COVID-19 IgG/IgM

Rapid Test Device

(Whole Blood/Serum/Plasma)

COV-W23M

INTENDED USE

The COVID-19 IgG/IgM Rapid Test Device is an *in vitro* immunoassay for the direct and qualitative detection of anti-SARS-CoV-2 IgM and anti-SARS-CoV-2 IgG in human whole blood, serum, or plasma as an aid in the diagnosis of COVID-19.The test is for professional use only.

INTRODUCTION

Coronaviruses are a large family of viruses that are common in many different species of animals, including camels, cattle, cats, and bats.
The two highly pathogenic viruses, SARS-CoV and MERS-CoV, cause severe respiratory syndrome in humans, and the other four human coronaviruses (HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1) induce only mild upper respiratory diseases in immunocompetent hosts, although some of them can cause severe infections in infants, young children and elderly individuals[1,2,3].
COVID-19 is the disease associated with SARS-CoV-2, which was identified in China at the end of 2019. Coronaviruses cause respiratory and intestinal infections in animals and humans[1].
The virus is transmitted mainly via respiratory droplets that people sneeze, cough, or exhale. The incubation period for COVID-19 is currently estimated at between two and 14 days. Common symptoms of COVID-19 infection include fever, cough and respiratory symptoms such as shortness of breath and breathing difficulties. More serious cases develop severe pneumonia, acute respiratory distress syndrome, sepsis and septic shock that can lead to the death of the patient. People with existing chronic conditions seem to be more vulnerable to severe illness.
Detection of IgM indicates recent infection and can be used for early diagnosis of infection. IgG antibodies gradually appear and increase in the late stage of infection, and the COVID-19 IgG/IgM Rapid Test Device is a simple lateral flow immunoassay for the direct detection of anti-SARS-CoV-2 IgG/IgM antibody. It will provide a presumptive diagnosis of COVID-19.

PRINCIPLE

The COVID-19 IgG/IgM Rapid Test Device detects anti-SARS-CoV-2 IgG/IgM antibody through visual interpretation of color development.
Anti-human IgG and anti-human IgM are used to detect specific antibodies in the human whole blood, serum, or plasma specimen. When specimen is added to the sample well, specific IgM and/or IgG antibodies, if present, will bind to the SARS-CoV-2 antigens conjugated to colored particles on the conjugate pad. As the specimen migrates along the strip by capillary action and interacts with reagents on the membrane, the complex will be captured by anti-human IgM and/or anti-human IgG antibodies immobilized on the test region(s). Excess colored particle are captured at the internal control region.
The presence of a red band(s) on the test region(s) indicates a positive result for the particular IgG and/or IgM antibodies, while its absence indicates a negative result. A red band at the control region (C) serves as a procedural control, indicating that membrane wicking is working.

REAGENTS AND MATERIALS

Materials Provided

- Individually packed test devices
- 5uLdisposable pipettes
- 10uLdisposable pipettes
- Buffer
- Package insert

Materials Required but Not provided

- Clock, timer or stopwatch
- Transfer pipette

PRECAUTIONS

- For *in vitro* Diagnostic Use Only.
- Read the Package Insert prior to use. Directions should be read and followed carefully.
- Do not use kit or components beyond the expiration date.
- The device contains material of animal origin and should be handled as a potential biohazard. Do not use if pouch is damaged or open.
- Test devices are packaged in foil pouches that exclude moisture during storage. Inspect each foil pouch before opening. Do not use devices that have holes in the foil or where the pouch has not been completely sealed. Erroneous result may occur if test reagents or components are improperly stored.
- Do not use the Buffer if it is discolored or turbid. Discoloration or turbidity may be a sign of microbial contamination.
- All patient specimens should be handled and discarded as if they are biologically hazardous. All specimens must be mixed thoroughly before testing to ensure a representative sample prior to testing.
- Care should be taken to store specimens as indicated in the document (refer to SPECIMEN COLLECTION AND STORAGE).
- Failure to bring specimens and reagents to room temperature before testing may decrease assay sensitivity. Inaccurate or inappropriate specimen collection, storage, and transport may yield false negative test results.
- Avoid skin contact with all components containing sodium azide which is a skin irritant.
- If infection with SARS-CoV-2 is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions and sent to state or local health departments for testing.

