Respiratory Viruses in Luxembourg (ReViLux)

Weekly report (28 December 2022)

Executive summary

The sentinel network detected a very high epidemic activity over the last week, based on 16.0% of consultations being associated with influenza-like illness.

Within the specimens collected by the sentinel network, Influenzavirus A was the most frequently detected virus over the last two weeks (50.6% positivity rate), followed by Human rhinovirus (14.6%) and Metapneumovirus (12.6%). Genotyping analyses showed that the most frequent Respiratory syncytial virus strain during the current season is RSV-B (71.3%), and the most frequent influenzavirus A is H3 (96.4%).

Regarding the SARS-CoV-2 genomic surveillance, The Omicron BQ.1 lineage is the most frequent one (67.6%, confidence interval: 61.8 - 73.5%), followed by Omicron BA.5 (19.7%, confidence interval: 14.7 - 24.7%).

IN THE SPOTLIGHT

Influenzavirus is the causative agent of flu (*grippe*). Currently, there is a generalised outbreak in the northern hemisphere driven by type A virus (and especially H3N2). In the Greater Region, the influenza activity remains very high in Luxembourg and France, and high in Germany.

BQ.1 and its sublineages are a subtype of Omicron BA.5. There are no data yet suggesting higher severity than other Omicron lineages, but it carries some mutations that have been associated to escape immunity from previous BA.5 infections, which suggests a higher reinfection risk. Vaccine protection against infection might be reduced, but protection against severe disease is not expected to be affected.

XBB is a recombinant of two SARS-CoV-2 lineages, BA.2.10.1 and BA.2.75. Early evidence suggests higher reinfection risk compared to other circulating lineages, due to the mutations it carries in the Receptor-Binding Domain of the spike protein. Nevertheless, there is no evidence suggesting an increase in severity.

Introduction

The Laboratoire national de santé, as **National Reference Laboratory for Acute Respiratory Infections** in Luxembourg, performs close surveillance on respiratory viruses, with a special focus on SARS-CoV-2. The main monitoring activities are:

- **The Sentinel Surveillance**. It provides a broad picture of respiratory diseases affecting the Luxembourgish population, based on clinical and laboratory data.

- **The SARS-CoV-2 Genomic Surveillance**. It enables detailed observation of SARS-CoV-2 variants and mutations through time and space, as well as studying specific groups of interest.

The objective of the ReViLux report is to inform public health actions in Luxembourg.

Sentinel Surveillance Network

The Sentinel Surveillance aims at monitoring the circulating respiratory viruses, from traditional ones like Influenza to more recent ones like SARS-CoV-2, and hence underpin public health actions. The Sentinel Network is a group of general practitioners and paediatricians spread over the country. They report the weekly number of patients showing symptoms suggestive of acute respiratory infection (ARI) and influenza-like illness (ILI), and those patients are then sampled and tested for a panel of respiratory viruses. The circulation of respiratory viruses in the north hemisphere is generally monitored by seasons that go from week 40 to week 20. The period between weeks 20 and 40 is usually called interseason.

Clinical results

Last week, 16.0% of consultations were reported as ILI, which represents a very high epidemic activity for Luxembourg, according to ECDC and the Moving Epidemic Method. The history of ILI consultations is displayed in Figure 1, and a detailed summary of the number of ARI and ILI cases during the last four weeks is included in Table 1.

