Respiratory Viruses in Luxembourg (ReViLux)

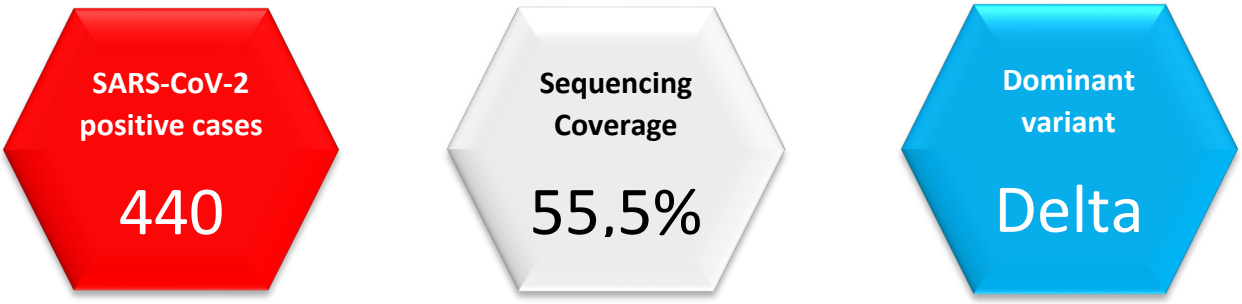
Weekly report (16 – 22 August 2021)

Executive Summary

The Sentinel Surveillance Network identified no cases of influenza-like illness, thus remaining below the recommended threshold for the interepidemic 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 244 Luxembourgish specimens in week 33/2021 (from 440 total cases in the Grand Duchy of Luxembourg, 55,5%). This exceeds the minimum coverage (10%) but does not reach the minimum sample size (254) recommended by the ECDC.

Community surveillance showed that Delta variant continues to be the dominant one in Luxembourg (99,1%), with low prevalence of the Gamma (0,9%). In respect to target group surveillance, all cases analysed were identified as VOC cases, and 15 post-vaccination breakthrough cases were assigned to Delta variant.



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).

Results of syndromic surveillance during week 33 (16 August 2021 – 22 August 2021) are displayed in Table 1 and the history of ILI consultations since the 2018-2019 season is shown in Figure 1. No cases of ILI were identified in week 33; therefore, **the percentage of ILI is below the threshold for the interepidemic season** (1,14%), according to the ECDC.

Regarding the virological surveillance, no data is available for week 33.

Table 1. Syndromic surveillance during week 33

Week	ARI		ILI		Total consultations
	N	%	N	%	
2021/30	19	8.02%	0	0.00%	237
2021/31	3	3.45%	1	1.15%	87
2021/32	15	8.47%	0	0.00%	177
2021/33	15	6.67%	0	0.00%	225

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 °C, systemic symptoms like myalgia or malaise…).

