IFU (Instructions for Use)

This IFU covers:

- Brevitest SARS-CoV-2 IgG Test

This test is:

- For prescription use only.
- For in vitro diagnostic use only.
- For use only as described by the FDA in the Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency.

Contents

Manufacturer information

Manufacturer: BreviTest Technologies, LLC (Brevitest).
Address: 3900 Essex Lane, Suite 575, Houston, TX 77027
Website: www.brevitest.com
Contact: info@brevitest.com

Scientific summary

Intended Use

The Brevitest SARS-CoV-2 IgG Test is an enzyme-linked immunoassay intended for the qualitative detection of IgG antibodies to SARS-CoV-2 in human plasma or serum. The 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. Tests should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, 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 human serum or plasma several days after initial infection, although the response of IgG antibodies to a SARS-CoV-2 challenge is not well characterized. Individuals may have detectable virus present for several weeks or months following seroconversion. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities. A positive IgG serology test does not preclude the presence of an active SARS-CoV-2 infection, and negative results do not preclude either a current or past SARS-CoV-2 infection. If acute infection is suspected, direct testing for the SARS-CoV-2 virus is recommended. False positive results for Anti-SARS-CoV-2 tests may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Due to the risk of false positive results, confirmation of positive results should be considered using a second, different IgA, IgG or IgM assay.

Scientific background

Coronaviruses are a large family of single-stranded RNA viruses that infect mammals and birds, causing respiratory infections. Severe acute respiratory syndrome coronavirus 2 (SARS coronavirus 2 or SARS-CoV-2), causes an infectious disease named COVID-19 (Coronavirus disease 2019). Those affected may develop a fever, dry cough, fatigue and shortness of breath. Those infected usually have antibodies (IgG, IgM and IgA) in the body. The amount of antibodies may vary by time after symptom onset. It is not yet definitively known when IgG antibodies specific to the SARS-CoV-2 virus will become detectable in serum or plasma during an infection, or how long the antibodies persist following infection. Antibodies are produced gradually by the immune response system after infection. The sensitivity of antibody detection is usually directly related to the time after infection when blood samples are collected.

Measurement principle

An ELISA test is a series of 2 binding events followed by an enzymatic reaction that generates a colorimetric readout. BreviTest automates the process to enable rapid (<11 minutes) result. The Brevitest platform is designed for quantitative analysis at the point of care (POC) by untrained

personnel, but the IgG serology test is qualitative and has not been validated for POC use, and may only be performed under the control of a high-complexity CLIA-certified lab.

Device details and test conditions

Components and reagents provided

1. Acuity™ Analyzer
2. Cartridges: these are individually sealed in pouches in a nitrogen rich environment and shipped and stored at 2-8˚C.
3. Others
    a. Instruction for use – included inside each box of cartridges
    b. Fact Sheet for Health Care providers
    c. Fact Sheet for Patients

Materials required but not provided

Standard laboratory supplies and equipment such as gloves, wipes, timer, and micropipettes are not provided.

Storage and handling requirements

1. Store cartridges at 2-8°C. Do not freeze.
2. The cartridge is stable up to and including the expiration date printed on the outer container. The cartridge should remain in the sealed pouch until ready for use. The Analyzer will not perform a test using a cartridge that is beyond the expiration date.

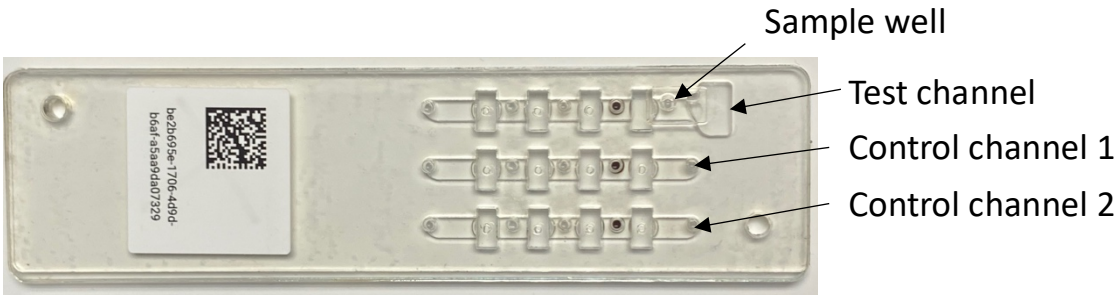
Warnings and Precautions

- For professional use only.
- **This test has not been reviewed by the FDA.**
- **Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.**
- **Results from antibody testing should not be used to diagnose or exclude SARS-CoV-2 infection or to inform infection status.**
- **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.**
- **Not for the screening of donated blood**
- Use of this product is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests.
- This test should be performed at 18 to 30℃ (64 to 86℉).
- Follow the instructions for use carefully. Reliability of assay results cannot be guaranteed if there is any deviation from the instructions in this package insert.
- Professionals must handle the potentially contaminated materials safely according to local requirements.
- Do not smoke, drink, eat, or use cosmetics in the working area. Wear Personal Protective Equipment and disposable gloves when working with samples and reagents. Wash hands after operations.

