MEDICAL/SCIENTIFIC AFFAIRS BULLETIN

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)

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, and Xpert Xpress CoV-2/Flu/RSV 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 genetic sequence and in other genomic regions[1-5]. As of November 2021, 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). 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	B.1.529#	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
VBM	B.1.1.7 and Q lineages	VOC-20DEC-01	Alpha
	B.1.351 and descendants	VOC-20DEC-02	Beta
	P.1 and descendants	VOC-21JAN-02	Gamma
	B.1.427 / B.1.429	ND	Epislon
	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
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.

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A better way.

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*** test also detects 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 4,000,000 from GISAID database as end of November 2021 https://www.gisaid.org/) since the launch of our Xpert **Xpress** SARS-CoV-2, Xpert **Xpress** SARS-CoV-2/Flu/RSV and Xpert **Xpress** CoV-2/Flu/RSV ***plus*** tests. These include the spike protein variant strains listed above.

Coverage is currently at ≥ 99% for the E target, ≥ 97% for the N2 target and >99% for the RdRp target based on *in silico* analysis. 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 and Xpert **Xpress** CoV-2/Flu/RSV ***plus*** tests are not impacted.

Due to our two- and three-target design, the tests' overall predicted inclusivity is 98-100% across all variants. For the recently emerged Omicron variant[6], *in silico* assessment of all available sequences at the date of this report predicts 100% inclusivity by all Cepheid Xpert 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.

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REFERENCES

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3 World Health Organization. Tracking SARS-CoV-2 Variants. Accessed Dec 2021. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

4 Accessed Dec 2021. https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html

5 Accessed Dec 2021. 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 Dec 2021. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

* 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 has 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.

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