

## Cross-Institutional Evaluation of the Abbott ARCHITECT SARS-CoV-2 IgG Immunoassay

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### ABSTRACT

**Objective:** To describe a cross-institutional approach to verify the Abbott ARCHITECT SARS-CoV-2 antibody assay and to document the kinetics of the serological response.

**Methods:** We conducted analytical performance evaluation studies using the Abbott ARCHITECT SARS-CoV-2 antibody assay on 5 Abbott ARCHITECT i2000 automated analyzers at 2 academic medical centers.

**Results:** Within-run and between-run coefficients of variance (CVs) for the antibody assay did not exceed 5.6% and 8.6%, respectively, for each institution. Quantitative and qualitative results agreed for lithium heparin plasma, EDTA-plasma and serum specimen types. Results for all SARS-CoV-2 IgG-positive and -negative specimens were concordant

among analyzers except for 1 specimen at 1 institution. Qualitative and quantitative agreement was observed for specimens exchanged between institutions. All patients had detectable antibodies by day 10 from symptom onset and maintained seropositivity throughout specimen procurement.

**Conclusions:** The analytical performance characteristics of the Abbott ARCHITECT SARS-CoV-2 antibody assay within and between 2 academic medical center clinical laboratories were acceptable for widespread clinical-laboratory use.

**Keywords:** antibody, COVID-19, EUA, immunoassay, SARS-CoV-2, serology

Coronavirus disease 2019 (COVID-19) was characterized as a global pandemic by the World Health Organization (WHO) on March 11, 2020, after first appearing in Wuhan, China in December 2019.<sup>1</sup> The highly contagious COVID-19 virus was identified to be a phylogenetic sister to the severe acute respiratory syndrome coronavirus (SARS-CoV) and has been named *severe acute respiratory coronavirus 2*

(SARS-CoV-2).<sup>2</sup> As of March 8, 2021, there are over 29 million people in the United States and over 117 million people around the world who have been confirmed as having SARS-CoV-2 infection. As of July 17, 2020, nearly 3.5 million people in the United States and nearly 14 million people around the world have been confirmed as having SARS-CoV-2 infection.<sup>3</sup> However, the full extent of the outbreak has yet to be determined, due to limited testing to detect current or past exposure to the novel contagion.<sup>4,5</sup>

### Abbreviations:

COVID-19, coronavirus disease 2019; WHO, World Health Organization; SARS-CoV, severe acute respiratory syndrome coronavirus; SAR-CoV-2, severe acute respiratory coronavirus 2; Ig, immunoglobulin; EUA, Emergency Use Authorization; PMA, premarket approval; N, nucleocapsid; S, spike surface; CMIA, chemiluminescent microparticle immunoassay; IRB, institutional review boards; UVA, University of Virginia; VCU, Virginia Commonwealth University; S/C, signal-to-calibrator; RT, real-time; CLSI, Clinical and Laboratory Standards Institute; CV, coefficient of variation; CI, confidence interval; IVD, in-vitro diagnostic

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In an effort to slow the spread of COVID-19 and to avoid straining vital health care resources, numerous countries around the world have implemented social behavioral restrictions for their citizens (ie, social distancing, lockdowns). Now, after a year of disrupted living and an economic crisis, government and scientific strategists are requesting accurate estimates of COVID-19 infection rates and immunity status as they prepare approaches to gradually lift these restrictions.<sup>6</sup> Consequently, a critical discussion point in returning to normal daily life has been centered on testing for human antibodies to SARS-CoV-2, to determine exposure rates and possible resistance to the virus.<sup>6,7</sup>

Recent preliminary reports<sup>8–10</sup> have attempted to quickly document the timeframe to detect antibodies to SARS-CoV-2 in infected individuals. Symptomatic individuals with SARS-CoV-2 infection typically did not demonstrate detectable antibodies to the virus in the first 7 days after symptoms.<sup>8,9</sup> In most hospitalized patients with a confirmed RNA viral load, detectable immunoglobulin (Ig)G antibodies appeared 14 to 28 days after symptoms onset.<sup>10</sup> Serology characteristics of IgM to SARS-CoV-2 has also been studied<sup>8,11</sup> and it appears to rise several days before IgG or simultaneously as previously described.<sup>8,11</sup>

Hundreds of SARS-CoV-2 antibody tests have rapidly emerged during the pandemic.<sup>11,12</sup> In the United States, manufacturers of these tests were not required by the FDA to go through their formal approval process.<sup>13</sup> However, this policy was changed, and now the FDA requires manufacturers to submit assay-performance data for review under the FDA Emergency Use Authorization (EUA) process.<sup>14</sup> However, due to the dynamic and evolving situation, typical assay validation and patient cohort studies through cross-institutional studies are still not being rigorously performed. These limitations have led to various questions regarding analytical performance characteristics that are typically vetted by the FDA 510(K) or premarket approval (PMA) review processes.<sup>15</sup>

The 2 most common analytical methods available to detect antibodies to SARS-CoV-2 rely on lateral flow immunochromatography or noncompetitive immunoassay technology.<sup>11</sup> These methods predominantly were designed to identify antibodies towards the SARS-CoV-2 nucleocapsid (N) or spike surface (S) proteins. A primary target for several assay developers has been directed towards the nonconserved S1 subunit of the SARS-CoV-2 spike protein. The S1 subunit is considered to be specific to each coronavirus strain, which could possibly mitigate cross-reactivity with the 4 common coronaviruses (eg, HKU1, NL63, OC43, 229E).<sup>11</sup> Initially large commercial manufacturers of laboratory tests started to distribute SARS-CoV-2 antibody tests for use on their automated immunoassay platforms, with or without EUA.<sup>11</sup>

Abbott Diagnostics recently developed a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma, which is run on the ARCHITECT i System.<sup>16</sup> Several performance evaluations of the assay<sup>17–22</sup> were

published recently. However, the studies were conducted at single institutions, multiple analyzers were not evaluated, and only 1 study evaluated different specimen-collection tube types. Therefore, the aim of this study is to report on a cross-institutional approach for validating the Abbott Architect SARS-CoV-2-IgG immunoassay, evaluate assay performance for different specimen-collection tube types, and to document the kinetics of the serological response.