Laboratory results

Over the last two weeks, the most frequently detected viruses (and their positivity rates) were Influenzavirus A (50.6%), Human rhinovirus (14.6%) and Metapneumovirus (12.6%). An overview of the viral circulation during the current season is displayed in Figure 2 and Table 2.
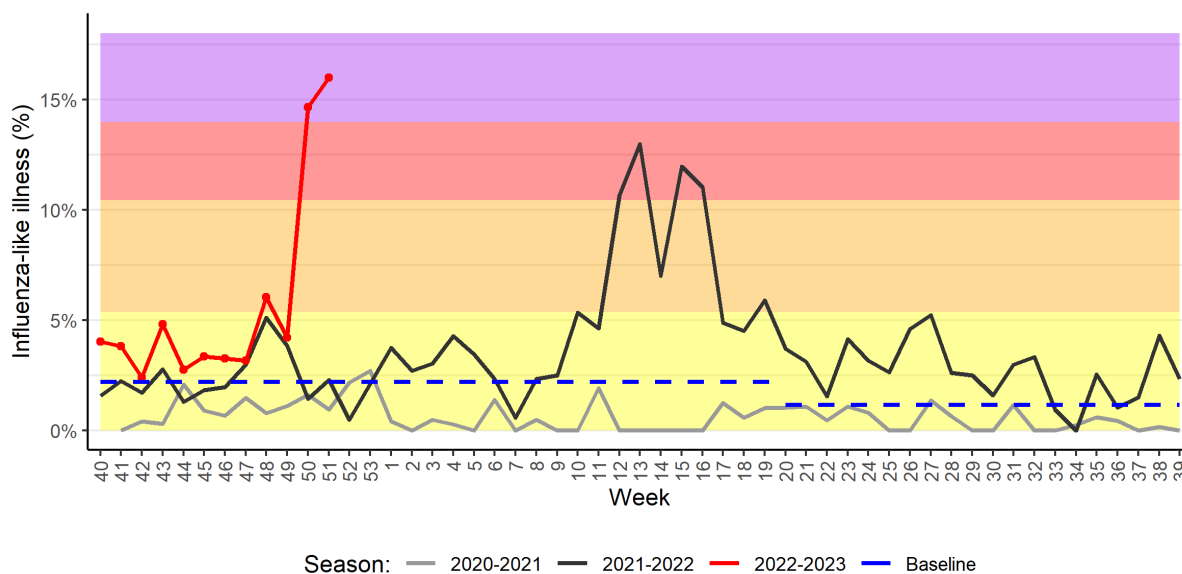
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Figure 1. Percentage of patients with influenza-like illness over the last three seasons
Background colours according to intensity of circulation: low, medium, high, very high.

Table 1. Syndromic surveillance over the last 4 weeks

Week	ARI		ILI		Total consultations
	N	%	N	%	
2022/48	129	21.61	36	6.03	597
2022/49	98	19.60	21	4.20	500
2022/50	82	17.15	70	14.64	478
2022/51	60	20.00	48	16.00	300

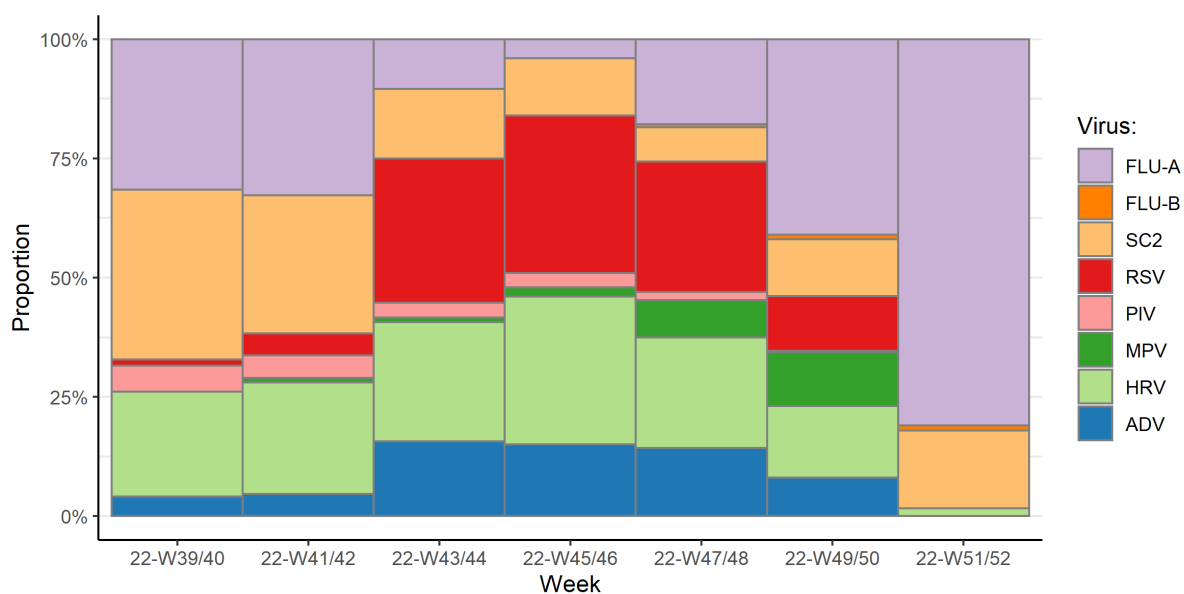*ARI: Acute Respiratory Infections; ILI: Influenza-Like Illness.*

