LNS LUXEMBOURG

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

Direction de la santé

Respiratory Viruses in Luxembourg (ReViLux)

Weekly report (Period 19/07/-25/07/2021)

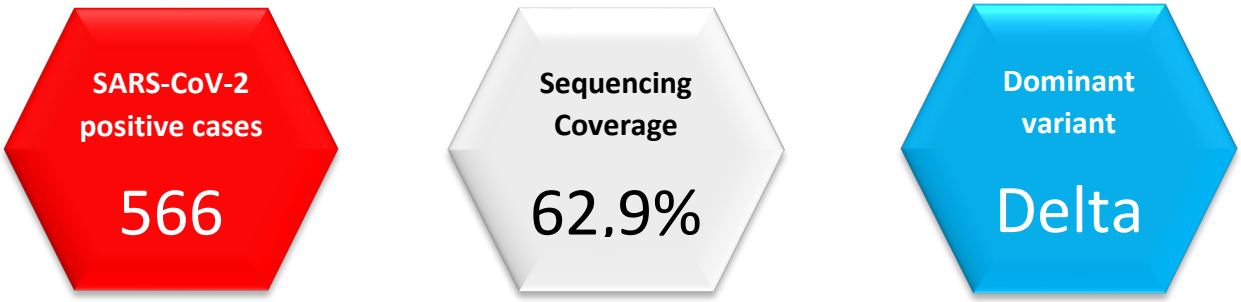
Executive Summary

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 356 specimens in week 29/2021 (from 566 total cases in the Grand Duchy of Luxembourg, 62,9%). This exceeds the minimum coverage (10%) and sample size recommended by the ECDC (which is 292 in our current epidemiological situation).

Community surveillance revealed a sharp fall of Gamma cases (-65,0% compared to week 28) and a mild increase of Delta variant cases, which remains on an increasing trend since week 24. Currently, the Delta variant continues to be the dominant variant in Luxembourg.

In respect to target group surveillance, all cases analysed were identified as VOC cases, and 13 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 29 (19 July 2021 – 25 July 2021) are displayed in Table 1 and the history of ILI consultations since the 2018-2019 season is shown in Figure 1. **The percentage of ILI remains below the threshold for the interepidemic season**, according to the ECDC.

Regarding the virological surveillance, no data is available for week 29.

Table 1. Syndromic surveillance during week 29

	Count	Percent
ARI consultations	32	11,4%
ILI consultation	0	0,0%
Total consultations	280	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…).