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## Methods and Materials

The study was considered to constitute research on nonhuman subjects, as defined by the institutional review boards (IRBs) of both institutions. Performance evaluation studies were conducted using the Abbott ARCHITECT qualitative SARS-CoV-2 IgG antibody assay, implemented on 2 Abbott ARCHITECT i2000SR immunoassay analyzers in the clinical laboratory at University of Virginia (UVA), and 3 ARCHITECT i2000SR immunoassay analyzers implemented in the clinical laboratory at Virginia Commonwealth University (VCU). Although the Abbott ARCHITECT SARS-CoV-2 IgG assay is a qualitative assay, quantitative evaluations of assay results were also performed using the numerical signal-to-calibrator (S/C) values. The assay cutoff for a positive result is 1.4 S/C or greater.

Blood was collected into BD Vacutainer SST II Advance tubes for serum-specimen studies, BD Vacutainer EDTA tubes for EDTA plasma studies, and BD Vacutainer PSTTM II tubes (all products by Becton, Dickinson and Company) for lithium heparin plasma specimens. Residual specimens were from patients with SARS-CoV-2 real-time (RT)-PCR results measured at VCU using the Xpert Xpress SARS-CoV-2 (Cepheid), BD SARS-CoV-2 (Becton, Dickinson and Company), or cobas SARS-CoV-2 (F. Hoffman-La Roche Ltd.) analytical systems. RT-PCR testing at UVA was performed by ABI 7500 (CDC assay) and Abbott m2000 (AbbVie Inc.). Prepandemic specimens had been collected in 2018 and 2019 and stored at  $-70^{\circ}\text{C}$  and were categorized as having SARS-Cov-2-negative results.

For the studies conducted at UVA, 105 specimen from 8 individual patients who had positive results via SARS-CoV-2 PCR testing and 54 specimens from 34 patients with negative results via SARS-CoV-2 PCR testing were collected.

Of those, 24 specimens from 4 patients tested positive for non-SARS-CoV-2 coronaviruses. To compare tube types, specimens from 20 patients were included when heparin lithium and EDTA plasma were available from the same phlebotomy draw: 40 specimens total.

UVA precision studies were performed as follows. Between-run imprecision was assessed by analyzing 2 levels of Abbott Architect SARS-CoV-2 IgG quality-control materials during a 5-day period; within-run imprecision was assessed by analyzing 10 replicates each of a SARS-CoV-2 IgG-positive and -negative patient specimen during a single run.

For the studies conducted at VCU, 116 specimens from 57 individual patients with positive results via SARS-CoV-2 PCR, 33 specimens from 32 patients testing negative via SARS-CoV-2 PCR, and 15 specimens collected before the pandemic were included. Fifteen of the specimens with negative SARS-CoV-2 PCR results were from 14 patients with positive results for the following non-SARS-CoV-2 respiratory viruses: 1 adenovirus, 1 influenza A, 4 rhinovirus/enterovirus, 4 coronavirus OC43 (3 individual patients), 3 coronavirus NL63, and 2 coronavirus HKU1. To compare tube types, specimens from 20 patients were included when heparin lithium and serum (red-top tube) were available from the same phlebotomy draw: 40 specimens total. VCU within-run and between-run precision studies were performed according to Clinical and Laboratory Standards Institute (CLSI) EP15.<sup>23</sup>

Because this study utilized residual specimens, the time duration between specimen collection for PCR testing and serology specimen collection varied. For all serology specimens except those collected in patients with other coronaviruses, specimens were collected between 1 and 26 days from non-SARS-CoV-2 PCR testing. For specimens from patients who tested

positive for other coronaviruses, 7 of 33 serology specimens were collected the same day that the corresponding non-SARS-CoV-2 coronavirus PCR specimens were collected.

Box and whisker, Passing Bablok Regression Fit, and difference plots were constructed using R statistical software. Also, sum of least squares linear regression and difference plots were generated by Microsoft Excel version for Mac 2011 version 14.7.7 (Microsoft Corporation). Imprecision studies and statistical analyses among analyzers and study groups were performed by ANOVA using GraphPad statistical software (GraphPad Software) and Analyse-it (a statistical-analysis add-in for Microsoft Excel).

## Results

### Results of Imprecision and Among-Instrument Comparisons Studies for the Abbott ARCHITECT SARS-CoV-2 IgG Assay

The Abbott ARCHITECT SARS-CoV-2 IgG antibody assay exhibited similar performance characteristics during independent EUA verification studies conducted at both institutions. In **Table 1**, we show the results of imprecision assessments using S/C values for ARCHITECT SARS-CoV-2 IgG quality-control materials or patient specimens categorized as having positive or negative results via SARS-CoV-2 PCR. We obtained 100% qualitative agreement vs expected value for all results. For quantitative S/C values, imprecision did not exceed 5.6% for within-run coefficient of variation (CV) estimates and 8.6% for between-run CV estimates.

