LNS LUXEMBOURG

LE GOUVERNEMENT
DU GRAND-DUCHÉ DE LUXEMBOURG
Ministère de la Santé

Direction de la santé

Respiratory Viruses in Luxembourg (ReViLux)

Weekly report (2 – 8 August 2021)

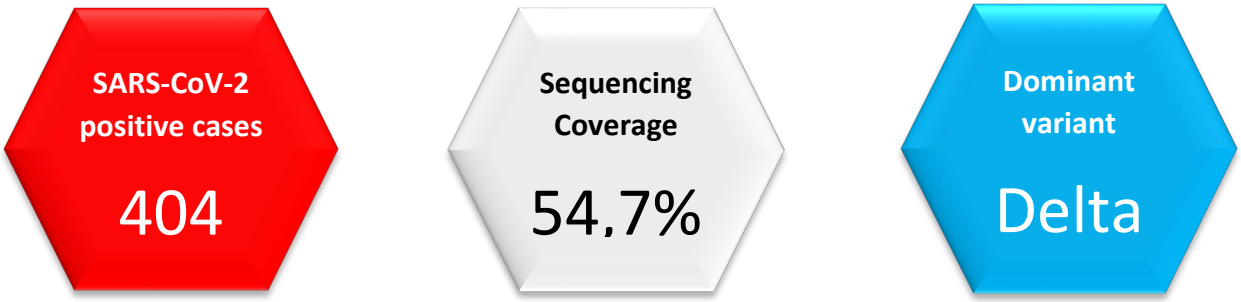
Executive Summary

The Sentinel Surveillance Network identified one case of influenza-like illness, which reaches the threshold that is applicable to 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 221 specimens in week 31/2021 (from 404 total cases in the Grand Duchy of Luxembourg, 54,7%), including 180 non-targeted specimens (44,6%). This exceeds the minimum coverage (10%) but does not reach the minimum sample size (242) recommended by the ECDC.

Community surveillance showed that Delta variant continues to be the dominant one in Luxembourg (94,4%), with low presence of the Gamma (4,4%) and other variants (1,1%).

In respect to target group surveillance, all cases analysed were identified as VOC cases and 16 post-vaccination breakthrough cases were identified as VOCs.



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 31 (02 August 2021 – 08 August 2021) are displayed in Table 1 and the history of ILI consultations since the 2018-2019 season is shown in Figure 1. Only 1 case of ILI was identified, but as the number of consultations dropped to 87, the proportion of ILI cases in week 31 exceeds the threshold for the interepidemic season (1,14%) according to the ECDC. A close look will be kept at the evolution of ILI cases next week.

Regarding the virological surveillance, no data is available for week 31.

Table 1. Syndromic surveillance during week 31

	Count	Percent
ARI consultations	3	3,45%
ILI consultation	1	1.15%
Total consultations	87	100%

