



Xpert® Xpress SARS-CoV-2 (EUA,* CE-IVD)
Xpert® Xpress SARS-CoV-2/Flu/RSV (EUA,* CE-IVD)
Xpert® Xpress CoV-2/Flu/RSV plus (EUA,* CE-IVD)
Xpert® Xpress CoV-2 plus (EUA,* CE-IVD)

SARS-CoV-2 Variants with Spike Protein Gene Mutations[^]
UPDATED INFORMATION on SARS-CoV-2 VARIANT COVERAGE

Disclaimer: This document, developed by Cepheid Medical/Scientific Affairs, is provided as a courtesy to Cepheid customers to offer guidance regarding Xpert Xpress SARS-CoV-2, Xpert Xpress SARS-CoV-2/Flu/RSV, Xpert Xpress CoV-2/Flu/RSV plus and and Xpert Xpress CoV-2 plus test results. It is your laboratory's responsibility to validate any test in accordance with federal, state/province, and local laws.

SARS-CoV-2 variants continue to emerge, containing multiple mutations in both the spike gene sequence and in other genomic regions.¹⁻⁵ As of June 2022 the current variants of concern (VOC), variants being monitored (VBM) or other variants[^] are listed below. With recent changes in variant classifications by the Centers for Disease Control and Prevention (CDC), at the date of this publication there are no variants of interest (VOI). Additionally, since the emergence of B.1.1.529 (Omicron), this lineage has been further classified into four sub-lineages, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5, and is reflected in the table below. For updates and history of variant classification, refer to the CDC SARS-CoV-2 Variant Classifications and Definitions website.⁴

VARIANT CLASSIFICATION	PANGO LINEAGE	PHE NAME	WHO DESIGNATION
VOC	BA.1	ND	Omicron
	BA.1.1	ND	Omicron
	BA.2	ND	Omicron
	BA.3	ND	Omicron
	BA.4	ND	Omicron
	BA.5	ND	Omicron
	B.1.617.2	VOC-21APR-02	Delta
	B.1.617.2 with K417N (B.1.617.2.1 / AY.1)	ND	Delta
	B.1.1.7 and Q lineages	VOC-20DEC-01	Alpha
	B.1.351 and descendants	VOC-20DEC-02	Beta
VBM	P.1 and descendants	VOC-21JAN-02	Gamma
	B.1.427 / B.1.429	ND	Epsilon
	B.1.525	VUI-21FEB-03	Eta
	B.1.526	ND	Iota
	B.1.617.1	VUI-21APR-01	Kappa
	B.1.617.3	VOC-21APR-03	ND
	P.2	VUI-21JAN-01	Zeta
	B.1.621, B.1.621.1	VUI-21JUL-01	Mu

VARIANT CLASSIFICATION	PANGO LINEAGE	PHE NAME	WHO DESIGNATION
Other Variants [^]	P.3	VUI-21MAR-02	Theta
	C.37 [#]	VUI21-JUN-01	Lambda [#]
	B.1.1.318	VUI-21FEB-04	ND
	B.1.1.7 with E484K	VOC-21FEB-02	ND
	B.1.324.1 with E484K	VUI-21MAR-01	ND
	A.23.1 with E484K	VUI-21FEB-01	ND
	C.1.2	ND	ND

ND: not determined

[^] Includes variants classified Variant Under Investigation or being monitored by Public Health England that are not included in CDC VBM classification.

[#] Analysis performed with limited number of sequences which may impact inclusivity assessment.

The Cepheid Xpert **Xpress** SARS-CoV-2 and Xpert **Xpress** SARS-CoV-2/Flu/RSV tests detect the nucleocapsid (N2) and envelope (E) genes of SARS-CoV-2. To mitigate effects of potential future genetic drift, the Cepheid Xpert **Xpress** CoV-2/Flu/RSV **plus** and Xpert **Xpress** CoV-2 **plus** tests also detect the RNA dependent RNA polymerase (RdRp) gene in addition to the nucleocapsid (N2) and envelope (E) genes of SARS-CoV-2. Cepheid continues to monitor strain surveillance data and has performed routine *in silico* analysis of SARS-CoV-2 sequences (over 11,000,000 from GISAID database at the end of May 2022 <https://www.gisaid.org/>) since the launch of our Xpert **Xpress** SARS-CoV-2, Xpert **Xpress** SARS-CoV-2/Flu/RSV, Xpert **Xpress** CoV-2/Flu/RSV **plus** and Xpert **Xpress** CoV-2 **plus** tests. These include the spike protein variant strains listed above.

