BioMedomics™

INFECTIOUS DISEASE

COVID-19

IgM-IgG Rapid Test

Instructions For Use

Intended Use |

The BioMedomics COVID-19 IgM-IgG Combined Antibody Rapid Test is a lateral flow immunoassay intended for the qualitative, differential detection of IgG and IgM antibodies to SARS-CoV-2 in human serum, plasma, or whole blood samples (capillary or venous) including samples prepared by commonly-used anticoagulants (K2EDTA, NaCitrate, Li-Heparin) from individuals with current or prior COVID-19 infection. The BioMedomics COVID-19 IgM-IgG Combined Antibody Rapid Test is intended for use as an aid in identifying patients 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 BioMedomics COVID-19 IgM-IgG Combined Antibody Rapid Test should not be used to diagnose acute SARS-CoV-2 infection.

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. Patients may have detectable virus present for several weeks following seroconversion.

The sensitivity of BioMedomics COVID-19 IgM-IgG Combined Antibody Rapid 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 BioMedomics COVID-19 IgM-IgG Combined Antibody Rapid Test 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 IgG or IgM assay.

Summary |

The novel coronaviruses belong to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the current epidemiological investigation, the incubation period is 1 to 14 days, mostly 3 to 7 days. The main manifestations include fever, fatigue and dry cough. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases.

Test Principle |

BioMedomics COVID-19 IgM-IgG Combined Antibody Test is immunochromatography based. The test card contains (1) colloidal gold-labeled recombinant novel coronavirus antigen, (2) two detection lines (G and M lines) and one quality control line (C) fixed on a nitrocellulose membrane. M is fixed with monoclonal anti-human IgM antibody for detecting the novel coronavirus IgM antibody. G is fixed with monoclonal anti-human IgG antibody for detecting the novel coronavirus IgG antibody. The quality control antibody is fixed on the C line.

When an appropriate amount of test sample is added to the sample well of the test cassette, the sample will move forward along the test card via capillary action. If the sample contains IgM antibody, the antibody will bind to the colloidal gold-labeled novel coronavirus antigen. The antibody/antigen complex will be captured by the anti-human IgM antibody immobilized on the membrane, forming a red M line and indicating a positive result for the IgM antibody.

If the sample contains IgG antibodies, the antibody will bind to the colloidal gold-labeled novel coronavirus antigen and the antibody/antigen complex will be captured by the antibody immobilized on the membrane, forming a red G line and indicating a positive result for the IgG antibody.

If neither antibody is present, a negative result is displayed. The card also contains a quality control line (C). Regardless of what antibodies are present the C line should appear to indicate that the sample has been transported properly through the membrane. If the C line does not appear it indicates that the test result is invalid and a new, unopened test cassette is required to repeat the test.

Contents of the Kit |

One test kit contains:
20 Test Cassettes | 1 Buffer Solution Bottle | 1 Package Insert

One test cassette contains:

- Dried reagents with stabilizers
- Colloidal gold-labeled novel coronavirus antigen
- Anti-mouse IgG polyclonal antibody
- Anti-human IgG monoclonal antibody
- Anti-human IgM monoclonal antibody

Materials not provided but required:
Sampling Devices | Alcohol Wipes | Gloves | Timer

Warnings and Precautions |

- For human in vitro clinical diagnostics only.
- The product should only be used by trained healthcare professionals.
- After opening the sealed cassette pouch the test should be used within one hour.
- Do not immerse test cassette in water.
- Do not freeze test cassette or buffer solution.
- Handle specimens in accordance to the OSHA Standard on Bloodborne Pathogens.
- Wear protective gloves, clothing, and eyewear.
- Wash hands thoroughly after handling specimens.
- Dispose of all used or damaged test cassettes, capillary samplers, or other kit components as biohazardous materials.
- Do not use test cassette, buffer solution, or any other kit components if the pouch is damaged or the seal is broken.
- Do not use samples containing lipids, hemolysis, or turbidity which can affect results.
- Not for use with heat inactivated or other inactivated human specimen (blood, serum, plasma).
- This package insert must be read completely before performing the test. Failure to follow directions in insert may yield inaccurate test results.
- Test results should be read between 10 and 15 minutes after a specimen is applied to the sample well. Results read after 15 minutes may give erroneous results
- Do not use test cassette, buffer solution, or any kit component beyond the indicated expiration date.
- Bring all reagents to room temperature (15-30°C) before use.

Storage Instructions |

The reagent should be stored in the dark at room temperature (2°C to 30°C) and has a shelf-life of 12 months. The container should be protected from light after being opened. Do not freeze.