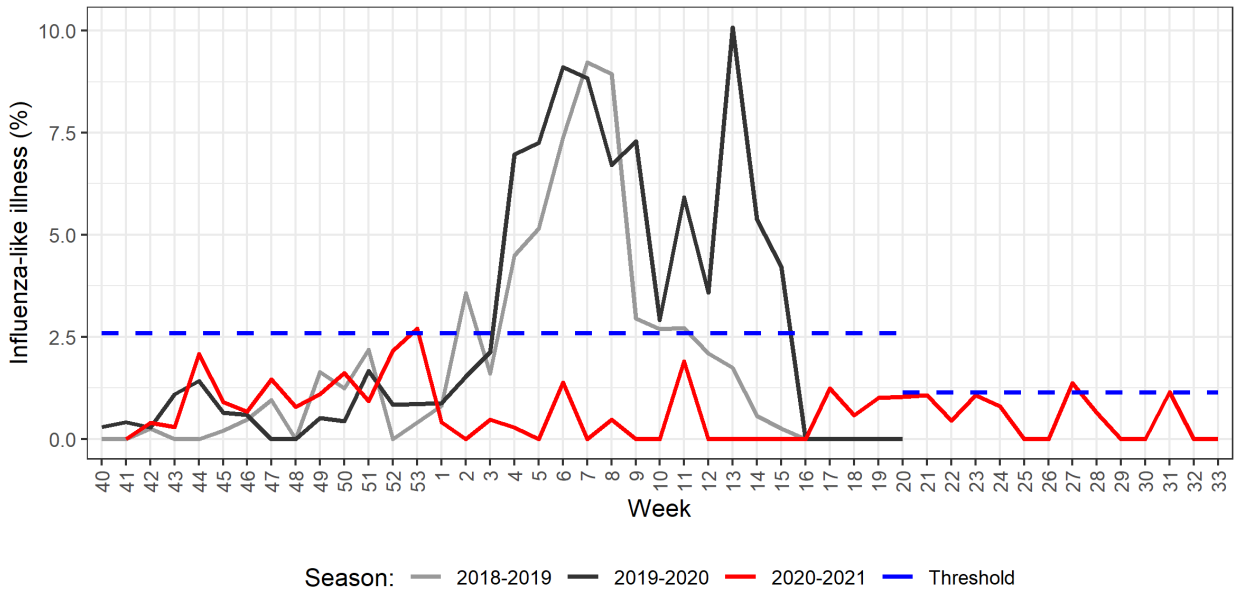


Figure 1. Percentage of patients with influence-like illness over the last three seasons

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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 for (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 sample of community cases.

The sample of community cases is a selection from all cases to detect emerging SARS-CoV-2 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 (v3.1.11, pangoLEARN 2021-08-09). 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 Annex 1.

Methodological note on Delta subtypes

The latest version of the pangoLEARN software included new lineages AY.4-AY.12. These are sublineages within B.1.617.2 (Delta variant), and were previously assigned to the B.1.617.2 lineage. However, due to their different geographic backgrounds they are now identified separately in order to allow a more detailed tracking. They are all classified as Delta variant by the World Health Organization.

Sequenced specimens

In week 33, 440 new cases were registered in Luxembourg; hence, the minimum sample size required to detect a 2.5% incidence is estimated to be 254 specimens (57,7%).

The microbial genomics unit at the LNS sequenced 319 specimens, with 244 specimens having been collected in week 33 from residents (55,5% coverage of the 440 total cases registered in Luxembourg; see coverage trend in Figure 2). This exceeds the minimum coverage (10%) but does not reach the minimum sample size (254) recommended by ECDC. The community sample size in week 33, after removal of 17 additional cluster cases, was 227.

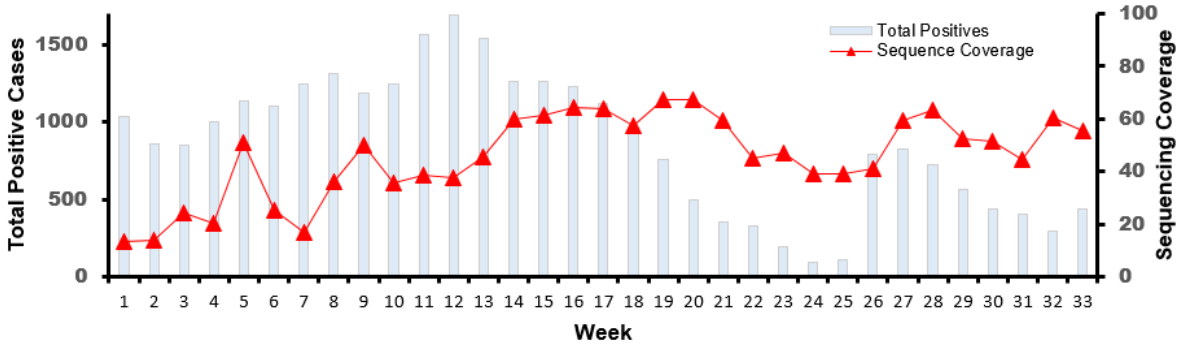

Figure 2. Sequence coverage based on weekly number of positive cases in Luxembourg during 2021

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Circulating lineage detection

The evolution of variants over the weeks is shown in Figure 3.

In week 33/2021, only Gamma and Delta variants (including 3 Delta subtypes) were detected within our population sequencing pool, after removal of cluster specimens, and excluding specimens collected from non-residents, as shown in Figure 4. The most prevalent variants are displayed in Table 2.

