Rapid™ Response

Liberty

COVID-19 IgG/IgM

Rapid Diagnostic Test for the Detection of SARS-CoV-2 IgG/IgM Ab

REF **COV- 13C25U**

For use under Emergency Use Authorization only
For *in vitro* diagnostic use only
For prescription use only

Package Insert

(Instructions for Use)

Intended Use

The Rapid Response™ Liberty COVID-19 IgG/IgM is an immunochromatographic lateral flow assay intended for the qualitative detection and differentia-tion of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibod-ies to SARS-CoV-2 in human serum, plasma (sodium citrate, sodium heparin, or dipotassium EDTA), venous whole blood (sodium citrate, sodium heparin, or dipotassium EDTA) and fingerstick whole blood. The Rapid Response™ Liberty COVID-19 IgG/IgM 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 Rapid Response™ Liberty COVID-19 IgG/IgM should not be used to diagnose or exclude acute SARS-CoV-2 infection.

Testing of serum, plasma and venous whole blood specimens is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, that meet requirements to perform high or moderate complexity tests.

Testing of fingerstick whole blood specimens is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate or waived complexity tests. Testing of fingerstick whole blood specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Results are for the detection of SARS-CoV-2 antibodies. IgM and 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 Rapid Response™ Liberty COVID-19 IgG/IgM early after infection is 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 Rapid Response™ Liberty COVID-19 IgG/IgM may occur due to cross-reactivity from pre-existng antibodies or other possible causes. Due to the risk of false positive results, confirma on of positive results should be considered using a second, different SARS-CoV-2 IgG or IgM assay.

The Rapid Response™ Liberty COVID-19 IgG/IgM is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation of the Test

Coronavirus disease 2019 (COVID-19) is a respiratory illness that can spread from person to person. This antibody test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, the virus that causes COVID-19, indicating recent or prior infection, by detecting antibodies to SARS-CoV-2 in human blood specimens. Although not everyone who is infected will develop an antibody response, appropriately validated serology tests, when used broadly, can be useful in understanding how many people have developed an adaptive immune response to the virus and how far the pandemic has progressed. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

Principles of the Test

The Rapid Response™ Liberty COVID-19 IgG/IgM test is an immunochromatographic assay for the detection and differentiation of SARS-CoV-2 IgM and/or IgG antibodies in human blood specimens. Control antibody, anti-human IgG, and streptavidin (test line for IgM) are immobilized onto a nitrocellulose membrane to form three distinct lines, the control line, the IgG test line, and the IgM test line. The nitrocellulose membrane is attached onto a plastic backing card and combined with the other reagents and pads to construct a test strip. The test strip is encased inside a plastic device. Blood samples, including human serum, plasma (sodium citrate, sodium heparin, or dipotassium EDTA), venous whole blood (sodium citrate, sodium heparin, or dipotassium EDTA), and fingerstick whole blood are added to the sample well of the test device to initiate a test. The sample specimens migrate sequentially through filter pad, conjugate pad, nitrocellulose membrane, and absorbent pad. SARS-CoV-2 antibodies in sample specimens interact with the recombinant SARS-CoV-2 antigen (SARS-CoV-2 nucleocapsid and spike protein S1 RBD) that is conjugated to colloidal gold nanobeads and biotin-conjugated anti-human antibodies to form an immune complex while they migrate through the conjugate pad. SARS-CoV-2 IgM antibodies react with the gold-conjugated SARS-CoV-2 antigen and biotin-conjugated anti-human IgM. SARS-CoV-2 antibod-ies only react with the gold-conjugated SARS-CoV-2 antigen. The immune complexes migrate through the nitrocellulose membrane and bind to each respective test line. The IgM immune complexes bind to the streptavidin region (IgM test line, "M") on the membrane to generate a purple-colored line to indicate a positive IgM result. The IgG immune complexes bind to the anti-human IgG region (IgG test line, "G") on the membrane to generate a purple-colored line to indicate a positive IgG result. The gold-conjugated chicken IgY migrates through the membrane and binds to the control antibody (anti-chicken IgY) in the control region to generate a red-colored line (control line, "C"). The test results should be interpreted 10 minutes after addition of buffer to the sample well. The test results should not be interpreted after 15 minutes. The color intensity in the test region will vary. Any faint colored line(s) in the test region(s) should be considered as positive.