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

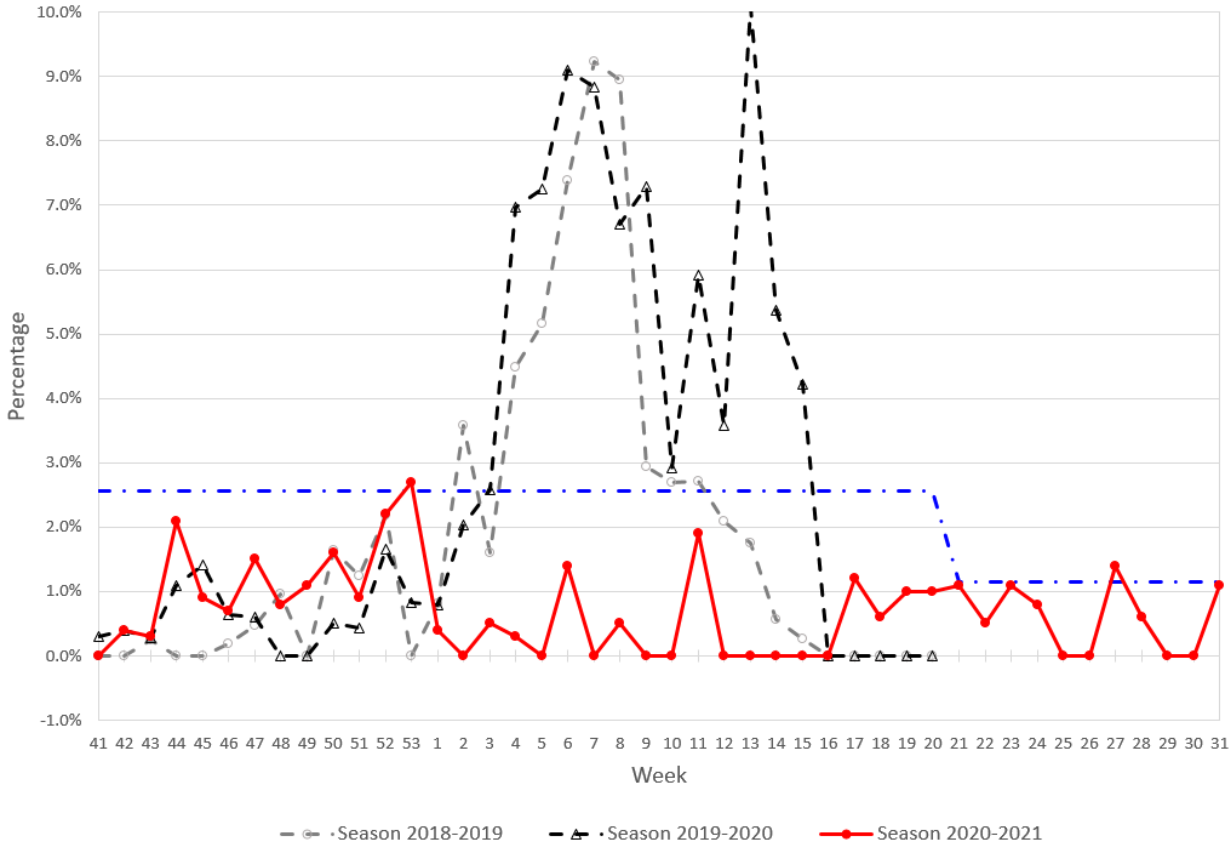


Figure 1. Percentage of patients with influence-like illness over the epidemiological weeks

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 hospitalized 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.

In week 31, 404 new cases were registered in Luxembourg; hence, the minimum sample size required to detect a 2.5% incidence is estimated to be 242 specimens (59,9%). The number of non-targeted specimens from Luxembourgish residents, successfully sequenced this week was 180 (44,6%), which exceeds the minimum coverage (10%) but does not reach the minimum sample size (242) recommended by ECDC.

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 (v3.1.10, pangoLEARN 2021-07-28). 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.

Sequenced specimens

Last week, the microbial genomics platform at the LNS sequenced 252 specimens, with 248 having been collected in week 31/2021. Among the latter, 61 specimens were reported to be part of a cluster or non-residents. The number of non-targeted specimens from Luxembourgish residents successfully sequenced this week was 180 (44,6% coverage of 404 total cases) (see coverage trend in Figure 2).