Sample Requirements |

- Suitable for human serum, plasma, or whole blood samples (capillary or venous) including samples prepared by commonly-used anticoagulants (K2EDTA, NaCitrate, Li-Heparin).
- Fresh samples should be collected and tested without inactivation.
- Not for use with heat inactivated or other inactivated human specimen (blood, serum, plasma).
- Serum and plasma samples can be stored at 2-8°C for 5 days. If long-term storage of serum or plasma samples is required, store at -20°C and avoid repeated freeze/thaw cycles.
- Anticoagulated whole blood samples can be stored at 2-8°C for 5 days.
- Before testing, samples stored in refrigerated or frozen storage should be slowly returned to room temperature (15-30° C) and stirred. When particulates are clearly visible in the sample the precipitate should be removed by centrifugation before testing.

Test Procedure |

Do not open pouch until ready to use. Prep necessary materials: Test cassette | Buffer solution | Sampling Device
Label Test cassette with patient ID

1 | Obtain a specimen using standard laboratory or provider protocols. Using appropriate sampling device, obtain 15µL of fingerstick or venous whole blood specimen, or 10µL of serum or plasma using appropriate titration device.

- For intravenous sampling follow standard laboratory protocols.

2 | Dispense the specimen into the Test Cassette sample well.

- Ensure that the entire sample is dispensed into the sample well.

3 | Remove colored cap of the Buffer Solution bottle and dispense 2-3 drops into the Test Cassette sample well.

- Remove any air bubbles in the dropper.
- Test on a level surface at room temperature.

4 | Allow test to run for 10 minutes. Read the results by viewing the detection window.

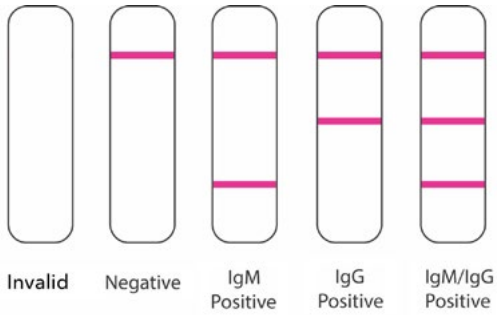
- Test results that have run over 15 minutes are invalid.

Test Method Limitations |

- This product can only be used to detect the IgG and IgM antibodies of the novel coronavirus in human whole blood (capillary or venous), serum, or plasma. It cannot be used with other body fluids or secretions.
- Proper sample collection is critical for optimum test performance. Failure to follow the collection and sampling requirements may give inaccurate results.
- This product is only for qualitative testing and the intensity of the test line does not necessarily correlate to SARS-CoV-2 antibody titer in the specimen.
- 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.
- Negative results may be caused by low concentrations of the novel coronavirus IgG/IgM antibody in the sample and therefore cannot completely rule out the possibility of infection.
- 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. Results should be used in combination with clinical observations and other testing methods.
- Test results can be affected by temperature and humidity.
- A negative or non-reactive result can occur if the virus has undergone minor amino acid mutation(s) in the epitope recognized by the antibody detected by the test.
- This test should not be used for screening of donated blood.

Display of Results/Expected Values |

A total of three detection lines are possible, with the control (C) line appearing when sample has flowed through the cassette.



1 | Invalid Result: If the quality control line (C) does not appear, then the test result is invalid and sample must be retested with a new cassette.

2 | Negative Result: If only the quality control line (C) appears and the detection lines G and M are not visible, then no novel coronavirus antibody has been detected and the result is negative.

3 | Positive Result, M only: If both the quality control line (C) and the detection line M appears, then the novel coronavirus IgM antibody has been detected and the result is positive for the IgM antibody.

4 | Positive Result, G only: If both the quality control line (C) and the detection line G appears, then the novel coronavirus IgG antibody has been detected and the result is positive for the IgG antibody.

5 | Positive Result, G and M: If the quality control line (C) and both detection lines G and M appear, then the novel coronavirus IgG and IgM antibodies have been detected and the result is positive for both the IgG and IgM antibodies.

Internal Quality Control Procedure |

Each Test Cassette device has a built-in control. A red colored line in the detection window at the Control line can be considered an internal positive procedural control. The Control line will appear if the test procedure has been correctly performed. If the Control line does not appear, the test is invalid and a new test must be performed. If the problem persists, please contact your local vendor or BioMedomics for technical support.

