

Qorvo Biotechnologies Omnia™ SARS-CoV-2 Antigen Test Detects Delta and Other Circulating COVID-19 Variants

SUMMARY

Genetic variants of the SARS-CoV-2 virus have been emerging and circulating globally throughout the COVID-19 pandemic. These viral mutations are monitored in the United States through genomic sequencing surveillance. As variants are detected in the general population, the diagnostic community attempts to ascertain the capability of commercial testing devices to detect the variants in patient specimens. Qorvo has undertaken external studies in partnership with the Rapid Acceleration of Diagnostics (RADx) Variant Taskforce, and internal studies using recombinant antigen for the major variants of national interest to assess the capability of the Qorvo Biotechnologies Omnia SARS-CoV-2 Antigen Test (Omnia Antigen Test) in variant detection. Both datasets support the ability to detect all variants tested, and importantly, the Delta variant.

QORVO BIOTECHNOLOGIES OMNIA™ SARS-CoV-2 TESTING PLATFORM

The Qorvo Biotechnologies Omnia™ Platform consists of a benchtop instrument and disposable antigen test cartridges (Figure 1). Bulk Acoustic Wave (BAW) detection technology is used to determine the presence of SARS-CoV-2 nucleocapsid proteins from anterior nasal swab specimens. The antigen test utilizes a sandwich immunoassay format whereby two sensors are activated on the device surface, one with mouse monoclonal antibodies to the SARS-CoV-2 nucleocapsid protein, and the second with a nonspecific reference antibody to achieve a high degree of specificity and sensitivity. The Omnia Antigen Test received Emergency Use Authorization (EUA) from the U.S. Food & Drug Administration (FDA) in April 2021 as a response to the SARS-CoV-2 pandemic.



Figure 1: Qorvo Biotechnologies' Omnia Instrument and SARS-CoV-2 Antigen Test Cartridge

SARS-CoV-2 VARIANTS

Since November 2020, the Centers for Disease Control and Prevention (CDC) has received patient specimens from public health agencies for genomic sequencing and evaluates emerging variants for their ability to spread disease, determine the severity of disease among the populace, evade detection by commercial diagnostic tests, evaluate their susceptibility to respond to medical therapies and their ability to evade natural or vaccine immunity¹.

The US Department of Health and Human Services (HHS) established an interagency group, SARS-CoV-2 Interagency Group (SIG), inclusive of members from the CDC, National Institute of Health (NIH), FDA, Biomedical Advanced Research and Development Authority (BARDA) and the Department of Defense (DOD) solely to coordinate efforts during the pandemic. SIG developed a Variant Classification system with three categories:

1. Variants of Interest² (VOI): a variant with specific genetic markers that are associated with changes to receptor binding, reduced neutralization by antibodies generated by previous infection or vaccination, reduced efficacy of treatments, potential diagnostic impact or predicted increase in transmission or disease severity. Currently, there are 6 variants in this class (B.1.427, B.1.429, B.1.525, B.1.526, B.1.617.1 and B.1.617.3).
2. Variants of Concern² (VOC): a variant with evidence of an increase in transmissibility, more severe disease, significant reduction in neutralization by antibodies, reduced effectiveness of treatments or vaccines and diagnostic detection failures. Currently, there are 4 variants in this class (B.1.1.7, B.1.351, B.1.617.2 and P1).
3. Variants of High Consequence² (VOHC): a variant with clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness relative to previously circulating variants. Currently, there are no variants in this class.

USA VARIANT PREVALENCE IN 2021³

Viruses constantly change through mutation and the SARS-CoV-2 virus is no exception. Multiple variants have emerged since the beginning of the pandemic. Figure 2 shows the emergence of the SARS-CoV-2 variants in the United States from January through August 2021.

