SARS-CoV-2 Sequencing Update
31 December 2021

Supported by the DSI and the SA MRC

Prepared by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory (NHLS) on behalf of the Network for Genomics Surveillance in South Africa (NGS-SA)
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 30 December at 08h36

Data license: https://www.gisaid.org/registration/terms-of-use/


Case data is based on specimen collection date. Cases from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports.weekly-epidemiological-brief/ Test data from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-testing-summary/
Bar graphs represent genomes sequenced per epiweek, with lines representing cases by collection date (weeks 18 – 51)
Genomes and cases presented as provincial total (percentage of national total) for epiweeks 18 – 51
PTP: percentage testing positive in week 50 (19 Dec – 25 Dec); the arrow indicates direction of change since the previous week (12 Dec – 18 Dec)
Total genomes: 26 390
2020 genomes: 6 462
2021 genomes: 19 928

Sequencing data ending epi week 51 (ending 25 December 2021)
Currently in epi week 52 (ending 1 January 2022)

*This represents the cleaned, de-duplicated dataset of unique sequences. This dataset will be used for all further figures.
All provinces, apart from GP, NC and WC, have comparable percentages of overall cases and overall sequenced genomes.
Omicron sub-lineage spike mutation profiles

BA.1
21K

BA.2
21L
Lacks 69-70del
Not detectable by S-Gene Target Failure

BA.3
21M

Lineage definitions based on https://github.com/cov-lineages/pango-designation/issues/367
Images from https://covdb.stanford.edu/page/mutation-viewer/
Omicron spike mutations compared to other VOC/VOIs

- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked to immune escape

<table>
<thead>
<tr>
<th>Spike mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA.1</td>
</tr>
<tr>
<td>BA.2</td>
</tr>
<tr>
<td>BA.3</td>
</tr>
<tr>
<td>C.1.2</td>
</tr>
<tr>
<td>Alpha+E484K</td>
</tr>
<tr>
<td>Gamma</td>
</tr>
<tr>
<td>Delta</td>
</tr>
<tr>
<td>Kappa</td>
</tr>
<tr>
<td>Eta</td>
</tr>
<tr>
<td>Iota</td>
</tr>
<tr>
<td>Lambda</td>
</tr>
<tr>
<td>Mu</td>
</tr>
</tbody>
</table>

Only lineage-defining mutations are pictured here. Low prevalence mutations can be seen on the following slide.

**Mutation impact key**
- **Unknown or unconfirmed impact**
- **Known/predicted immune escape**
- **Enhanced infectivity**

NGS-SA
Network for Genomic Surveillance in South Africa
Mutational profile of Omicron is largely shared amongst all sequences. Low mutation frequencies for N417N, N440K, G446S and N764K are most likely a result of poor coverage due to primer drop off.
Omicron has been detected in 109 countries across the globe (detections based on GISAID).
Delta dominated in South Africa until October at >80%. Omicron dominated November and early December at >95%.
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in October – December 2021

The Delta variant dominated at >80% in October in South Africa, while Omicron was detected at 0.3% (2/768). Omicron dominated in November, at 83% (1063/1289) and continues to dominate in December (98%, 807/820).
Detection Rates: Beta, Delta, C.1.2 and Omicron

C.1.2 has been detected at ≤ 4% of sequences monthly. Beta prevalence increased slightly in October but has since remained at low levels in November and December. Omicron has been dominant since November (>80% in November, >98% in December).
Free State Province, 2021, n = 1063

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Gauteng Province, 2021, n = 5475

GP (N=5475)

Number of genomes

Number of cases

Percent of genomes

Epiweek

GP (N=5475)

Epiweek

Cases

Omicron (21K)
Omicron (21M)
Beta (20H, V2)
Delta (21A)
Delta (21I)
Delta (21J)
Kappa (218)
Eta (21D)
20A
20B
20C
20D
unassigned
19A
19B

Network for Genomic Surveillance in South Africa

NGS-SA
KwaZulu-Natal Province, 2021, n = 2474
Limpopo Province, 2021, n = 1168
Mpumalanga Province, 2021, n = 1114
Northern Cape Province, 2021, n = 1341

Graph showing the number of cases and percent of genomes from 2021 in the Northern Cape Province, South Africa. The graph includes data from various weeks, with peaks and trends indicating the spread of different viral variants.
North West Province, 2021, n = 1276