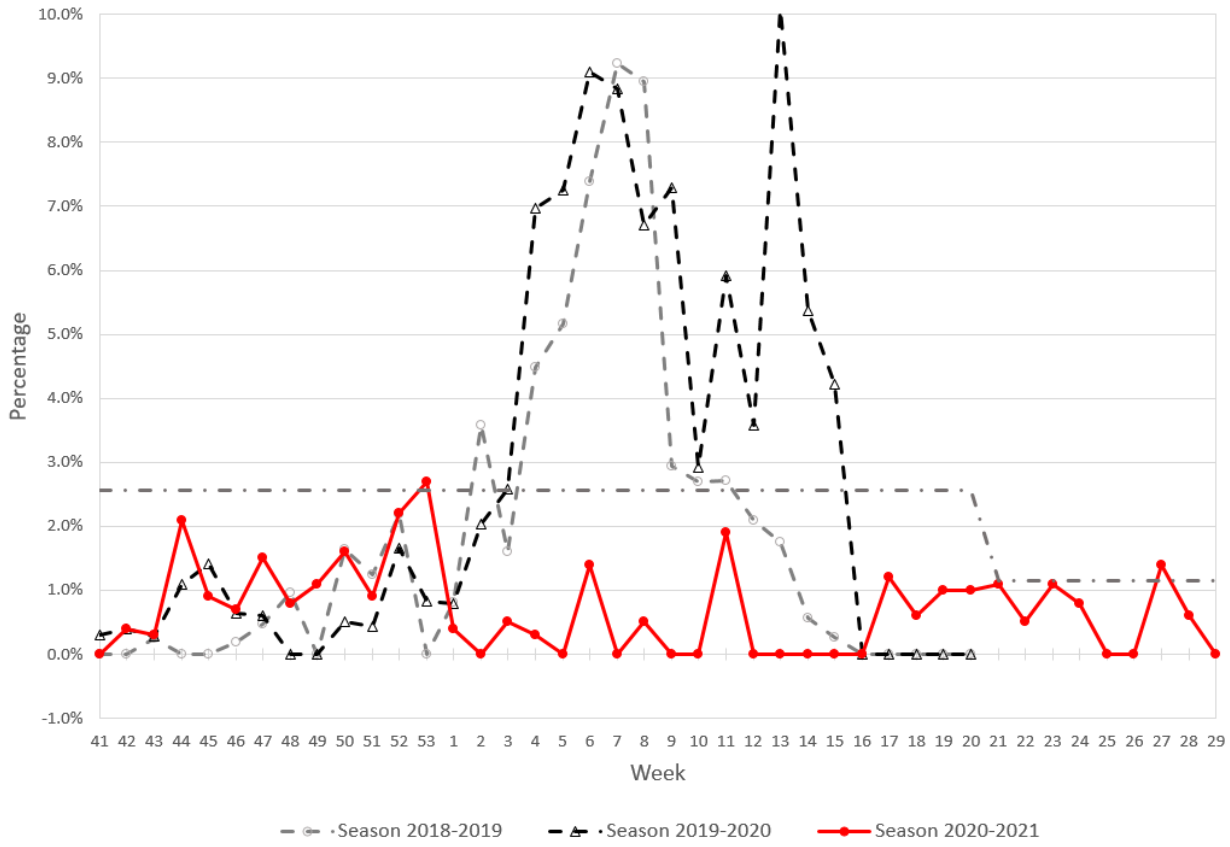


Figure 1. Percentage of patients with influence-like illness over the epidemiological weeks

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 representative sample of community cases.

The representative 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 29, 566 new cases were registered in Luxembourg; hence, the minimum sample size required to detect a 2.5% incidence is estimated to be 292 specimens (51,6%). The number of non-targeted specimens from Luxembourgish residents successfully sequenced this week was 297 (52,5%), which exceeds the minimum coverage (10%) and minimum sample size (292) 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 (v3.1.7, pangoLEARN version 2021-07-09). 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.

Sequenced specimens

Last week, the microbial genomics platform at the LNS sequenced 588 specimens, with 391 having been collected in week 29/2021. Among the latter, 74 specimens were reported to be part of a cluster or vaccine failure investigation, and 35 specimens were from non-residents (15 specimens overlapping). The number of non-targeted specimens

from Luxembourgish residents successfully sequenced this week was 297 (52,5% coverage of 566 total cases) (see coverage trend in Figure 2).

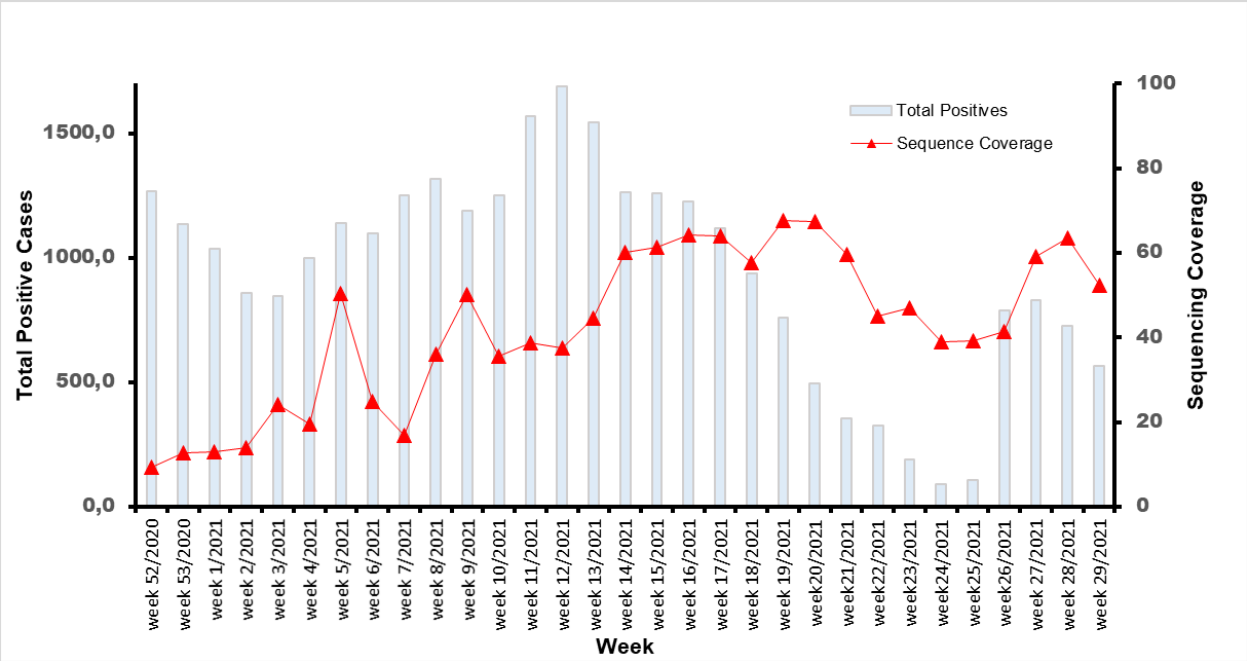


Figure 2. Sequence coverage based on total number of positive cases in Luxembourg in between week 52/2020 and week 29/2021

Circulating lineage detection

The evolution of variants over the weeks is shown in Figure 3. Delta variant showed a constant increase, in absolute values, during the last seven weeks, and remains the dominant variant.