Figure 2. Distribution of respiratory viruses detected within the Sentinel Network, by two-week periods. Results from last weeks are not yet consolidated.
FLU-A: influenzavirus A; FLU-B: influenzavirus B; PIV: parapneumovirus; RSV: respiratory syncytial virus; ADV: adenovirus; MPV: metapneumovirus; HRV: human rhinovirus; SC2: SARS-CoV-2.

Table 2. Distribution of respiratory viruses detected within the Sentinel Network over the last 2 weeks compared to the interseason period.

Virus	Last 2 weeks		Season 2022/2023	
	N*	Positivity rate (%)	N*	Positivity rate (%)
Influenzavirus A	247	50.6	322	27.5
Human rhinovirus	30	14.6	177	21.3
SARS-CoV-2	50	10.3	154	14.4
Respiratory syncytial virus	15	7.3	149	17.9
Adenovirus	12	5.8	86	10.3
Metapneumovirus	26	12.6	52	6.3
Parainfluenzavirus	1	0.5	18	2.2
Influenzavirus B	3	0.6	6	0.5
Total	**384**		**964**	

*Co-infection cases counted once for each virus detected.

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Genotyping analyses

In order to assess the circulation of viral strains, genotyping analyses were also performed for Influenzavirus A and Respiratory syncytial virus (RSV) (Figure 3). During the current season, the most frequently detected strain for Influenzavirus A was H3 (96.4%), and for RSV it was type B (71.3%).
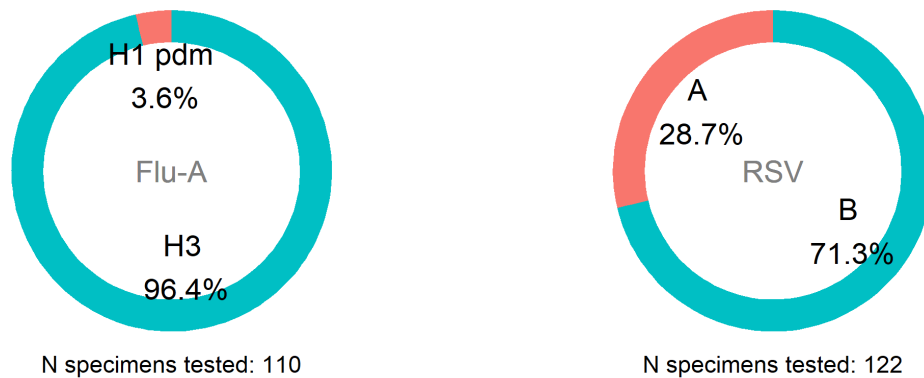

N specimens tested: 110   N specimens tested: 122

Figure 3. Detection of influenzavirus-A (Flu-A) and Respiratory syncytial virus (RSV) strains in sentinel samples during the current season.

SARS-CoV-2 Genomic Surveillance

SARS-CoV-2 has posed a serious threat to the world population since 2020, and it is still a challenge for health systems. For this reason, the National Reference Laboratory for Acute Respiratory Infections at LNS continues to monitor the genomic characteristics of the SARS-CoV-2 virus detected in Luxembourg.

LNS receives positive specimens (nasopharyngeal or oropharyngeal swabs analysed by RT-PCR) from the national network of laboratories. All hospital specimens are sequenced, as well as a representative selection of community specimens. Illumina and Nanopore devices are used respectively. When needed, an additional screening by targeted PCR is also performed to enable earlier evaluation of the spread of newly emerging variants.

Bioinformatic analyses are based on a standardised pipeline, and lineage assignment is performed through the PANGOLin software (4.1.3, pango-data 1.16, mode UShER). In order to allow easier visualisation, WHO and Nextstrain categorisations are also used.

