ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
BABSON DIAGNOSTICS AC19G1
(BABSON DIAGNOSTICS, INC.)

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only

(The Babson Diagnostics aC19G1 will be performed at Babson Diagnostics, Inc., which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high-complexity tests as per Babson Diagnostics, Inc. instructions for use that was reviewed by the FDA under this EUA.)

INTENDED USE

The Babson Diagnostics aC19G1 test is an indirect sandwich chemiluminescent immunoassay performed on the Atellica IM Analyzer intended for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma (potassium EDTA, lithium heparin). The Babson Diagnostics aC19G1 test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The Babson Diagnostics aC19G1 test should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to Babson Diagnostics, Inc., which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity tests.

Results are for the detection of SARS CoV-2 antibodies. IgG antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

The sensitivity of the Babson Diagnostics aC19G1 test early after infection in unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for the Babson Diagnostics aC19G1 test may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The Babson Diagnostics aC19G1 test is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The Babson Diagnostics aC19G1 is an indirect sandwich immunoassay. The sample is

incubated with Capture Reagent containing recombinant biotinylated SARS-CoV-2 S1 antigen immobilized on streptavidin latex magnetic microparticles. Antigen-antibody complexes will form if SARS-CoV-2 antibody is present in the sample. Detection Reagent containing mouse monoclonal anti-human IgG antibody labelled with acridinium ester is used to detect IgG antibodies to SARS-CoV-2 in the sample. The test is a two-pass assay run on the Siemens Atellica IM analyzer.

COMPONENTS SPECIFIC TO THE TEST

The following components are specific to the Babson Diagnostics aC19G1:

Component Name	Component Description
Babson Diagnostics aC19G1 Primary Reagent Pack	Reagent pack containing Babson Diagnostics aC19G1 Capture Reagent and Babson Diagnostics aC19G1 Detection Reagent
Babson Diagnostics aC19G1 Capture Reagent	Recombinant biotinylated SARS-CoV-2 S1 antigen immobilized on streptavidin latex magnetic particles
Babson Diagnostics aC19G1 Detection Reagent	Mouse monoclonal anti-human IgG antibody labeled with acridinium ester
Babson Diagnostics aC19G1 Calibrator	Pooled human serum determined to be positive for the presence of IgG antibodies to SARS-CoV-2 and preserved in sodium azide at 0.09%
Babson Diagnostics aC19G1 Negative Quality Control	Pooled human serum determined to be negative for the presence of IgG antibodies to SARS-CoV-2 and preserved in sodium azide at 0.09%
Babson Diagnostics aC19G1 Positive Quality Control	Pooled human serum determined to be positive for the presence of IgG antibodies to SARS-CoV-2 and preserved in sodium azide at 0.09%

COMPONENTS REQUIRED BUT NOT SPECIFIC TO THE TEST

Standard Siemens Healthineers solutions including Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. In addition, Siemens Healthineers Atellica IM Analyzer with Atellica Sample Handler or Atellica Direct Load is needed to perform the assay.

CONTROLS TO BE USED WITH THE BABSON DIAGNOSTICS AC19G1

Babson Diagnostics aC19G1 Negative Quality Control and Babson Diagnostics aC19G1 Positive Quality Control should be used with the assay.

INTERPRETATION OF RESULTS

Results are automatically calculated as Index Values by the Atellica IM analyzer.

The Index Value is calculated as the RLU (Relative Light Units) for the test sample divided by the RLU at the cut-off value.

A result with Index Value <1.0 is interpreted as the specimen being “Nonreactive” or “Negative” for IgG antibodies to SARS-CoV-2. A result with Index Value ≥1.0 is interpreted as the specimen being “Reactive” or “Positive” for IgG antibodies to SARS-

CoV-2 (see **Table 1**).

Table 1. Interpretation of results.

Index Value	Interpretation	Description
<1.00	Nonreactive or Negative	IgG antibodies to SARS-CoV-2 were not detected in the sample.
≥1.00	Reactive or Positive	IgG antibodies to SARS-CoV-2 were detected in the sample.

PERFORMANCE EVALUATION

1) Analytical Sensitivity:

There is no standard reference SARS-CoV-2 antigen material available; accordingly, absolute analytical sensitivity cannot be calculated.

2) Analytical Specificity

Reactivity/lnclusivity
Although mutations in the SARS-CoV-2 genome have been identified as the virus has spread, no serologically unique strains have been described relative to the originally isolated virus (this research is limited at present).