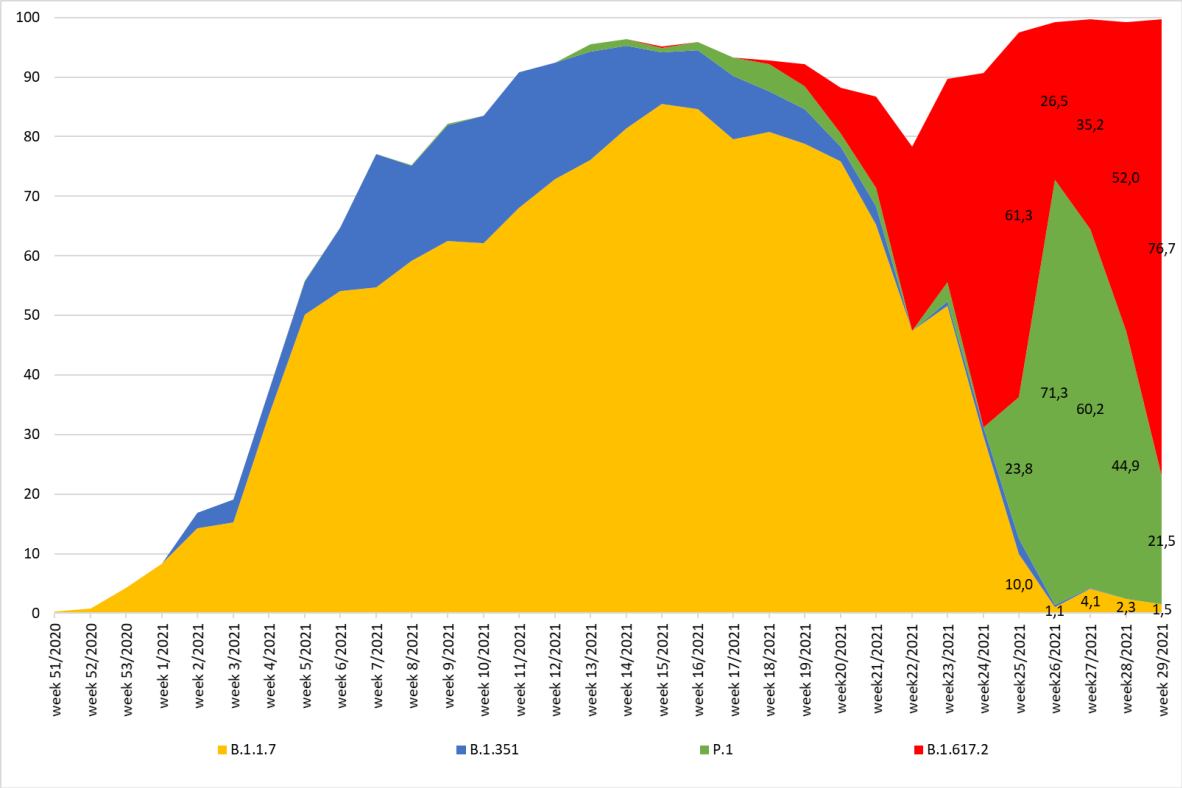


Figure 3. Evolution of variants in sequencing pool of all specimens including targeted sequencing (clusters, non-residents) since first detection of B.1.1.7 in Luxembourg

In week 29/2021, 4 circulating SARS-CoV-2 variants were detected within our representative 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 lineages detected within the community (cluster and non-resident cases excluded) in weeks 28 and 29/2021 (week 28 cases updated by retrospective sequencing)

VOC	Week 29			Week 28		
	N	%	CI	N	%	CI
B.1.1.7 (Alpha)	6	2.0%	0.4% - 3.6%	11	2.6%	1.1% - 4.1%
B.1.351 (Beta)	0	0.0%	-	0	0.0%	-
P.1 (Gamma)	71	23.9%	19.1% - 28.8%	203	47.8%	43.0% - 52.5%
B.1.617.2 (Delta)	219	73.7%	68.7% - 78.7%	209	49.2%	44.4% - 53.9%
Others	1	0.3%	0.0% - 1.0%	2	0.4%	0.0% - 1.1%
Total	**297**	**100.0%**		**425**	**100.0%**	