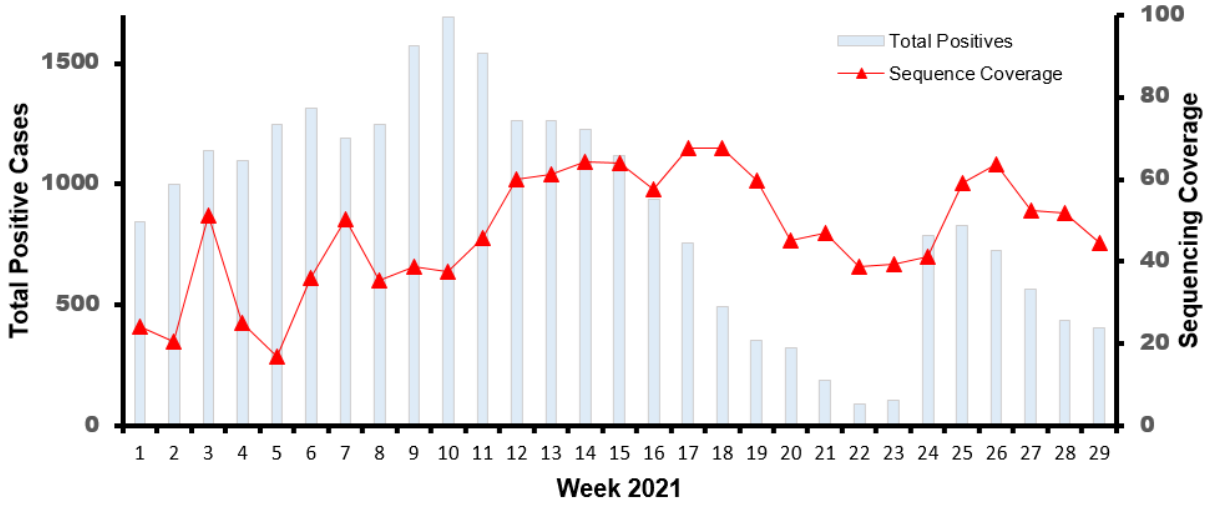


Figure 2. Sequence coverage based on total number of positive cases in Luxembourg in between week 52/2020 and week 31/2021

Circulating lineage detection

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

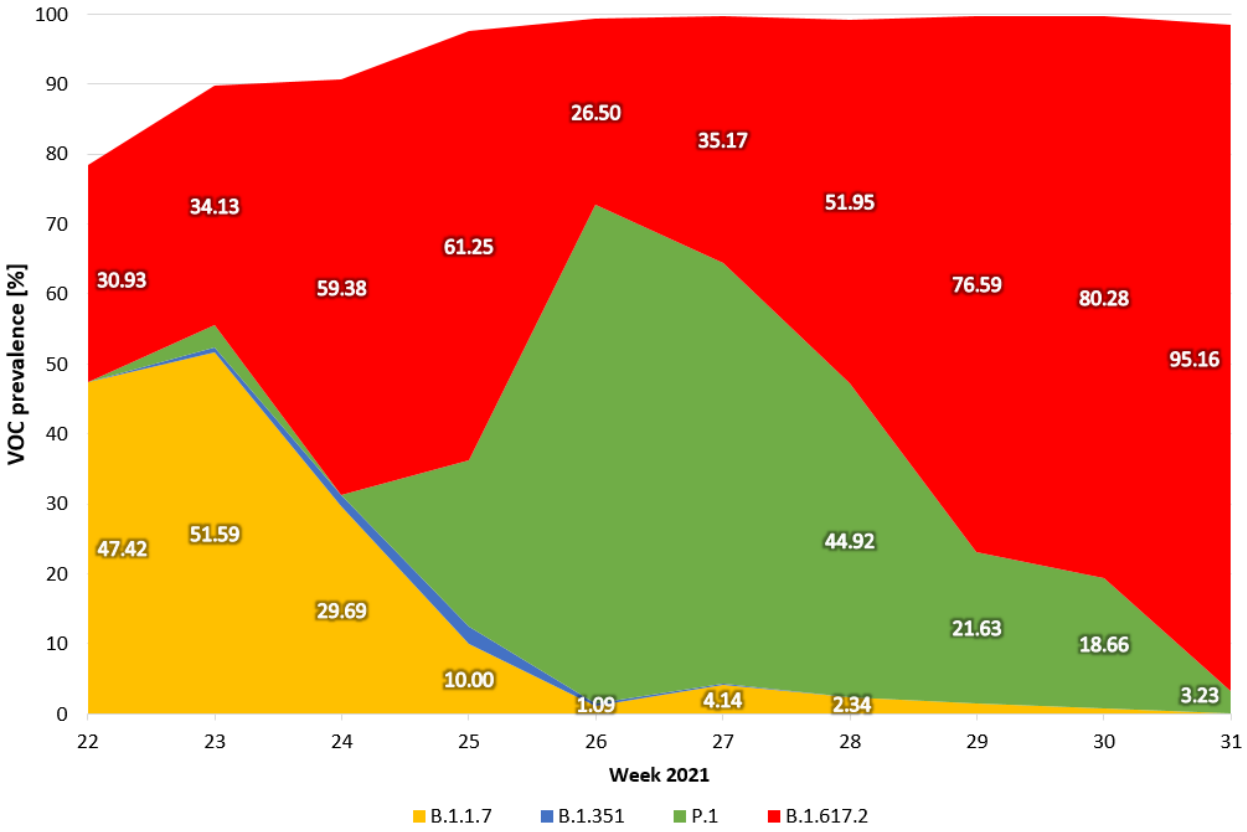


Figure 3. Evolution of variants in sequencing pool of all specimens including targeted sequencing (clusters, non-residents) over the last 10 weeks in Luxembourg.