External Quality Control Procedure |

- Good laboratory practice recommends the use of external positive and negative controls to ensure the function of the test reagents and to evaluate the user ability to properly perform a test. It is recommended that external controls be performed with each new lot or shipment. If the controls do not perform as expected, review the instructions and repeat the test. Consult the laboratory director before performing patient tests and reporting results.
- Test performance can be evaluated using the COVID-19 External Control Kit available from BioMedomics. Follow instructions included in the kit for preparation, use, storage, and determination of appropriate values. Frequency of external control testing should be determined by your laboratory director and according to your laboratory standard quality control protocols. Upon confirmation of the expected results, the test is ready to use with patient specimens.
- The COVID-19 External Control Kit includes positive external control. The positive control is formulated by spiking humanized anti-SARS-Cov-2 antibodies in negative human serum. The positive control may be reactive to the IgM line, IgG line or both.
- The COVID-19 External Control Kit includes negative human serum as a negative external control. The negative control will yield an affirmative result (red line) for the control (C) line only, when the test has been performed correctly and the test device is properly functioning.
- The use of negative and positive controls from other commercial kits has not been established.

Performance Characteristics |

Clinical Agreement Validation Study | The BioMedomics COVID-19 IgM-IgG Rapid Test was tested using clinical samples at Jiangsu Provincial Center for Disease Control and Prevention (Jiangsu CDC), Nanjing, China. The COVID-19 IgM-IgG Rapid Test is intended to test IgM and IgG separately. The test was validated against a panel of previously frozen samples consisting of twenty six (26) SARS-CoV-2 antibodies (both IgM and IgG) positive and eighty (80) antibody-negative plasma samples. The antibody-positive samples were collected from clinically-confirmed COVID-19 infected patients and the presence of anti-SARS-Cov-2 antibodies were confirmed with a chemiluminescent IgM and IgG assay (magnetic particles). Within the 26 positive samples, 22 samples tested positive for both IgM and IgG antibodies by BioMedomics COVID-19 IgM-IgG Rapid Test, 4 samples tested positive for only IgG. All 80 negative specimens were collected from healthy donors and confirmed SARS-CoV-2 antibody negative with both the COVID-19 IgM-IgG Rapid Test and the chemiluminescent IgM and IgG assay. Testing was performed using one lot of the COVID-19 IgM-IgG Rapid Test. Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008). The results and data analysis are shown in the tables below.

The BioMedomics COVID-19 IgM-IgG Rapid Test displayed a combined sensitivity of 100% (95% CI:86.77%-100%) and a combined specificity of 98.75% (95% CI:93.23%-99.97%).

Table 1: Summary Results, Clinical Agreement Study

COVID-19 IgM-IgG Rapid Test Kit	Comparator Method			Antibody Negative	
	Antibody Positive				
	IgM+	IgM+	IgM-	Negative	Total
	IgG+	IgG-	IgG+		
IgM+,IgG+	22				22
IgM+,IgG-				1	1
IgM-,IgG+	4				4
IgM-,IgG-				79	79
Total	26			80	106

Table 2: Summary Statistics, Clinical Agreement Study

Measure	Estimate	95% Confidence Interval
IgM Sensitivity	84.62% (22/26)	65.13%-95.64%
IgM Specificity	98.75% (79/80)	93.23%-99.97%
IgG Sensitivity	100% (26/26)	86.77%-100%
IgG Specificity	100% (80/80)	95.49%-100%
Combined Sensitivity	100% (26/26)	86.77%-100%
Combined Specificity	98.75% (79/80)	93.23%-99.97%

Venous Blood/Serum/Plasma Stability & Performance | A study was conducted at the Immunology/Histocompatibility and Immunogenetics Laboratories of University of North Carolina hospital to validate the COVID-19 human specimen storage stability and performance of BioMedomics COVID-19 IgM-IgG Rapid Test. Serological specimen (K2EDTA whole blood, serum and plasma) weree collected from COVID-19 positive patients (confirmed by RT-PCR). The samples were stored at (2 to 8 °C, or 36 to 46 °F). The samples were tested with BioMedomics COVID-19 IgM-IgG Rapid Test at 0, 1, 2, 3, 6 and 7 days. At each time point, the sample was tested in duplicate. All specimen types had consistent and same test results when tested at each storage time point.