**Table 1. Imprecision Study Results<sup>a</sup>**

Institution	Negative SARS-CoV-2 IgG Result		Positive SARS-CoV-2 IgG Result	
	Within-run CV% (S/C)	Between-run CV% (S/C)	Within-run CV% (S/C)	Between-run CV% (S/C)
UVA	0.0% (0.02)	8.6% (0.05)	1.6% (4.10)	3.4% (3.14)
VCU	5.6% (0.05)	5.6% (0.05)	2.1% (3.35)	3.2% (3.35)

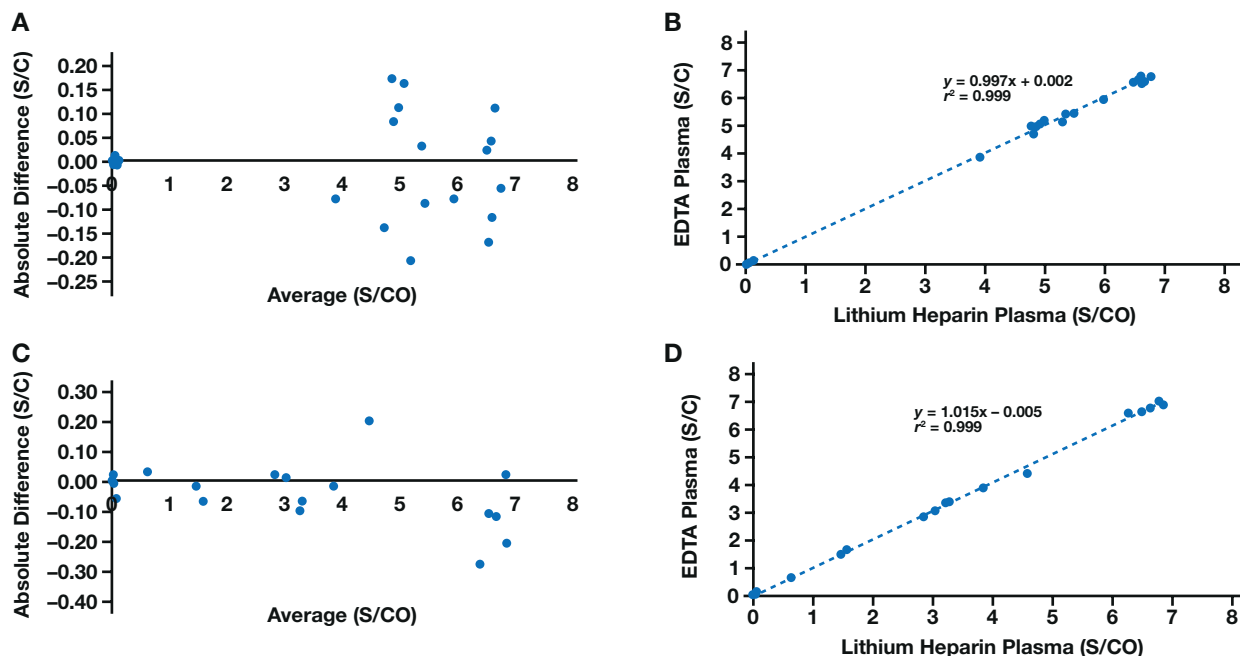
SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IgG, immunoglobulin G; CV, coefficient of variation; S/C, signal-to-calibrator; UVA, University of Virginia; VCU, Virginia Commonwealth University.

<sup>a</sup>Control specimens that tested negative and positive via Abbott ARCHITECT SARS-CoV-2 IgG assay were analyzed at UVA for between-run and at VCU for within-run and between-run imprecision estimates, the results are the average of the calculated imprecision values. A patient specimen with positive and negative results via SARS-CoV-2 IgG PCR testing was analyzed at UVA for within-run imprecision estimates.

A specimen-collection tube-type evaluation was performed independently at the 2 institutions. EDTA plasma specimens and corresponding lithium heparin plasma specimens collected from the same patients were analyzed at UVA. Lithium heparin plasma specimens and corresponding serum specimens collected from the same patients were analyzed at VCU. All qualitative results among tube types were 100% concordant, and the quantitative S/C results agreed (Figure 1). The difference plots showed average bias of  $-0.01$  S/C, with maximum differences of  $0.17$  to  $-0.21$  S/C for EDTA and lithium plasma; the slope of the linear regression for S/C values was  $0.997$  (95% confidence interval [CI],  $0.985$ – $1.008$ ), with an intercept of  $0.002$  ( $-0.046$  to  $0.049$ ). For serum and lithium plasma, the difference plots showed average bias of  $-0.04$  S/C with maximum differences of  $0.20$  to  $-0.28$  S/C for EDTA; the slope of the linear regression for S/C values was  $0.984$  (95% CI,  $0.968$ – $0.999$ ), with an intercept of  $0.008$  ( $-0.051$  to  $0.067$ ).