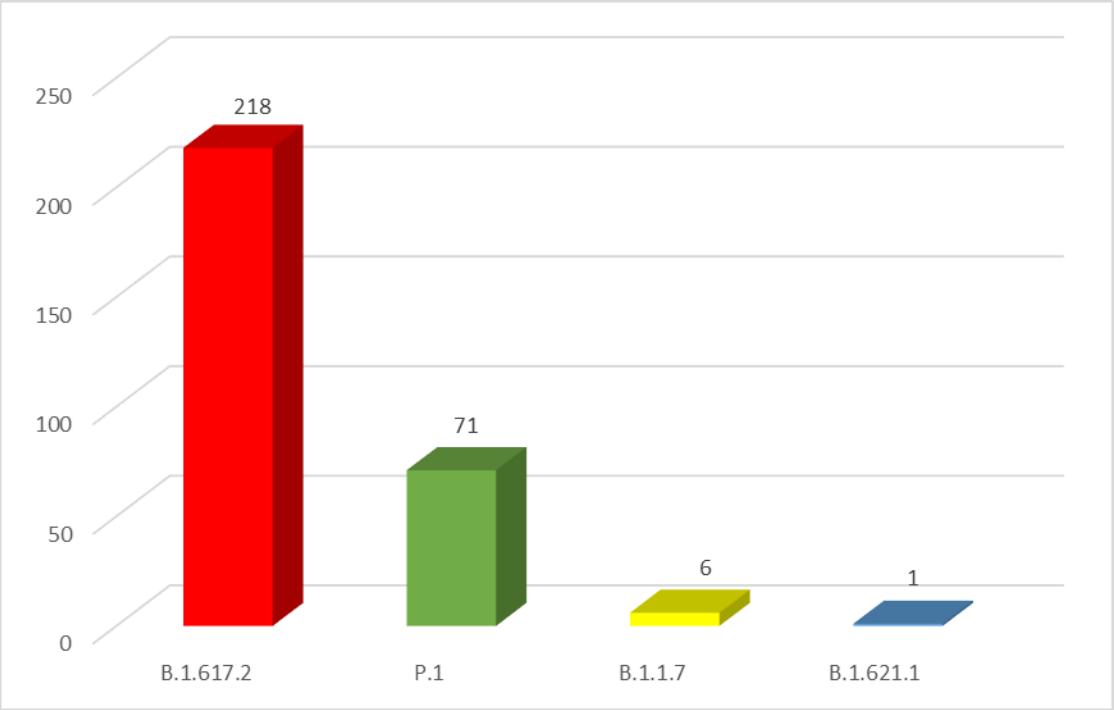


Figure 4. Number of SARS-CoV-2 variants in representative sample for week 29/2021

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. 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 between 1 Sep 2020 and 25 Jul 2021 (N=16080), as well as the frequencies in week 29/2021.

Table 3. Analysis of clinically relevant mutations identified during week 29/2021 sequencing

Mutation	Gene	Genomic Position in reference	Frequency Overall [%]	Frequency Week 29/2021 [%]	Characteristics	Reference
D614G	S gene	23402	95.5	99.3	Higher infectivity, higher case fatality rate, higher transmission; replaced original Wuhan strain, became globally dominant form of the virus	Eaaswarkhanth 2020 Becerra-Flores 2020, Hu 2020, Plante 2020
P323L	ORF1ab	14407	88.5	95.5	Higher severity	Biswas & Mudi 2020
R203K	N gene	28880	57.3	23.3	Fitness advantage for the virus	Leary 2020
G204R	N gene	28883	57.3	23.3	Fitness advantage for the virus	Leary 2020
N501Y	S gene	23063	56.2	22.4	501Y.V1/V2; Improved ACE2 binding affinity/higher transmissibility	Filip Fratev 2020 COVID-19 Genomics Consortium UK, 2020
E484K	S gene	23012	16.4	21.4	501Y.V2 / possible impact on antibody neutralization activity (escape mutation), improved ACE2 binding affinity	Greaney 2020
Y144del	S gene	21991-21993	44.7	2.5	possible impact on antibody binding affinity	Dawood 2020
H69/V70del	S gene	21765-21770	44.1	1.7	possible impact on antibody neutralization activity and reinfection; included in "mink" mutation	Kemp 2020
P681H	S gene	23604	41.9	2.0	immediately adjacent to the furin cleavage site, a known location of biological significance	COVID-19 Genomics Consortium UK, 2020
L37F	Nsp6	11081	3.5	3.2	Favored viral infection, higher severity	Aiewsakun 2020
Q57H	ORF3a	25561	21.2	0.2	Higher severity	Biswas & Mudi 2020
K417N	S gene	22813	7.6	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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Rambaut A., Holmes E., O'Toole Á., Hill V., McCrone J., Ruis C. et al. (2020). A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nature Microbiology*, *5*(11), 1403-1407. doi: 10.1038/s41564-020-0770-5

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.