Respiratory Viruses in Luxembourg (ReViLux)

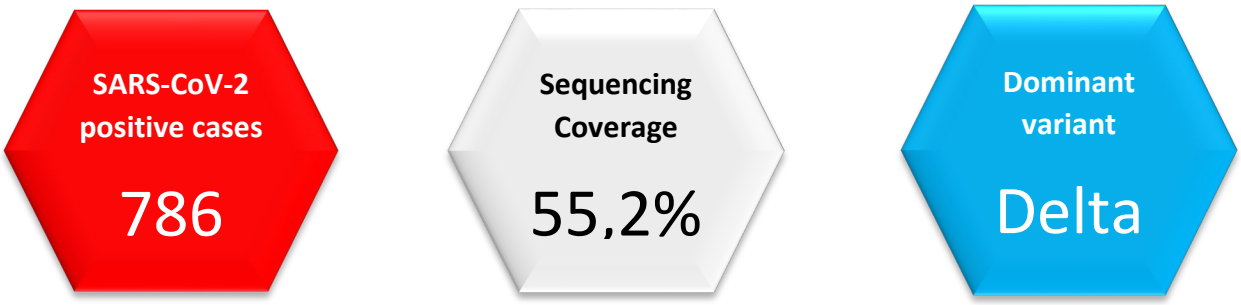
Weekly report (11– 17 October 2021)

Executive Summary

The Sentinel Surveillance Network identified 12 cases of influenza-like illness, thus remaining below 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 Laboratoire national de santé analysed 434 specimens from residents in Luxembourg in week 41/2021 (from 786 total cases in the Grand Duchy of Luxembourg, 55,2% sequencing coverage). This exceeds the minimum sample size (341) recommended by the ECDC to detect emerging variants at a 2.5% incidence at the epidemic situation in the country.

All specimens were assigned to the Delta variant. Community surveillance showed that parental lineage B.1.617.2 continues to be the most frequent one (65,1%), followed by AY.25 (7,9%) and AY.34 (6,7%). In respect to target groups, AY lineages were found in 36,2% of hospital specimens and 33,6% of post-vaccination breakthrough cases. As for the mutations under surveillance, they revealed no outstanding behaviour, remaining in agreement with the lineages observed.



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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 three active projects:

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.

The COVVAC Serology Project. It assesses the post-vaccination serological status in long-term care facilities and its evolution over time.

The ReViLux provides updates on the first two projects.

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 week 41 are displayed in Table 1 and the history of ILI consultations since the 2019-2020 season is shown in Figure 1. Twelve cases of ILI were identified in week 41 (out of 535 consultations); therefore, **the percentage of ILI (2,24%) remains below 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.

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Table 1. Syndromic surveillance during week 41

Week	ARI		ILI		Total consultations
	N	%	N	%	
2021/38	105	14.79	1	0.14	710
2021/39	73	21.53	0	0.00	339
2021/40	79	24.69	5	1.56	320
2021/41	107	20.00	12	2.24	535

ARI: Acute Respiratory Infections (acute respiratory syndrome like bronchitis, pharyngitis, rhinitis, pneumonia… with or without fever).
ILI: Influenza-Like Illness (acute respiratory syndrome <10 days, fever 38 ºC, systemic symptoms like myalgia or malaise…).

