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 locations such as the nucleocapsid protein or the spike protein region of the virus.

The LumiraDx SARS-CoV-2 tests and variants

The LumiraDx SARS-CoV-2 Ag, LumiraDx SARS-CoV-2 Ag Ultra, LumiraDx SARS-CoV-2 & Flu A/B and LumiraDx SARS-CoV-2 & RSV tests use antibodies (not nucleic acid based-primers like PCR) to capture SARS-CoV-2 nucleocapsid antigen (not the spike protein). Antibodies typically recognize 9-10 amino acid target sequences (equivalent to 27-30 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 have an effect 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%, according to the GISAID database. The LumiraDx SARS-CoV-2 Ag assay is used in the LumiraDx SARS-CoV-2 Ag test, LumiraDx SARS-CoV-2 & Flu A/B test, LumiraDx SARS-CoV-2 Ag Ultra test and LumiraDx SARS-CoV-2 & RSV test. Table 1 is a summary of the performance of this assay with Variants of Concern as designated by the WHO[6]. Evaluation has been carried out using *in silico* analysis, direct testing using recombinant nucleocapsid protein containing the specific mutations, live viral culture 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

- **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.

*No longer VOC according to WHO. From 15 March 2023, the WHO will consider Omicron sublineages independently for classification as VOCs.
† The mutations possessed by BA.1, BA.2, BA.3, BA.4, BA.5, XE and lineages estimated to be >5% prevalent in the UK (England)17 and US14 (as of 23rd October 2024) are shown in Table 2.

OS-04286-01
APPROVED FOR USE IN THE US.
EMERGENCY USE AUTHORIZED ONLY.

Table 2:

Nucleocapsid mutations possessed by Omicron lineages and results of recombinant protein testing.

Omicron lineage	Nucleocapsid protein muations[1]	Comments	Recombinant protein testing summary
B.1.1.529	P13L, E31-, R32-, S33-, R203K, G204R	None	All mutations detected at 50 pg/mL*
BA.1	P13L, E31-, R32-, S33-, R203K, G204R	None	All mutations detected at 50 pg/mL*
BA.2	P13L, E31-, R32-, S33-, R203K, G204R, S413R	None	Same mutations in the nucleocapsid protein as XE
BA.3	P13L, E31-, R32-, S33-, R203K, G204R, S413R	None	Same mutations in the nucleocapsid protein as XE
BA.4	P13L, E31-, R32-, S33-, P151S, R203K, G204R, S413R	None	All mutations detected at 50 pg/mL*
BA.5	P13L, E31-, R32-, S33-, R203K, G204R, S413R	None	Same mutations in the nucleocapsid protein as XE
XE	P13L, E31-, R32-, S33-, R203K, G204R, S413R	BA.1/BA.2 recombinant[10]	Protein detected at 50 pg/mL
BF.7	P13L, G30-, E31-, R32-, S33F, R203K, G204R, S413R	Sublineage of BA.5[14]	Protein detected at 50 pg/mL
XEC	P13L, E31-, R32-, S33-, R203K, G204P, Q229K, S413R	Estimated >5% prevalent in England and US (26 February 2025)	Same mutations in the nucleocapsid protein as XE aside from Q229K and G204P. Q229K and G204P have no impact on LumiraDx SARS-CoV-2 Ag test detection as per completed in silico analysis.
KP.3.1.1	P13L, E31-, R32-, S33-, R203K, G204R, Q229K, S413R	Estimated >5% prevalent in England & US (26 February 2025)	Same mutations in the nucleocapsid protein as XE aside from Q229K. Q229K has no impact on LumiraDx SARS-CoV-2 Ag test detection as per completed in silico analysis.
JN.1	P13L, G30-, E31-, R32-, S33-, R203K, Q229K, S413R	Estimated >5% prevalent in England (26 February 2025)	Same mutations in nucleocapsid as XE and BF aside from Q229K. Q229K has no impact on LumiraDx SARS-CoV-2 Ag test detection as per completed in silico analysis.
LP.8.1	P13L, G30-, E31-, R32-, S33-, R203K, G204R, Q229K, S413R †	Estimated >5% prevalent in England & US (26 February 2025)	Same mutations in nucleocapsid as XE and BF aside from Q229K. Q229K has no impact on LumiraDx SARS-CoV-2 Ag test detection as per completed in silico analysis.

*All mutations were tested separately. All mutations except P151S are also present in the XE nucleocapsid protein.

† Present mutations determined through mutation frequencies occurring at ≥70% mined from GISAID database for Jan2025.

- **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.
- **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.

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 3) 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), Delta (B.1.617.2) and Omicron (B.1.1.529 and B.1.1.529 sub lineage BA.2) variants.

Table 3: Estimation of analytical performance carried out by the Liverpool School of Tropical Medicine, demonstrating comparable LoD across all variants tested.

Variant strain	Verified LoD concentration
UK Wild type (B.1)[7]	1.0 x 10^2 pfu/mL
Alpha (B.1.1.7)[7]	5.0 x 10^2 pfu/mL
Gamma (P.1)[7]	1.0 x 10^2 pfu/mL
Delta (B.1.617.2)[7]	2.5 x 10^1 pfu/mL
Omicron (B.1.1.529)[11]	1.0 x 10^3 pfu/mL
Omicron (B.1.1.529) sub lineage BA.2[12]	1.0 x 10^2 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.

As the WHO ended the public health emergency of international concern status of COVID-19 in May 2023[15], and the disease is beginning to transition from a pandemic to epidemic state, the focus of LumiraDx variant monitoring is moving from wet testing to in silico surveillance of circulating and newly arising variants.

OS-04286-01
APPROVED FOR USE IN THE US.
EMERGENCY USE AUTHORIZED ONLY.

Definitions

Ag	Antigen
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
VOC	Variant of concern
WHO	World Health Organisation
PCR	Polymerase Chain Reaction
LoD	Limit of Detection
FIND	Foundation for Innovative New Diagnostics
pg	Picogram
pfu	Plaque Forming Unit

1. GISAID Regeneron Database - mutation details (https://gisaid.org/hcov19-variants/) (Accessed 20 November 2024).
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 October 2023
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)
10. World Health Organisation (https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/) Accessed October 2023
11. Data on File (Feb 2022)
12. Data on File (May 2022)
13. UKHSA Technical Briefing 55 (https://www.gov.uk/government/publications/investigation-of-sars-cov-2-variants-technical-briefings)
14. CDC (https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html#anchor_1632154493691) (Accessed October 2023)
15. Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic (https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-%282005%29-emergency-committee-regarding-the-coronavirus-disease-%28covid-19%29-pandemic)(Accessed 11Mar2025)

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.

The LumiraDx SARS-CoV-2 Ag Ultra, LumiraDx SARS-CoV-2 & Flu A/B and LumiraDx SARS-CoV-2 & RSV tests are not available in the US.