Serology Test Evaluation Report for “Architect i1000 SARS-CoV-2 IgG” from Abbott

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1 Introduction

The Architect i1000 SARS-CoV-2 IgG from Abbott was tested on 2020-05-20 at the Hemostasis Laboratory Branch, Division of Blood Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). Tests were from lot number 15016M800. The Architect i1000 SARS-CoV-2 IgG is intended to qualitatively detect IgG.

1.1 Panel composition

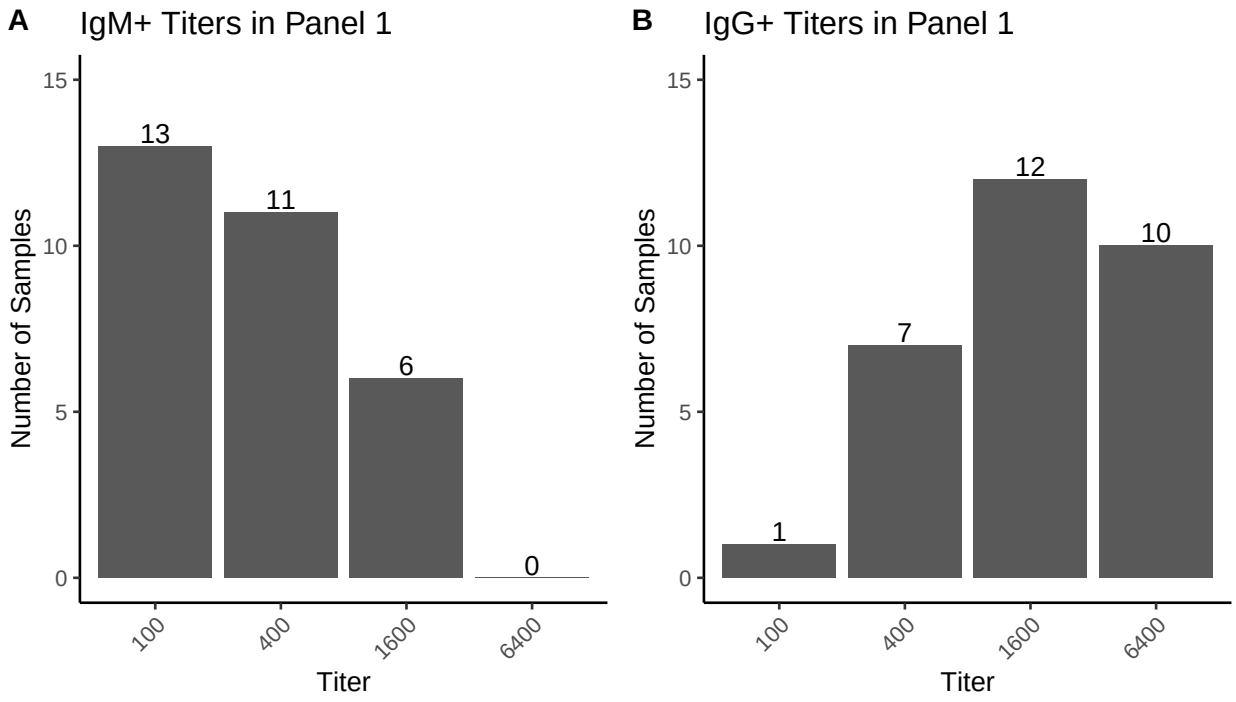

Figure 1: Titer levels for (A) IgM+ and (B) IgG+ samples according to the CDC SARS-CoV-2 Spike antigen assay

The test was evaluated against “Panel 1,” which includes frozen SARS-CoV-2 antibody-positive serum samples ($n = 30$) and frozen antibody-negative serum and plasma samples ($n = 80$). The panel size and composition were chosen to enable a laboratory-based evaluation and to provide reasonable estimates and confidence intervals for test performance in the context of limited sample availability. The sample size is comparable to that of a typical sample size used to support Emergency Use Authorization (EUA) by FDA for tests of this type.

