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Swiss national RSV, SARS-CoV-2 and Influenza genomic surveillance program: January to May 2025

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1. Summary:

This report covers the samples collected between 17th January, 2025 and May 21 (depending on the virus), corresponding to the fourth sequencing batch of the integrated RSV, SARS-CoV-2 and influenza genomic surveillance program of the 2024/2025 season.

Many of the samples (63/156, 40%) originate from the Sentinella program (21 (IA) + 33 (IB) + 5 (RSV) + 4 (SC2)), complemented by a random selection of samples originating from 5 hospital laboratories (Table 1, Table 2 and Table 3).

A total of 156 samples were processed at the Health 2030 Genome Center, yielding 146 sequences successfully submitted to GISAID: **66 SARS-CoV-2**, **58 influenza** (26 A [15 H1N1, 11 H3N2], 32 B), **and 22 RSV** (8 RSV-A, 14 RSV-B).

The proportion of SARS-CoV-2, influenza, and RSV viruses across the batch reflects continued co-circulation of multiple respiratory viruses in Switzerland during the late winter and spring period.

The most common lineage for SARS-CoV-2 was LP.8.1, currently decreasing in frequency and represent 49% of positive sequences. According to GISAID, two sequences (3%) of the new NB.1.8.1 variant under monitoring have been retrieved in the last sequencing batch. For influenza viruses, 55% of the sequences were Influenza B and 45% were Influenza A: of the Influenza A sequences, 58% (15/26) belonged to the H1N1 subtype, while 42% (11/26) belonged to the H3N2 subtype. For RSV, 36% (8/22) of the sequences were RSV-A, and 64% (14/22) were RSV-B.

No influenza mutations associated with resistance to oseltamivir or baloxavir were identified. RSV samples showed no mutations associated with resistance to nirsevimab or palivizumab. Likewise, no high-level nirmatrelvir/ritonavir resistance mutations were observed in the circulating SARS-CoV-2 strains.

Sequencing success overall was high: 90% (66/73) for SARS-CoV-2, 95% (58/61) for influenza, and 100% (22/22) for RSV. The next sequencing batch will be the last of this phase including only SARS-CoV-2 positive specimens and is expected to be sent for sequencing in September 2025

Table 1: Origin of the samples and success of the sequencing

	SARS-CoV-2	Influenza	RSV
Sentinella	4	54 (21 A(10 H1N1 and 11 H3N2), 33 B)	5 (3 A, 2 B)
Laboratory network	69	7 (6 A (6 H1N1 and 0 H3N2), 1 B)	17 (5 A, 12 B)
Total	73	61 (27 A, 34 B)	22 (8 A, 14, B)
Number of sequences successfully deposited in GISAID	66	58 (26 A (15 H1N1 and 11 H3N2), 32 B)	22 (8 A, 14 B)

Table 2: Sentinella positive specimens (from 21.03.2025 to 21.05.2025)

	SARS-CoV-2	Influenza	RSV
Total number of positive specimens	10	84 (39 A, 45 B)	17
Meeting sequencing criteria*	4	54 (21 A, 33B)	5
Included**	4	54 (21 A, 33 B)	5

Table 3: Detailed origin of samples by originating lab.

Site	SARS-CoV-2	Influenza	RSV
CHUV	15	4	0
HUG	27	0	0
ICH	0	0	0
IFIK	4	3	0
IMV	13	0	7
USB	10	0	10
Total	69	7	17

SARS-CoV-2 lineages

Figure 1: The proportion of Swiss sequences belonging to each pango lineage is available online at https://covariants.org/per-country?region=World.

Of note, sequencing analyses revealed the presence of two N.1.8.1 samples, both from the canton of Vaud and collected on May 19, 2025 according to GISAID.

Escape mutation prevalence

Currently, no monoclonal antibodies available in Switzerland are effective at neutralizing the vast majority of the SARS-CoV-2 sub-lineages circulating in Switzerland and the rest of the world. The 3CL protease inhibitor, nirmatrelvir/ritonavir Paxlovid®, remains effective against SARS-CoV-2, and we are monitoring the prevalence of mutations that have been shown to reduce its efficacy by 5-fold or more (table 4).

No resistance mutations were spotted in Switzerland.

Table 4: Prevalence NSP5 mutations of SARS-CoV-2 leading to resistance from nirmatrelvir/ritonavir Paxlovid®

Mutation	Switzerland	Mutation	Switzerland
T25A	0	P168Del	0
F140L/S	0	H172L/N/Q/Y	0
G143S	0	A173V	0
S144A/E/L/P	0	R188G	0
M165R/T	0	Q189K	0
E166A/G/K/V	0	Q192A/C/D/E/F/G/H/I/K/L/P/R/S/T/V/W/Y	0
L167F	0	P252L	0

Data based on the Stanford University 3CLpro inhibitors mutation list (only mutations causing more than a 5-fold reduction in nirsevimab susceptibility are depicted here).

Influenza lineages

45 percent of influenza sequences belonged to Influenza A, and 55% belonged to Influenza B.
Of the Influenza A sequences, 58% were assigned to the H1N1 subtype, while 42% were assigned to the H3N2 subtype.

