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.

GISAID, NEXTstrain and Pango are established systems that name and track virus variants of concern and variants of interest, these systems are designed to give scientists a common language in which they can discuss and investigate the evolution of SARS-CoV-2[1]. WHO have released a variant naming system based on the Greek alphabet for use by the General public (Table 1).

Table 1[1] – Variants listed by WHO[1], ECDC[2], UK PHE[3] as VOC

WHO label	Pango lineages	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	201 (V1)	UK Sept 2020	18-Dec-2020
Beta	B.1.351 B.1.351.2 B.1.351.3	GH/501Y.V2	20H (V2)	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2 P.1.4 P.1.6 P.1.7	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2 AY.3 AY.3.1	G/478K.V1	21A	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

The LumiraDx SARS-CoV-2 Ag Test and Variants

The LumiraDx SARS-CoV-2 Ag Test uses 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 SARS-CoV-2 Ag Test. 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 Ag Test

The following table shows the performance of the LumiraDx SARS-CoV-2 Ag Test with VoCs a Variants of Interest (VOI) and VUI (Variants Under Investigation. In-house evaluation has been carried out using in silico analysis and direct testing using either recombinant nucleocapsid protein or independent testing with the viral isolate:

- **Alpha Variant[6], Beta Variant[7] and Gamma Variant[7]** – detection was demonstrated in patient samples by UK Department of Health and Social Care, COVID-19 Technologies Validation Group.
- **Beta Variant[8]** – demonstrated by the South African National Health Laboratory Service.
- **Delta Variant[9]** – detection has been demonstrated in patient samples as discussed by the UK Department of Health and Social Care, COVID-19 Technologies Validation Group.

Table 2

Variant strain	Nucleocapsid protein mutation	LumiraDx SARS-CoV-2 Ag Test Result – Pos/Neg
Alpha VOC-20DEC-01 VOC-202012/01 B.1.1.7	D3L, R203K, G204R, S235F	Positive
Beta VOC-20DEC-02 VOC-202012/02 B1.351	T205I	Positive
Gamma VOC-21JAN-02 VOC-202101/02 (P.1)	P80R	Positive
Delta VOC 11-MAY-2021 N/A B1.617	D3Y, R203M, D377Y	Positive
Eta VOI-17-MAR-2021 B1.525 (previously UK 1188)	A12G	Positive
Theta VUI-21MAR-02 N/A P.3	R203K, G204R	Positive
VUI-21MAR-01 VUI-202103/01 B1.324.1 with E484K	M234I	Positive

As part of an ongoing project we are also monitoring new mutations in the SARS-CoV-2 viral genome as they arise. The following variants representing the most abundant mutations on the Regeneron Covid-19 Dashboard[5], which is one of the collaborations enabled by the data from GISAID, have so far been tested:

Table 3

Mutation	N° of clones sequenced	Observed frequency	Reactivity in LumiraDx Antigen Assay
N 203 R K	1101346	58.70%	Reactive
N 204 G R	1033746	55.10%	Reactive
N 235 S F	843133	44.94%	Reactive
N 3 D L	834054	44.46%	Reactive
N 220 A V	164505	8.77%	Reactive
N 199 P L	133993	7.14%	Reactive
N 234 M I	116756	6.22%	Reactive
N 205 T I	102374	5.46%	Reactive
N 67 P S	95405	5.09%	Reactive
N 194 S L	70487	3.76%	Reactive
N 204 G P	66257	3.53%	Reactive
N 377 D Y	68151	2.42%	Reactive
N 203 R M	36560	1.95%	Reactive
N 80 P R	32614	1.74%	Reactive
N 63 D G	31980	1.70%	Reactive
N 376 A T	29381	1.57%	Reactive
N 215 G C	21999	1.17%	Reactive
N 365 P S	18607	0.99%	Reactive
N 13 P L	18358	0.98%	Reactive
N 377 D Y	68151	-	Reactive

1. www.who.int (accessed 16th August 2021)
2. ECDC - European Center for Disease Prevention and Control. Variants of Interest. https://www.ecdc.europa.eu/en/covid-19/variants-concern. (accessed 26th August 2021)
3. www.gov.uk - UK Public Health (accessed 25th August 2021)
4. CDC – Center for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html (accessed 27th August 2021)
5. GISAID Regeneron Database (Regeneron COVID-19 Dashboard) accessed September 2021.
6. 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)
7. UK DHSC COVID-19 TVG: Personal Communication by email (March 2021) Data on File
8. South African National Health Laboratory Service: Laboratory Evaluation Report (April 2021) Data on File
9. UK DHSC COVID-19 TVG: Personal Communication (Data on File May 2021)