



## Case Report

# Longitudinal Performance Validation of Siemens SARS-CoV-2 Spike Protein Serologic Assay

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### 1. Introduction

The Siemens Centaur® SARS-CoV-2 IgG Antibody assay, which received Food and Drug Administration Emergency Use Authorization (FDA EUA), serologically detects the presence of circulating IgG antibodies to SARS-CoV-2 in human serum or plasma using the Siemens Centaur® Immunoassay Systems. This new semiquantitative test was validated in February 2021 at the Core facility of Pacific

Diagnostics Laboratories (PDL), the largest clinical reference laboratory in coastal California between Los Angeles and San Francisco. It is recognized that this commercially available test correlates well with circulating neutralizing antibody (nAb) titers [1-3] and is capable of assessing specific antibody production without any current claim by the FDA regarding immunity to COVID-19 infection. This was reaffirmed when the FDA issued their safety communication on 19 May 2021; however, many recent studies [4, 5] reported during the summer of 2021 have clearly demonstrated waning levels of circulating

antibodies to SARS-CoV-2 over the course of several months post vaccination. This is the rationale for the FDA [6] authorizing a booster dose for select populations at least 6 months after completion of the primary series of Pfizer BioNTech COVID-19 vaccine. At the present time, neutralizing antibodies are the primary and determinative correlate “to protective immunity to SARS-CoV-2 induced either through natural infection or through vaccination” [3]. Commercially available enzyme-linked immunoassays (EIA) similar to this Siemens assay do not directly measure nAb; however, recently published studies [3] have demonstrated that this Siemens EIA demonstrated the highest correlation for commercial assays with the gold-standard Plaque Reduction Neutralization Test (PRNT) and “best agreement” with the newly FDA EUA approved cPass Neutralization Antibody Assay.

## 2. Methods

This validation study was conducted utilizing a traditional laboratory correlation protocol (as prescribed under CFR Title 42 requirements) that is designed to assess the performance metrics of any new clinical assay in comparison to the FDA Instructions for Use (IFU). In this context, 57 of 57 uninfected laboratory staff, who were tested in March 2020, prior to vaccination, were resulted negative with an index value  $< 1.00$ . In February 2021, we validated the new semiquantitative assay and 28 of the original members with no prior COVID-19 infection and who were at least 14 days post 2<sup>nd</sup> dose of the Pfizer BioNTech (BNT162b2) COVID-19 vaccine, were retested.

## 3. Results

Of this longitudinal cohort (spanning a time interval of 6-8 months), 25 of the 28 who were tested 2-4 weeks after second

vaccine dose, demonstrated maximal response with an index value  $> 150$  (limit of the analytic measurement range instituted by the manufacturer at that time) and then retested at 6 months. 3 of the 28, who had values less than this maximal value, were vaccinated early and thus were actually tested 6-7 weeks after their second dose and thus their retest time interval essentially represents an expanded (7- 8 month) time span. This same group of three were clustered into the lowest tier on the August 2021 retest. These observations clearly appear to demonstrate that circulating antibodies start to decline sometime after the 2-4-week post vaccination period and continue to show larger quantitative decrements as the months progress. Individuals tested during the 7-8-month time frame had noticeably lower index values than index values for those tested at the 6-month interval. Of note, the largest single 6-month decrement was in an individual older than 60 that is similar to the observations published in the large Israeli study [7].

Although this sample size is small, the 6-month average index value decrement was large enough to be considered highly statistically significant ( $p < 0.001$ ) as illustrated in Figure 1. None of the 28 individuals dipped below the index value of 1.00, which is qualitatively resulted as negative. Specifically, this means that the level of circulating Spike (S1 RBD) antibody cannot be analytically distinguished from the cohort of 57 uninfected individuals tested as part of the original PDL validation studies, performed prior to the release of vaccine, who demonstrated index values  $< 1.00$  consistent with the performance characteristics as submitted to the FDA. The Siemens SARS-CoV-2 IgG Spike (S1 RBD) Antibody performed on the Siemens Centaur<sup>®</sup> must generate an index value  $\geq 4.8$  in order to meet the FDA requirement to be categorized as a high-titer COVID-19 Convalescent Plasma donor [2]. Although none of 28 individuals dropped

below an index value of 1.00, 6 of the 28 (21%) after 6 months and 3 of 3 (100%) after 7 months demonstrated index

values < 4.8, which is a numerical cutoff recognized as an immunity transference milestone.