Cross reactivity

a. Cross reactivity was evaluated by spiking specimens determined to be SARS-CoV-2 seronegative using Babson Diagnostics aC19G1 with Bio-Rad VIROTROL I and VIROTROL II, which have published representative reactivities using a variety of methods (**Table 2**). The column labeled "n" indicates the number of test runs performed by Bio-Rad in order to confirm reactivity. These control reagents are prepared from human plasma or serum reactive for respective antibodies.

Table 2. Cross-reactivity samples characterization methods.

Spiker	Antibody in Spiker	Characterization Method	n
VIROTROL I	Anti-HIV-1	Bio-Rad GS HIV-1/HIV-2 Plus 0 EIA Abbott ARCHITECT HIV Ag/Ab Combo Ortho VITROS ECi Anti-HIV 1 + 2	6 9 6
VIROTROL I	Anti-HBc	Bio-Rad MONOLISA Anti-HBC EIA Ortho HBc ELISA	6 20
VIROTROL I	Anti-HCV	Ortho HCV Version 3.0 ELISA Abbott ARCHITECT Anti-HCV	24 24
VIROTROL I	Anti-CMV	bioMérieux VIDAS CMV IgG	6
VIROTROL I	Anti-HTLV-1	Abbott PRISM HTLV-I/HTLV-II	20
VIROTROL II	Anti-HBs	Abbott ARCHITECT AUSAB Ortho VITROS ECi Anti-HBs DiaSorin ETI-AB-AUK PLUS	25 24 10
VIROTROL II	Anti-HAV	Bio-Rad MONOLISA Anti-HAV EIA	4

		DiaSorin ETI-AB-HAVK PLUS	10

Five specimens that had tested negative on Babson Diagnostics aC19G1 were spiked with VIROTROL I (900 µL native specimen spiked with 300 µL VIROTROL I). Contrived specimens were confirmed to be HCV Ab positive at Clinical Pathology Laboratories (Austin, TX). Each contrived specimen was tested in duplicate on Babson Diagnostics aC19G1, and all ten runs were negative for SARS-CoV-2 IgG.

Five specimens that had tested negative on Babson Diagnostics aC19G1 were spiked with VIROTROL II (900 µL native specimen spiked with 300 µL VIROTROL II). Contrived specimens were confirmed for HBs Ab at Clinical Pathology Laboratories (Austin, TX), with four of five REACTIVE, and the fifth NON-REACTIVE but detectable at 5.72 MIU/ML. Each contrived specimen was tested in duplicate on Babson Diagnostics aC19G1, and all ten runs were negative for SARS-CoV-2 IgG.

Five specimens that had tested negative on Babson Diagnostics aC19G1 were spiked with VIROTROL I (900 µL native specimen spiked with 300 µL VIROTROL I). Contrived specimens were confirmed for HIV 1/2 Ab at Clinical Pathology Laboratories (Austin, TX), with all five SCREEN REACTIVE and all five CONFIRMATION NON-REACTIVE. Confirmatory testing was performed on Bio-Rad GS HIV-1/HIV-2 Plus O EIA, which was used to characterize VIROTROL I at 3.39 Mean/Cutoff. Each contrived specimen was tested in duplicate on Babson Diagnostics aC19G1, and all ten runs were negative for SARS-CoV-2 IgG

b. Cross reactivity for ANA was evaluated by combining four Bio-Rad Liquichek ANA Controls in a 1:1:1:1 ratio. The Liquicheck controls are prepared from pre-diluted human serum. The pooled ANA QC was run in triplicate on Babson Diagnostics aC19G1, and all three runs were negative for SARS-CoV-2 IgG. Positivity of each of the controls on HEp-2 is published by Bio-Rad in the Certificate of Analysis.

c. Nine specimens that had tested positive for one or more of Influenza A IgG, Influenza A IgM, Influenza B IgG, and Influenza B IgM at ARUP (Salt Lake City, UT) were tested in duplicate on Babson Diagnostics aC19G1, and all eighteen runs were negative for SARS-CoV-2 IgG.

d. Additionally, 100 pre-pandemic samples from a population with a high prevalence of vaccination and/or infection against the following were tested to evaluate potential cross reactivity:

- Influenza A
- Influenza B
- Rhinovirus
- Haemophilus Influenzae

No cross reactivity was observed.