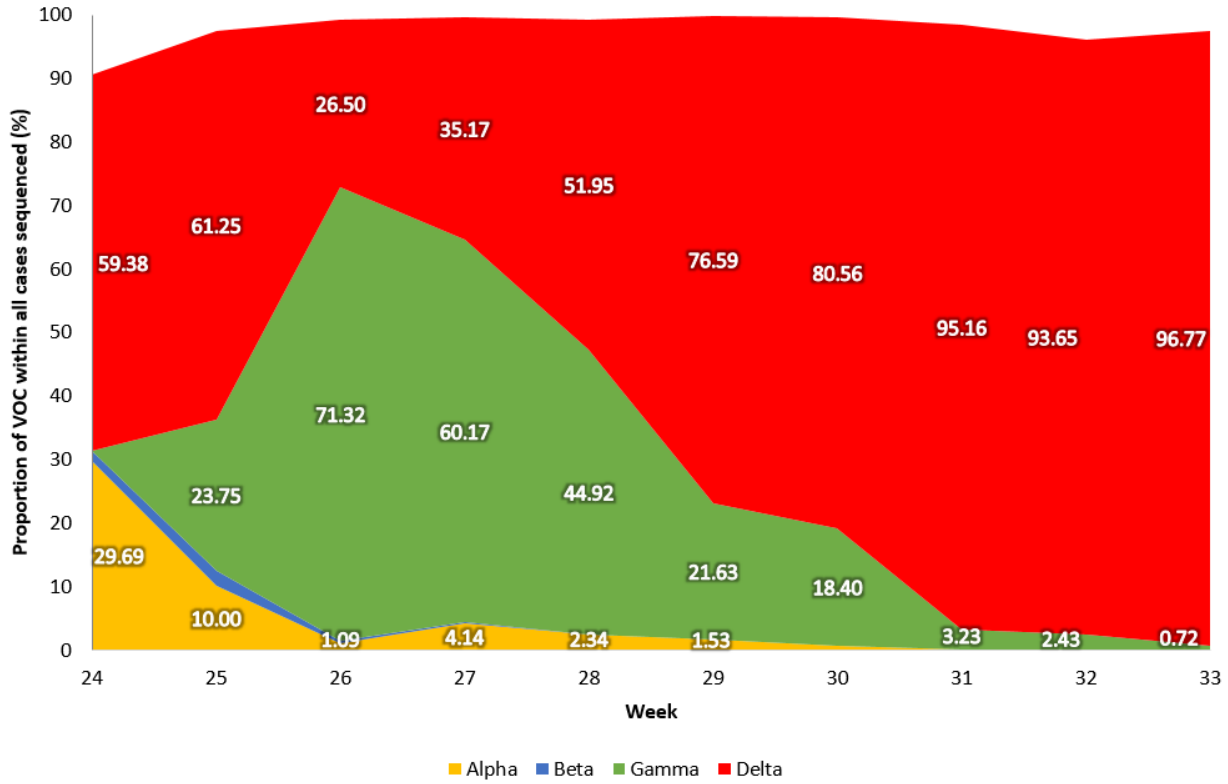

Figure 3. Evolution of VOCs distribution within all specimens sequenced, including target groups (clusters, non-residents) over the last 10 weeks in Luxembourg

Table 2. Distribution of SARS-CoV-2 lineages detected within the community (cluster and non-resident cases excluded) in weeks 32 and 33/2021 (previous cases updated by retrospective sequencing)

VOC	Week 32			Week 33		
	N	%	CI %	N	%	CI %
Alpha	0	0.0	-	0	0.0	-
Beta	0	0.0	-	0	0.0	-
Gamma	5	3.3	0.5 - 6.1	2	0.9	0.0 - 2.2
Delta	147	96.7	93.9 - 99.5	218	99.1	97.8 - 100.0
Others	0	0.0	-	0	0.0	-
Total	**152**	**100.0**		**220**	**100.0**	