The presence of two lines marked by "C" and "G" indicates a SARS-CoV-2 IgG positive result. The presence of two lines marked by "C" and "M", indicates a SARS-CoV-2 IgM positive result. The presence of three lines "C", "G," and "M", indicates positive results for both SARS-CoV-2 IgG and IgM. The appearance of only the control line "C" indicates negative. If the control line does not appear, regardless of the presence of "G" or "M" test lines, the test result is not valid. With an invalid result, it is recommended to repeat the using a new, unopened device following the instructions.

Reagents and Materials Provided

Contents Name	Quantity (in a kit)	Description
Test device	25 each	Foil pouched test device containing one test strip which is encased on plastic devices cassette
Assay buffer	1 each	Na_2CO_3 <0.1% sodium azide as a preservative.
Blood transfer pipette	25 each	For blood transfer.
Alcohol swab	25 each	Use to clean a collection site prior to sampling the fingerstick whole blood.
Sterile safety lancet	25 each	Single-use lancets intended for sampling fingerstick whole blood.
Package insert	1 each	Instructions for use
Quick Reference Instructions (QRI)	1 each	Quick reference instructions

***Materials not supplied**

- Timer
- Pair of safety gloves
- External positive and negative controls (available for purchase separately)

Optional materials:

- 20 µl micropipette

Warnings and Precautions

- For prescription and in vitro diagnostic use only. For use under an Emergency Use Authorization Only.
- This product has not been FDA cleared or approved; but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories
- This product has been authorized only for detecting the presence of IgM and IgG antibodies against SARS-CoV-2, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(l) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(l), unless the declaration is terminated or authoriza-tion is revoked sooner.
- Testing of serum, plasma and venous whole blood specimens is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, that meet requirements to perform high or moderate complexity tests.
- Testing of fingerstick whole blood specimens is limited to laborato-ries certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate or waived complexity tests. Testing of fingerstick whole blood specimens is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.
- As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
- Immediately use after opening the test device in the pouch.
- Immediately add the assay buffer to the test device after the specimen is applied.
- In order to obtain accurate results, the test must follow this package insert.
- Do not interpret the test result before 10 minutes and after 15 minutes following the addition of buffer to the sample well.
- Do not use if the test device package is damaged.
- Do not use the kit contents beyond the expiration date.
- Do not eat, drink, or smoke in the area where the specimens and kit contents are handled.
- Use appropriate precautions in the collection, handling, storage, and disposal of patient samples and used kit contents.
- Dispose of used contents as biohazardous wastes in accordance with federal, state, and local requirements.
- Nitrile or latex gloves should be worn when performing this test.
- If the assay buffer contacts the skin or eye, flush with copious amounts of water.
- Handle all specimens as though they contain infectious agents.
- Adding additional blood sample volume to the sample well may cause false positive or invalid results.
- Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens.
- Reagents contain sodium azide, which is harmful if inhaled, swallowed, or exposed to skin. Contact with acids produces a very toxic gas. If there is contact with skin, wash immediately with plenty of water. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.
- Do not interchange kit contents from different lots.
- Do not re-use any contents in the kit as they are single-use only.

Storage and Stability

- Store the test kit as packaged between 1- 30°C.
- The reagents and materials in the Rapid Response™
- Liberty COVID-19 IgG/IgM are stable until the expiration date printed on the outer packaging. Do not use beyond the expiration date.
- The test device must remain in the sealed pouch until use.
- Do not freeze any contents of the kit.

Quality Control

Internal Quality Control:

The Rapid Response™ Liberty COVID-19 IgG/IgM contains a built-in internal procedural control in the test device. A red-colored line appearing in the control region "C" is designed as an internal procedural control. The appearance of the procedural control line indicates that sufficient flow has occurred, and the functional integrity of the test device has been maintained. If the procedural control line does not develop in 10 minutes, the test result is considered invalid, and retesting with a new device is recommended. If the internal procedural control line is still absent in the retest, please contact the manufacturer or distributor.

External Control:

It is recommended to follow the laboratory regulations or quality control procedures to perform external controls in the Rapid Response™ Liberty COVID-19 IgG/IgM. Controls are available through Access Bio under catalog number: SCLM-02571 or SCLM-10071.