Class Specificity
Babson Diagnostics aC19G1 Detection Reagent uses a mouse monoclonal anti-human IgG antibody labeled with acridinium ester. This antibody has class-specific

reactivity only to human IgG isotypes. In addition, The Babson Diagnostics aC19G1 was evaluated for class specificity to IgG antibodies in a study designed to evaluate the potential for human IgM to cross react and therefore produce false positive results for IgG.

Seven specimens were tested for class specificity. Five specimens were native patient specimens and two specimens were control materials (VIROTROL and VIROCLEAR). Bio-Rad VIROTROL SARS-CoV and VIROCLEAR SARS-CoV are research use only control materials.

Two aliquots were made from each specimen: the control and the treated with DTT aliquots. The DTT aliquot was prepared by spiking the specimen with DTT in PBS. The PBS aliquot was prepared by spiking the specimen with PBS (without DTT) as a control. Both aliquots were mixed and incubated for 30 minutes at room temperature.

The PBS and DTT aliquots were tested with an FDA-authorized serological assay to confirm IgG/IgM reactivity and DTT activity.

The PBS and DTT aliquots were run on Babson Diagnostics aC19G1 in duplicate, and the results are presented in **Table 3**. Class specificity was determined based on 100% percent agreement between PBS Result and DTT Result for each replicate on Babson Diagnostics aC19G1.

Table 3. Results of testing class specificity samples with Babson Diagnostics aC19G1.

Specimen (antibody class reactivity status)	Replicate	aC19G1 PBS Result (Index)	aC19G1 DTT Result (Index)	aC19G1 DTT Expected	Agreement
190670 (IgM+/IgG+)	1	+ (2.56)	+ (2.50)	+	Yes
	2	+ (2.50)	+ (2.27)	+	Yes
190677 (IgM+/IgG+)	1	+ (1.82)	+ (2.00)	+	Yes
	2	+ (1.75)	+ (1.96)	+	Yes
190828 (IgM+)	1	– (0.48)	– (0.58)	–	Yes
	2	– (0.51)	– (0.58)	–	Yes
190779 (IgM+/IgG+)	1	+ (2.63)	+ (2.50)	+	Yes
	2	+ (2.56)	+ (2.44)	+	Yes
20141001 (IgM+/IgG+)	1	+ (2.86)	+ (2.70)	+	Yes
	2	+ (2.78)	+ (2.44)	+	Yes
VIROTROL (IgM+/IgG+ control)	1	+ (2.56)	+ (2.33)	+	Yes
	2	+ (2.50)	+ (2.38)	+	Yes
VIROCLEAR (negative control)	1	– (0.00)	– (0.00)	–	Yes
	2	– (0.00)	– (0.00)	–	Yes

Matrix Equivalency

Matrix sets were collected from five donors negative for SARS-CoV-2 IgG when tested by the Babson Diagnostics aC19G1. A serum tube, a potassium EDTA plasma tube, and a lithium heparin plasma tube were collected from each donor. Each sample was used to create four contrived samples with analytes at the following levels:

- Negative (no spike)
- High Negative (spiked with known positive serum)
- Low Positive (spiked with known positive serum)
- Positive (spiked with known positive serum)

Positive serum for contrived samples used in the study was from a single donor who had tested positive for SARS-CoV-2 using an FDA-authorized PCR method. The serum sample was further confirmed as IgG antibody positive using an FDA authorized IgG antibody test.

Each of the contrived samples was tested with the Babson Diagnostics aC19G1 in triplicate. Results were consistent across all replicates, and all positive samples were positive and all negative samples were negative in all evaluated matrices. A Deming regression analysis was performed for all samples evaluated in the matrix equivalency study regressing the mean index values from samples from each candidate tube versus the serum index values. R^2 for both graphs were 0.997 showing equivalent performance of the Babson Diagnostics aC19G1 when using potassium EDTA plasma, lithium heparin plasma, and serum samples as matrices.

3) Clinical Performance

Clinical Sensitivity

Clinical sensitivity was evaluated by conducting a retrospective study testing a total of 34 specimens collected from individuals confirmed to be positive for SARS-CoV-2 by an FDA-authorized PCR assay based on nasopharyngeal and oropharyngeal swab collection methods. Out of the 34 specimens collected, 20 specimens were serum specimens. Of these 20 specimens, 18 were from individuals who had COVID-19 symptoms, while two were from asymptomatic individuals. Fourteen specimens were EDTA plasma specimens from individuals with one or more documented positive FDA-authorized PCR results. Out of the 34 specimens collected, the remaining 14 were EDTA plasma specimens from individuals who had COVID-19 symptoms.

