzerland/00213/2023
2023-Mar-14	EPI_ISL_18101381	A/Switzerland/10945/2023
2023-Mar-14	EPI_ISL_18101382	A/Switzerland/11159/2023
2023-Mar-17	EPI_ISL_18101414	B/Switzerland/54058/2023
2023-Mar-20	EPI_ISL_18101415	B/Switzerland/77230/2023
2023-Mar-21	EPI_ISL_18101383	A/Switzerland/77757/2023
2023-Mar-22	EPI_ISL_18101416	B/Switzerland/00528/2023
2023-Mar-23	EPI_ISL_18101384	A/Switzerland/20498/2023
2023-Mar-27	EPI_ISL_18101417	B/Switzerland/45220/2023
2023-Mar-28	EPI_ISL_18101418	B/Switzerland/45191/2023
2023-Mar-30	EPI_ISL_18101419	B/Switzerland/68807/2023
2023-Mar-31	EPI_ISL_18101420	B/Switzerland/89489/2023
2023-Apr-03	EPI_ISL_18101421	B/Switzerland/01331/2023
2023-Apr-04	EPI_ISL_18101422	B/Switzerland/13177/2023
2023-Apr-06	EPI_ISL_18101423	B/Switzerland/55100/2023
2023-Apr-05	EPI_ISL_18101424	B/Switzerland/24464/2023
2023-Apr-17	EPI_ISL_18101425	B/Switzerland/21410/2023
2023-Apr-17	EPI_ISL_18101426	B/Switzerland/21226/2023
2023-Apr-18	EPI_ISL_18101427	B/Switzerland/21682/2023
2023-Apr-24	EPI_ISL_18101385	A/Switzerland/85043/2023
2023-Apr-26	EPI_ISL_18101428	B/Switzerland/07551/2023
2023-May-03	EPI_ISL_18101429	A/Switzerland/77731/2023