NOTE: The external controls are available for separate purchase. Positive

- External Control: Mixture of human chimeric SARS-CoV-2 IgM and IgG spike S1 antibodies in heat inactivated SARS-CoV-2 antibody-negative confirmed serum.
- Negative External control: Heat inactivated SARS-CoV-2 antibody negative confirmed serum.

Specimen Type

Acceptable specimen types for testing with the Rapid Response™ Liberty COVID-19 IgG/IgM are human serum, plasma (sodium citrate, sodium heparin, or dipotassium EDTA), venous whole blood (sodium citrate, sodium heparin, or dipotassium EDTA), and fingerstick whole blood. 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

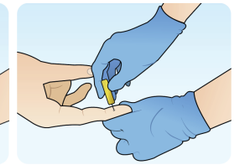
Procedural Notes

1. The Rapid Response™ Liberty COVID-19 IgG/IgM can be performed using human serum, plasma (sodium citrate, sodium heparin, or dipotassium EDTA), venous whole blood (sodium citrate, sodium heparin, or dipotassium EDTA), and fingerstick whole blood.
2. Allow test devices, reagents, and specimens to equilibrate up to room temperature (15~30°C) prior to testing.
3. Remove the Rapid Response™ Liberty COVID-19 IgG/IgM test device from its foil pouch immediately before testing.

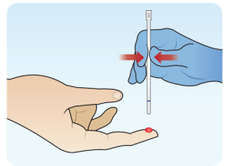
Fingerstick whole blood

1. Collect the specimen wearing safety gloves to avoid contact and contamination.
2. Use only the provided blood lancet, alcohol swab, and blood transfer pipette for human fingerstick whole blood specimen collection.
3. Process the fingerstick sample immediately after collection.
4. Testing should be performed immediately after specimen collection.

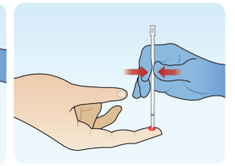
1. Clean the fingertip to be pierced with an alcohol swab.



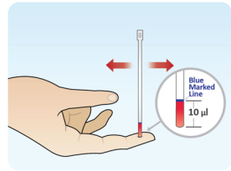
2. Squeeze the end of the fingertip and pierce the cleaned area using a blood lancet. Properly discard the blood lancet.



3.Press the top part of the provided blood transfer pipette.



4. Touch the blood using the pipette tip while still pressing the pipette.



5.Fill the pipette with the blood sample up to the blue marked line by releasing slowly.

- **Venous Whole Blood:**

Draw venous whole blood following the general laboratory procedures by a trained operator. Collect the blood sample in a commercially available blood collection tube containing anticoagulants including sodium citrate, sodium heparin, or dipotassium EDTA. Swirl the tube gently as needed. It is recommended to test whole blood specimens immediately after blood collection.

- **Serum:**

Collect venous whole blood into a container NOT containing anticoagulants. Wait for the blood clot and separate the serum by centrifugation.

- **Plasma:**

Collect venous whole blood into a container containing anticoagulants (sodium citrate, sodium heparin, or dipotassium EDTA). Separate the plasma by centrifugation.

- Use only the provided blood transfer pipette or micropipette for sample loading to the test device.
- Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed specimens.
- Testing should be performed immediately after specimen collection. 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. For long term storage, serum and plasma specimens should be kept below -20°C for up to one month. It is recommended to test whole blood specimens immediately after blood collection.
- Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Specimens cannot 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.

Description of Symbols

IVD — ***In vitro* diagnostic medical device** — Indicates a medical device that is intended to be used as an *in vitro* diagnostic medical device

Consult instructions for use — Indicates the need for the user to consult the instructions for use

Manufacturer — Indicates the medical device manufacturer

LOT — **Batch code** — Indicates the manufacturer's batch code so that the batch or lot can be identified

Do not re-use — Indicates a medical device that is intended for a single-use, or uses on a single patient during a single procedure

Use by date — Indicates the date after which the medical device is not to be used

Prescription-only

REF — **Catalog number** — Indicates the manufacturer's catalog number so that the medical device can be identified

Caution — Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself

Date of manufacture — Indicates the date when the medical device was manufactured

Temperature limit — Indicates the temperature limits to which the medical device can be safely exposed

Do not use if the package is damaged — Indicates a medical device that should not be used if the package has been damaged or opened

Σ <n> — **Contains sufficient for <n> tests** — Indicates the total number of *in vitro* diagnostic tests that can be performed with *in vitro* diagnostic medical device

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BTNX INC.