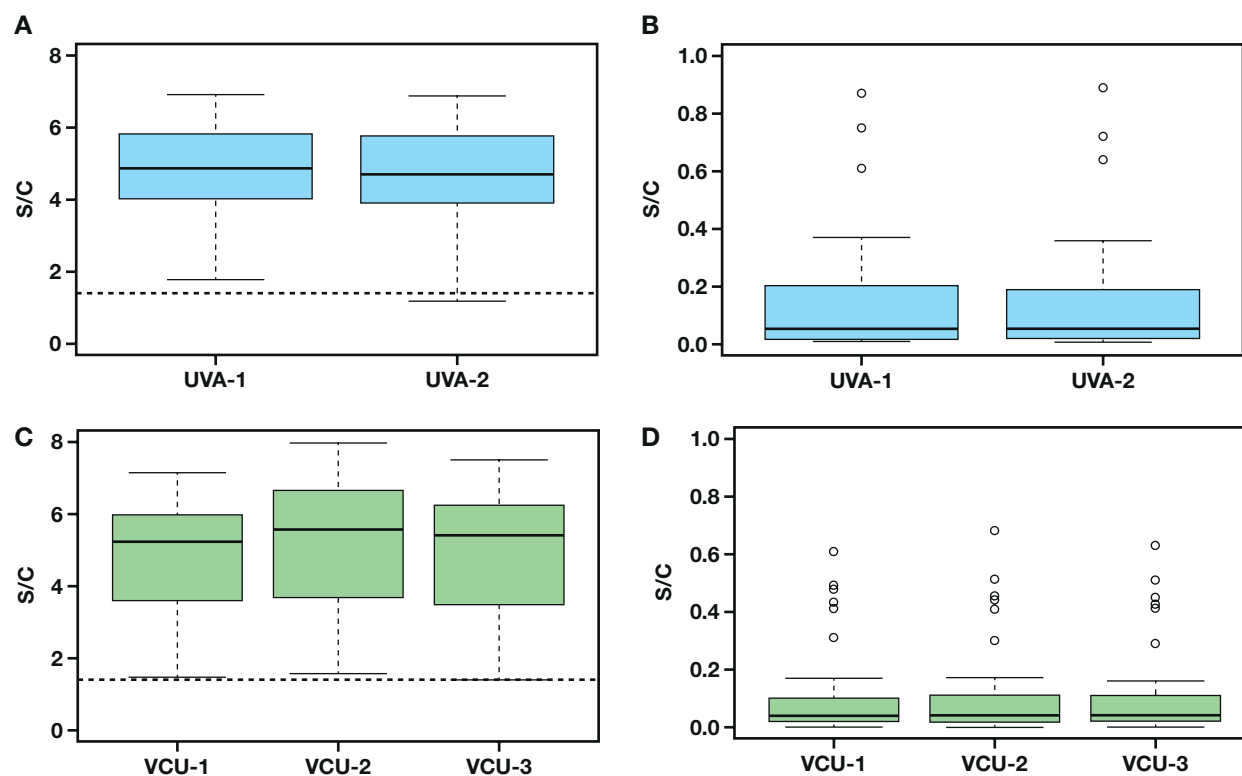
Among-instrument comparison studies were performed independently at each institution, using multiple analyzers, and evaluated for qualitative and quantitative agreement. Qualitative measurements at UVA for 2 ARCHITECT i2000 analyzers were concordant, with the exception of 1 specimen. One specimen, from a patient who tested positive for SARS-CoV-2 via PCR assay, tested negative via the ARCHITECT SARS-CoV-2 IgG assay on a single analyzer, with an S/C value below the  $1.4$  cutoff for positivity, as confirmed by repeat analysis. This specimen had been collected from a patient 11 days after symptoms; the patient experienced seroconversion on day 6 after symptoms, with all other specimens testing positive after day 6.

Quantitative S/C values for IgG-positive and IgG-negative results are shown in Figure 2. Median S/C values for IgG-positive results at UVA (Figures 2A and 2B) were  $4.86$  and  $4.72$ , respectively, and  $0.06$  and  $0.06$ , respectively, for IgG-negative results via each analyzer. The results of



**Figure 1**

Comparison of the means of the signal-to-calibrator (S/C) values obtained from different specimen-collection tube types. S/C values from 30 specimen of lithium heparin plasma and corresponding EDTA-plasma specimen (from the same patients) were measured on analyzer A (A) and analyzer B (B) at the University of Virginia (UVA). S/C values from 21 specimens of lithium heparin plasma (C) and corresponding serum specimens from the same patients (D) were analyzed at Virginia Commonwealth University (VCU) on the same analyzer. Absolute-difference plots and ordinary least-squares regressions were calculated.



**Figure 2**

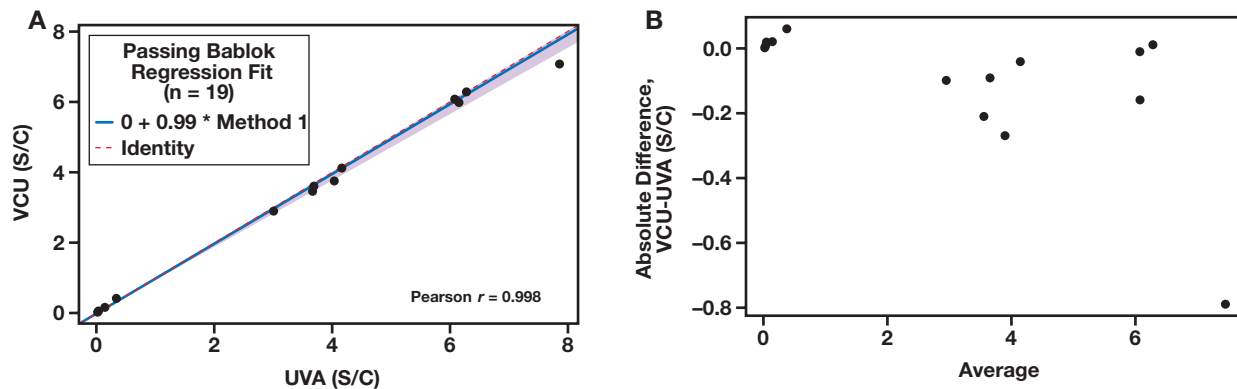
Lithium heparin specimens were analyzed on different analyzers at the University of Virginia (UVA) and Virginia Commonwealth University (VCU). At UVA, 64 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin (IgG)-positive specimens (**A**) and 59 IgG-negative (**B**) specimens were analyzed on 2 analyzers. At VCU, 78 IgG-positive specimens (**C**) and 86 IgG-negative specimens (**D**) were assayed on 3 analyzers. The dotted line at the bottom of panels A and C represent the assay cutoff of signal-to-calibrator (S/C) results, of 1.4. The heavy line is the median, the ends of the boxes are the 25<sup>th</sup>- and 75<sup>th</sup>-percentile values, and the end caps represent the maximum and minimum S/C values observed, with the open circles representing potential outliers.