FDA-authorized PCR methods used in the clinical sensitivity study included the following: Roche cobas SARS-CoV-2, Quest SARS-CoV-2 rRT-PCR, Qiagen QIAstat-Dx Respiratory SARS-CoV-2 Panel, Abbott M2000 RealTime SARS-CoV-2 assay, and Luminex NxTAG CoV.

All specimens included in the clinical sensitivity study were tested using the Babson Diagnostics aC19G1 at a single site (Babson Diagnostics laboratory, Austin, TX) by two operators trained on laboratory procedures for the instrument and the test method. Results of the clinical study by day post symptom onset are presented in **Table 5**.

Table 4. Results of the retrospective clinical study with samples collected from subjects confirmed to be SARS-CoV-2 positive by an FDA-authorized PCR by day from symptom onset.

Days Post Symptom Onset	Number Tested	Positive with aC19G1	PPA	95% CI
8 - 14	3	2	66.67%	20.76% - 93.86%
≥15	29	29	100.00%	88.31% - 100.00%
N/A (Asymptomatic)	2	2	100.00%	34.24% - 100.00%
Total	**34**			

Since two samples were collected from asymptomatic patients, and not able to be stratified by "days from symptom onset", samples were also stratified by days from positive PCR. Positive Percent Agreement (PPA) and 95% confidence intervals are shown in **Table 6.**

Table 5. Results of the retrospective clinical study with samples collected from subjects confirmed to be SARS-CoV-2 positive by an FDA-authorized PCR by day from positive PCR.

Days from Positive PCR	Number Tested	Positive with aC19G1	PPA	95% CI
8 - 14	10	9	90.00%	59.59% - 98.21%
≥15	24	24	100.00%	86.20% - 100.00%
Total	**34**			

Results of the retrospective study by matrix are presented in **Table 7** (EDTA plasma) and **Table 8** (serum).

Table 6. Results of the clinical study with retrospective EDTA plasma samples.

Days from Positive PCR	Number Tested	Positive with aC19G1	PPA	95% CI
8 - 14	6	6	100.00%	60.97% - 100.00%
≥15	8	8	100.00%	67.56% - 100.00%
Total	**14**			

Table 7. Results of the clinical study with retrospective serum samples.

Days from Positive PCR	Number Tested	Positive with aC19G1	PPA	95% CI
8 - 14	4	3	75.00%	32.57% - 95.44%
≥15	16	16	100.00%	80.64% - 100.00%
Total	**20**			

Clinical Specificity

Clinical specificity was evaluated by testing 100 retrospectively collected (between September 25, 2019 and October 7, 2019) serum and plasma specimens. All these specimens were negative when tested with the Babson Diagnostics aC19G1. Negative

Percent Agreement (NPA) is therefore 100%, and 95% CI is 96.30% - 100.00%.

Warnings

- This test has not been cleared or approved by the US Food and Drug Administration.

- This test has been authorized by FDA under an emergency use authorization only for use by the authorized laboratory, Babson Diagnostics, Inc., which is certified under CLIA, and meets requirements to perform high complexity tests.

- This test has been authorized only for the detection of IgG antibodies to SARS-CoV-2, not for any other viruses or pathogens.

- This test is 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.

Limitations

- For In Vitro Diagnostic Use Only
- Rx Only
- Not for the screening of donated blood
- For Professional Use Only
- For Use Under the Food and Drug Administration's Emergency Use Authorization Only
- For Use at Babson Diagnostics, Inc.
- Detection of IgG antibodies against SARS-CoV-2 is not yet established to determine long term immunity to the virus or to protect against infection by the virus
- Results should only be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings
- The assay performance characteristics have not been established for matrices other than serum and plasma (potassium EDTA, lithium heparin)
- Do not test samples collected prior to 14 days from symptom onset with the Babson Diagnostics AC19G1 test because there is an increased risk of false negative results.
- Results from antibody testing should not be used to diagnose or exclude active SARS-CoV-2 infection
- Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Testing with a molecular diagnostic should be considered to evaluate for active infection in symptomatic individuals
- Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E
- A positive result may not indicate previous SARS-CoV-2 infection. Consider other information including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune

response.

- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.