Sequencing activity

In week 50, 1464 new cases were registered in Luxembourg; hence, the minimum sample size required to detect emerging variants at a 5% incidence is estimated to be 244 specimens (16.7%). The microbial genomics unit at LNS sequenced 358 specimens from the week of study, including 307 national ones (sequencing coverage: 21.0%; see Figure 4). This reaches the recommended sample size.
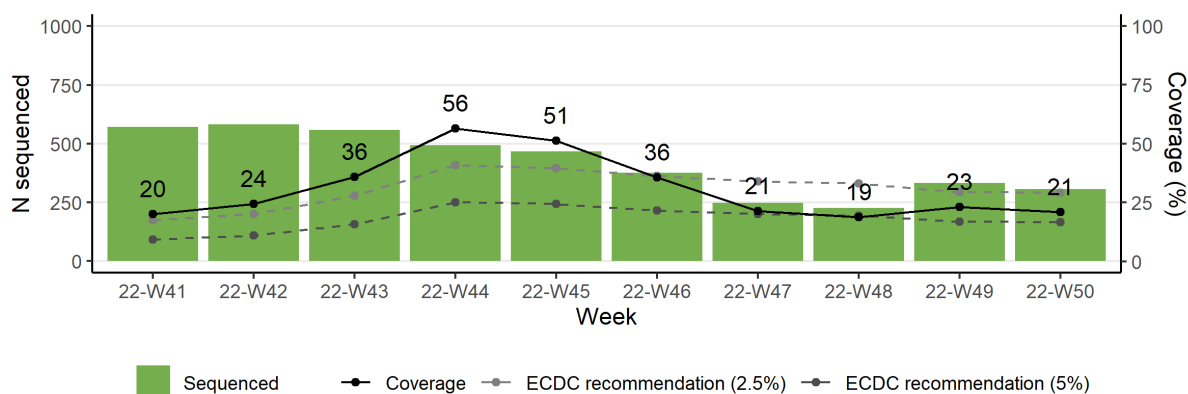

Figure 4. Number of specimens sequenced and national coverage based on weekly number of positive cases in Luxembourg. The coverage from the last two weeks is not consolidated yet.

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Variant circulation

The Omicron variant remains the main one detected within the representative sample, the most frequent subvariant being Omicron BQ.1 (67.6%), followed by Omicron BA.5 (19.7%).

An overview of the variants and lineages circulating over the last weeks is displayed in Figure 5, and further details are shown in Table 3. The history of the circulation of each variant since January 2021 is displayed in Figure 6.
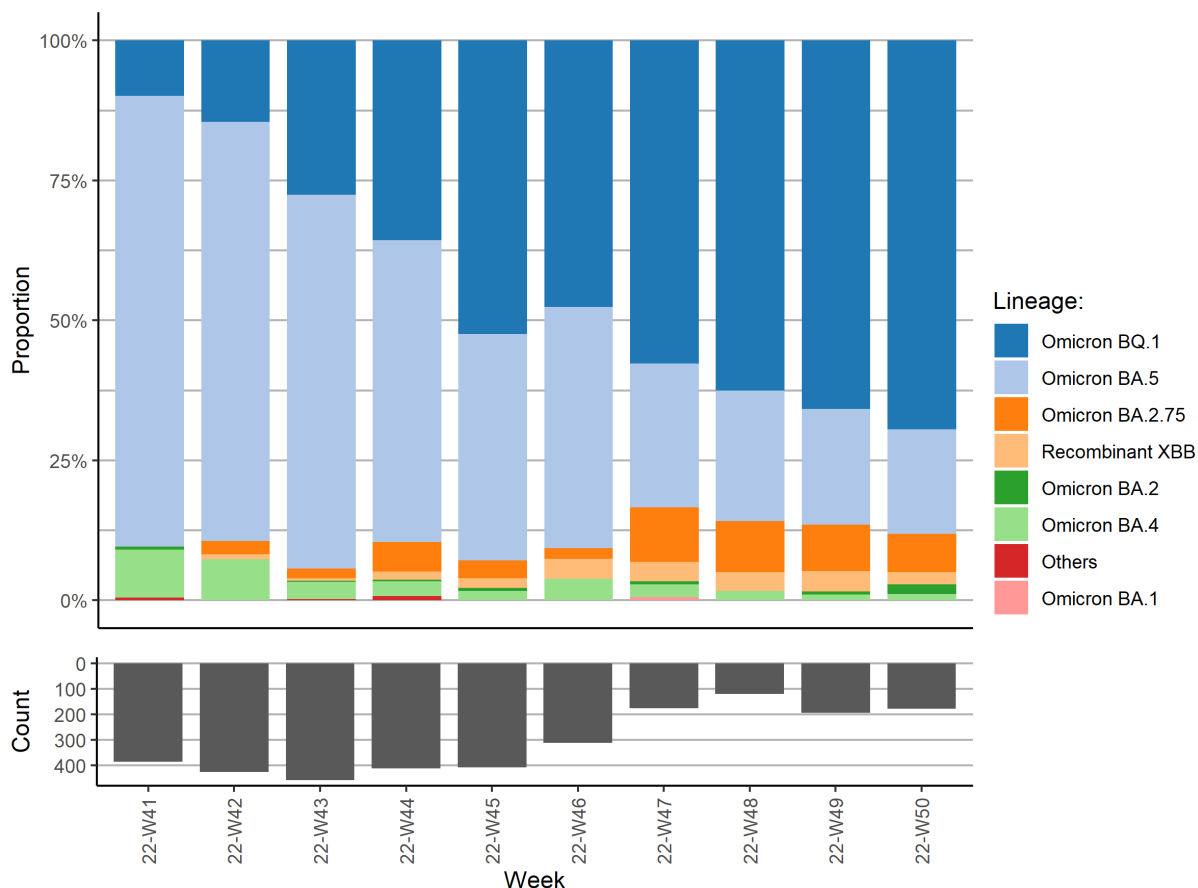