Table 3: Venous Blood/Serum/Plasma Results

	Blood		Serum		Plasma	
Day	IgM	IgG	IgM	IgG	IgM	IgG
0	+	+	+	+	+	+
1	+	+	+	+	+	+
2	+	+	+	+	+	+
3	+	+	+	+	+	+
6	+	+	+	+	+	+
7	+	+	+	+	+	+

Cross Reactivity | A cross-reactivity study was performed using forty-four commercially obtained sera specimens (serum or sodium citrate plasma). The full specimen list and donor demographic information can be found in the study report. All specimens were associated with a COVID-19 respiratory negative PCR result or were collected prior to the COVID-19 outbreak. Each specimen was tested in duplicate for a total of 88 sample results. Both negative and positive controls were additionally tested. Three blinded readers independently read each cassette. Results were collated at the end of the study and adjudicated based on agreement of two of three readers. Cassettes were also read by a Hamamatsu reflectance reader. The protocol followed the established instructions for use. For each test 10 µl of sample was applied to the cassette, allowed to sit for 10 minutes before interpretation. Cross-Reactivity Results for the BioMedomics COVID-19 IgM-IgG Rapid Test are shown in the table below.

Table 4: Cross-Reactivity Results

Condition	Specimen Type	Sample N	IgG Negative	IgG Positive	IgM Negative	IgM Positive
Anti-COV HKU1	Serum	3	6	0	6	0
Anti-COV NL63	Serum	2	4	0	4	0
Anti-COV OC43	Serum	1	2	0	2	0
Anti-Flu A	Plasma	2	4	0	4	0
Anti-Flu A/B	Plasma	5	8	2	10	0
Anti-Flu B	Plasma	3	6	0	6	0
Anti-Haemophilus influenza	Serum	5	10	0	8	2
Anti-HBV	Serum	5	10	0	10	0
Anti-HCV	Serum	5	10	0	8	2
Anti-HIV	Serum	5	10	0	10	0
Anti-RSV IgG	Plasma	3	6	0	4	2
Antinuclear Antibody	Serum	5	10	0	8	2

The positive IgM and IgG bands for all replicates except Anti-HCV (IgM) were observed as faint and therefore not considered significant interference. However, false positive results due to cross-reactivity with antibodies to anti-HCV could occur.

Point-of-Care Usage with Capillary Blood | The clinical performance of the BioMedomics COVID-19 IgM-IgG Rapid test performed with capillary whole blood samples by non-laboratory users (e.g., doctors, nurses, nursing assistants, physician or nursing students, physician office medical assistant, outreach clinic medical staff) in a point-of-care setting was evaluated by clinical testing conducted by the University of North Carolina at Chapel Hill, via Health on Wheels Mobile Medical Unit Van and the Respiratory Diagnostic Center (RDC) located in Chapel Hill, NC, USA. One capillary (fingerstick) whole blood and nasopharyngeal (NP) swab specimen was collected from each study participant on Day 1 and Day 28 of study. The blood samples were tested with BioMedomics COVID-19 IgM/IgG Rapid Test by a trained non-laboratory user at the point of care according to the Instructions for Use. The NP samples were transported to the reference laboratory for SARS-CoV-2 RT-PCR testing. A total of nine PCR positive samples and seven PCR negative capillary samples were tested. The antibodies tests were conducted at day 28. The results are summarized in the below table. Both positive samples and negative samples have 100% test concordance with PCR results.

Table 5: Summary Results, Capillary Blood POC Study

Subject	PCR Result	Days after Initial Visit	IgM	IgG
COV-001	Pos @ Day 0	28	+	++
1-002	Pos @ Day 7	28	+	++
1-002	Neg	28	-	-
COV-002-001	Neg	28	-	-
COV-004	Pos @ Day 0	28	-	++
4-001	Pos @ Day 1	28	+	++
4-002	Pos @ Day 1	28	-	++
COV-005	Pos @ Day 1	28	-	++
5-001	Neg	28	-	-
COV-006	Pos @ Day 1	28	-	+
6-001	Neg	28	-	-
6-002	Neg	28	-	-
COV-008	Pos @ Day 1	28	+	++
8-001	Pos @ Day 2	28	++	++
COV-010-002	Neg	1	-	-
COV-011-001	Neg	2	-	-

Table 6: Summary Statistics, Capillary Blood POC Study

Measure	Estimate	95% Confidence Interval
IgM PPA	55.6% (5/9)	20%-86%
IgM NPA	100% (7/7)	59%-100%
IgG PPA	100% (9/9)	66%-100%
IgG NPA	100% (7/7)	59%-100%
IgG/IgM PPA	100% (9/9)	66%-100%
IgG/IgM NPA	100% (7/7)	59%-100%

PPA = Positive Percent Agreement
NPA = Negative Percent Agreement

Do Not Reuse

Manufacturer

Expiration Date

For In Vitro Diagnostic Use Only

Batch Code

Storage Temperature Range

Catalog Number

Contains <n> tests

Buffer Solution

Consult Instructions

Test Cassette

Instructions For Use

Part Number

Authorized EU Representative

Scan for instructions in other languages

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