among-instrument comparison studies performed at VCU demonstrated 100% qualitative agreement among 3 analyzers. Median S/C values at VCU (**Figures 2C** and **2D**) were 5.23, 5.56, and 5.40, respectively, for positive results, and 0.04, 0.04, and 0.04, respectively, for negative results via each analyzer.

For quantitative results, there were no statistically significant differences for median S/C values among analyzers for IgG-positive results at UVA ( $P = .66$ ) or VCU ( $P = .30$ ), or IgG-negative results at UVA ( $P = .91$ ) or VCU ( $P = .97$ ). Also, there were no statistically significant differences for median IgG S/C values among the 2 independent sample sets for IgG-positive specimens ( $P = .51$ ) or among the 2 independent sample sets for IgG-negative specimens ( $P = .15$ ).

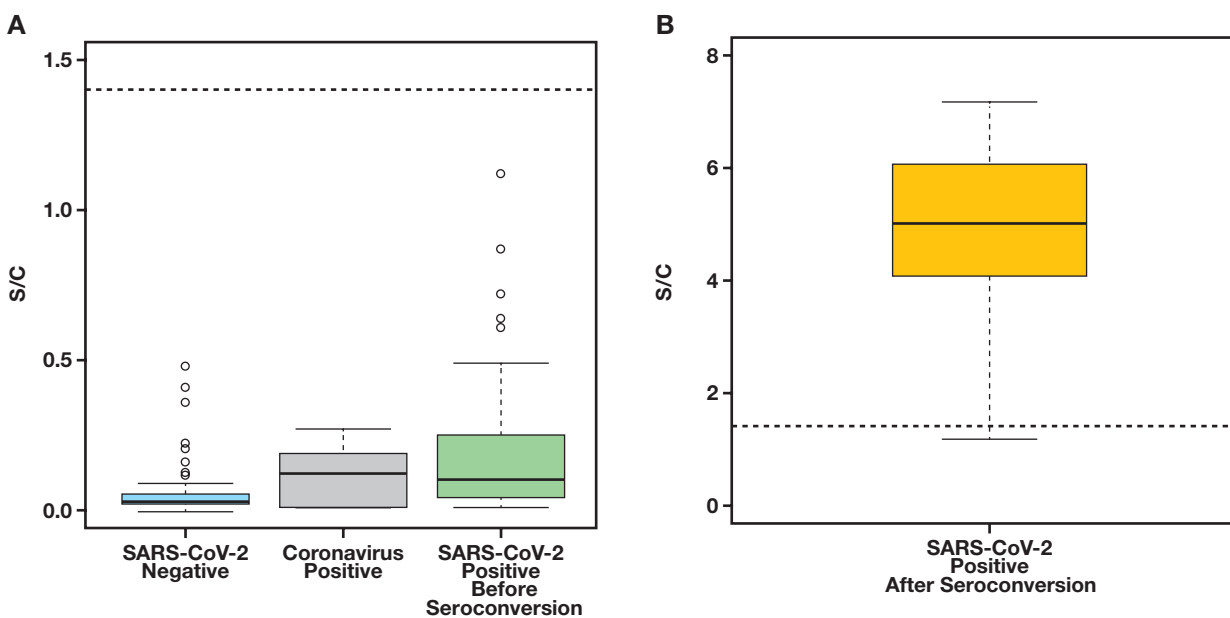
To evaluate agreement of results for the IgG assay implemented at 2 different institutions, 9 lithium heparin specimens from patients with positive results via SARS-CoV-2 PCR and 10 lithium heparin specimens from patients with negative results via SARS-CoV-2 PCR were exchanged between the institutions; the S/C values were then compared. There was 100% concordance for qualitative IgG results for all specimens.

**Figure 3** shows Passing-Bablok regression and an absolute difference plot of the S/C results of the exchanged specimens. S/C results showed quantitative agreement and no biases for specimens with S/C values less than 6.29. The slope of the regression was 0.990 (95% CI, 0.942–1.000), with an intercept of 0 (0–0.012), and the average bias was  $-0.08$  S/C. One specimen exhibited a



**Figure 3**

Comparison of results from specimens run at the University of Virginia (UVA) and Virginia Commonwealth University (VCU). Lithium heparin specimens ( $n = 19$ ) were exchanged between institutions; the results are shown as Passing Bablok regression (A) and absolute-difference (B) plots.