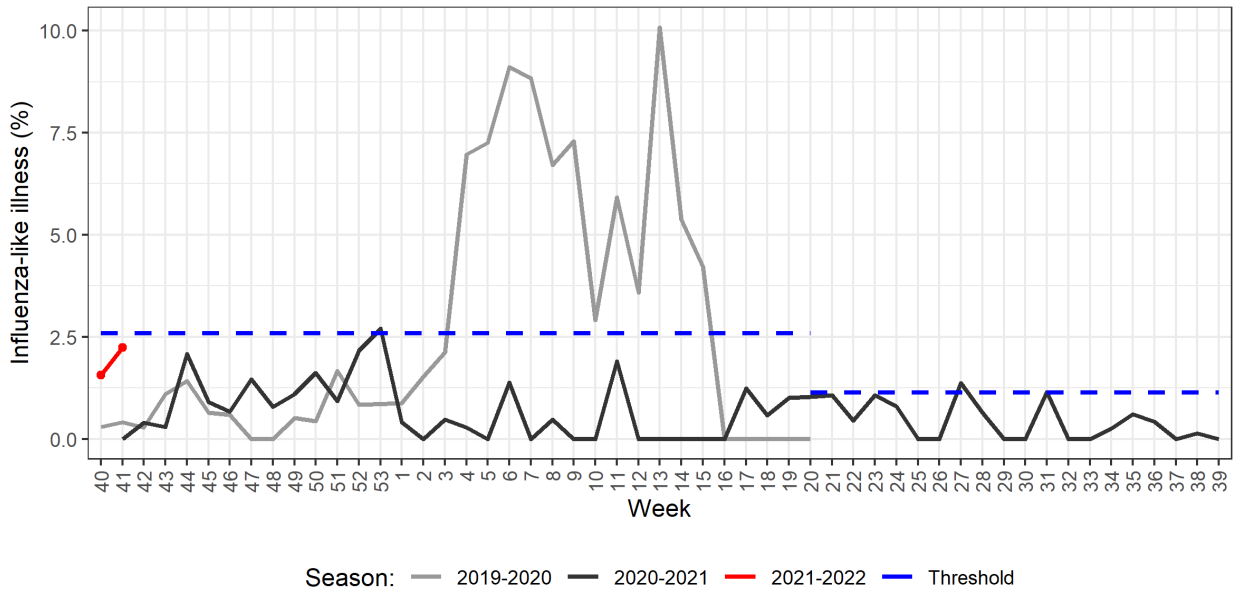

Figure 1. Percentage of patients with influenza-like illness over the last three seasons

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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 reinfection and post-vaccination cases.
3) Sequencing all specimens from cluster cases.
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.

The LNS shares its sequencing results with GISAID EpiCov database (www.gisaid.org) periodically. SARS-CoV-2 lineages (variants) have been assigned based on Rambaut et al. using Phylogenetic Assignment of Named Global Outbreak LINeages (pangolin) software (v3.1.14, pangoLEARN 2021-10-13). The ReViLux continues to use the Pango nomenclature, in addition to the WHO nomenclature, to allow easier visualization of links between any evolving variants and their ancestor (https://cov-lineages.org). See nomenclature equivalences in the Annex 1.

Methodological notes

Since 3 September 2021, the ECDC no longer considers B.1.1.7 and B.1.1.7+E484K lineages (Alpha variant) as variants of concern. This decision is based in both their low circulation and the high effectiveness of vaccines in controlling them.

Delta sublineages nomenclature is in constant review. This report is based on the pangoLEARN version v2021-10-13. Previously assigned lineages might differ after retrospective analysis of the sequences, based on the updated pangoLEARN version.

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Sequenced specimens

In week 41, 786 new cases were registered in Luxembourg; hence, the minimum sample size required to detect emerging variants at a 2.5% incidence is estimated to be 341 specimens (43,4%).

The microbial genomics unit at the LNS sequenced 474 specimens from week 41, with 434 specimens having been collected in week 41 from residents (55,2% coverage of the 786 total cases registered in Luxembourg; see coverage trend in Figure 2). This exceeds the minimum sample size (341) to detect a 2.5% incidence recommended by the ECDC. The representative sample of community cases is built by systematic selection.

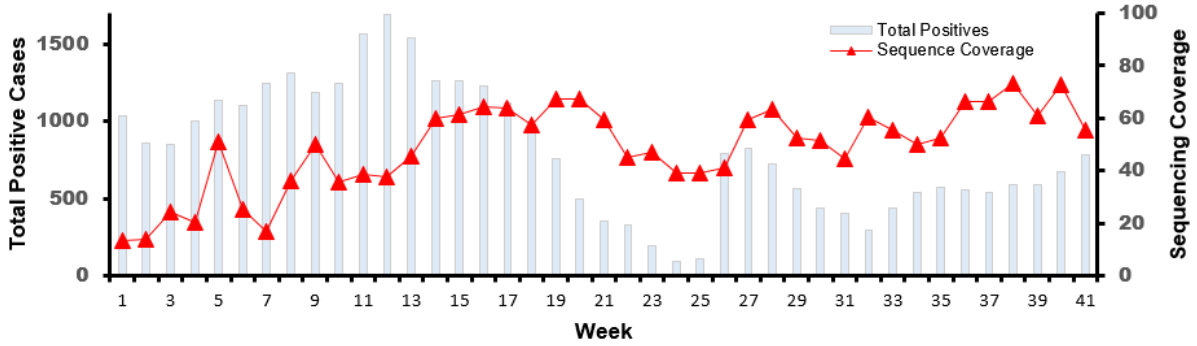

Figure 2. Sequence coverage (red) based on weekly number of positive cases in Luxembourg (light blue) during 2021.

Circulating lineage detection

In week 41/2021, only Delta variant cases were detected among all specimens sequenced in the representative sample of community cases, including 12 Delta subtypes. The distribution of VOCs is displayed in Table 2 and their evolution over the weeks is shown in Figure 3. **The parental lineage B.1.617.2 continues to be the most frequent one (65,1%), followed by AY.25 (7,9%) and AY.34 (6,7%).** The distribution of lineages for week 40 displayed in this report differs from the one published in the previous one due to an update of the source software (more details in the *Methodological note*).

Table 2. Distribution of SARS-CoV-2 lineages detected within the Luxembourgish representative sample in weeks 40 and 41/2021 (previous cases might be updated by retrospective analysis).