Figure 5. Distribution of lineages within the representative sample during the last 10 weeks.

Table 3. Distribution of SARS-CoV-2 lineages detected within the representative sample during the last two weeks. Previously reported cases might be updated by retrospective analysis.

Lineage*	Week 49		Week 50	
	%	CI %	%	CI %
Omicron BQ.1	58.8	52.7 - 65.0	67.6	61.8 - 73.5
Omicron BA.5	28.0	22.3 - 33.6	19.7	14.7 - 24.7
Omicron BA.2.75	7.8	4.4 - 11.2	7.0	3.8 - 10.2
Recombinant XBB	4.1	1.6 - 6.6	2.5	0.5 - 4.4
Omicron BA.2	0.0	-	2.0	0.3 - 3.8
Omicron BA.4	1.2	0.0 - 2.6	1.2	0.0 - 2.6

*CI: Confidence Interval at 95%. *Sub-lineages BA.2.75 and BQ.1 are not included in the count of their parental lineages (BA.2 and BA.5, respectively).*
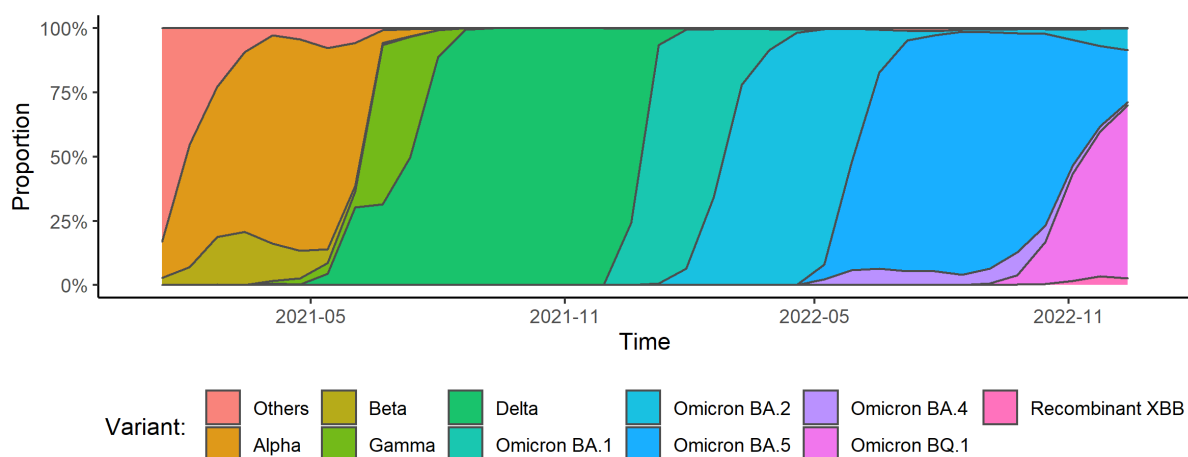
Figure 6. Proportion of each variant circulating in Luxembourg since January 2021.