1.1.1 Positive samples

Positive samples used in Panel 1 were from patients previously confirmed to have SARS-CoV-2 infection with a nucleic acid amplification test (NAAT). Time between symptom onset, NAAT testing, and sample collection is not known for all samples. Both SARS-CoV-2 IgM and IgG antibodies are present in all Panel 1 positive samples. The Centers for Disease Control and Prevention (CDC) detected the presence of IgG and IgM antibodies at their laboratory using their SARS-CoV-2 spike enzyme-linked immunosorbent assay (ELISA) tests.[1] The presence of antibodies was confirmed at the Frederick National Laboratory for Cancer Research (FNLCR), a Federally Funded Research and Development Center (FFRDC) sponsored by the National Cancer Institute (NCI), using CDC's developed ELISAs (Pan-Ig, IgG, and IgM) as well as an IgG Receptor Binding Domain (RBD) ELISA developed by the Krammer Laboratory at the Icahn School of Medicine at Mount Sinai.[2] The positive samples selected may not reflect the distribution of antibody levels in patient populations that would be evaluated by such a test. Because all samples are positive for both IgM and IgG, this evaluation cannot verify that tests intended to detect IgM and IgG antibodies separately detect these antibodies independently.

Positive samples were assessed at dilutions of 1:100, 1:400, 1:1600, and 1:6400 by CDC on their Pan-Ig assay, their IgM assay, and their IgG assay. Some samples were run at additional dilutions. Any samples that were positive at a dilution greater than 1:6400 were assigned a titer of 6400 because 1:6400 was the highest dilution at which all Panel 1 positive samples were assessed. Two of these samples, C0107 and C0176, were positive for IgG antibodies at a dilution of 1:25600.

1.1.2 Negative samples

All Panel 1 negative samples were collected prior to 2020, before the SARS-CoV-2 virus is known to have circulated in the United States. Panel 1 groups include:

- "Negatives" ($n = 70$): selected without regard for clinical status. This group includes a sample, C0063, that showed reactivity in the Pan-Ig CDC spike ELISA at FNLCR. It includes another sample, C0087, that showed reactivity in the IgG RBD ELISA at FNLCR.
- "HIV+" ($n = 10$): selected from banked serum from HIV+ patients.[3] This group includes 3 samples, C0018, C0155, and C0182, that showed reactivity in the IgG RBD ELISA at FNLCR.

[1] See `https://www.cdc.gov/coronavirus/2019-ncov/lab/serology-testing.html`, which notes "CDC's serologic test is designed and validated for broad-based surveillance and research that will give us information needed to guide the response to the pandemic and protect the public's health. The test is not currently designed to test individuals who want to know if they have been previously infected with COVID-19."

[2] An implementation of this test, the COVID-19 ELISA IgG Antibody Test, has been granted an EUA authorization by FDA for use at the Mount Sinai Laboratory (MSL), Center for Clinical Laboratories, a division of the Department of Pathology, Molecular, and Cell-Based Medicine, New York, NY. See `https://www.fda.gov/media/137029/download`.

[3] HIV+ samples were deemed appropriate for inclusion in the panel: (1) to increase the sample size and reduce the confidence interval; and (2) to identify any possibility of cross-reactivity with HIV+ samples. It is anticipated that other types of samples, as they become available, may also be evaluated in any future analyses.

All Panel 1 negative samples were assessed at dilutions of 1:100 and 1:400 by CDC on their Pan-Ig assay. A subset of samples was assessed in parallel at additional dilutions and on the CDC IgM and IgG assays. All Panel 1 negative samples were negative at a dilution of 1:100 on the CDC Pan-Ig assay. These samples were assigned an undetectable titer (represented as zero (0) in the line data) for the Pan-Ig assay, the IgM assay, and the IgG assay.

1.2 Analysis

Samples used in this evaluation were not randomly selected, and sensitivity (PPA) and specificity (NPA) estimates in this report may not be indicative of the real-world performance of the Abbott Architect i1000 SARS-CoV-2 IgG. Sensitivity and specificity were calculated for each antibody (e.g., IgM, IgG, IgA, and Pan-Ig, as applicable) separately. In addition, sensitivity and specificity were estimated in a combined manner, where a positive result for any antibody the Abbott Architect i1000 SARS-CoV-2 IgG is intended to detect was considered as a positive test result and a negative result meant that a sample tested negative for all antibodies the Abbott Architect i1000 SARS-CoV-2 IgG is intended to detect. Positive and negative predictive values were calculated for combined sensitivity and specificity assuming a prevalence of 5%. Cross-reactivity with HIV+ was evaluated, and results are presented separately. If cross-reactivity was detected, the samples with HIV+ were not included in calculations of specificity.

Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008).[4] Confidence intervals for PPV and NPV were calculated using the values from the 95% confidence intervals for sensitivity and specificity. For evaluation of cross-reactivity with HIV+, it was evaluated whether an increased false positive rate among antibody negative samples with HIV was statistically higher than the false positive rate among antibody negative samples without HIV (for this, a confidence interval for the difference in false positive rates was calculated per a score method described by Altman.[5])

1.3 Important caveats

Sensitivity and specificity estimates in this report may not be indicative of the real world performance of the Abbott Architect i1000 SARS-CoV-2 IgG.

These results are based on serum and plasma samples only and may not be indicative of performance with other sample types, such as whole blood, including finger stick blood.

Information about anticoagulants used is not known.

The number of samples in the panel is a minimally viable sample size that still provides reasonable

[4] CLSI. *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline—Second Edition*. CLSI document EP12-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2008. See `https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard__identification_no=31791`.

[5] Statistics with Confidence: Confidence Intervals and Statistical Guidelines. (2013). Wiley.

estimates and confidence intervals for test performance, and the samples used may not be representative of the antibody profile observed in patient populations.

1.4 Notes about the evaluation procedure

- The Abbott Architect i1000 SARS-CoV-2 IgG was used per the manufacturer's package insert.
- Devices were tested within any expiration dates provided.
- Devices were not obviously defective / compromised.
- Devices were stored at CDC within their labeled conditions.
- A single operator conducted the automated test with assistance from a second technician who performed sample ID quality checks on tube labeling and data entry.
- The personnel who performed the testing were blinded to the identity / code of the sample and the expected results.
- The testing was performed after calibration and control samples were run on the instrument.

2 Results

Table 1: Summary Results

	Comparator Method			Collected pre-2020		
	Antibody Positive			Antibody Negative		
Architect i1000 SARS-CoV-2 IgG	IgM+, IgG+	IgM+, IgG-	IgM-, IgG+	Negative	HIV+	Total
IgG+	27					27
IgG-	3			70	10	83
Total	30			70	10	110

Table 2: Summary Statistics

Measure	Estimate	Confidence Interval
IgG Sensitivity	90.0% (27/30)	(74.4%; 96.5%)
IgG Specificity	100% (80/80)	(95.4%; 100%)
Combined Sensitivity	90.0% (27/30)	(74.4%; 96.5%)
Combined Specificity	100% (80/80)	(95.4%; 100%)
Combined PPV for prevalence = 5.0%	100%	(46.1%; 100%)
Combined NPV for prevalence = 5.0%	99.5%	(98.6%; 99.8%)
Cross-reactivity with HIV+	0.0% (0/10), not detected	

3 Line Data

In the table below, “Days” refers to “Days from symptom onset to blood collection.”

Table 3: Line Data

Sample Number	IgM Result	IgG Result	IgA Result	Pan Ig Result	(IgM / IgG) Result	Control	Sample ID	Type	CDC Spike Pan-Ig Titer	CDC Spike IgM Titer	CDC Spike IgG Titer	Days	Group
1		Negative				Pass	C0155	Plasma	0	0	0		HIV+
2		Negative				Pass	C0197	Plasma	0	0	0		HIV+
3		Negative				Pass	C0182	Plasma	0	0	0		HIV+
4		Negative				Pass	C0093	Plasma	0	0	0		HIV+
5		Negative				Pass	C0099	Plasma	0	0	0		HIV+
6		Negative				Pass	C0089	Plasma	0	0	0		HIV+
7		Negative				Pass	C0138	Plasma	0	0	0		HIV+
8		Negative				Pass	C0054	Plasma	0	0	0		HIV+
9		Negative				Pass	C0150	Plasma	0	0	0		HIV+
10		Negative				Pass	C0018	Plasma	0	0	0		HIV+
11		Negative				Pass	C0179	Plasma	0	0	0		Negatives
12		Negative				Pass	C0008	Plasma	0	0	0		Negatives
13		Negative				Pass	C0185	Plasma	0	0	0		Negatives
14		Negative				Pass	C0079	Plasma	0	0	0		Negatives
15		Negative				Pass	C0198	Plasma	0	0	0		Negatives
16		Negative				Pass	C0051	Plasma	0	0	0		Negatives
17		Negative				Pass	C0063	Plasma	0	0	0		Negatives
18		Negative				Pass	C0199	Plasma	0	0	0		Negatives
19		Negative				Pass	C0004	Plasma	0	0	0		Negatives
20		Negative				Pass	C0193	Plasma	0	0	0		Negatives