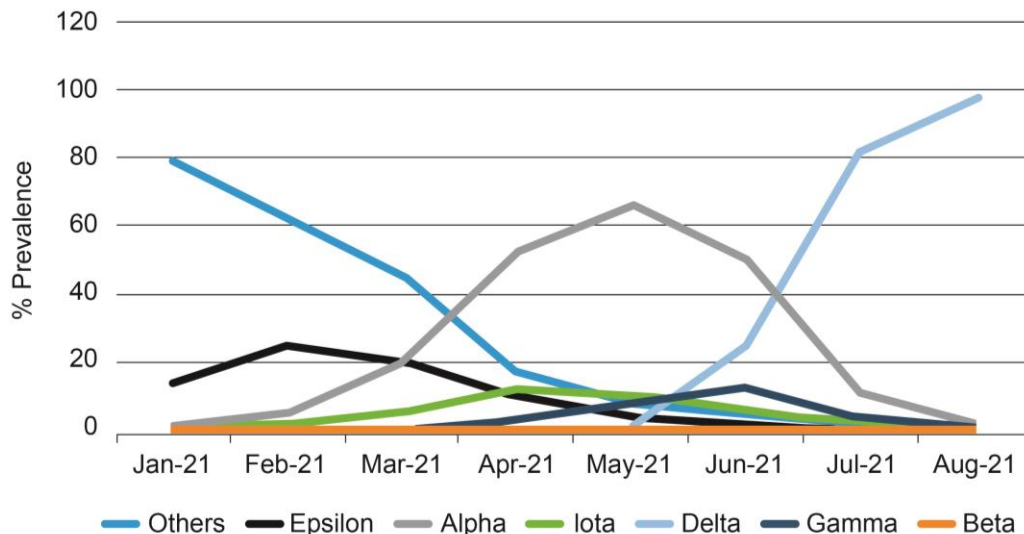


Figure 2: 2021 US Variant Prevalence (%)

In January 2021, the Epsilon variant accounted for 14% while the majority of variants determined as 'Others' represented 79%. In March 2021, the Alpha variant started to rise at 21%, peaked in May at 66% and then declined to 2% in August. In May 2021, the Delta variant appeared at 1% and drastically increased to 25% in June, 82% in July and in August, represents 97% of the infections in the US. The emergence of variants in the population is concerning to clinicians and the general public and raises the following questions:

- How infectious are the variants?
- Will the emerging variants cause an increase in illness severity or death?
- Will the commercially available vaccines help patients that contract the variants?
- Are the commercial SARS-CoV-2 tests capable of detecting variants in clinical samples?

VACCINE RESPONSE TO VARIANTS⁴

A recent study at the Oregon Health & Science University was performed to evaluate age dependency on neutralization of the SARS-CoV-2 (original strain) and the P.1 (Gamma) variant in individuals that received two doses of the Pfizer-BioNTech vaccine. Antibody titers in samples collected 14-days post-vaccination displayed a significant negative association with participant age which may account for breakthrough infections in vaccinated older adults. Emerging variants of concern, P.1 (Gamma), B.1.1.7 (Alpha) and B.1.351 (Beta) have been reported to be less neutralized by vaccine-induced antibodies and are responsible for a majority of breakthrough infections⁵.

With the increased incidence of breakthrough infections in the vaccinated population combined with the rising levels of infection among the unvaccinated population in the US, the importance of diagnostic tests and their ability to detect emerging variants is critical in the war against SARS-CoV-2 infections.

EXTERNAL RADx EVALUATION OF VARIANTS USING THE OMNIA SARS-CoV-2 ANTIGEN TEST⁶

Variant Study Specimen Preparation

The Qorvo Omnia Instrument and Antigen Test were selected by the NIH-funded Atlanta Center for Microsystems Engineered Point-of-Care Technologies (RADx ACME-POCT) team for an internal study in May 2021 (excluding the Delta variant) to determine if the Antigen Test could detect variants. Test panels containing VOI and VOC variants were prepared at Emory University (Table 1). Each panel was prepared using pools of 8-10 heat-inactivated remnant clinical samples. Serial dilutions of each panel were prepared in Pooled Nasal Fluid Matrix from Innovative Research, Inc. to span a range of viral loads with a cycle threshold (Ct) between 18 – 35. A similar study was performed in July with the Delta variant and a control strain utilizing 4 different individual remnant samples and dilutions of each remnant to span a similar Ct range. Emory University performed quality control on the dilutions by extracting total RNA and analyzing using a RT-PCR assay using the CDC's EUA primers/probe set. Omnia LOD was determined in terms of these Ct measurements and results within 3 Cts of the control group were considered equivalent.