- Wipe and wash any surfaces splashed with sample with highly effective disinfectant. Avoid splashing and the formation of aerosols.
- Use a new clean disposable sample dispensing plastic dropper or tip for every sample to avoid cross contamination.
- Decontaminate and dispose of all samples, cartridges, and potentially contaminated materials as if they were infectious waste, in a biohazard waste container.
- Use the unpacked cartridge as soon as possible.
- Do not use the cartridge beyond the expiry date indicated on the outer container.
- Do not use the cartridge if the pouch is damaged or the seal is broken.
- The cartridge cannot be reused.
- Do not allow strong magnetic sources within 12 inches of the cartridge.

Control procedure

- Two internal procedural controls are embedded in each cartridge. These appear as two channels beside the test channel. One of the channels contains a negative control assay (no analyte) and the other contains a positive control assay (using antibodies mimicking the analyte being tested).



- The sample well is visible through the top of the cartridge.
- Separate external positive and negative controls are not supplied with this kit because of the embedded controls.

Specimen Type

Specimen Type Acceptable specimen types for testing are human serum and plasma. Proper specimen collection methods must be followed. Inadequate specimen collection and/or improper specimen handling may yield false results; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality to obtain accurate test results.

Specimen Collection and Handling Procedures

Collect the specimen wearing safety gloves to avoid contact and contamination.

Serum: Collect venous whole blood into a container NOT containing anticoagulants. Wait for the blood clot and separate the serum by centrifugation. If your laboratory has a standard validated method for serum collection, you may follow your method.

Plasma: Collect venous whole blood into a container containing anticoagulants (sodium citrate, sodium heparin, or dipotassium EDTA). Separate the plasma by centrifugation. If your laboratory has a standard validated method for plasma collection, you may follow your method.

Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed specimens. Do not leave the serum and plasma specimens at room temperature beyond 8 hours. Serum and plasma specimens may be stored at 2-8°C for up to 48 hours before use. For long term storage, serum and plasma specimens may be kept below -20°C for up to one month.

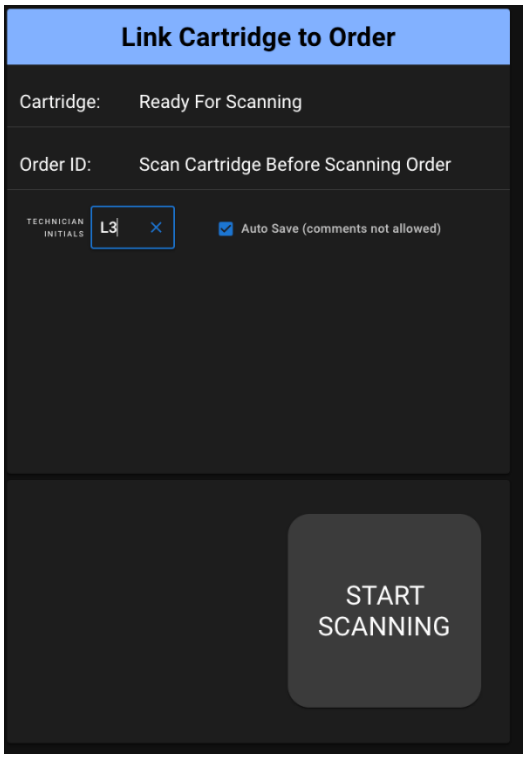
Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Specimens should not be frozen and thawed more than once. If specimens are to be shipped, they should be packed in compliance with local regulations covering the transportation of etiologic agents.

