Respiratory Viruses in Luxembourg (ReViLux)

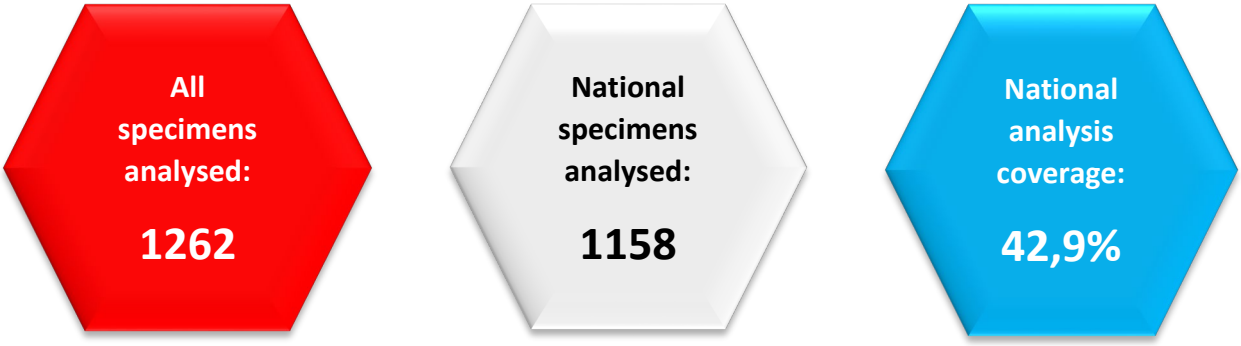
Weekly report (29 Nov – 05 Dec 2021)

Executive Summary

The Sentinel Surveillance Network identified 27 cases of influenza-like illness, thus exceeding the recommended threshold for the new epidemic season, according to the European Center for Disease Prevention and Control (ECDC) guidelines.

Regarding SARS-CoV-2 genomic surveillance, the LNS analysed 812 specimens from residents in Luxembourg in week 48/2021 (from 2699 total cases in the Grand Duchy of Luxembourg, 30,1%). This does not reach the new ECDC recommendations to detect emerging variants at 1% prevalence (minimum sample size of 927). Including complementary screening results by PCR, 1158 national specimens were analysed globally.

All specimens sequenced in week 48 were assigned to the Delta variant. The first Omicron case has been detected among specimens from week 49. The most frequent lineages are AY.43 (34,8%), AY.4 (11,8%) and AY.98.1 (8,4%). A similar distribution was observed for target groups (hospital specimens and post-vaccination breakthrough cases). As for the mutations under surveillance, they revealed no outstanding behaviour, remaining in agreement with the lineages observed.



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. There are currently two active projects on which the ReViLux provides updates:

The Sentinel Surveillance Network. It provides a broad picture of respiratory diseases affecting the Luxembourgish population, based on its double monitoring system (syndromic and virological).

The National SARS-COV-2 Genomic Surveillance Program. It enables detailed observation of SARS-CoV-2 mutations and variants through time and space, and also monitoring specific groups of interest.

Sentinel Surveillance Network

The **Sentinel Surveillance Network** aims at monitoring the circulating respiratory viruses, including SARS-CoV-2, and hence underpin public health actions. Following the World Health Organization (WHO) and European Centre for Disease Prevention and Control (ECDC) guidance, it focuses on cases of acute respiratory infection (ARI) and influenza-like illness (ILI).

Week 40 marked the beginning of the new influenza season 2021-2022. Results of syndromic surveillance during the last four weeks are displayed in Table 1 and the history of ILI consultations since the 2019-2020 season is shown in Figure 1. The number of ILI cases identified in week 47 was 27 (out of 528s consultations); therefore, **the percentage of ILI (5,11%) exceeds the threshold for the epidemic season** (2,59%), according to the ECDC.

Regarding the virological surveillance, a partnership among the CNS, private laboratories and the LNS recently started and will enable us to monitor the presence of several respiratory viruses. Results from the first analyses will be published soon.