Table 3: Line Data *(continued)*

Sample Number	IgM Result	IgG Result	IgA Result	Pan Ig Result	(IgM / IgG) Result	Control	Sample ID	Type	CDC Spike Pan-Ig Titer	CDC Spike IgM Titer	CDC Spike IgG Titer	Days	Group
21		Negative				Pass	C0121	Plasma	0	0	0		Negatives
22		Negative				Pass	C0117	Plasma	0	0	0		Negatives
23		Negative				Pass	C0005	Plasma	0	0	0		Negatives
24		Negative				Pass	C0065	Plasma	0	0	0		Negatives
25		Negative				Pass	C0059	Plasma	0	0	0		Negatives
26		Negative				Pass	C0098	Plasma	0	0	0		Negatives
27		Negative				Pass	C0109	Plasma	0	0	0		Negatives
28		Negative				Pass	C0095	Plasma	0	0	0		Negatives
29		Negative				Pass	C0032	Plasma	0	0	0		Negatives
30		Negative				Pass	C0156	Plasma	0	0	0		Negatives
31		Negative				Pass	C0140	Plasma	0	0	0		Negatives
32		Negative				Pass	C0041	Plasma	0	0	0		Negatives
33		Negative				Pass	C0101	Plasma	0	0	0		Negatives
34		Negative				Pass	C0016	Serum	0	0	0		Negatives
35		Negative				Pass	C0118	Serum	0	0	0		Negatives
36		Negative				Pass	C0001	Serum	0	0	0		Negatives
37		Negative				Pass	C0048	Serum	0	0	0		Negatives
38		Negative				Pass	C0062	Serum	0	0	0		Negatives
39		Negative				Pass	C0087	Serum	0	0	0		Negatives
40		Negative				Pass	C0116	Serum	0	0	0		Negatives
41		Negative				Pass	C0083	Serum	0	0	0		Negatives
42		Negative				Pass	C0173	Serum	0	0	0		Negatives
43		Negative				Pass	C0011	Serum	0	0	0		Negatives
44		Negative				Pass	C0094	Serum	0	0	0		Negatives

Table 3: Line Data *(continued)*

Sample Number	IgM Result	IgG Result	IgA Result	Pan Ig Result	(IgM / IgG) Result	Control	Sample ID	Type	CDC Spike Pan-Ig Titer	CDC Spike IgM Titer	CDC Spike IgG Titer	Days	Group
45		Negative				Pass	C0115	Serum	0	0	0		Negatives
46		Negative				Pass	C0073	Serum	0	0	0		Negatives
47		Negative				Pass	C0058	Serum	0	0	0		Negatives
48		Negative				Pass	C0014	Serum	0	0	0		Negatives
49		Negative				Pass	C0126	Serum	0	0	0		Negatives
50		Negative				Pass	C0169	Serum	0	0	0		Negatives
51		Positive				Pass	C0191	Serum	400	100	400	22	Positives
52		Positive				Pass	C0136	Serum	6400	400	6400		Positives
53		Positive				Pass	C0074	Serum	400	100	400	24	Positives
54		Positive				Pass	C0092	Serum	1600	100	1600		Positives
55		Positive				Pass	C0102	Serum	400	400	400	25	Positives
56		Positive				Pass	C0160	Serum	1600	100	1600	17	Positives
57		Positive				Pass	C0053	Serum	1600	1600	1600	28	Positives
58		Negative				Pass	C0037	Serum	400	100	1600	19	Positives
59		Positive				Pass	C0049	Serum	400	400	400	23	Positives
60		Positive				Pass	C0080	Serum	1600	400	1600	29	Positives
61		Positive				Pass	C0164	Serum	1600	400	6400	23	Positives
62		Positive				Pass	C0061	Serum	1600	100	1600	26	Positives
63		Positive				Pass	C0107	Serum	6400	400	6400	36	Positives
64		Positive				Pass	C0010	Serum	1600	400	1600	29	Positives
65		Positive				Pass	C0084	Serum	6400	100	6400	24	Positives
66		Positive				Pass	C0038	Serum	100	100	100	20	Positives
67		Positive				Pass	C0180	Serum	6400	1600	6400	24	Positives
68		Positive				Pass	C0090	Serum	1600	100	1600	22	Positives