**Figure 4**

Comparison of signal-to-calibrator (S/C) results from patient specimens. Specimens were categorized based on patient severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) status. A box-and-whiskers plot shows the specimens with negative results (A), which are grouped by specimens testing SARS-CoV-2 negative (negative via PCR testing and collected before the pandemic: 68 patients, 68 specimens), specimens testing negative via SARS-CoV-2 PCR testing and others that tested positive for coronavirus via PCR testing (12 patients, 33 specimens), and specimens from patients who had tested positive for SARS-CoV-2 via PCR testing but had not yet experienced seroconversion (13 patients, 37 specimens). The specimens testing positive for SARS-CoV-2 via PCR (B) included all specimens collected after the first positive IgG result from patients in whom serial specimens were collected (9 patients, 65 specimens). The dotted lines at the bottom of the plots represent the positivity cutoff at S/C of 1.4. The heavy line is the median, the ends of the boxes are the 25<sup>th</sup>- and 75<sup>th</sup>-percentile values, and the end caps represent the maximum and minimum S/C values observed, with the open circles representing potential outliers.

bias of  $-0.80$  S/C for VCU vs UVA at a S/C of 7.5; however, the bias did not affect the qualitative interpretation of the result.

### Performance of the Abbott ARCHITECT SARS-CoV-2 IgG Antibody Assay in Different Patient Populations

Data from the independent method-comparison studies at each institution were combined to evaluate the IgG antibody assay performance for different patient populations.

**Figure 4** shows S/C results of specimens that were classified into 1 of the following 4 categories: negative results via SARS-CoV-2 PCR ( $n = 68$ ); negative results via SARS-CoV-2 PCR but positive results for non-SARS-CoV-2 coronaviruses via PCR ( $n = 33$ ); serial specimens from patients with positive SARS-CoV-2 results via PCR but who had IgG-negative results and presumably had not yet experienced seroconversion ( $n = 37$  specimens from 13 patients); and serial specimens from patients with SARS-CoV-2 positivity via PCR, who had positive IgG results ( $n = 65$ ). The median S/C values for the different patient groups were as follows: patients with SARS-CoV-2 negativity via PCR, 0.03; patients with other coronaviruses, 0.12; patients that had SARS-CoV-2 positivity via PCR but did not reach the cutoff for IgG positivity, 0.10; and SARS-CoV-2 positivity via PCR along with IgG positivity, 5.01.

Of the patients who tested negative for SARS-CoV-2 via PCR (**Figure 4A**), all had S/C results less than 1.12 (median, 0.04), and those results were well below the cutoff of 1.4, including specimens that tested positive for other coronaviruses. **Figure 4B** shows all specimens used in this study that had positive results via IgG for SARS-CoV-2, via IgG, including all specimens collected after the first positive IgG result was obtained from serial specimens. There was 1 discrepant specimen (**Figure 2**) that had false negativity via 1 analyzer and positivity via the other analyzer, after the patient experienced seroconversion (as mentioned in first section of the Results). Otherwise, all other data were greater than the cutoff for a positive result.

The medians were significantly different for patients with negative SARS-CoV-2 results via PCR testing ( $P < .01$ ), patients with non-SARS-CoV-2 coronaviruses ( $P < .01$ ), and those with SARS-CoV-2 positivity via PCR testing ( $P < .01$ ) (**Figure 4A**). However, those values did not reach the cutoff for IgG positivity, compared with SARS-CoV-2 positivity via PCR and IgG positivity (**Figure 4B**). Also, median results for

patients with other coronaviruses (0.12) and SARS-CoV-2 positivity via PCR but for whom values did not reach the cutoff for IgG positivity (0.10) were significantly larger than the median for patients with SARS-CoV-2 negativity via PCR (0.03;  $P < .05$  and  $P < .01$ , respectively; **Figure 4A**). We note that the median S/C value for specimens from patients who positive for other coronaviruses (0.12) and positive for SARS-CoV-2 via PCR (0.10), but for whom values were below the cutoff for IgG positivity, were not significantly different ( $P = .27$ ).

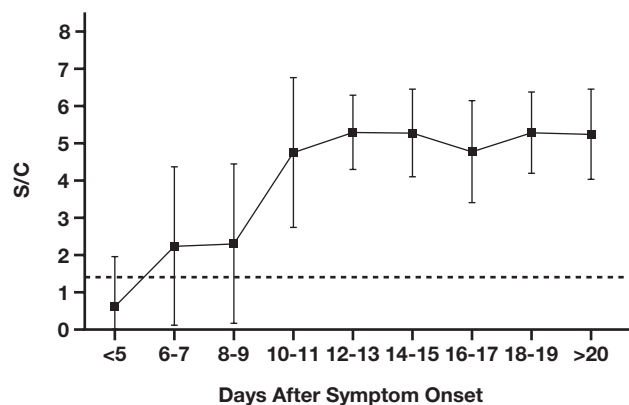
### Seroconversion Across Serial Specimens in Patients with Positive Results Via PCR

Results from serial specimens from patients testing SARS-CoV-2 positive via PCR, beginning at the date of symptom onset, were examined to characterize the kinetics of seroconversion. The data were collected independently at the 2 institutions and were combined to generate **Figure 5**. We included 13 different patients in the evaluation, and by onset of symptoms after day 10, all patients had detectable IgG and maintained seropositivity for the remainder of the specimen-collection period.

## Discussion

Before an in-vitro diagnostic (IVD) clinical assay is cleared by the FDA, the assay will go through an extensive, multisite clinical evaluation period.<sup>24,25</sup> This evaluation is performed to ensure that the analytical performance characteristics of the assay provide equivalent results among instruments and correspond to clinical outcomes in specified patient populations and clinical settings. In emergency situations, such as the current worldwide COVID-19 pandemic, the FDA provides IVD companies with the option to submit their tests through an EUA process.<sup>26</sup> This route is provided to expedite measurement technologies that can be rapidly deployed in a clinical setting for rapidly evolving medical conditions. However, the accelerated authorization may not identify performance issues that might otherwise have been identified during a normal review process.