Test Procedure

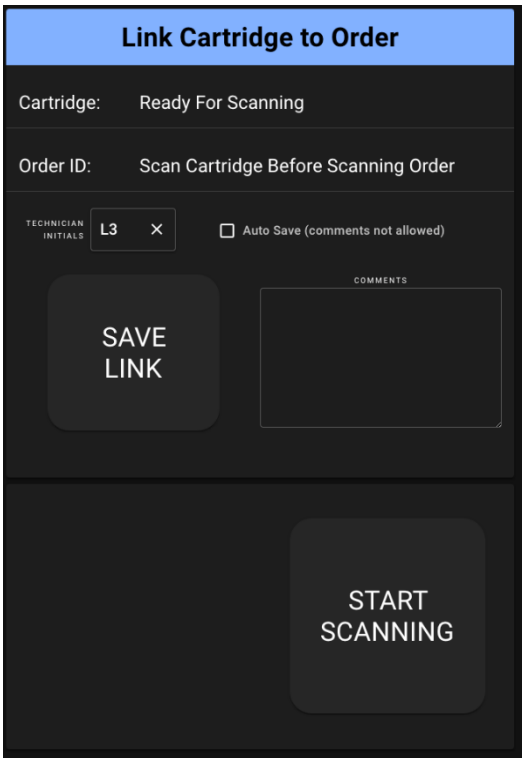
Preparation for Test

1. If not already on, power up analyzer by connecting to mains power, at least 10 minutes before testing.
    a. If the analyzer is properly connected to the mains power, the light on the analyzer will be illuminated.
    b. The analyzer must be connected to the internet to function and connects automatically to the internet using its built-in Particle chip. When the analyzer first starts, the light will blink green. Once it connects to the internet, it will blink cyan (blue-green) as it attempts to connect with the Brevitest system. Once the connection is complete, the light will be steady red. This sequence only occurs when the analyzer is turned on for the first time.
    c. If the analyzer is not at the proper temperature, the light will be steady red as it heats up to its operating temperature.
    d. Typically, the analyzer will be ready in less than 10 minutes.
    e. When it is ready for use, the light will turn green and pulse in a “breathing” pattern – slowly getting brighter, then slowly getting darker, thus cycling bright/dark continuously.
2. Remove a cartridge from its pouch and place it on a clean, flat, and dry surface with the barcode on the cartridge facing up.
3. Electronically link the sample identification barcode (on the collection tube) to the cartridge code (on the cartridge).
    a. Use any device (e.g. tablet or smartphone) with a camera and web browser.
    b. Go to https://brevitest-labtech.com/ on the device. Credentials are provided by Brevitest and are required to use the system.
    c. Enter the initials of the technician running the test.
    d. Tap or click on the START SCANNING button.
    e. To add comments that are retained with the test, turn off the Auto Save button
    f. Scan the code on the cartridge.
    g. Scan the code on the tube.
    h. If Auto Save is off:
        i. Enter comments
        ii. Tap or click SAVE LINK button
    i. Tap or click the STOP SCANNING button.

Auto Save Mode

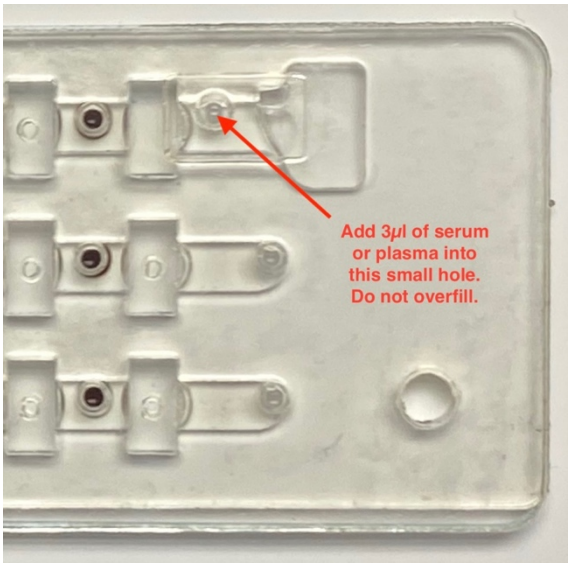


Technician Comment Mode



Adding the Sample

Transfer 3µl of undiluted serum or plasma into the sample well using standard pipetting techniques.



Running the Test

1. Insert cartridge into analyzer. DO NOT INSERT A CARTRIDGE INTO AN ANALYZER WITH A STEADY RED LIGHT. The light must be “breathing” green.

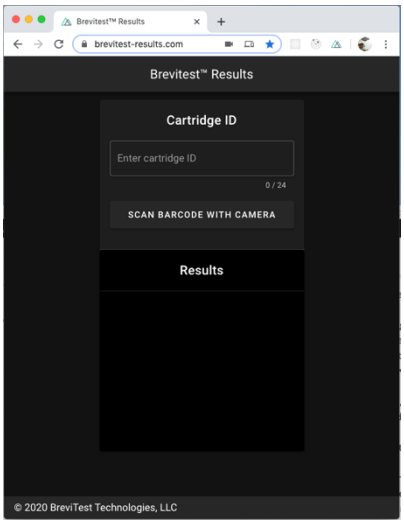
a. After inserting the cartridge, color of the light on the analyzer changes from breathing green to steady red, indicating the test has started to run.
b. Approximately, 10 minutes later, the test will finish running. This will be indicated by a slowly repeating light beeping sound, as well as a change of the light back to breathing green.
c. If the test fails, the analyzer will flash red and beep rapidly and repeatedly. Remove the cartridge and repeat the test with the same sample in a new cartridge.