Variants	SIG Classification ²	Nucleoprotein Mutations (mutations within Omnia binding epitope denoted by *)	RADx variant taskforce testing with inactivated virus (within 3 Ct of control)
B.1.2	N/A		PASS
B.1.1.7 (Alpha)	VOC	D3L, R203K, G204R, S235F	PASS
B.1.351 (Beta)	VOC	T205I	PASS
B.1.427 (Epsilon)	VOI	T205I	PASS
B.1.429 (Epsilon)	VOI	T205I, M234I	PASS
B.1.525 (Eta)	VOI	S2M, D3Y, A12G, T205I	PASS
B.1.526 (Iota)	VOI	P199L, M234I	PASS
B.1.617.2 (Delta)	VOC	D63G*, R203M, G215C, D377Y	PASS
P.1 (Gamma)	VOC	P80R*, R203K, G204R	PASS
P.2 (Zeta)	VOI	A119S*, R203K, G204R, M234I	PASS

Table 1

EXTERNAL STUDY RESULTS⁶

The initial blinded study in May 2021 was completed in two days. External quality control was performed daily on eight Qorvo Omnia instruments. The variant panels were tested in triplicate following the test procedure in the Omnia antigen test Instructions for Use. A similar follow-on study was completed in July 2021 to evaluate the Delta variant using duplicate measurements. After testing was complete, the results were unblinded and reviewed by the RADx Variant Task Force (VTF). The VTF concluded that the Omnia antigen test adequately detects the variants evaluated in this study (see Table 1).

QORVO BIOTECHNOLOGIES INTERNAL EVALUATION OF VARIANTS USING THE OMNIA SARS-CoV-2 ANTIGEN TEST⁷

This paper focuses on the capability of the Omnia Antigen Test to detect the variants circulating in the United States. Qorvo Biotechnologies conducted internal studies beyond the RADx activity to determine if the assay could detect the epitope mutations of the variants within the known binding epitope of the antibodies used in the Omnia test. The test panels used recombinant samples of the variants.

Figures 3 and 4 illustrate the signal obtained using the nucleoprotein mutations at various dilution levels. The Omnia Antigen Test will flag a test result as 'positive' when the signal is ≥ 1 AU/mL. The nucleoprotein mutation in the Delta variant, D63G, is detected by the Omnia Antigen Test at all dilution levels evaluated in the study, and importantly at greater than two times the levels of the original Wuhan strain upon which the EUA submission was based. Likewise, the P80R mutation in the Gamma variant, the P67S mutation of the B.1.2 variant and the B.1.1.7 Alpha variant are detected at all dilution levels evaluated in the study.