We conducted a cross-institutional and multianalyzer evaluation of the Architect SARS-CoV-2 IgG antibody test implemented on the Abbott ARCHITECT i2000 platform



**Figure 5**

Serial specimens collected from 13 patients at different institutions and graphed by signal-to-calibrator (S/C) result. The x-axis represents postsymptom onset during a period of days; the sample size is  $\leq 5$  days ( $n = 18$ ), 6–7 days ( $n = 15$ ), 8–9 days ( $n = 13$ ), 10–11 days ( $n = 10$ ), 12–13 days ( $n = 7$ ), 14–15 days ( $n = 12$ ), 16–17 days ( $n = 6$ ), 18–19 days ( $n = 8$ ) and  $\geq 20$  days ( $n = 17$ ). The error bars indicate SD.

with 2 separate study-patient populations. Evaluations of the Abbott SARS-CoV-2 IgG antibody test have been published.<sup>17–21</sup> However, in each of these study reports, the authors do not evaluate assay performance among multiple ARCHITECT analyzers, and only 1 study evaluated different specimen-collection tube-type comparisons.

Similar to the findings of previously published studies, our assessment showed excellent analytical performance within and between both of our institutions. Assay imprecision was acceptable across both institutions for IgG antibody-negative and -positive specimens. Our specimen-tube evaluation demonstrated equivalent assay performance for lithium heparin plasma, EDTA plasma, and serum specimens. This finding is consistent with the updated manufacturer-provided instructions-for-use claims that all 3 specimen types are acceptable.<sup>16</sup> In contrast, the findings of a recent study<sup>22</sup> showed significant differences between plasma- and serum-based testing in other commercially available antibody assays; these findings highlight the importance of performing specimen-type verification studies.

For within-institution method comparison studies, all IgG antibody results were concordant among analyzers or with patient SARS-CoV-2 PCR result, with the exception of 1 specimen at 1 institution. For that specimen, the IgG antibody result was below the assay cutoff; however, but the patient had a positive result via SARS-CoV-2 PCR testing, and positive IgG results had been obtained for specimens collected before that specimen, which suggests a preanalytical error, false-negative assay result, or technical

error. Analysis of the same 19 specimens at both institutions yielded 100% qualitative concordance among the 5 analyzers at both institutions, demonstrating equivalent assay performance across institutions and analyzers. Also, no statistically significant differences were obtained for S/C results within institutions, suggesting equivalent quantitative performance.

Cross-reactivity in SARS-CoV-2 antibody tests has been a concern from the medical community. In our study, we included specimens from patients who had tested negative via SARS-CoV-2 PCR, had tested positive for other coronaviruses via PCR, and had had specimens collected before the pandemic. All of these 101 specimens had negative qualitative results via the Abbott ARCHITECT assay, supporting lack of cross-reactivity with immunoglobulins produced in response to other viral infections.

One finding that interested us was a slightly larger median S/C value for patients diagnosed with non-SARS-CoV-2 coronaviruses compared to specimens obtained from patients with a negative SARS-CoV-2 result via PCR. This result could suggest partial interference from non-SARS-CoV-2 IgG antibodies. However, if there was potential interference, it was not substantial enough to affect the qualitative result. Also, the S/C values for patients with positive results via PCR before seroconversion had significantly larger values, compared with patients having negative results via PCR. This finding suggests the possible presence of SARS-CoV-2 IgG antibodies at a concentration lower than the cutoff for the assay. This observation



agrees with previously published findings.<sup>18</sup> Our results are consistent with those of previously published studies<sup>17–21</sup> evaluating the specificity of the Abbott ARCHITECT SARS-CoV-2 assay.

Seroconversion studies included specimen from both institutions. For all 13 patients who tested positive for SARS-CoV-2 via PCR testing who were included in the seroconversion study, seroconversion was detected by the IgG antibody assay within 10 days of symptom onset. This finding is consistent with those of previous studies.<sup>8,9,18</sup>

The present study has some limitations. A limitation of the cross-reactivity assessment was that for 6 patients who tested positive via PCR for non-SARS-CoV-2 coronaviruses, specimens were collected for serological testing within 4 days of specimen collection for the viral PCR assay and an unknown time period from the time of symptom onset. Therefore, the patients from whom the specimens were obtained may have had insufficient time to develop a robust IgG response and, thus, the specimen may not have been suitable for assessment of cross-reactivity in the ARCHITECT SARS-CoV-2 IgG antibody assay.

Another limitation is the relatively small number of specimens included in the seroconversion study. Because the specimens were obtained from among specimens submitted for purposes other than this research, our ability for specimen acquisition was limited. It is possible that seroconversion kinetics may have differed if specimens had been obtained on a daily basis for all patients. Also, the number of serial specimens and time of specimen collection for IgG antibody testing relative to PCR testing varied, and time of symptom onset was unknown for the specimens from other patients in this study. These factors could complicate comparison of S/C values among the different patient categories shown in **Figure 4**. Further research is needed to define the relationships of S/C values in patients infected with non-SARS-CoV-2 coronavirus, as well as in patients testing positive for SARS-CoV-2 via PCR before seroconversion vs after seroconversion.

In conclusion, the Abbott ARCHITECT SARS-CoV-2 IgG assay performed similarly for 3 specimen types and across 5 analyzers at 2 different institutions. This finding suggests acceptable performance of this assay and analyzer for widespread clinical laboratory use. **LM**

## Personal and Professional Conflicts of Interest

None reported.