Table 3: Line Data *(continued)*

Sample Number	IgM Result	IgG Result	IgA Result	Pan Ig Result	(IgM / IgG) Result	Control	Sample ID	Type	CDC Spike Pan-Ig Titer	CDC Spike IgM Titer	CDC Spike IgG Titer	Days	Group
69		Positive				Pass	C0119	Serum	1600	100	1600	20	Positives
70		Positive				Pass	C0176	Serum	6400	400	6400	19	Positives
71		Negative				Pass	C0122	Serum	400	100	400	24	Positives
72		Positive				Pass	C0064	Serum	1600	1600	6400	20	Positives
73		Positive				Pass	C0040	Serum	1600	400	1600	24	Positives
74		Positive				Pass	C0144	Serum	6400	1600	6400	21	Positives
75		Positive				Pass	C0071	Serum	6400	1600	6400	20	Positives
76		Positive				Pass	C0127	Serum	400	400	1600	23	Positives
77		Negative				Pass	C0153	Serum	400	100	400	31	Positives
78		Positive				Pass	C0132	Serum	1600	1600	6400		Positives
79		Positive				Pass	C0172	Serum	1600	400	1600	19	Positives
80		Positive				Pass	C0161	Serum	400	100	400	25	Positives
81		Negative				Pass	C0081	Serum	0	0	0		Negatives
82		Negative				Pass	C0043	Serum	0	0	0		Negatives
83		Negative				Pass	C0050	Serum	0	0	0		Negatives
84		Negative				Pass	C0181	Serum	0	0	0		Negatives
85		Negative				Pass	C0110	Serum	0	0	0		Negatives
86		Negative				Pass	C0165	Serum	0	0	0		Negatives
87		Negative				Pass	C0044	Serum	0	0	0		Negatives
88		Negative				Pass	C0067	Serum	0	0	0		Negatives
89		Negative				Pass	C0100	Serum	0	0	0		Negatives
90		Negative				Pass	C0139	Serum	0	0	0		Negatives
91		Negative				Pass	C0066	Serum	0	0	0		Negatives
92		Negative				Pass	C0072	Serum	0	0	0		Negatives

Table 3: Line Data *(continued)*

Sample Number	IgM Result	IgG Result	IgA Result	Pan Ig Result	(IgM / IgG) Result	Control	Sample ID	Type	CDC Spike Pan-Ig Titer	CDC Spike IgM Titer	CDC Spike IgG Titer	Days	Group
93		Negative				Pass	C0174	Serum	0	0	0		Negatives
94		Negative				Pass	C0024	Serum	0	0	0		Negatives
95		Negative				Pass	C0002	Serum	0	0	0		Negatives
96		Negative				Pass	C0027	Serum	0	0	0		Negatives
97		Negative				Pass	C0186	Serum	0	0	0		Negatives
98		Negative				Pass	C0158	Serum	0	0	0		Negatives
99		Negative				Pass	C0128	Serum	0	0	0		Negatives
100		Negative				Pass	C0120	Serum	0	0	0		Negatives
101		Negative				Pass	C0034	Serum	0	0	0		Negatives
102		Negative				Pass	C0131	Serum	0	0	0		Negatives
103		Negative				Pass	C0012	Serum	0	0	0		Negatives
104		Negative				Pass	C0146	Serum	0	0	0		Negatives
105		Negative				Pass	C0069	Serum	0	0	0		Negatives
106		Negative				Pass	C0029	Serum	0	0	0		Negatives
107		Negative				Pass	C0020	Serum	0	0	0		Negatives
108		Negative				Pass	C0033	Serum	0	0	0		Negatives
109		Negative				Pass	C0200	Serum	0	0	0		Negatives
110		Negative				Pass	C0070	Serum	0	0	0		Negatives