NW (N=1276)

Number of genomes

Number of cases

percent of genomes

Number of cases

Omicron (21K)  Omicron (21M)  Beta (20H, V2)  Delta (21A)  Delta (21I)  Kappa (21B)  Eta (21I)  20A  20B  20C  20D  unassigned  19A  19B

Cases
Western Cape Province, 2021, n = 4133
Summary

- **Variant of Concern Omicron**
  - **South Africa:**
    - Dominated November sequencing data at 82.5% of genomes (n=1063/1289) and December sequencing data at 98% of genomes (n=807/830)
    - Detected in all provinces
  - **Global:**
    - Detected in 109 countries worldwide
    - Split into three lineages based on different mutational profiles: BA.1 (21K), BA.2 (21L), BA.3 (remains in 21M with parent lineage B.1.1.529 as does not meet requirements for new clade)

- Delta variant dominated in all provinces until end October
  - Delta sub-lineages varied by province

- C.1.2 lineage detected in all provinces of South Africa with prevalence of <4% of genomes per month and continues to be detected at low frequency
Supported by the DSI and the SA MRC

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Multiple labs from NGS-SA and collaborating public and private laboratories are contributing to sequencing, both as originating and as submitting (pictured here) laboratories.
## Variants of Concern (VOC)

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Pango lineage•</th>
<th>GISAID clade</th>
<th>Nextstrain clade</th>
<th>Additional amino acid changes monitored*</th>
<th>Earliest documented samples</th>
<th>Date of designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha</td>
<td>B.1.1.7</td>
<td>GRY</td>
<td>20I (V1)</td>
<td>+S:484K</td>
<td>United Kingdom, Sep-2020</td>
<td>18-Dec-2020</td>
</tr>
<tr>
<td>Gamma</td>
<td>P.1</td>
<td>GR/501Y.V3</td>
<td>20J (V3)</td>
<td>+S:681H</td>
<td>Brazil, Nov-2020</td>
<td>11-Jan-2021</td>
</tr>
</tbody>
</table>


• Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.

* See TAG-VE statement issued on 26 November 2021

* Only found in a subset of sequences
## Currently designated Variants of Interest (VOI)

<table>
<thead>
<tr>
<th>WHO label</th>
<th>Pango lineage*</th>
<th>GISAID clade</th>
<th>Nextstrain clade</th>
<th>Earliest documented samples</th>
<th>Date of designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambda</td>
<td>C.37</td>
<td>GR/452Q.V1</td>
<td>21G</td>
<td>Peru, Dec-2020</td>
<td>14-Jun-2021</td>
</tr>
<tr>
<td>Mu</td>
<td>B.1.631</td>
<td>GH</td>
<td>21H</td>
<td>Colombia, Jan-2021</td>
<td>30-Aug-2021</td>
</tr>
</tbody>
</table>


*Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.
Submission of routine specimens for sequencing

• representative of multiple geographic regions (provinces/districts/health facilities) from individuals of
  • all ages
  • over as many time periods during the SARS-CoV-2 epidemic in South Africa

• requested that testing laboratories in both the private and public sectors, submit respiratory samples to their closest NGS-SA sequencing laboratory on a routine basis (ideally every week) as follows, depending on the capacity of the testing laboratory:
  • All positives samples should be sent every week (NGS-SA laboratory will perform random sampling as described below) OR
  • A weekly selection of approximately 10%-20% of randomly selected positive samples should be sent every week. Number of selected samples will depend on the size of laboratory and how many other laboratories are drained by the submitting laboratory.
Submission of special interest specimens for sequencing

In addition to routine samples mentioned above, please send specimens separately to above and clearly marked if:

• Suspected vaccine breakthrough (≥14 days after vaccine), especially if hospitalised and clinically severe
• Suspected re-infection (≥90 days after previous episode), especially if hospitalised and clinically severe
• Prolonged shedding with high SARS-CoV-2 viral loads (i.e. Ct values less than 30 for more than 1 month post-primary diagnosis) in immunocompromised individuals
• Possible animal-to-human transmission
• Suspected cases of importation from another country, especially countries known to harbour SARS-CoV-2 variants of concern or countries with little available information
• Clusters of “unusual” cases (e.g., in terms of disease presentation, patient groups affected, etc.)