## References

1. WHO Director-General's opening remarks at the media briefing on COVID-19. Published March 11, 2020. Accessed February 20, 2021. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>
2. Gorbalenya AE, Baker SC, Baric RS, et al. The species *severe acute respiratory syndrome-related coronavirus*: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020;5:536–544.
3. COVID-19 Map. Johns Hopkins Coronavirus Resource Center. Last updated February 20, 2021. Accessed February 20, 2021. <https://coronavirus.jhu.edu/map.html>. Accessed March 8, 2021.
4. IDSA Releases Antibody Testing Primer. Updated April 20, 2020. Accessed February 20, 2021. <https://www.idsociety.org/news-publications-new/articles/2020/emphasizing-need-for-more-information-idsa-releases-antibody-testing-primer/>
5. The New York Times website. Mandavilli A. Coronavirus Antibody Tests: Can You Trust the Results? Published April 24, 2020. Accessed February 20, 2021. <https://www.nytimes.com/2020/04/24/health/coronavirus-antibody-tests.html>
6. The New York Times website. Eder S, Twohey M, Mandavilli A. Antibody Test, Seen as Key to Reopening Country, Does Not Yet Deliver. Accessed February 20, 2021. <https://www.nytimes.com/2020/04/19/us/coronavirus-antibody-tests.html>
7. Weitz JS, Beckett SJ, Coenen AR, et al. Intervention Serology and Interaction Substitution: Modeling the Role of 'Shield Immunity' in Reducing COVID-19 Epidemic Spread. Published April 3, 2021. Accessed February 20, 2021. <https://www.medrxiv.org/content/10.1101/2020.04.01.20049767v1>
8. Lou B, Li T-D, Zheng S-F, et al. Serology characteristics of SARS-CoV-2 infection since the exposure and post symptoms onset. Published March 27, 2020. Accessed February 20, 2021. <https://www.medrxiv.org/content/10.1101/2020.03.23.20041707v1>
9. Liu L, Liu W, Zheng Y, et al. A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients. Accessed February 20, 2021. <https://www.medrxiv.org/content/10.1101/2020.03.06.20031856v1>
10. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature.* 2020;581(7809):465–469.
11. Long Q-X, Liu B-Z, Deng H-J, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med.* 2020;26(6):845–848.
12. Torres R, Rinder HM. Double-edged spike: are SARS-CoV-2 serologic tests safe right now? *Am J Clin Pathol.* 2020;aaqaa071.
13. Wall Street Journal. Burton TM. FDA sets standards for coronavirus antibody tests in crackdown on fraud. Updated May 4, 2020. Accessed February 20, 2021. <https://www.wsj.com/articles/fda-sets-standards-for-coronavirus-antibody-tests-in-crackdown-on-fraud-11588605373>
14. FDA. Insight into FDA's Revised Policy on Antibody Tests: Prioritizing Access and Accuracy. Updated May 4, 2020. Accessed February 20, 2021. <https://www.fda.gov/news-events/fda-voices/insight-fdas-revised-policy-antibody-tests-prioritizing-access-and-accuracy>
15. FDA. Center for Devices and Radiological Health. Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised). Published May 2020. Accessed February 20, 2021. <https://www.fda.gov>

- [gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised)
16. Farnsworth CW, Anderson NW. SARS-CoV-2 serology: much hype, little data. *Clin Chem*. 2020;66(7):875–877.
  17. Abbott. SARS-CoV-2 Immunoassays: Advancing Diagnostics of COVID-19. Accessed February 20, 2021. <https://www.corelaboratory.abbott/us/en/offerings/segments/infectious-disease/sars-cov-2>
  18. Bryan A, Pepper G, Wener MH, et al. Performance characteristics of the Abbott Architect SARS-CoV-2 IgG assay and seroprevalence in Boise, Idaho. *J Clin Microbiol*. 2020;58(8):e00941-20.
  19. Tang MS, Hock KG, Logsdon NM, et al. Clinical performance of two SARS-CoV-2 serologic assays. *Clin Chem*. 2020;66(8):1055–1062.
  20. Kohmer N, Westhaus S, Rühl C, Ciesek S, Rabenau HF. Brief clinical evaluation of six high-throughput SARS-CoV-2 IgG antibody assays. *J Clin Virol*. 2020;129:104480.
  21. Nicol T, Lefevre C, Serri O, et al. Assessment of SARS-CoV-2 serological tests for the diagnosis of COVID-19 through the evaluation of three immunoassays: two automated immunoassays (Euroimmun and Abbott) and one rapid lateral flow immunoassay (NG Biotech). *J Clin Virol*. 2020;129:104511.
  22. Theel ES, Harring J, Hilgart H, Granger D. Performance characteristics of four high-throughput immunoassays for detection of IgG antibodies against SARS-CoV-2. *J Clin Microbiol*. 2020;58(8):e01243-20.
  23. Haselmann V, Kittel M, Gerhards C, et al. Comparison of test performance of commercial anti-SARS-CoV-2 immunoassays in serum and plasma samples. *Clin Chim Acta*. 2020;510:73–78.
  24. Carey RN, Durham AP, Hauck WW, et al. *User Verification of Precision and Estimation of Bias; Approved Guideline*. Clinical Laboratory Standards Institute; 2014.
  25. FDA. Overview of IVD Regulation. Updated September 16, 2019. Accessed February 20, 2021. <https://www.fda.gov/medical-devices/ivd-regulatory-assistance/overview-ivd-regulation>
  26. FDA. *Regulatory Controls*. Published March 27, 2018. Accessed February 20, 2021. <https://www.fda.gov/medical-devices/overview-device-regulation/regulatory-controls>
  27. FDA. *Emergency Use Authorization*. Updated February 19, 2021. Accessed February 20, 2021. <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>