I. Intended Use

The Biomerica COVID-19 IgG/IgM Rapid Test is a lateral flow chromatographic immunoassay for rapid, qualitative, and differential detection of IgG and IgM antibodies specific to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human capillary whole blood, serum, or plasma specimens. The test is intended for professional *in vitro* diagnostic use only.

II. Summary and Explanation

Coronaviruses (CoVs) belong to the subfamily *Orthocoronavirinae* in the family *Coronaviridae* and the order *Nidovirales*. Coronaviruses are a large family of viruses that are common in people and many different species of animals, including camels, cattle, cats, and bats. Rarely, animal coronaviruses can infect people and then spread between people. A human coronavirus (SARS-CoV) caused the severe acute respiratory syndrome coronavirus (SARS) outbreak in 2003 followed by MERS-CoV in 2012.[1] Most recently, a SARS-related CoV was implicated as the etiological agent responsible for the outbreak in Wuhan, central China. This outbreak is estimated to have started on 12th December 2019.[2] This virus has been called COVID-19, novel coronavirus (2019-nCoV), SARS-CoV-2, and other similar names. The virus has rapidly spread to other countries by travelers from China.[2] Typical symptoms are fever, malaise, shortness of breath and in severe cases, pneumonia, severe acute respiratory syndrome, kidney failure and even death.[3-5] The disease was first called unidentified viral pneumonia.

The SARS-CoV-2 virus is a betacoronavirus, like MERS-CoV and SARS-CoV. All three of these viruses have their origins in bats. The sequences from U.S. patients are similar to the one that China initially posted, suggesting a likely single, recent emergence of this virus from an animal reservoir.[1]

Early on, many of the patients at the epicenter of the outbreak in Wuhan, Hubei Province, China had some link to a large seafood and live animal market, suggesting animal-to-person spread. Later, a growing number of patients reportedly did not have exposure to animal markets, indicating person-to-person spread. Person-to-person spread was subsequently reported outside Hubei and in countries outside China, including in the United States. Some international destinations now have ongoing community spread with the virus that causes COVID-19, as do some parts of the United States. Community spread means some people have been infected and it is not known how or where they became exposed.[1] Spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein are four major structural proteins of SARS-CoV-2. Tests are typically designed to detect antibodies to (N) and (S) structural proteins.

Serological time courses were followed for COVID-19 patients who were initially negative for IgG and/or IgM antibodies and underwent seroconversion. [6,7] The median day of seroconversion for both IgG and IgM was 12-14 days post-symptom onset in these studies. Moreover, it was observed that 100% of patients exhibited anti-SARS-CoV-2 antibodies >14 days after symptom onset. While these studies also have shown that antibodies can be observed earlier, the use of antibody tests is best applied >14 days post-symptom onset, to allow seroconversion to occur.

III. Principle of the Test

Recombinant SARS-CoV-2 nucleocapsid antigen conjugated to colloidal gold is immobilized onto a conjugate pad. Anti-human IgM and anti-human IgG are coated in the test line region. The specimen reacts with SARS-CoV-2 antigen-gold conjugate and then migrates upward on the membrane chromatographically to react with anti-human IgM and anti-human IgG. A pink/red colored band will appear next to the "IgM" in the test window if the sample contains IgM antibodies to SARS-CoV-2 and a second pink/red colored band will appear next to the "IgG" in the test window if contains IgG antibodies to SARS-CoV-2. If the specimen does not contain antibodies to SARS-CoV-2, no pink/red colored line(s) will appear in next to the "IgM" or "IgG" in the test window which indicates a negative result. A built-in control band will always show next to the "C" in the test window indicating that the proper volume of sample and test buffer has been added to the test device.

IV. Materials Provided

1. Test device in sealed foil pouch with desiccant
2. Test buffer
3. Instructions for use
4. 20 µL capillary tubes

V. Materials Required but Not Provided

1. Timer
2. Personal protective equipment, such as protective gloves, medical mask, goggles and lab coat or gown
3. Pipette and pipette tip
4. Lancets (capillary whole blood only)
5. Centrifuge (for serum and plasma only)
6. Appropriate biohazard waste container and disinfectants

VI. Special Notes for Laboratories and Healthcare Workers at the Point-of-Care

1. This test has not been reviewed by the FDA.
2. Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
3. Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
4. 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.
5. Not for the screening of donated blood.
6. This test does not produce an actual test report. Laboratories and healthcare workers at the point-of-care performing this test must include the results from the COVID-19 IgG/IgM Rapid Test in their own test report.