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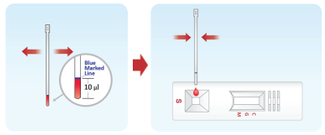
1. Place a device on a clean, flat surface after removing it from the pouch. Write the patient's ID on the device if required.
2. Transfer serum, plasma sample, venous whole blood, or fingerstick whole blood:

a) using a provided blood transfer pipette:

Press the top part of the provided blood transfer pipette and touch the sample with the pipette tip while pressing the pipette. Release the press slowly to fill the pipette with the sample up to the **blue marked line (approximately 10 µl)**. Add the blood sample to the **sample well "S"** of the test device by pressing the top part of the blood transfer pipette.



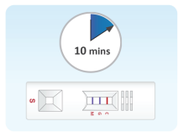
NOTE: Excessive blood may cause false positive or invalid test results.

b) using a micropipette:

Transfer **10 µl** of the **venous whole blood, serum or plasma** sample to the **sample well "S"** of the test device using a micropipette.

3. Open the cap and invert the assay buffer bottle and hold vertically above the sample well. Squeeze the bottle gently to add **one (1) drop** of the assay buffer solution to the **sample well "S"** immediately after sample loading.

4. Start a timer. Read the result **at 10 minutes**. The test results should not be read earlier than 10 minutes and after 15 minutes.



Interpretation of Results

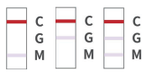
NOTE: The test results should be read and interpreted not earlier than 10 minutes after the sample application and the reading and interpretation of the results should not exceed 15 minutes. The test results should not be interpreted using any instruments.

IgM Positive : two distinct lines appear
One red-colored line next to "C" and one purple-colored line next to "M" indicate SARS-CoV-2 IgM positive result.

IgG Positive : two distinct lines appear
One red-colored line next to "C" and one purple-colored line next to "G" indicate SARS-CoV-2 IgG positive result.

IgG/IgM Positive : three distinct lines appear
One red-colored line next to "C", one purple-colored line next to "M", and one purple-colored line next to "G" indicate SARS-CoV-2 IgM and IgG positive result.

***Result with faint colored line(s)* :**
The color intensity in the test region will vary. Any faint colored line(s) in the test region(s) should be considered as positive.



Negative :
Only one line next to "C" indicates a negative result.

Invalid* : *no control line appears
If the control line "C" is not visible, the result is invalid. Re-run the test using a new test device. If the same invalid result persists, contact the manufacturer or distributor before continuing to test samples.

Expected Results of the External Controls

Positive Control: three distinct lines appear.
One red-colored line next to "C", one purple-colored line next to "M", and one purple-colored line next to "G" indicates SARS-CoV-2 IgM and IgG positive result.

Negative Control: one distinct line appears.
Only one red-colored line next to "C" indicates a negative result.

NOTE: If the test result for either the Negative Control or the Positive Control is not as expected, the test should be repeated using a new Test Device. If the test result for any of the controls is not as expected upon retesting, contact Technical Support.