Table 5: Resistance mutations to influenza antivirals mostly used in Switzerland

A(H1N1)pdm09			A (H3N2)			Influenza B		
Mutation	Switzerland	Europe	Mutation	Switzerland	Europe	Mutation	Switzerland	Europe
NAI : Oseltamivir			NAI : Oseltamivir			NAI : Oseltamivir		
S110F	0	0	**E119I/V**	0	0	**G104E**	0	0
E119A/D/V	0	0	D151E	0	0	E105K	0	0
R152K	0	0	**R224K**	0	0	**G108E**	0	0
D199E/G/Y	0	0	N245Y	0	0	**E117A/D/G/V**	0	0
I223K/L/R/T	0	1/0/0/3	**Del245-248f**	0	0	**P139S**	0	0
S247G/R	0	1	**Del247-250f**	0	0	**G140R**	0	0
H275Y	0	55	K249E	0	3	T146K/P	0	0
R293K	0	0	E276D	0	0	**R150K**	0	0
N295S	0	0	**R292K**	0	0	K152M/N	0	0
I427T	0	0	**N294S**	0	0	D197E/N/**Y**	0	0
I436N	0	0	N329K/R	0	0	A200T	0	0
P458T	0	0	S331R	0	7	**I221L/N/T**	0	0
			R371K	0	0	A245T	0	0
			Q391K+K249E	0	0	H273Y	0	0
			E119V+T148I	0	0	**R292K**	0	0
			E119V+I222L/V	0	0	N294S	0	0
						R374K	0	0
						A395E	0	0
						H439P	0	0
						Y142H+G145R	0	0
						T146P+N169S	0	0
PAI: Baloxavir			Baloxavir			Baloxavir		
I38S/T	0	0/1	**I38T**	0	0	I38F/M/T/V	0	0
I38F/L/M/V	0	1/0/0/1	I38F/L/M/N/S/V	0	0			
			L28P	0	0			
E23 G/K/R	0	1/2/0	E23G/K/R	0	0	E23K	0	0
K34R	0	1	K34R	0	0			
			A36V	0	0			
A37T	0		A37T	0	0			
			E119D	0	0			
E198 K	0		E198K	0	0			
E199D/G	0		E199G	0	0			
						E120De	0	0
						G199R	0	0

Mutations depicted in this table cause reduced inhibition (RI) (for influenza A: 10 to 100 fold increase in IC_{50} values; for influenza B: 5 to 50 fold increase in IC_{50} values), or highly reduced inhibition, in bold (HRI) (for influenza A: >100 fold increase in IC_{50} value; for influenza B: > 50 fold increase in IC_{50} value).
NAI: neuraminidase inhibitor (resistance mutation located in the neuraminidase protein)
PAI: inhibitor of the cap endonuclease of the acidic protein baloxavir (resistance mutation located in the PA). Data based on last WHO algorithm (v2023).

RSV

RSV has two main immunogenic targets, the F-protein and the G- Protein. Currently available monoclonal antibodies target the F-protein. F-protein and G-protein mutations were common.

Table 6 : Resistance mutations to monoclonal antibodies available in Switzerland with a anti-RSV activity

RSV-A		
Mutation	Switzerland	Europe
Resistance to nirsevimab		
N671 + N208Y	0	
K68E	0	
Resistance to palivizumab		
K272 M/T	0	
S275F	0	

RSV-B		
Mutation	Switzerland	Europe
Resistance to nirsevimab		
I64T	0	
I64M + K65R	0	
K68E/Q	0	
K68N	0	
N201S/T	0	
N208S/D	0	
K65Q/T	0	
Resistance to palivizumab		
K272N/Q	0	
K272R	0	
KN63R	0	

Mutations depicted in this table cause either have shown to cause a proven resistance to the mAb (highlighted in bold), either to possibly reduce the neutralization by the mAb. Only resistance causing more than a 5 fold reduced neutralization are presented here.
List of mutations originates from the last ANRS – MIE Respiratory viruses group mutation list combined with literature review (https://virusfrenchresistance.org/virus-french-resistance-rsv/, *Fourati*, Lancet, 2024).

Escape mutation prevalence

No escape mutation conferring a high resistance to anti-RSV mAbs available in the Swiss market have been retrieved in the sequencing batch.

Methods:

Samples originate from the **Sentinella** surveillance program (40% in this batch), which reflects the circulation of viruses in the outpatient community. These are complemented by samples collected from six major tertiary hospital laboratories (60%): **Institut für Medizinische Virologie (IMV)** in Zurich, **Centre Hospitalier Universitaire Vaudois (CHUV)** in Lausanne, **Hôpitaux Universitaires de Genève (HUG)** in Geneva, **Universitätsspital Basel (USB)**, **Institut Central des Hôpitaux (ICH)** in Sion, and **Institut für Infektionskrankheiten (IFIK)** in Bern. Samples are obtained from both outpatient departments and hospital wards to reach a predefined target of approximately **200 samples per batch**. In this batch only 158 samples were received by the Genome Center.
Only samples that meet the **sequencing criteria*** are sent for sequencing.

Note that all Sentinella specimen are processed at the Geneva University Hospitals laboratory of virology.

*Sequencing criteria

- Influenza and RSV : Ct values ≤ 25; SARS-CoV-2: Ct value ≤ 28
- AND absence of co-infection with another respiratory virus

**Reasons for Sentinella specimen meeting sequencing criteria not to be sent to sequencing: missing tube, not enough volume, other reason

Samples are processed with the Illumina Respiratory Virus Oligo Panel according to manufacturer's instructions. Analyses are performed by the 2030 Health Genome Center and transferred to the Swiss Pathogen Surveillance platform (SPSP) before submission in GISAID, as recommended by WHO.

Analysis of resistance mutation is performed by the team of Richard Neher, based on specific mutations list for each virus determined either by WHO documentation, literature review, or other available algorithms.

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https://bsse.ethz.ch/cevo/research/sars-cov-2/swiss-sars-cov-2-sequencing-consortium.html

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