VII. Warnings and Precautions

1. This test is for *in vitro* diagnostic use only.
2. This package insert must be read completely before performing the test. Failure to following directions may yield inaccurate test results.
3. The test results should be read between 10 and 20 minutes after a specimen is applied to the test device. Results read after 20 minutes may give erroneous results.
4. All specimens should be treated as capable of transmitting diseases. Use appropriate precautions and follow Biosafety Level 2 or higher guidelines.
5. Wear appropriate personal protective equipment (e.g. gowns, gloves, masks, eye protection) in the collection, handling, storage and disposal of patient samples and used kit contents.
6. Proper specimen collection storage and transport are critical to the performance of this test.
7. Do not run the test with hemolyzed, lipemic, or icteric samples.
8. The test is single use only. Discard after use.
9. Do not touch the test window of the device.
10. Do not use test beyond the expiration date.
11. Do not use the device if the pouch is punctured or not sealed.
12. This test should only be used by professionally trained staff using sample(s) that have been collected by qualified medical personnel.
13. The test result should be interpreted by a physician or qualified medical professional along with clinical findings and other laboratory test results.
14. Do not open the test device (cassette) and/or remove any labeling on the test device (cassette).
15. BIOHAZARDOUS WASTE DISPOSAL: All specimens and the used device components carry risk of infection. The process of disposing of used device components must follow the local regulations for biohazardous waste disposal.

VIII. Storage and Stability

Store the tests at room temperature or refrigerated (2-30°C); **DO NOT FREEZE**. The tests are usable through the expiration date printed on the sealed pouch. Do not use beyond the expiration date. The tests must remain in the sealed pouch until used.

IX. Quality Control

A procedural control is included in the test. A pink/red colored line appearing in the control region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking, and correct procedural technique.

Positive and Negative Controls are not supplied with this kit. Users should follow Good Laboratory practices which recommend the daily use of positive and negative controls to confirm the test procedure and to verify proper test performance. Users should follow all applicable federal, state, and local guidelines concerning the frequency of assaying external quality control materials.

X. Sample Collection

The Biomerica COVID-19 IgG/IgM Rapid Test can be performed on human capillary whole blood, serum, and plasma specimens.

Specimen Collection:

Capillary Fingerstick Whole Blood Sample Collection: Wash the patient's hands with soap and warm water or wipe the finger you intend to stick with an alcohol swab. Allow to dry.

1. Holding finger tight, squeeze the blood toward the tip of the finger.
2. Puncture skin using a sterile lancet. Wipe away first drop of blood.
3. Gently squeeze hand from palm to finger, making sure to get a large hanging drop of blood.
4. Touch the tip of the capillary tube to the drop of blood until filled (approximately 20 µL). Avoid air bubbles.

Venous Whole Blood Collection: Using standard phlebotomy practices, collect desired sample(s) as follows: red top (serum), or lavender top (venous whole blood) tube.

Whole Blood Testing and Storage:

Capillary Fingerstick Whole Blood: Testing of capillary whole blood must be performed immediately after specimen collection. **DO NOT STORE CAPILLARY FINGERSTICK WHOLE BLOOD**.

Serum Specimen Processing and Storage:

Serum Processing: Allow whole blood collected without anticoagulant to clot at room temperature for 45-120 minutes prior to centrifugation to collect serum.

Serum Storage: Once serum has been collected, store at 2-8°C within 30 minutes. Serum specimens may be stored at 2-8°C for up to 7 days. For long term storage, serum specimens should be kept frozen below -20°C. Multiple freeze/thaw cycles should be avoided.

Plasma Specimen Processing and Storage: Separate plasma from blood as soon as possible to avoid hemolysis. Venous whole blood specimens should not be stored at room temperature for more than 30 minutes. **Do not freeze whole blood specimens.** Only clear, non-hemolyzed specimens should be used.

- Collect sample in a lavender top (EDTA) tube.
- Sample should not be left at room temperature for an extended time period. Plasma samples may be stored at 2-8°C for up to 7 days or for long term storage, kept below -20°C. Multiple freeze/thaw cycles should be avoided.

