SARS-CoV-2 Sequencing Update
25 February 2022

Supported by the DSI and the SA MRC
Msmoi N. Milisana K. et al. Lancet Microbe 2020

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 25 February 2022 at 11h11

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 gives weekly percentage testing positive rates, 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 39 [2021] – 7 [2022]).

Genomes and cases presented as provincial total (percentage of national total) for epiweeks 39 (2021) – 7 (2022).

PTP: percentage testing positive in week 7 (13 Feb 2022 – 19 Feb 2022); the arrow indicates direction of change since the previous week (6 Feb 2022 – 12 Feb 2022).

743 genomes deposited in the past week.
**Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022**

(N=31,812*)

Total genomes: 31,795
- 2020 genomes: 6,539
- 2021 genomes: 23,289
- 2022 genomes: 1,983

Sequencing data ending epi week 6 (ending 12 February 2022)

Currently in epi week 8 (ending 26 February 2022)

*This represents the cleaned, de-duplicated dataset of unique National and Pneumonia Surveillance 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.
Delta dominated in South Africa until October at >80%. Omicron has dominated from November onwards.
Omicron dominated in December (99%, 3560/3589) and January (99%, 1907/1922), and continues to dominate in February (98%, 59/60) with sub-lineage BA.2 increasing in prevalence.
Detection Rates: Beta, Delta, C.1.2 and Omicron

Omicron has been dominant since November (>80% in November, >99% in December and January). BA.2 increased in frequency in January, making up 36% of genomes. BA.2 dominates in February (78%) but more sequencing data is required to confirm its prevalence.
South Africa, 2021-2022, n = 25188*

*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.
Eastern Cape Province, 2021-2022, n = 2363
Free State Province, 2021-2022, n = 1314

Clade key (bar graph)
- Omicron (21L/BA.2)
- Omicron (21K/BA.1.1)
- C.1.2 (20D)
- Delta (21I)
- Beta (20H.2)
- Alpha (20I.1)
- Kappa (21B)
- Eta (21D)
- 20A
- 20B
- 20C
- 20D
- unassigned
- 19A
- 19B

Weekly percentage testing positive key (line graph)
- ≤ 5
- 6 - 10
- 11 - 20
- 21 - 30
- 31 - 40
- 41 - 50
- 51 - 55
Gauteng Province, 2021-2022, n = 6732
KwaZulu-Natal Province, 2021-2022, n = 3220

Clade key (bar graph)

Weekly percentage testing positive key (line graph)
Limpopo Province, 2021-2022, n = 1675

Clade key (bar graph)

Weekly percentage testing positive key (line graph)
Western Cape Province, 2021-2022, n = 5063

Clade key (bar graph)

Weekly percentage testing positive key (line graph)
Summary

- Variant of Concern Omicron
  - Detected in at least 153 countries and dominating globally
  - Split into different lineages based on different mutational profiles. Predominant lineages currently BA.1 (21K), BA.1.1 (21K, BA.1+spike R346K), BA.2 (21L), BA.3 (21M). More lineages are being assigned but defining mutations are not yet available.

- South Africa (detected in all provinces):
  - Dominated December, January and February sequencing data at >99% of genomes
  - While BA.1 was the predominant sub-lineage in December (85%) and January (53%), the proportion of BA.2 increased from 5% in December and 36% in January to 78% in February

- Low frequency of previously circulating variants such as Delta still detected in recent data
Omicron sub-lineage spike mutation profiles

**BA.1**

21K

Lacks 69-70del
Not detectable by S-Gene Target Failure

**BA.2**

21L

**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

Only lineage-defining mutations are pictured here. Low prevalence mutations can be seen on the following slide.
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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 +S:452R</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.)