Table 1. Syndromic surveillance during week 48

Week	ARI		ILI		Total consultations
	N	%	N	%	
2021/45	84	17.07	9	1.83	492
2021/46	53	12.96	8	1.96	409
2021/47	65	17.62	11	2.98	369
2021/48	128	24.24	27	5.11	528

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

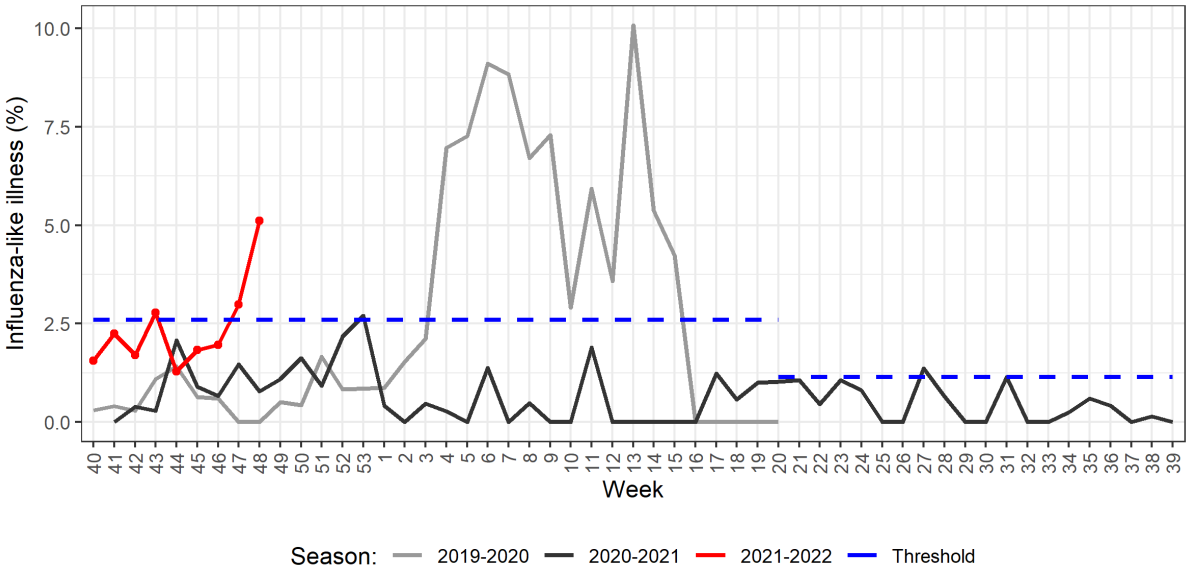


Figure 1. Percentage of patients with influenza-like illness over the last three seasons

SARS-CoV-2 Genomic Surveillance

The current sequencing strategy

The National Reference Laboratory for Acute Respiratory Infections at LNS receives SARS-CoV-2 positive samples (nasopharyngeal or oropharyngeal swabs analysed by RT-PCR) from the national network of laboratories and proceeds as follows:

1) Sequencing all specimens from hospital cases.
2) Sequencing all specimens from post-vaccination cases.
3) Sequencing specimens from clusters with high transmission.
4) Sequencing a representative sample of community cases.

The representative sample of community cases is a systematic selection from all SARS-CoV-2 positive cases registered in Luxembourg to detect emerging variants and early increases in their incidence and transmission within the community in Luxembourg. This sample is selected according to the ECDC guidelines.

Due to the **emergence of the new Omicron variant of concern**, as well as the high incidence rates in the European context, the LNS is currently expanding its sequencing capacity and reactivity. Additionally, targeted PCR tests are carried systematically in order to detect potential Omicron cases within 24h from reception of the specimen. These potential cases are then prioritised for confirmation by sequencing.