Limitations

1. Use of the Rapid Response™ Liberty COVID-19 IgG/IgM is limited to laboratory personnel who have been trained. Not for home- use.
2. The test is limited to the qualitative detection of anti-COVID-19 antibody levels in human serum and ACD plasma samples and does not indicate the quantity of the antibodies. The intensity of the test line does not necessarily correlate to the SARS-CoV-2 antibody titer in the specimen.
3. The test results should be interpreted 10 minutes after starting the test. The test results should not be interpreted after 15 minutes.
4. This test can only be used for the analysis of human serum, plasma (sodium citrate, sodium heparin, or dipotassium EDTA), venous whole blood (sodium citrate, sodium heparin, or dipotassium EDTA), and fingerstick whole blood samples.
5. Negative results do not preclude SARS-CoV2 infection and should not be used as the sole basis for patient management decisions. IgM antibodies may not be detected in the first several days of infection; the sensitivity of the Rapid COVID-19 IgG/IgM Combo Test Kit early after an infection is unknown. False-positive results for IgM and IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
6. A negative result can occur if the quantity of antibodies for 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 antibody used in the test.
7. The test may have lower sensitivity for IgG and IgM detection in symptomatic individuals prior to15 days since symptom onset.
8. Direct testing with a molecular diagnostic test should be performed to evaluate for acute SARS-CoV-2 infection in symptomatic individuals.
9. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection or to determine infection status.
10. It is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.
11. Positive results may not indicate previous SARS-CoV-2 infection. Consider other information including clinical history and local disease prevalence, in assessing the need for an alternative serology test to confirm an adaptive immune response. 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.
12. This test will only indicate the presence of SARS-CoV-2 IgM and/or IgG antibodies in the specimen.
13. The detection of SARS-CoV-2 IgG/IgM antibodies is dependent upon proper specimen collection, handling, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results.
14. This device has been evaluated for use with human specimen material only.
15. This test cannot rule out diseases caused by other bacterial or viral pathogens.
16. This device should not be used for the screening of donated blood.
17. The performance of this device has not been established in individuals that have received a COVID-19 vaccine. The clinical significance of a positive or negative antibody result following COVID-19 vaccination has not been established, and the result from this assay should not be interpreted as an indication or degree of protection from infection after vaccination.
18. The performance of this test was established based on the evaluation of a limited number of clinical specimens (serum and plasma) collected from March 27, 2016 to May 21, 2020 from three sites in the US (California and Illinois). The clinical performance characteristics of the *Rapid Response™ Liberty* COVID-19 IgG/IgM test for POC testing was evaluated in a multi-site prospective study in the U.S (California and New Mexico). The clinical performance has not been established in 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.

Conditions of Authorization for Laboratories

The Rapid Response™ Liberty COVID-19 IgG/IgM, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, Letter of Authorization and other authorized labeling are available on the FDA website:

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas

Authorized Laboratories using the Rapid Response™ Liberty COVID-19 IgG/IgM ("your product" in the conditions), must adhere to the Conditions of Authorization indicated in the Letter of Authorization listed as follows:

1. Authorized laboratories[a] must use the Rapid Response™ Liberty IgG/IgM must include with test result reports, all 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 must use the Rapid Response™ Liberty COVID-19 IgG/IgM as outlined in the authorized labeling. 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 Rapid Response™ Liberty COVID-19 IgG/IgMare not permitted.
3. Authorized laboratories that receive the Rapid Response™ Liberty COVID-19 IgG/IgM must notify the relevant public health authorities of their intent to run the Rapid Response™ Liberty COVID-19 IgG/IgM prior to initiating testing.
4. Authorized laboratories using the Rapid Response™ Liberty COVID-19 IgG/IgM must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories must collect information on the performance of the Rapid Response™ Liberty COVID-19 IgG/IgM and report to Division of Microbiology Devices (DMD)/Office of Health Technology7 (OHT7)-(Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH EUA Reporting@fda.hhs.gov) and Access Bio, Inc. Technical Support (via email: TShelp@accessbio.net) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the assay of which they become aware.
6. All laboratory personnel using the Rapid Response™ Liberty COVID-19 IgM/IgG must be appropriately trained in immunochromatographic techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the Rapid Response™ Liberty COVID-19 IgG/IgM 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 Rapid Response™ Liberty COVID-19 IgG/IgM.
7. Access Bio, Inc., Intrivo Diagnostics, Inc. and authorized laboratories using the Rapid Response™ LibertyCOVID-19 IgG/IgM must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

[a] The letter of authorization refers to "authorized laboratories" as the following: Testing of serum,plasma and venous wholeblood specimens is limited to laboratories certifiedunder the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C.263a, that meet requirements to perform high or moderate complexity tests. Testing of fingerstick whole blood specimens is limited to laboratories certifiedunder theClinicalLaboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, thazt meet the requirements to perform high, moderate or waived complexity tests.Testing of fingerstick wholeblood specimens is authorized for useat thePoint of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Performance Characteristics

Clinical Agreement

Study I: Retrospective Study – Serum and Plasma

The clinical performance of the Rapid Response™ Liberty COVID-19 IgG/IgM was evaluated using retrospectively collected SARS-CoV-2 serum and plasma samples at 3 sites by 10 operators in the U.S. A total of 246 samples, 211 plasma (47 positive and 164 pre-COVID) and 35 serum (17 positive and 18 negative), collected in the U.S. were tested in this study. A total of 164 pre-COVID samples were collected before December 2019 in the U.S. All the collected positive serum and plasma samples were confirmed by FDA authorized SARS-CoV-2 RT-PCR tests as comparators.