VOC	**Week 40**			**Week 41**		
	N	***%***	***CI %***	***N***	***%***	***CI %***
Delta B.1.617.2	226	71.1	66.1 - 76.1	222	65.1	60.0 – 70.2
Delta AY.25	3	0.9	0.0 – 2.0	27	7.9	5.1 – 10.8
Delta AY.34	33	10.4	7.0 - 13.7	23	6.7	4.1 – 9.4
Delta AY.4	9	2.8	1.0 - 4.7	15	4.4	2.2 – 6.6
Delta AY.10	4	1.3	0.0 - 2.5	13	3.8	1.8 – 5.8
Delta AY.22	5	1.6	0.2 - 2.9	11	3.2	1.4 – 5.1
Delta AY.39	5	1.6	0.2 - 2.9	10	2.9	1.1 – 4.7
Delta AY.5	8	2.5	0.8 - 4.2	9	2.6	0.9 – 4.3
Delta AY.3	2	0.6	0.0 - 1.5	4	1.2	0.0 – 2.3
Delta AY.33	20	6.3	3.6 – 9.0	3	0.9	0.0 – 1.9
Delta AY.26	0			2	0.6	0.0 – 1.4
Delta AY.35	0			1	0.3	0.0 – 0.9
Delta AY.4.5	0			1	0.3	0.0 – 0.9
Delta AY.9	2	0.6	0.0 - 1.5	0		
Delta AY.4.2	1	0.3	0.0 - 0.9	0		
Total	**318**	**100**	**-**	**341**	**100**	**-**

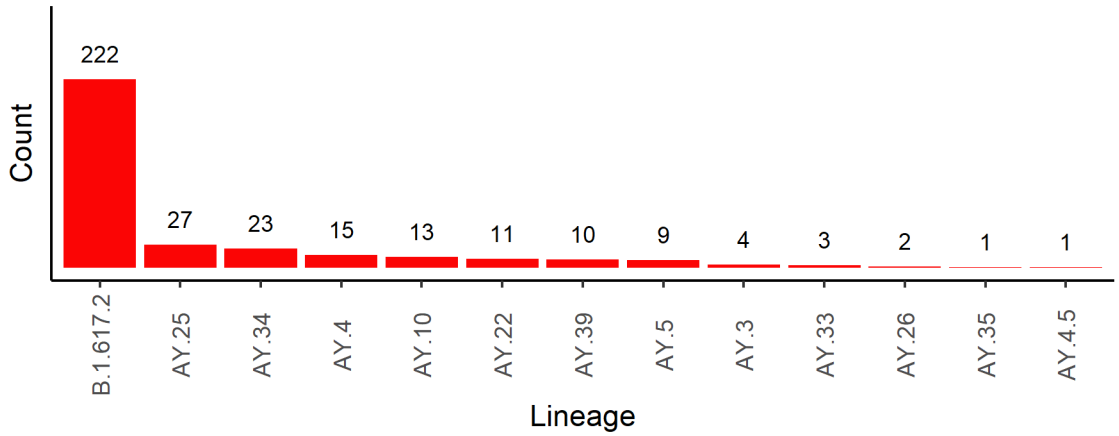

Figure 3. Number of SARS-CoV-2 variants in the representative sample for week 41/2021

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 15 mutations to the spike protein frequently associated to VOCs and variants of interest (VOIs). Table 3 provides the cumulative frequencies of these mutations, detected in the lineage-assignable genome sequences since 1 Sep 2020 (N = 20 483), as well as the frequencies for the last 3 weeks.

In broad terms, the mutations identified were expected according to the lineages assigned during this week. No mutation showed an outstanding behaviour.

Table 3. Analysis of a selection of mutations of concern identified in successfully sequenced specimens during the last 3 weeks (previous frequencies updated by retrospective sequencing)

Mutation	**Relative frequence by week (%)**				**Variants associated (VOC & VOI)**
	39	40	41	cumul.	
A701V	0.0	0.0	0.0	5.9	Beta
D614G	98.5	99.2	99.1	97.9	Beta, Gamma, Delta, B.1.620, Lambda, Mu
E484K	0.0	0.0	0.0	13.5	Beta, Gamma, B.1.620, Mu
F490S	0.0	0.0	0.0	1.0	Lambda
H655Y	0.0	0.0	0.0	6.3	Gamma
K417N	0.0	0.0	0.0	6.1	Beta
K417T	0.0	0.0	0.0	6.6	Gamma
L452Q	0.0	0.0	0.0	0.0	Lambda
L452R	93.2	94.3	88.3	26.6	Delta
N501Y	0.0	0.2	0.0	45.6	Beta, Gamma, Mu
P681H	0.0	0.0	0.0	33.7	B.1.620, Mu
P681R	95.8	96.1	92.3	26.5	Delta
R346K	0.0	0.0	0.0	0.1	Mu
S477N	0.9	0.4	2.0	9.0	B.1.620
T478K	95.0	95.3	90.1	26.8	Delta

Cumul: cumulative frequence since 1 Sept 2020. VOC: variant of concern; VOI: variant of interest.

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Annexes

Annex 1. SARS-CoV-2 variants naming

Table A1. 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: transmissibility	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)

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

**All sub-lineages included.*

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

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Table A2. 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

**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/)

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