The LNS shares its sequencing results with GISAID EpiCov database periodically. SARS-CoV-2 lineages have been assigned based on Rambaut et al. using the Phylogenetic Assignment of Named Global Outbreak LINeages (pangolin) software (v3.1.16, pangoLEARN 2021-11-25). The Pango nomenclature is used in addition to the WHO nomenclature to enable easier visualization of links between any evolving variants and their ancestor (See nomenclature equivalences in Appendix 1). Delta lineages nomenclature is in constant review. The original Delta B.1.617.2 lineage is being re-classified into more specific AY lineages in order to enable a more precise tracing of the cases. This report is based on the latest nomenclature, and previously assigned lineages might have been updated to remain consistent with the latest nomenclature.

Sequenced specimens

In week 48, 2699 new cases were registered in Luxembourg. Given the epidemiological situation after the emergence of the new Omicron variant, achieving a 1% incidence detection capacity is preferrable than the usual 2.5%, according to the ECDC. For that, the recommended sample size is estimated in 973 specimens (36.1%).

Last week, the microbial genomics unit at the LNS analysed 906 specimens from week 48, with 812 specimens having been collected in week 48 from residents. As this sample did not reach the ECDC-recommended sample size, another 346 specimens from residents were tested by targeted PCR for the Omicron variant (overall, 42,9% coverage of the 2699 total cases registered in Luxembourg; see coverage trend in Figure 2).

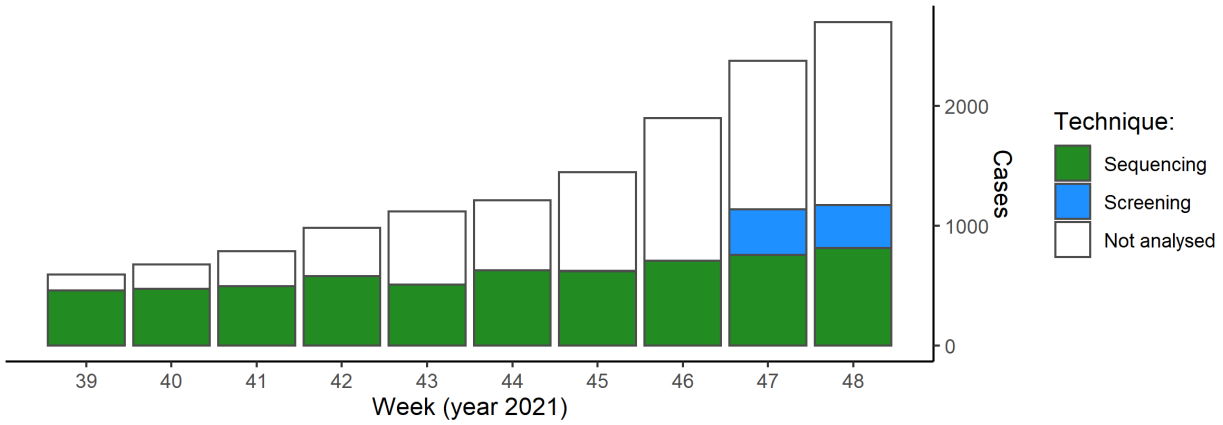


Figure 2. National coverage based on weekly number of positive cases in Luxembourg. The coverage from the latest weeks might not be consolidated yet.

Circulating lineage detection

The distribution of successfully assigned lineages within the representative sample is shown in Figure 3. Regarding Delta AY sublineages, only a selection is displayed, based on their pevalence during the last 10 weeks (min. 1%). This distribution is further detailed for the last 2 weeks in Table 2. **The lineage AY.43 continues to be the most frequent one (34,8%)**, followed by AY.4 (11,8%), while the remaining lineages show frequencies lower than 10%. No Omicron cases were assigned in week 48, but the first case has been sequenced in a national specimen collected in week 49.