2. Remove cartridge from analyzer. Beeping sound will stop. Analyzer will be ready for use again.
3. Appropriately dispose of the cartridge and samples.

Waste Disposal

Patient samples, sample-buffer mixtures, and used cartridges should be handled as infectious waste. All reagents must be disposed of in accordance with local disposal regulations.

Obtaining results for the laboratory



A successfully run test ends with the analyzer recording data using the built-in sensors. The analyzer sends this data to a database on the web (cloud storage). In the cloud, the absorption data is processed using proprietary algorithms into a result (positive/ negative). The Brevitest software, including the cloud storage, does not contain any patient identifiable information which should be limited to the laboratory's Lab Information System.

Following analysis, the Brevitest system will make available the results as positive for IgG or negative for IgG. This information is solely linked to the cartridge number and not to any patient information. To obtain the results:

- The laboratory can obtain the result directly from the Brevitest database by going to the webapp on *brevitest-results.com* and scanning or manually entering in the cartridge number

The result can also be communicated back to the laboratory along with the cartridge identifier by Brevitest if it has been so agreed to previously. It can be transmitted immediately, or at defined intervals (e.g. daily) via secured email (since no patient identification data is included) or as a paper copy.

Sample code #	Cartridge #	Result
ABC-0000	BT-0000-0000-0000	Positive
ABC-0001	BT-0000-0000-0001	Negative

Performance Characteristics

1. Clinical Performance:

Our Clinical Agreement Study tested samples from a total of 33 positive patients, confirmed using an acceptable comparator RT-PCR method, and 78 negative subjects (samples obtained prior to the beginning of the COVID-19 pandemic). The results showed overall positive percent agreement

(PPA)/sensitivity of 100% (95% CI: 89.6% - 100%) and overall negative percent agreement (NPA)/specificity of 100% (95% CI: 95.3% - 100%).

Total Clinical Performance Analysis for IgG

		Reference method		
		Positive	Negative	Total
Brevitest test results	Positive	33	0	33
	Negative	0	78	78
	Total	33	78	111

1) Sensitivity (Positive percent agreement): 100% (95% CI @ 5%: 89.6% - 100%)

2) Specificity (Negative percent agreement): 100% (95% CI @5%: 95.3% - 100%)

When estimating the sensitivity of IgG over time from onset of symptoms to time of sample collection, the percent of IgG positive subjects reached a peak of 100% when the test was performed >14 days after symptom onset.

Sensitivity Estimates for IgG Over Time

		Test Results		
Days after Onset of Symptoms (days):	Samples Tested	IgG positive	IgG PPA	95% CI
<8	0	0	N/A	N/A
8-14	0	0	N/A	N/A
>14	33	33	100%	89.6% - 100%

Limitations

1. A positive result may not indicate current or previous SARS-CoV-2 infection. Consider other information, including clinical history and local disease prevalence, in assessing the need for a direct test for SARS-CoV-2 virus or a second but different serology test to confirm an immune response. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.
2. Only use serum or plasma as the test material. Other analytes may give erroneous results.
3. Removing cartridge from analyzer prior to test completion will result in a canceled test with no reported results.
4. Negative results do not preclude current or past SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions.
5. IgG antibodies may not be detected in the first few days of infection; the sensitivity of the Brevitest IgG Serum/Plasma Serology test for SARS-CoV-2 early after infection is unknown.
6. False positive results for IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Samples with positive results should be confirmed with alternative testing method(s) and clinical findings before a diagnostic determination is made.
7. The tests are limited to the qualitative detection of IgG antibodies in serum or plasma against the SARS-CoV-2 virus.

8. A negative result may occur if the quantity of antibodies against the SARS-CoV-2 virus present in the specimen is below the detection limit of the assay, or if the virus has undergone minor amino acid mutation(s) in the epitope recognized by the patient's antibody such that the antibody no longer recognizes the viral capture protein used in the test.
9. This test should not be used for matrices other than serum or plasma.

Conditions of authorization for the laboratory

Authorized laboratories using the Anti-SARS-CoV-2 Test ("product" in the conditions below), must adhere to the following conditions:

1. Authorized laboratories using the product will include with result reports of the product using authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
2. Authorized laboratories using the product will use the product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use the product are not permitted.
3. Authorized laboratories that receive the product will notify the relevant public health authorities of their intent to run the product prior to initiating testing.
4. Authorized laboratories using the product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories will collect information on the performance of the product and report to DMD/OHT7- OIR/OPEQ/ CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Brevitest Technologies, LLC (info@brevitest.com) any suspected occurrence of false reactive or false nonreactive results and significant deviations from the established performance characteristics of the product of which they become aware.
6. All laboratory personnel using the product must be appropriately trained in immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product
7. Authorized distributors, and authorized laboratories using the product will ensure that any records associated with this test are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.