In week 31/2021, 5 circulating SARS-CoV-2 variants 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 lineages are displayed in Table 2 and information about the lineages is provided in Annex 2.

Table 2. Distribution of SARS-CoV-2 VOCs detected within the community (cluster and non-resident cases excluded) in weeks 30 and 31/2021 (previous cases updated by retrospective sequencing)

VOC	Week 31			Week 30		
	N	%	CI %	N	%	CI %
Alpha	0	0.0	-	2	0.9	0.0 - 2.1
Beta	0	0.0	-	0	0.0	-
Gamma	8	4.4	1.4 - 7.5	41	18.1	13.1 - 23.2
Delta	170	94.4	91.1 - 97.8	183	81.0	75.9 - 86.1
Others	2	1.1	0.0 - 2.6	0	0.0	-
Total	**180**	**100.0**		**226**	**100.0**	

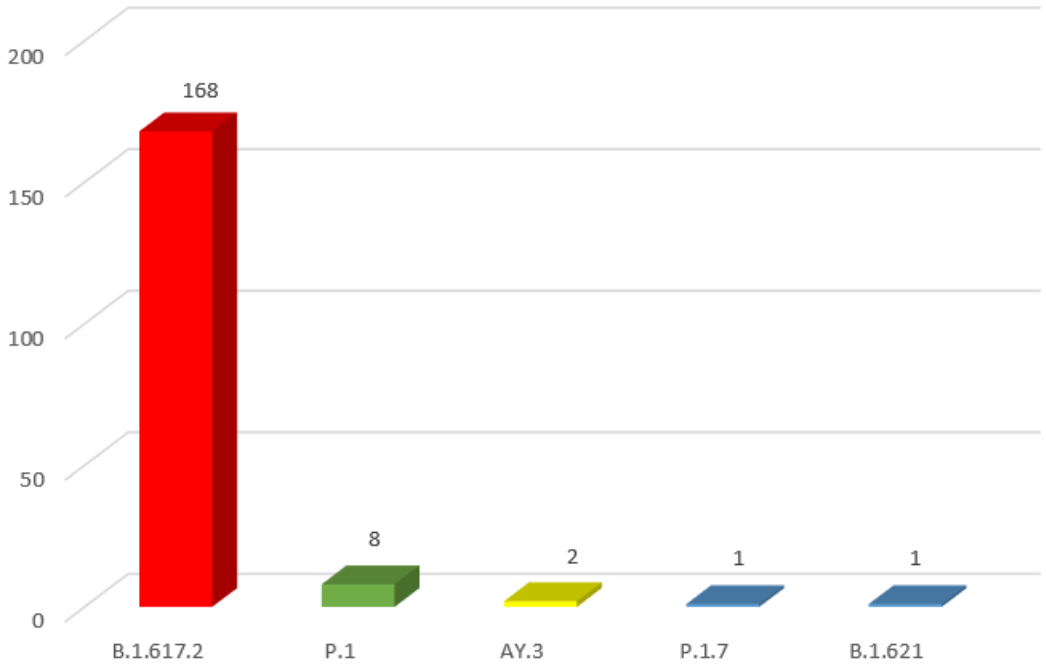


Figure 4. Number of SARS-CoV-2 variants in community sample for week 31/2021

Mutation surveillance

In addition to the surveillance of SARS-CoV-2 variants by whole genome sequencing, the LNS monitors the occurrence of SARS-CoV-2 mutations assumed to have a clinical and epidemiological relevance. Currently, 13 mutations are being observed, and this list is updated continually.

Table 3 provides the overall frequencies of these mutations, detected in the lineage-assignable genome sequences, analyzed since 1 Sep 2020 (N=16679), as well as the frequencies in week 31/2021.