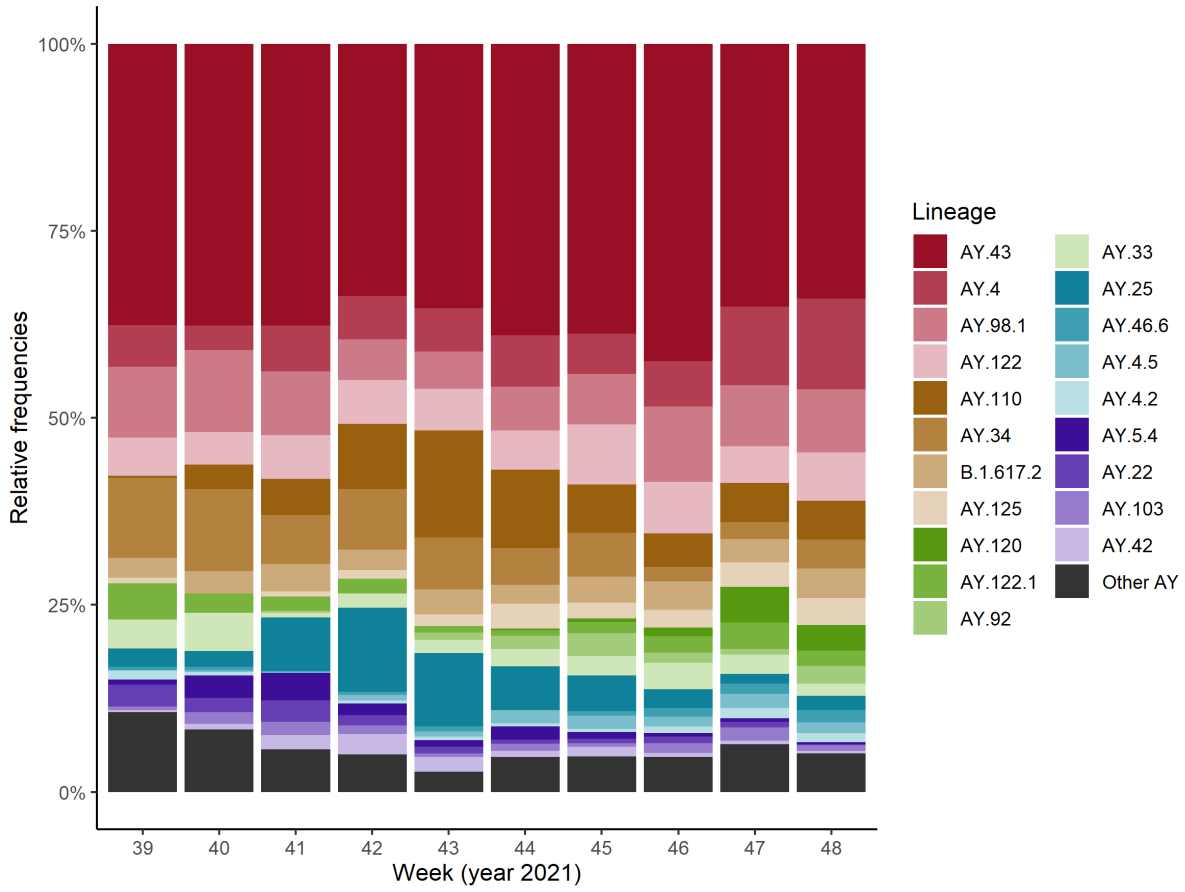


Figure 3. Distribution of lineages within the national representative selection during the last 10 weeks

Table 2. Distribution of SARS-CoV-2 lineages detected within the national representative sample in weeks 46 and 47/2021 (previously reported cases might be updated by retrospective analysis).