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Clinical and epidemiological factors

In this section, the lineage distribution of all specimens sequenced over the last month is assessed by demographics (sex and age group, Figure 7) and sampling setting (community vs. hospital, Table 4).
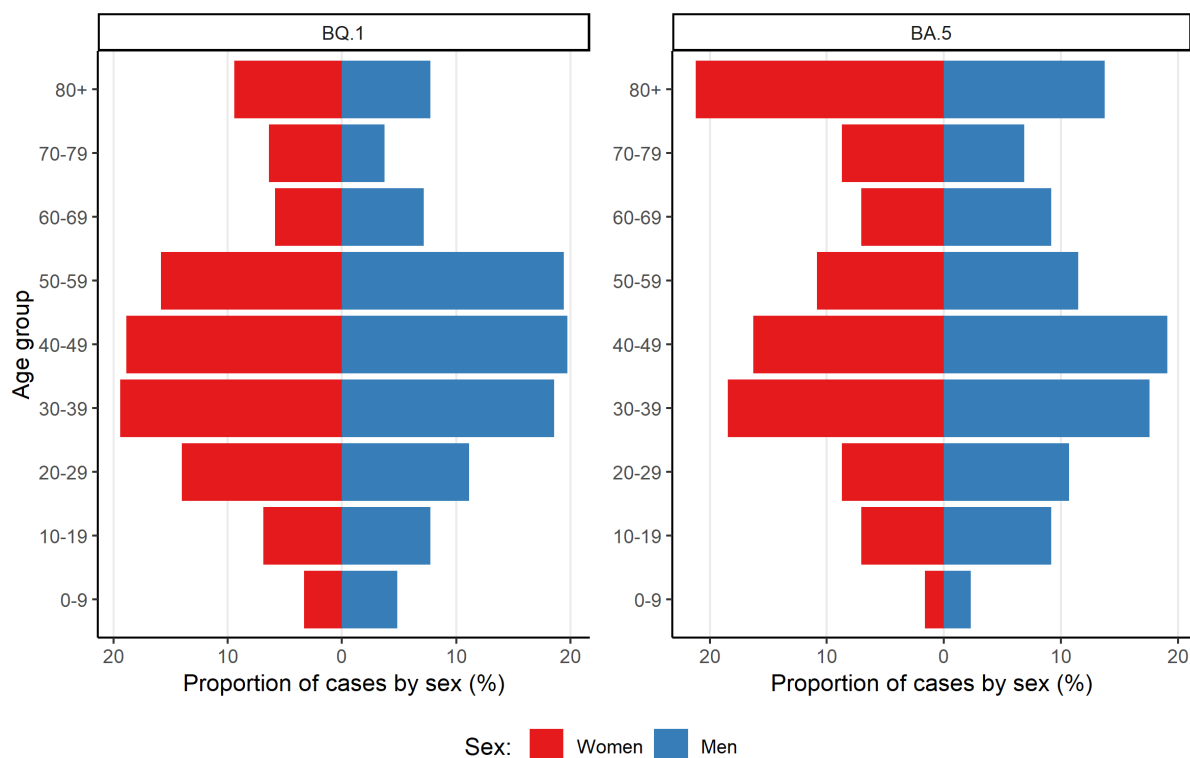

Figure 7. Age group and sex distribution of specimens sequenced over the last 4 weeks, by lineage.

Table 4. Comparison of lineage distribution by sampling setting.

Lineage	Community			Hospital		
	Women	Men	**Total**	Women	Men	**Total**
Omicron BQ.1	72.7%	75.4%	**74.0%**	61.5%	68.5%	**64.5%**
Omicron BA.5	27.3%	24.6%	**26.0%**	38.5%	31.5%	**35.5%**
Total	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**

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Mutation surveillance

In addition to the surveillance of SARS-CoV-2 variants, the LNS monitors the occurrence of SARS-CoV-2 mutations, as their early detection might be key to foresee changes in the epidemic evolution. The LNS is currently monitoring mutations to the spike protein, following ECDC guidance, and comparing their prevalence to that observed in Europe (according to GISAID).

Among the specimens collected over the last four weeks, no mutation was detected at a higher circulation in Luxembourg compared to Europe.

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