Table 3. Analysis of clinically relevant mutations identified during week 31/2021 sequencing

Mutation	Gene	Genomic Position in reference	Frequency Overall [%]	Frequency Week 31/2021 [%]	Characteristics	Reference
D614G	S gene	23402	95.6	87.8	Higher infectivity, higher case fatality rate, higher transmission	Eaaswarkhanth 2020 Becerra-Flores 2020, Hu 2020, Plante 2020
P323L	ORF1ab	14407	88.7	83.3	Higher severity	Biswas & Mudi 2020
R203K	N gene	28880	55.7	3.1	Fitness advantage for the virus	Leary 2020
G204R	N gene	28883	55.7	3.1	Fitness advantage for the virus	Leary 2020
N501Y	S gene	23063	54.6	3.1	501Y.V1/V2; Improved ACE2 binding affinity/higher transmissibility	Filip Fratev 2020 COVID-19 Genomics Consortium UK, 2020
E484K	S gene	23012	16.2	3.1	501Y.V2 / possible impact on antibody neutralization activity (escape mutation), improved ACE2 binding affinity	Greaney 2020
Y144del	S gene	21991-21993	43.2	0.0	possible impact on antibody binding affinity	Dawood 2020
H69/V70del	S gene	21765-21770	42.6	0.0	possible impact on antibody neutralization activity and reinfection; included in "mink" mutation	Kemp 2020
P681H	S gene	23604	40.4	0.7	immediately adjacent to the furin cleavage site, a known location of biological significance	COVID-19 Genomics Consortium UK, 2020
L37F	Nsp6	11081	3.4	1.0	Favored viral infection, higher severity	Aiewsakun 2020
Q57H	ORF3a	25561	20.5	0.3	Higher severity	Biswas & Mudi 2020
K417N	S gene	22813	7.3	0.0	501Y.V2 / possible impact on antibody binding affinity (escape mutation)	Kemp 2020
N439K	S gene	26143	0.8	0.0	Improved ACE2 binding affinity	Zhou 2020

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European Centre for Disease Prevention and Control. Guidance for representative and targeted genomic SARS-CoV-2 monitoring – 3 May 2021. ECDC : Stockholm ; 2021

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Hadfield J., Megill C., Bell S., Huddleston J., Potter B., Callender C. et al. (2018). Nextstrain: real-time tracking of pathogen evolution. *Bioinformatics*, *34*(23), 4121-4123. doi: 10.1093/bioinformatics/bty407

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Annexes

Annex 1. SARS-CoV-2 variants naming

The ReViLux continues to use the (Pango) system to allow easier visualisation of links between any evolving variants and their ancestor. Equivalence for most frequently used VOC nomenclatures are shown in Table A1 (adapted from WHO).

Table A1. Variants of concern nomenclature by 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 B.1.351.2 B.1.351.3	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

Adapted from WHO - Tracking SARS-CoV-2 variants

Annex 2. Summary of evidence regarding the most frequently detected variants in the Great Duchy of Luxembourg

Lineage B.1.1.7 is characterized by several spike protein mutations, including N501Y, H69/V70del and P861H. The variant seems to have a considerable epidemiological impact, as it has a higher transmissibility rate.

Lineage B.1.351 holds numerous spike protein mutations, of which three are located in the receptor binding domain (K417N, E484K and N501Y), and are therefore relevant for antibody binding. As for B.1.1.7, a higher transmissibility rate and viral loads seem to be associated with this variant. Due to the K417N and E484K mutations, an impact on vaccination efficacy and possibility of reinfection is subject to scientific investigation.

Lineage P.1 (descendent of B.1.1.28), initially found in the Amazon region, has a similar mutation profile as the South African variant, including E484K and N501Y. Concerns are, as for the South African variant, higher transmissibility and a decreased protection by neutralizing antibodies.

Lineage B.1.525 carries several mutations of biological significance, including E484K, Q677H and F888L. It does not carry N501Y, but a set of deletions similar to the B.1.1.7 variant.

Lineage B.1.617 is a variant first detected in India and was designated “Under Investigation” on 1st April 2021 by Public Health England. It contains a number of spike mutations associated with antigenic escape or found in other variants of concern, including L452R, E484Q and P681R. Subtype B.1.617.2 does not carry S:E484Q and seems to be more transmissible than B.1.1.7 (increasing confidence). Neutralization studies show reductions in cross-neutralizing activity between B.1.1.7 and B.1.351.