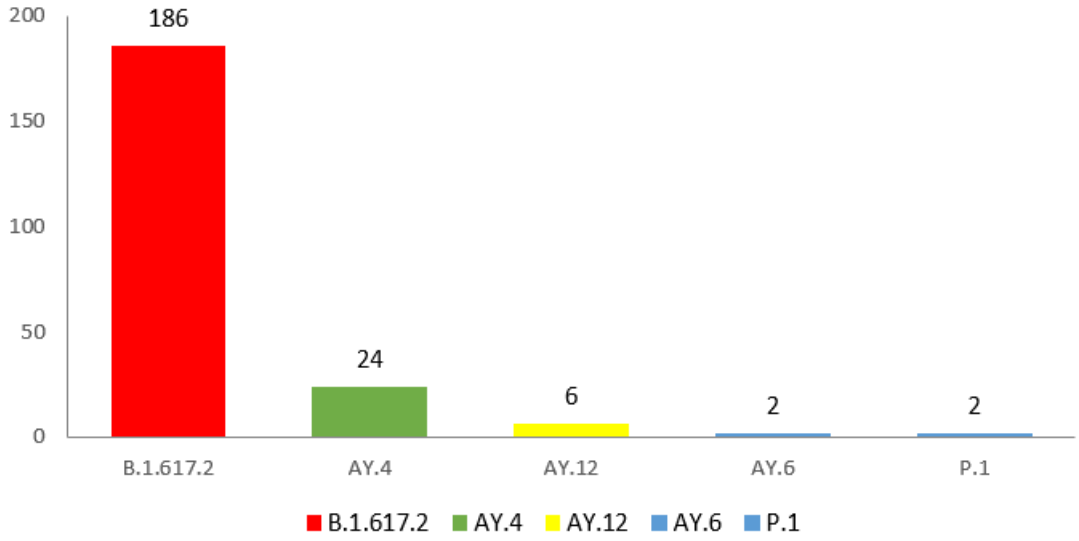

Figure 2. Number of SARS-CoV-2 variants in representative sample for week 33/2021

Mutation surveillance

In addition to the surveillance of SARS-CoV-2 variants, the LNS monitors the occurrence of SARS-CoV-2 mutations assumed to have a clinical and epidemiological relevance.

Table 3 provides the overall frequencies of these mutations, detected in the lineage-assignable genome sequences, analyzed since 1 Sep 2020 (N=17166), as well as the frequencies in week 33/2021.

Table 3. Analysis of clinically relevant mutations identified during week 33/2021 sequencing

Mutation	Gene	Genomic Position in reference	Frequency Overall [%]	Frequency Week 33/2021 [%]	Characteristics	Reference
D614G	S gene	23402	95.7	99.7	Higher infectivity, higher case fatality rate, higher transmission	Eaaswarkhanth 2020 Becerra-Flores 2020, Hu 2020, Plante 2020
P323L	ORF1ab	14407	88.9	94.4	Higher severity	Biswas & Mudi 2020
R203K	N gene	28880	54.2	0.7	Fitness advantage for the virus	Leary 2020
G204R	N gene	28883	54.2	0.7	Fitness advantage for the virus	Leary 2020
N501Y	S gene	23063	53.2	0.7	501Y.V1/V2; Improved ACE2 binding affinity/higher transmissibility	Filip Fratev 2020 COVID-19 Genomics Consortium UK, 2020
E484K	S gene	23012	15.8	0.7	501Y.V2 / possible impact on antibody neutralization activity (escape mutation), improved ACE2 binding affinity	Greaney 2020
Y144del	S gene	21991-21993	42.0	0.0	possible impact on antibody binding affinity	Dawood 2020
H69/V70del	S gene	21765-21770	41.5	0.0	possible impact on antibody neutralization activity and reinfection; included in "mink" mutation	Kemp 2020
P681H	S gene	23604	39.4	0.0	immediately adjacent to the furin cleavage site, a known location of biological significance	COVID-19 Genomics Consortium UK, 2020
L37F	Nsp6	11081	3.4	2.4	Favored viral infection, higher severity	Aiewsakun 2020
Q57H	ORF3a	25561	19.9	0.0	Higher severity	Biswas & Mudi 2020
K417N	S gene	22813	7.1	0.0	501Y.V2 / possible impact on antibody binding affinity (escape mutation)	Kemp 2020
N439K	S gene	26143	0.7	0.0	Improved ACE2 binding affinity	Zhou 2020

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Annexes

Annex 1. SARS-CoV-2 variants naming

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. Equivalence for VOC are shown in Table A1 (adapted from WHO).

Table A1. 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 World Health Organization - Tracking SARS-CoV-2 variants