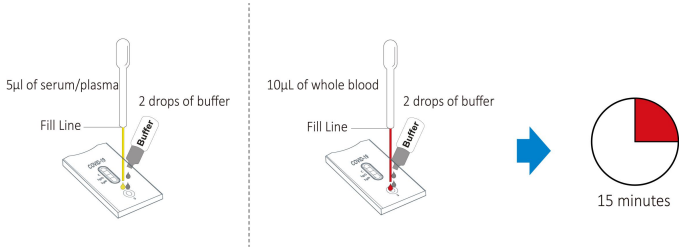
STORAGE AND STABILITY

- Store the COVID-19 IgG/IgM Rapid Test Device at 2~30℃when not in use.
- **DO NOT FREEZE**.
- Kit contents are stable until the expiration dates marked on their outer packaging and containers.
- Perform testing immediately after specimen collection. Do not leave specimens at room temperature for prolonged periods. Serum and plasma specimens may be stored at 2-8°C for up to 7 days. For long term storage, serum or plasma specimens should be kept below -20°C. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 3 days after collection. Do not freeze whole blood specimens.
- Containers containing anticoagulants such as EDTA, citrate, heparin or oxalate should be used for whole blood storage.
- Bring specimens to room temperature prior to testing. Frozen serum or plasma specimens must be completely thawed and mixed well prior to testing. Avoid repeated freezing and thawing of specimens.
- If specimens are to be shipped, pack them in compliance with all applicable regulations for transportation of etiological agents.

TESTPROCEDURE

Specimen Collection:
Allow the test device, specimen, buffer, and/or controls to reach room temperature (15-30°C) prior to testing.

1. Bring the pouch to room temperature before opening. Remove the test device from the sealed pouch and use it as soon as possible.
2. Place the test device on a clean and level surface. Label the test with patient or control identification.
   For Serum or Plasma Specimens:
   a) Using the provided 5μL disposable pipette, draw the specimen up to the Fill Line, and transfer 1 drop of the specimens (appr. 5 μL) onto the specimen well of the test device, then add 2 drops of buffer and start the timer.
   For Whole Blood Specimens:
   a) Using the provided 10μL disposable pipette, draw the specimen up to the Fill Line, and transfer 1 drop of whole blood (appr. 10 μL) onto the specimen well of the test device, then add 2 drops of buffer and start the timer.
3. Wait for the colored line(s) to appear. Read results at 15 minutes.
   Note: Specimens can also be applied using a micropipette.



RESULT INTERPRETATION

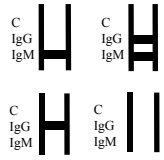
For COVID-19 IgG/IgM Test:

IgM Positive:*The colored line in the control region (C) changes from blue to red, and a colored line appears in the IgM test region. The result is positive for COVID-19 virus specific-IgM antibodies.

IgG Positive:*The colored line in the control region (C) changes from blue to red, and a colored line appears in the IgG test region. The result is positive for COVID-19 virus specific-IgG antibodies.

IgM and IgG Positive:*The colored line in the control region (C) changes from blue to red, and two colored lines should appear in IgG and IgM test regions. The color intensities of the lines do not have to match. The result is positive for IgM and IgG antibodies.

Negative: The colored line in the control region (C) changes from blue to red. No line appears in IgM or IgG test regions.



Invalid: Control line (C) is still completely or partially blue, and fails to completely change from blue to red. Insufficient buffer volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the procedure with a new test device. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

NOTE:

1. The color intensity in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of color in the test region should be considered positive. Note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

QUALITY CONTROL

Internal Procedural Controls
The COVID-19 IgG/IgM Rapid Test Device has built-in (procedural) controls. Each test device has an internal standard zone to ensure proper sample flow. The user should confirm that the CORLED band located at the "C" region is present before reading the result.
External Positive and Negative Controls
Good laboratory practice suggests testing positive and negative external controls to ensure that the test reagents are working and that the test is correctly performed.

LIMITATIONS OF THE TEST

1. The COVID-19 IgG/IgM Rapid Test Device is for professional *in vitro* diagnostic use, and should only be used for the qualitative detection of anti-SARS-CoV-2 IgM and anti-SARS-CoV-2 IgG. The intensity of color in a positive band should not be evaluated as "quantitative or semi-quantitative".
2. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
3. Failure to follow the TEST PROCEDURE and RESULT INTERPRETATION may adversely affect test performance and/or invalidate the test result.
4. Results obtained with this assay, particularly in the case of weak test lines that are difficult to interpret, should be used in conjunction with other clinical information available to the physician.
5. A negative result may occur ,If the number of IgG and/or IgM antibodies to novel coronavirus present in the specimen is below the detection limit of the test, or the specimen are collected at a stage of disease where antibodies have not yet been produced.
6. A high dose "hook effect" may occur where the color intensity of test band decreases as the concentration of anti-SARS-CoV-2 IgG/IgM increases. If a "hook effect" is suspected, dilution of specimens may increase color intensity of the test band.
7. Negative results do not preclude COVID-19 and should be confirmed via molecular assay.