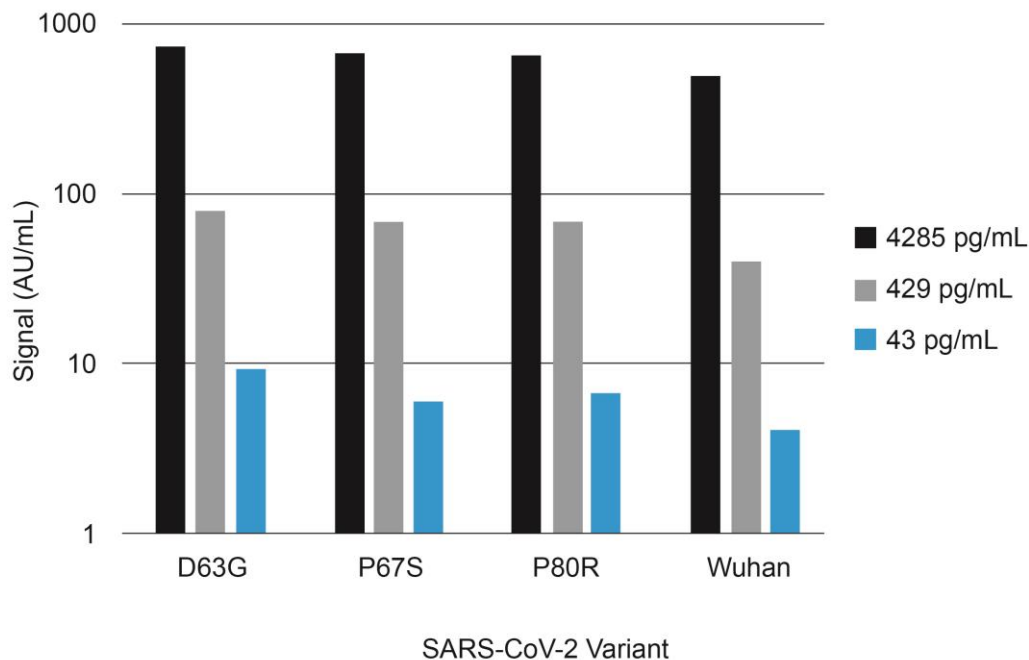


Figure 3

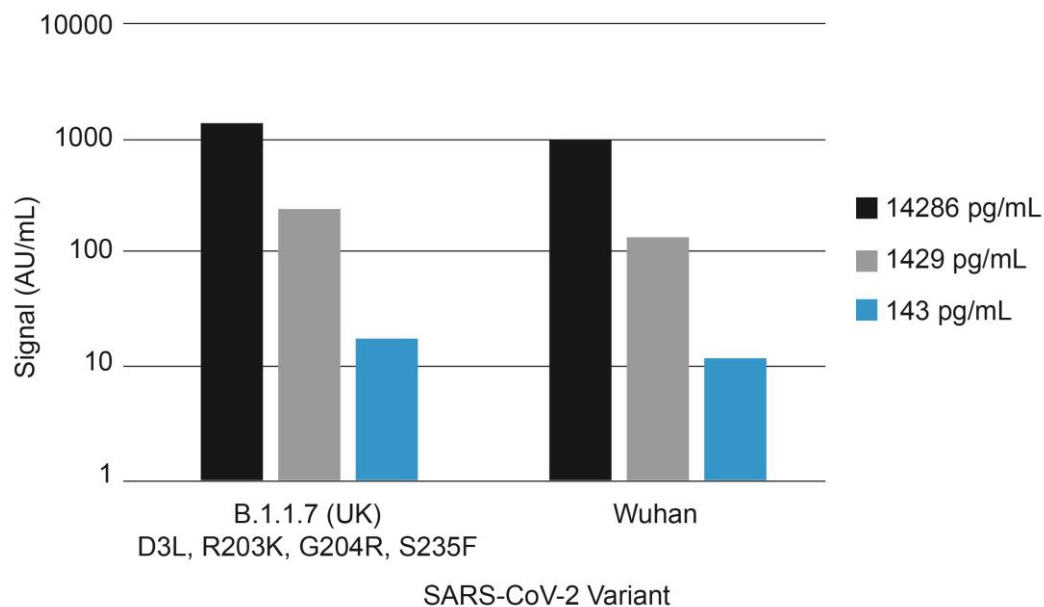


Figure 4

In summary, the dominant mutations (Delta, Gamma and Alpha) within the binding epitope of the antibodies used in the Omnia Antigen Test are detected with high sensitivity. Qorvo Biotechnologies' internal studies, using recombinant samples, illustrate the Omnia antigen test's ability to detect the variants currently in circulation.

Conclusion

SARS-CoV-2 variants continue to emerge in 2021. Infection rates in the US are dramatically increasing due to the emerging Delta variant and clinicians need diagnostic tests that can accurately detect the variants in patient samples.

Independently, Qorvo Biotechnologies' internal studies using recombinant samples and the external RADx ACME-POCT study using heat-inactivated clinical samples both demonstrate that the Omnia Antigen Test can detect the current variants in circulation in the USA. The robustness of the antibodies used in the Omnia antigen test is illustrated by their ability to detect the variant's nucleoprotein mutations.

- Qorvo continues to verify performance of the Omnia antigen test against new variants as they emerge. With RADx support, Qorvo is able to access the ACME-POCT team for this testing in conjunction with our own testing on recombinant antigens with the mutations specific to the variants. Recent work focused on the Delta variant due to significant national and international interest. Both datasets support the ability to detect all variants tested, and importantly, the Delta variant.

REFERENCES

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5. COVID-19 vaccine breakthrough infections reported to CDC—United States, January 1-April 30, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(21):792–793. doi:10.15585/mmwr.mm7021e3
6. The data was generated and analyzed by NIH-funded Atlanta Center for Microsystems Engineered Point-of-Care Technologies as part of the RADx Tech Team 6198, May 2021
7. Internal data on file, Qorvo Biotechnologies, Plymouth, Minnesota

**This product has not been FDA cleared or approved but has been authorized by FDA under an EUA for use by authorized laboratories. This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens; and the emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner. This product is not currently available for sale in any geography outside of the United States.*

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