Variant	**Week 47**			**Week 48**		
	N	***%***	***CI %***	***N***	***%***	***CI %***
Delta AY.43	236	35.2	31.6 – 38.8	241	34.8	31.3 – 38.4
Delta AY.4	70	10.4	8.1 – 12.7	82	11.8	9.4 – 14.3
Delta AY.98.1	55	8.2	6.1 – 10.3	58	8.4	6.3 – 10.4
Delta AY.122	33	4.9	3.3 – 6.6	44	6.4	4.5 – 8.2
Delta AY.110	35	5.2	3.5 – 6.9	35	5.1	3.4 – 6.7
Delta B.1.617.2	21	3.1	1.8 – 4.4	27	3.9	2.5 – 5.3
Delta AY.34	15	2.2	1.1 – 3.4	26	3.8	2.3 – 5.2
Delta AY.125	22	3.3	1.9 – 4.6	25	3.6	2.2 – 5.0
Delta AY.120	32	4.8	3.2 – 6.4	23	3.3	2.0 – 4.7
Delta AY.92	5	0.7	0.1 – 1.4	16	2.3	1.2 – 3.4
Delta AY.122.1	24	3.6	2.2 – 5.0	15	2.2	1.1 – 3.3
Delta AY.25	9	1.3	0.5 – 2.2	13	1.9	0.9 – 2.9
Delta AY.33	17	2.5	1.3 – 3.7	11	1.6	0.7 – 2.5
Delta AY.46.6	9	1.3	0.5 – 2.2	11	1.6	0.7 – 2.5
Delta AY.4.5	13	1.9	0.9 – 3.0	10	1.4	0.6 – 2.3
Delta AY.4.2	9	1.3	0.5 – 2.2	8	1.2	0.4 – 2.0
Delta AY.103	12	1.8	0.8 – 2.8	7	1.0	0.3 – 1.8
Delta other AY	54	-	-	40	-	-
Beta	0	-	-	0	-	-
Gamma	0	-	-	0	-	-
Omicron	0	-	-	0	-	-
Other	0	-	-	0	-	-
Total	**671**	**100**	**-**	**692**	**100**	**-**

Mutation surveillance

In addition to the surveillance of SARS-CoV-2 variants, the LNS monitors the occurrence of SARS-CoV-2 mutations reported to have a clinical and epidemiological relevance. This complementary surveillance enables us to detect unexpected mutations among the specimens sequenced. It is expected that VOC defining mutations share the same distribution as their corresponding VOCs. However, newly acquired mutations may occur and their early detection might be key to expect changes in the epidemic evolution.

Following ECDC guidance, the LNS is currently monitoring 42 mutations to the spike protein frequently associated to VOCs. **Accordingly to the distribution lineages, most of the mutations found during the last 2 weeks are linked to Delta cases. No specimen displayed a mutation pattern suspicious of Omicron variant.**

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Appendices

Appendix 1: SARS-CoV-2 variants of concern

According to the ECDC

Table A1-a. Nomenclature for variants of concern by the European Centre for Disease Prevention and Control (ECDC)

WHO label	Pango lineage*	Spike mutations of interest	First detection	Evidence for impact on: transmission	immunity	severity
Beta	B.1.351	K417N, E484K, N501Y, D614G, A701V	South Africa, Sept 2020	Yes (v) (1)	Yes (v) (1, 2)	Yes (v) (3, 4)
Gamma	P.1	K417T, E484K, N501Y, D614G, H655Y	Brazil, Dec 2020	Yes (v) (5)	Yes (v) (6)	Yes (v) (4)
Delta	B.1.617.2	L452R, T478K, D614G, P681R	India, Dec 2020	Yes (v) (7)	Yes (v) (8-10)	Yes (v) (9, 11)
Omicron	B.1.1.529	**	South Africa, Botswana, Nov 2021	-	-	-

WHO: World Health Organization. (v): evidence derived from the variant itself; (m): evidence derived from mutations associated with the variant.

**All sub-lineages included.*

***A67V, Δ69-70, T95I, G142D, Δ143-145, Δ211-212, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F.*

Adapted from ECDC – SARS-CoV-2 variants of concern (https://www.ecdc.europa.eu/en/covid-19/variants-concern)

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According to the WHO

Table A1-b. Nomenclature for variants of concern by the World Health Organization (WHO)

WHO label	Pango lineage*	GISAID clade/lineage	Nextstrain clade	Additional amino acid changes monitored	Earliest documented samples	Date of designation
Alpha	B.1.1.7[#]	GRY (formerly GR/501Y.V1)	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2[§]	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron	B.1.1.529	GR/484A	21K	-	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

**All sublineages included. [#] includes all Q sublineages. [§] includes all AY sublineages.*

Adapted from WHO - Tracking SARS-CoV-2 variants (https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/)