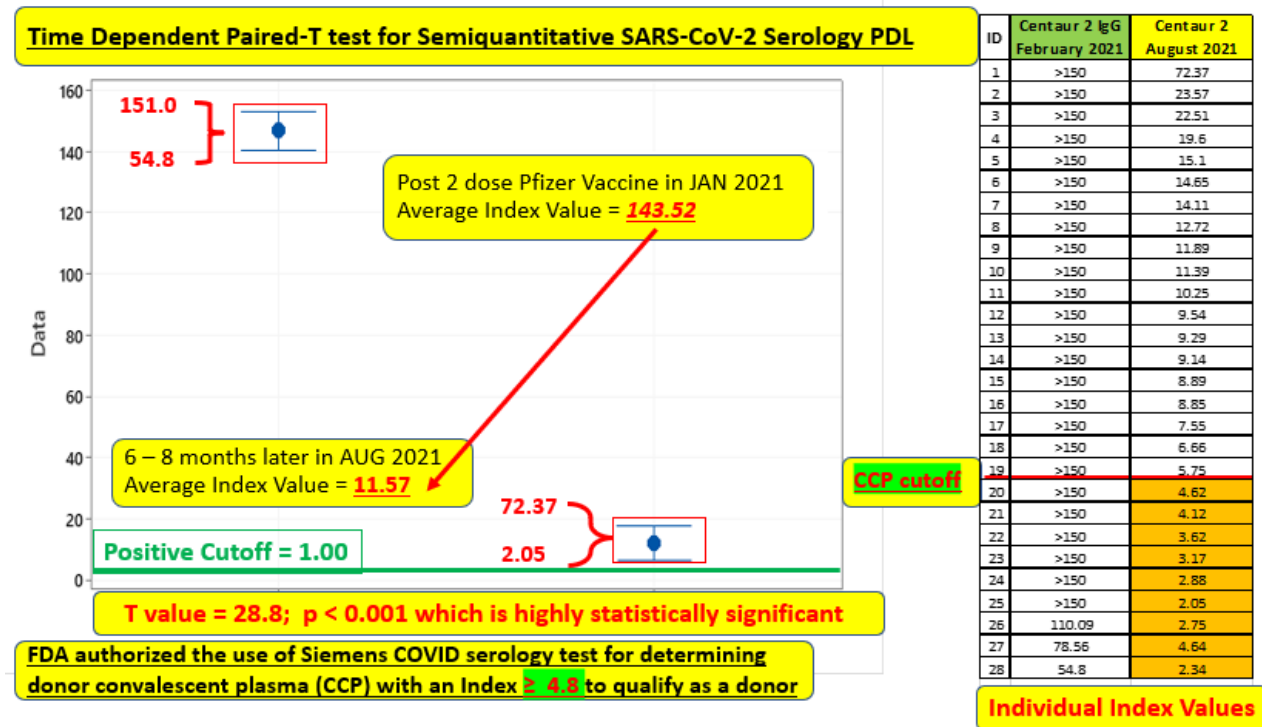


Figure 1: Time Dependent Paired-T test of average index value for 28-member cohort 6-8 months post vaccination.

#### 4. Conclusion

The intent of this longitudinal validation study was to corroborate the temporal pattern in waning circulating antibodies as recently reported in multiple studies [3, 4, 6, 7] using a commercially available assay, which has been recognized [3] as having demonstrated excellent agreement with FDA-EUA approved SARS-CoV-2 nAb and PRNT assays. Although limited in sample size, the decrement is highly statistically significant and the time interval of our longitudinal validation was 180-225 days, which exceeds those time intervals of 70, 146 and 150 days previously reported [4, 7, 8]. Our time interval and eventual results tends

to parallel the decay interval as recently reported in an expansive and comprehensive predictive study [5] that specifically evaluated multiple vaccine and convalescent studies and mathematically modeled “the decay of neutralization titers over the first 250 days after immunization.”

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### Conflict of Interest Disclosures

None

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