All the negative and positive samples were tested in a blinded fashion. Each sample was assigned with a unique subject identification code during collection and randomized prior to the testing. The expected results of the samples were completely blinded to the operators in this study. All the samples were tested according to the Rapid Response™ Liberty COVID-19 IgG/IgM testing procedures.

A total of 246 samples were considered evaluable in this study.

Rapid Response™ Liberty COVID-19 IgG/IgM Performance against the Comparator Methods - Serum and Plasma

For IgG antibody detection, the positive percent agreement (PPA) of Rapid Response™ Liberty COVID-19 IgG/IgM was 96.88% (62/64) (95% CI of 89.30 – 99.13%). For IgM antibody detection, the PPA was 89.06% (57/64) (95% CI of 79.10 - 94.60%). The overall NPA (either IgG positive or IgM positive counted as positive) was 98.90% (180/182) (95% CI 96.08 – 99.70%).

IgG results stratified by days post-onset of symptoms - serum and plasma

Days from Symptom Onset	Total number of samples	Non-reactive	Reactive	PPA	95% CI
0 - 7	-	-	-	-	-
8 - 14	1	0	1	100% (1/1)	20.65 – 100%
≥ 15	62	2	60	96.77% (60/62)	88.98 – 99.11%
Unknown	1	0	1	100% (1/1)	20.65 – 100%

IgM results stratified by days post-onset of symptoms - serum and plasma

Days from Symptom Onset	Total number of samples	Non-reactive	Reactive	PPA	95% CI
0 - 7	-	-	-	-	-
8 - 14	1	0	1	100% (1/1)	20.65 – 100%
≥ 15	62	7	55	88.71% (55/62)	78.48 - 94.42%
Unknown	1	0	1	100% (1/1)	20.65 – 100%

Study II: Independent Clinical Agreement Validation

The Rapid Response™ Liberty COVID-19 IgG/IgM from Access Bio was tested on Jun 2, 2020 at the Frederick National Laboratory for Cancer Research (FNLCR) sponsored by the National Cancer Institute (NCI). The test was validated against a panel of previously frozen samples consisting of 30 SARS-CoV-2 antibody-positive serum samples and 80 antibody-negative serum and plasma samples. Each of the 30 antibody-positive samples was confirmed with a nucleic acid amplification test (NAAT) and both IgM and IgG antibodies were confirmed to be present in all 30 samples. The presence of antibodies in the samples was confirmed by several orthogonal methods prior to testing with the Rapid Response™ Liberty COVID-19 IgG/IgM. The presence of IgM and IgG antibodies specifically was confirmed by one or more comparator methods. Antibody-positive samples were selected at different antibody titers.

All antibody-negative samples were collected prior to 2020 and include: i) Seventy (70) samples selected without regard to clinical status, "Negatives" and ii) Ten (10) samples selected from banked serum from HIV+ patients, "HIV+". Testing was performed by one operator using one lot of the Rapid Response™ Liberty COVID-19 IgG/IgM. Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008).

For the evaluation of cross-reactivity with HIV+, it was determined 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). The results and data analysis are shown in the tables below:

	Comparator Method			Collected pre-2020		
	Antibody Positive			Antibody Negative		
CareStart™ COVID-19 IgM/IgG	IgM+, IgG+	IgM+, IgG-	IgM-, IgG+	Negative	HIV+	Total
IgM+, IgG+	27					27
IgM+, IgG-				1		1
IgM-, IgG+	3			1		4
IgM-, IgG-				68	10	78
Total	30			70	10	110