Specimen Quality: Only clear, non-hemolyzed specimens should be used. Hemolyzed, lipemic, and icteric samples should not be used.

XI. Test Procedure

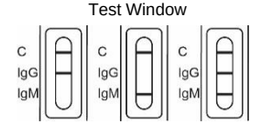
Allow test device, sample, and test buffer to reach room temperature (15° - 30°C) for 30 minutes prior to testing. Use test device within one hour after removing from sealed pouch.

1. Remove the test device from its sealed pouch and place the device on a level surface.
2. Set a timer for 10 minutes.
3. **For Serum/Plasma samples:**
   Transfer 10 µL of sample to the sample well (S), add 2 drops of test buffer to the sample well (S) (approximately 80 µL), and start the timer.

   For Capillary Fingerstick Whole Blood samples:
   Fill the capillary tube and transfer approximately 20 µL of capillary fingerstick whole blood sample to the sample well (S) of test cassette, add 2 drops of test buffer to the sample well (S) (approximately 80 µL) and start the timer.

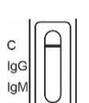
   NOTE: Do not move the test after buffer addition and before reading the results.
4. Pink/red-colored control and test line(s) should appear. Read results at 10 minutes. Do not interpret results after 20 minutes.

XII. Interpretation of Results



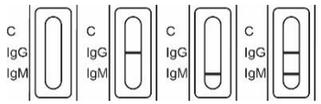
Positive Results

POSITIVE: If the sample contains IgM antibodies to SARS-CoV-2, a pink/ red-colored band next to the "IgM" in the test window will appear. If the sample contains IgG antibodies to SARS-CoV-2, a pink/red-colored band will appear next to the "IgG" in the test window.
NOTE: Any shade of pink/red color next to either the "IgM" or "IgG" should be considered positive.



Negative Results

NEGATIVE: Only one pink/red-colored colored band appears next to the "C". No pink/red-colored band(s) appear next to the "IgM" or "IgG".



Invalid Results

INVALID: An absence of a colored band next to the "C" regardless of the appearance of colored band(s) next to "IgM" and/or "IgG". Note: Insufficient sample volume, procedural errors, or a deteriorated test device are the most common reasons for invalid results. The sample should be retested using a new test device.

XIII. Performance Characteristics

Sensitivity and Specificity

The Biomerica COVID-19 IgG/IgM Rapid Test was compared with a commercial PCR (China-FDA, EUA) (Novel Coronavirus 2019-nCov PCR Kit (fluorescent PCR method), Shanghai BioGerm Medical Biotechnology Co., Ltd.).

IgM Result:

		PCR	
		Positive	**Negative**
COVID-19 IgG/IgM Antibody Test	**Positive**	17	3
	Negative	3	77

Relative Sensitivity: 85.0% (95%CI*: 62.1%-96.8%)
Relative Specificity: 96.3% (95%CI*: 89.4%-99.2%)
Accuracy: 94.0% (95%CI*: 87.4%-97.8%)
*Confidence Interval

IgG Result:

		PCR	
		Positive	**Negative**
COVID-19IgG/IgM Antibody Test	**Positive**	20	1
	Negative	0	79

Relative Sensitivity: 100.0% (95%CI*: 83.2%-100%)
Relative Specificity: 98.8% (95%CI*: 93.2%-100%)
Accuracy: 99.0% (95%CI*: 94.6%-100%)
*Confidence Interval

Combined IgG and/or IgM Results

		PCR	
		Positive	**Negative**
COVID-19 IgG/IgM Antibody Test	**Positive**	20	4
	Negative	0	76

Combined Sensitivity: 100% (95%CI*: 83.2% to 100.00%)
Combined Specificity: 95.0% (95%CI*: 87.7% to 98.6%)
Combined Accuracy: 96.0% (95%CI*: 90.1% to 98.9%)
*Confidence Interval

Cross-reactivity

Specimens that tested positive to the following potentially cross-reacting organisms were tested with the Biomerica COVID-19 IgG/IgM Rapid Test without any effect on the expected results.

