# SARS-CoV-2 variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Sometimes new variants emerge and disappear. Other times, new variants emerge and persist. Many variants of the virus that cause COVID-19 have been detected globally during this pandemic. A variant may contain one or multiple mutations and these mutations can occur in the nucleocapsid protein or the spike protein region of the virus.

### What is a "Variant of Concern" (VOC)?

A variant may be classified as "Of Concern" when there is evidence of an increase in transmissibility, more severe disease, significant reduction in neutralization by antibodies, reduced effectiveness of treatments or diagnostic detection failures.

### The LumiraDx SARS-CoV-2 Tests and Variants

The LumiraDx SARS-CoV-2 Ag, LumiraDx SARS-CoV-2 Ag Pool and LumiraDx SARS-CoV-2 & Flu A/B tests use antibodies (not nucleic acid based-primers like PCR) to capture SARS-CoV-2 **nucleocapsid antigen** (not the spike protein). Antibodies typically recognize 8-15 amino acid target sequences (equivalent to 24-45 nucleotide sequences). Thus, single nucleic acid point mutations are not likely to affect the performance of the LumiraDx tests. Furthermore, mutations outside of the nucleocapsid viral coding region (eg. Spike protein) are highly unlikely to affect on the performance of the test.

### Testing Status of SARS-CoV-2 Variants with the LumiraDx tests

LumiraDx is actively monitoring for new mutations in the SARS-CoV-2 viral genome as they arise. The reactivity of the LumiraDx tests is assessed against all mutations prevalent in the population at a level of greater than 1.0% on the Regeneron COVID-19 Dashboard[1] which is one of the collaborations enabled by the data in the **gisaid.org** website. Table 1 is a summary of the performance of the LumiraDx SARS-CoV-2 Ag assay used in the LumiraDx SARS-CoV-2 Ag test, LumiraDx SARS-CoV-2 Ag Pool test and the LumiraDx SARS-CoV-2 & Flu A/B test for Variants of Concern as designated by the WHO[6] at the time of writing this technical bulletin. Evaluation has been carried out using in silico analysis, direct testing using recombinant nucleocapsid protein of the specific mutations, live viral isolate testing and testing of positive live clinical samples.

Table 1: Summary of testing with the LumiraDx Ag test

| WHO Label[6] | Pango Lineage[6] | Country in which first detected[6] | Nucleocapsid mutation[1] | LumiraDx Test Result |
|---|---|---|---|---|
| **Alpha** | B.1.1.7 | UK,Sep 2020 | D3L, R203K,G204R, S235F | Positive |
| **Beta** | B.1.351 | South Africa, May 2020 | T205I | Positive |
| **Gamma** | P.1 | Brazil, Nov 2020 | P80R, R203K, G204R | Positive |
| **Delta** | B.1.617.2 | India, Oct 2020 | D63G, R203M, G215C, D377Y | Positive |
| **Omicron*** | B.1.1.529 | Multiple countries, Nov 2021 | R203K, G204R, P13L, E31-, R32- and S33- | Positive |

* Descendent Pango lineages of Omicron, BA.2 and BA.3, have the additional nucleocapsid mutation S413R, which was tested in-house using recombinant protein and tested positive at 50pg/mL on the LumiraDX SARS-CoV-2 Antigen Test.

- **Alpha Variant[2], Beta Variant[3] and Gamma Variant[3]** – Detection was demonstrated in patient samples by UK Department of Health and Social Care, COVID-19 Technologies Validation Group.
- **Beta Variant[4]** – Detection was demonstrated in patient samples by the South African National Health Laboratory Service.
- **Delta Variant[5]** – Detection was demonstrated in patient samples as discussed by the UK Department of Health and Social Care, COVID-19 Technologies Validation Group.
- **The Omicron Variant** – Testing with patient live samples was completed by LumiraDx.[8] In addition, a prospective clinical study was carried out by Medical Research Network Diagnostics.[9] Both studies showed that Omicron is detected by the LumiraDx SARS-CoV-2 Ag test with comparable sensitivity to the Delta variant.

In addition, the LumiraDx SARS-CoV-2 Ag test has been evaluated as part of the Foundation for Innovative New Diagnostics (FIND) process (www.finddx.org). For the COVID-19 response, FIND has commissioned independent evaluations of in vitro diagnostics following an Expression of Interest (EOI) process available on FIND's website by which all test submissions were scored according to their regulatory status and time to market; the manufacturing and distribution capacity of the supplier; and the supplier-reported clinical and analytical performance.[7]

As part of this evaluation, the Analytical sensitivity, i.e., Limit of detection (LoD), was performed at the Liverpool School of Tropical Medicine, U.K in which standardized serial dilutions of cultured viral isolate were prepared. Viral dilution was applied directly to the LumiraDx SARS-CoV-2 Ag Test strip. Dilutions were tested in triplicate and the LoD was defined as the last dilution where all repeats were interpreted as positive. The data (Table 2) demonstrate that the LumiraDx SARS-CoV-2 Ag Test can detect the U.K Wild Type (B.1), Alpha (B.1.1.7), Gamma (P.1), and Delta (B.1.617.2) variants. At the time of this LoD testing the Omicron variant was not in circulation.

Table 2: Estimation of analytical performance carried out by the Liverpool School of Tropical Medicine, demonstrating comparable LoD across all variants tested.[7]

| Variant (lineage) | Verified LoD concentration |
|---|---|
| **UK Wild type (B.1)** | 1.0 x $10^2$ pfu/mL |
| **Alpha (B.1.1.7)** | 5.0 x $10^2$ pfu/mL |
| **Gamma (P.1)** | 1.0 x $10^2$ pfu/mL |
| **Delta (B.1.617.2)** | 2.5 x $10^1$ pfu/mL |

**Conclusion**

All testing to date has demonstrated that the LumiraDx SARS-CoV-2 Ag Test can detect all the SARS-CoV-2 variants of concern with comparable sensitivity.

1. GISAID Regeneron Database (Regeneron COVID-19 Dashboard) accessed 22nd February 2022
2. UK Department of Health and Social Care (UK DHSC), COVID-19 Technologies Validation Group (TVG) report on LumiraDx SARS-CoV-2 Antigen test Report (January 2021)
3. UK DHSC COVID-19 TVG: Personal Communication by email (March 2021) Data on File
4. South African National Health Laboratory Service: Laboratory Evaluation Report (April 2021) Data on File
5. UK DHSC COVID-19 TVG: Personal Communication (Data on File May 2021)
6. World Health Organisation (https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/) Accessed September 2021
7. FIND Report on the LumiraDx SARS-CoV-2 Ag Test https://www.finddx.org/wp-content/uploads/2021/10/Lumira_Ag-Public-Report_v2_20211008.pdf
8. Data on File (Jan 2022)
9. Data on File (Feb 2022)

Not all products are available in all countries and regions. Please check with your local LumiraDx sales representative or distributor for availability in specific markets.

LumiraDx SARS-CoV-2 Ag Pool and LumiraDx SARS-CoV-2 & Flu A/B tests are not available in the US