Measure	Estimate	Confidence Interval
IgM Sensitivity	90.0% (27/30)	74.4%; 96.5%
IgM Specificity	98.8% (79/80)	93.3%; 99.8%
IgG Sensitivity	100% (30/30)	88.7%; 100%
IgG Specificity	98.8% (79/80)	93.3%; 99.8%
Combined Sensitivity	100% (30/30)	88.7%; 100%
Combined Specificity	97.5% (78/80)	91.3%; 99.3%
Combined PPV for prevalence = 5.0%	67.8%	35%; 88.4%
Combined NPV for prevalence = 5.0%	100%	99.4%; 100%
Cross-reactivity with HIV+	0.0% (0/10), not detected	-

Important limitations of the study:

1. Samples were not randomly selected, and sensitivity and specificity estimates may not be indicative of the real-world performance of the device. These results are based on serum and plasma samples only and may
2. not be indicative of performance with other sample types, such as whole blood, including finger stick blood.
   Information about anticoagulants used is not known.
3. The number of samples in the panel is a minimally viable sample size
4. that still provides reasonable estimates and confidence intervals for test performance, and the samples used may not be representative of the antibody profile observed in patient populations.

Study III: Prospective Fingerstick Study (POC)

The clinical performance characteristics of the Rapid Response™ Liberty COVID-19 IgG/IgM test was evaluated in a multi-site prospective study in the U.S. against an FDA authorized RT-PCR molecular assay as a comparator method. A total of two (2) Point-of-Care investigational sites in the U.S. (California and New Mexico) participated in the study. To be enrolled in the study, the positive patients had to be confirmed as positive by an FDA authorized RT-PCR and exhibit signs/symptoms of the COVID-19-like illness within 5 to 28 days prior to testing with the devices under evaluation. The negative subjects had to be confirmed as negative by an FDA authorized RT-PCR and currently present no signs or onset of symptoms and no previous infection history.

Testing was performed by eight (8) operators with no laboratory experience and who were representative of the intended users. Operators only used the QRI for the test without any training provided and complet-ed an ease-of-use questionnaire indicating favorable responses to all questions asked after completing the study.

The clinical study tested 75 samples (32 were collected from RT-PCR positive subjects and 43 were collected from RT-PCR negative subjects). Of the 32 RT-PCR positive clinical samples, date of symptom onset was known for 26 samples and unknown for 6 samples. Results were assessed stratified by (A) the days post symptom onset and (B) the days post RT-PCR testing in comparison to multiple FDA authorized assays as comparators:

IgG and IgM PPA results stratified by days post symptoms onset – fingerstick

Days from Symptom Onset	No. of RT-PCR Positive	IgG Reactive	IgG PPA	95% CI	IgM Reactive	IgM PPA	95% CI
0 – 7 days	1	1	100%	20.65 – 100%	1	100%	20.65 – 100%
8 – 14 days	12	12	100%	75.76 – 100%	12	100%	75.76 – 100%
≥ 15 days	13	13	100%	77.19 – 100%	13	100%	77.19 – 100%
Total	**26**	**26**	**100%**	**87.13 – 100%**	**26**	**100%**	**87.13 – 100%**

IgG and IgM PPA results stratified by days post RT-PCR result – fingerstick

Days post RT-PCR positive	No. of RT-PCR Positive	IgG Reactive	IgG PPA	95% CI	IgM Reactive	IgM PPA	95% CI
0 – 7 days	11	11	100%	74.12 – 100%	11	100%	74.12 – 100%
8 – 14 days	11	11	100%	74.12 – 100%	11	100%	74.12 – 100%
≥ 15 days	10	10	100%	72.25 – 100%	10	100%	72.25 – 100%
Total	**32**	**32**	**100%**	**89.28 – 100%**	**32**	**100%**	**89.28 – 100%**

The overall NPA of the Rapid Response™ COVID-19 IgG/IgM Rapid Test Device for IgG/IgM in fingerstick whole blood samples is 100% (43/43) (95% CI 91.80 – 100.0%).