Anti-influenza A virus	Anti-influenza B virus	Anti-RSV	Anti-Adenovirus
HBsAg	Anti-Syphilis	Anti-H. Pylori	Anti-HIV
Anti-HCV			

Interference Study

The following substances were found not to interfere with the test:

Ascorbic Acid	20 mg/dL	Bilirubin	60 mg/dL
Hemoglobin	1000 mg/dL	Total cholesterol	6 mmol/L
Triglyceride	50 mg/dL		

Inter-day, Inter-lot, Study

A negative specimen, an IgM positive specimen, and an IgG positive specimen were run individually on 3 separate days using the same lot of COVID-19 IgG/IgM Rapid Test. Results were rated visually as negative or positive at 10 minutes and 20 minutes after specimen application.

A negative specimen, an IgM positive specimen, and an IgG positive specimen were run in triplicates in 3 separate lots of COVID-19 IgG/IgM Rapid Test. Results were rated as positive or negative at 10 and 20 minutes after sample application.

All test results were consistent between runs and lots of the COVID-19 IgG/IgM Rapid Test.

Normal Population Study100 donor serum specimens collected from apparently healthy individuals prior to January 2019 were run on the COVID-19 IgG/IgM Rapid Test. Results were rated as positive or negative at 10 and 20 minutes after sample application. Results are shown below.

	IgG	**IgM**
# NEG	95	95
# POS	5	5
TOTAL	100	100
% NEGATIVE	95%	95%
SPECIFICITY	95%	95%

XIV. Limitations of the Test

1. The COVID-19 IgG/IgM Rapid Test should be used for the qualitative detection of IgG and IgM antibodies to SARS-CoV-2 in human capillary whole blood, serum, or plasma specimens. This test is not intended to determine the quantitative concentration or rate of increase of IgG and/or IgM antibodies to SARS-CoV-2.
2. The COVID-19 IgG/IgM Rapid Test will only indicate the presence of IgG and/or IgM antibodies to SARS-CoV-2 in the specimen and should not be used as the sole criteria for the diagnosis of SARS-CoV-2 infections. As with all diagnostic tests, all results must be considered with other clinical information available to the physician (e.g. signs and symptoms of COVID-19 and other diagnostic tests for SARS-CoV-2).
3. In conjunction with antibody test results, it is recommended to use nucleic acid detection for confirmation of SARS-CoV-2 infection. A definitive diagnosis should only be made after all clinical and laboratory findings have been evaluated.
4. The accuracy of the test depends on the sample collection process. Improper sample collection, improper sample storage, or repeated freezing and thawing of the sample will affect the test results.
5. Positive results using whole blood should be repeated with a serum sample. Do not run hemolyzed, lipemic, or icteric samples as it may affect the test results.
6. Positive test results do not rule out co-infections with other pathogens including other coronavirus species.
7. A negative result of this test can be caused by:
   a) Improper sample transfer or handling.
   b) The level of IgG and/or IgM antibodies to SARS-CoV-2 is below the detection limit of the test.
   c) IgG and/or IgM antibodies to SARS-CoV-2 have not appeared at the time of the sample was collected.
   d) Variations in viral genes may cause changes in antibody affinity for the SARS-CoV-2 test reagent.
8. If the test results are negative and clinical symptoms persist, additional follow-up testing using other clinical and laboratory methods is suggested.
9. Hematocrit level of the whole blood needs to be between 25% and 65% for accurate results.
10. Color blind operators should not read or interpret test results.
11. Performance characteristics of the test were determined in a clinical study in patients from China. Performance characteristics have not been established for other countries except the Normal Population Study.

XV. References

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For Export Only

COVID-19 IgG/IgM Rapid Test

July 2020

REF **1507A**

Immunoassay test kit for the qualitative detection of IgG and IgM antibodies specific to SARS-CoV-2 in human capillary whole blood, serum, or plasma specimens.

For professional *in vitro* diagnostic use only

BIOMERICA

Telephone: +1 949-645-2111
Fax: +1 949-553-1231
e-mail: info@biomerica.com
www.biomerica.com

Biomerica, Inc.,
17571 Von Karman Ave.
Irvine, CA 92614 USA

IVD

2°C 30°C

CE

EC REP

according to IVDD 98/79/ EC
MDSS GmbH, Schiffgraben 41
D-30175 Hannover, Germany