PERFORMANCE CHARACTERISTICS

Clinical Evaluation:

79 specimens were collected from patients exhibiting pneumonia or respiratory symptoms. 83 specimens were also collected from convalescent patients. 227 negative specimens were collected in the study.

For IgM detection:

Method		PCR+	PCR-	Total
COVID-19 IgG/IgM Rapid Test	IgM+	74	2	76
	IgM-	5	225	230
Total		79	227	306

Relative sensitivity: 93.7% (86.0%-97.3%)*

Relative specificity: 99.1% (96.8%-99.8%)*

Overall agreement: 97.7% (95.4%-98.9%)*

*95% Confidence Interval

For IgG detection:

Method		Convalescent samples	PCR-	Total
COVID-19 IgG/IgM Rapid Test	IgG+	82	3	85
	IgG-	1	224	225
Total		83	227	310

Relative sensitivity: 98.8% (93.5%-99.8%)*

Relative specificity: 98.7% (96.2%-99.5%)*

Overall agreement: 98.7% (96.7%-99.5%)*

*95% Confidence Interval

Cross Reactivity

There was no cross-reactivity with any of the unrelated infections tested. No inhibition was observed with any of the specimens.

ANA+	Anti-HSV-I IgM +	HAMA +
Anti-Chikungunya +	Anti-HSV-II IgM +	HBsAg +
Anti-Chlamydia +	Anti-Rubella IgM +	Lyme disease+
Anti-CMV IgM +	Anti-Syphilis +	P. falciparum +
Anti-Dengue virus +	Anti-Tuberculosis +	P. vivax +
Anti-HAV IgM +	Anti-Yellow fever +	RF + (high titer)
Anti-HCV +	Anti-Zika virus +	Toxoplasmosis +
Anti-HEV IgM +	Chagas IgG+	Typhoid IgM +
Anti-HIV+	EBV IgG +	

Interfering Substances

the sensitivity and specificity of the COVID-19 IgG/IgM Rapid Test are not affected by the substances listed below

Interfering substances	Concentration of analyte
Blood analytes	
Albumin	5 g/dL
Bilirubin	5 mg/dL
Hemoglobin	20 g/dL
Triglycerides	500 mg/dL
Anticoagulants	
EDTA	3.4 µmol/L
Heparin	3000 U/L
Sodium citrate	5 mg/mL
Potassium oxalate	2 mg/mL
Abnormal blood sample	
Visual hemolysis	NA
Icteric	NA
Lipemic	NA
Common medicines	
Acetylsalicylic acid	3.62 mmol/L
Ascorbic acid (Vitamin C)	342 µmol/L
Amoxicillin	206 µmol/L
Aspirin	4.34 mmol/L
Fluconazole	245 µmol/L
Ibuprofen	2425 µmol/L
Loratadine	0.78 µmol/L
Nadolol	3.88 µmol/L
Naproxen	2170 µmol/L
Paroxetine	3.04 µmol/L
Anti-malarial medicines	
Quinine	148 µmol/L
Anti-tuberculosis medicines	
Rifampicin	78.1 µmol/L
Isoniazid	292 µmol/L
Ethambutol	58.7 µmol/L
Common consumables	
Coffee (caffeine)	308 µmol/L
Alcohol (ethanol)	86.8 mmol/L

LITERATURE REFERENCES

1. Masters, P. S. & Perlman, S. in Fields Virology Vol. 2 (eds Knipe, D. M. & Howley, P. M.) 825–858 (Lippincott Williams & Wilkins, 2013).
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4. Kan, B. et al. Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. J. Virol. 79, 11892–11900 (2005).
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GLOSSARY OF SYMBOLS

REF	Catalog number		Temperature limitation
	Consult instructions for use	LOT	Batch code
IVD	*In vitro* diagnostic medical device		Use by
	Manufacturer		Do not reuse