Cross-Reactivity (Exclusivity)

The cross-reactivity study was conducted by testing a total of 87 plasma or serum samples, including 14 non-SARS-CoV-2 pathogens and one (1) autoantibody. All the plasma and serum samples tested as negative showed no cross-reactivity and resulted in 100% agreement between the Rapid Response™ Liberty COVID-19 IgG/IgM test result and the expected result as presented in the table table below:

Samples	Sample number and type	Test results (# of positive / # of replicate)	
		IgM Results	IgG Results
Anti-Influenza A	5 plasma	0/5	0/5
Anti-Influenza B	5 plasma	0/5	0/5
Anti-HCV	8 plasma, 2 serum	0/10	0/10
Anti-HBV	5 serum	0/5	0/5
Anti-229E (alpha coronavirus)	3 plasma	0/3	0/3
Anti-NL63 (alpha coronavirus)	7 plasma	0/7	0/7
Anti-OC43 (beta coronavirus)	9 plasma	0/9	0/9
Anti-HKU1 (beta coronavirus)	5 plasma	0/5	0/5
Antinuclear antibodies (ANA)	5 serum	0/5	0/5
Anti-respiratory syncytial virus	1 plasma, 5 serum	0/6	0/6
Anti-HIV	10 plasma	0/10	0/10
Anti-Dengue virus	5 plasma	0/5	0/5
Anti-T. pallidum (Syphilis)	5 serum	0/5	0/5
Anti-Rhinovirus	2 plasma	0/2	0/2
Anti-Hepatitis B	5 plasma	0/5	0/5

Interfering Substances

To assess substances with the potential to interfere with the performance of the Rapid Response™ Liberty COVID-19 IgG/IgM, SARS-CoV-2 IgG, IgM positive, and negative samples were tested with the addition of potentially interfering substances. The Rapid Response™ Liberty COVID-19 IgG/IgM test performance was not affected by any of eight potentially interfering substances tested.

- Acetaminophen
- Acetylsalicylic acid
- Albendazole Chloroquine
- diphosphate
- HAMA
- Hemoglobin
- Ibuprofen
- Rifampicin

The interfering effects of biotin concentrations ranging between 10 ng/ml and 100 µg/ml were tested in a separate study. Biotin concentrations up to 2.5 µg/ml did not lead to false results. Biotin concentrations >5 µg/ml can cause false-negative IgM results with the Rapid Response™ Liberty COVID-19 IgG/IgM. None of the IgG positive samples tested produced false negative in all biotin concentrations tested.

Class Specificity

The Rapid Response™ Liberty COVID-19 IgG/IgM was evaluated to determine that the assay accurately detects each SARS-CoV-2 IgM and IgG antibody class on its corresponding test lines. A total of five (5) IgM and IgG positive serum samples were treated with DTT to determine class specificity of the test. All samples treated with DTT showed no visible IgM line with the Rapid Response™ Liberty COVID-19 IgG/IgM, whereas the IgG results were not affected by DTT treatment. IgM and IgG results after DTT treatment showed 100% agreement to the expected results.

Matrix Equivalency

The matrix equivalency study was performed by spiking SARS-CoV-2 IgG/IgM positive sample into negative sample matrices for serum, venous whole blood, and plasma using different anticoagulants. All testing matrices were collected from the same donor and a total of five donors was evaluated with the Rapid Response™ Liberty COVID-19 IgG/IgM. The venous whole blood samples were collected from each individual in four different containers to prepare serum (no anticoagulant), and three matrices each of venous whole blood (sodium citrate, sodium heparin, and dipotassium EDTA) and plasma (sodium citrate, sodium heparin, and dipotassium EDTA). To prepare positive sample panels, each sample matrix was spiked with SARS-CoV-2 IgG/IgM positive serum sample at low positive and moderate positive levels and randomized for testing. The samples were tested in duplicate with the Rapid Response™ Liberty COVID-19 IgG/IgM. All the test results of seven different matrices from the individual showed 100% agreement to the expected results.

Sample type	Test results (# of positive / # of replicate (% agreement))					
	LP results		MP results		Negative results	
	IgM	IgG	IgM	IgG	IgM	IgG
Venous whole blood (EDTA)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Venous whole blood (Heparin)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Venous whole blood (Citrate)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Plasma (EDTA)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Plasma (Heparin)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Plasma (Citrate)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)
Serum	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (100%)	0/10 (100%)

Technical Support

For questions, or to report a problem, please call Technical Support at +1-888-339-9964, Ext. 803 or support@btnx.com .