Coverage is currently at $\geq 99\%$ for the E target, $\geq 99\%$ for the N2 target and $>100\%$ for the RdRp target based on *in silico* analysis of all sequences available. Data from field reports are consistent with this analysis and there have been no reported false-negative test results due to current circulating variants. The implications of these findings are that for the Xpert **Xpress** SARS-CoV-2 test a PRESUMPTIVE POSITIVE callout may occur for strains with point mutations in the N2 target, whereas the results from the Xpert **Xpress** SARS-CoV-2/Flu/RSV, Xpert **Xpress** CoV-2/Flu/RSV **plus** and Xpert **Xpress** CoV-2 **plus** tests are not impacted.

Due to our two- and three-target design, the assays' overall predicted inclusivity is 99-100% across all variants. For all Omicron sub-lineages, including BA.2.12.1,⁶ *in silico* assessment of all available sequences at the date of this report predicts 100% inclusivity by all Cepheid Xpert Xpress SARS-CoV-2 tests. For BA.1.1 sub-lineage of Omicron variant, *in silico* assessment of all available sequences at the date of this report predicts $\geq 99.5\%$ inclusivity by all Cepheid Xpert Xpress SARS-CoV-2 tests.

Acknowledgement: SARS-CoV-2 genome sequences used for this *in silico* analysis were collected from GISAID. Cepheid gratefully acknowledges the originating and submitting laboratories responsible for generating and sharing SARS-CoV-2 sequencing data via the GISAID Initiative.

Version 10. Released June 2022.

REFERENCES

- 1 Public Health England. Investigation of novel SARS-CoV-2 variant: Technical briefing. Accessed Jun 2022. <https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201>
- 2 Tegally H, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. medRxiv 2020. doi: 10.1101/2020.12.21.20248640 Accessed Jun 2022.
- 3 World Health Organization. Tracking SARS-CoV-2 Variants. Accessed Jun 2022. <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>
- 4 Accessed Jun 2022. <https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html>
- 5 Accessed Jun 2022. <https://virological.org/t/genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-manaus-preliminary-findings/586>
- 6 World Health Organization. Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern. Accessed Jun 2022. [https://www.who.int/news/item/26-11-2021-classification-of-omicron-\(b.1.1.529\)-sars-cov-2-variant-of-concern](https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern)
- 7 Accessed Jun 2022. [https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-\(b.1.1.529\)-technical-brief-and-priority-actions-for-member-states](https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states)

* In the United States, these tests have not been FDA cleared or approved. These tests have been authorized by FDA under an EUA for use by authorized laboratories. Xpert **Xpress** SARS-CoV-2 and Xpert **Xpress** CoV-2 **plus** have been authorized only for the detection of nucleic acids from SARS-CoV-2, and not for any other viruses or pathogens. Xpert **Xpress** SARS-CoV-2/Flu/RSV and Xpert **Xpress** CoV-2/Flu/RSV **plus** have been authorized only for the simultaneous qualitative detection and differentiation of nucleic acids from SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV), and not for any other viruses or pathogens. These tests are only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

CORPORATE HEADQUARTERS

904 Caribbean Drive
Sunnyvale, CA 94089 USA

TOLL FREE 1.888.336.2743
PHONE 1.408.541.4191
FAX 1.408.541.4192

EUROPEAN HEADQUARTERS

Vira Soleih
81470 Maurens-Scopont France

PHONE 33.563.82.53.00
FAX 33.563.82.53.01
EMAIL cepheid@cepheideurope.fr

www.Cepheid.com

© 2022 Cepheid 0819-10