COVID-19 IgG/IgM Rapid Test Device (Whole Blood/Serum/Plasma)
Product Insert
REF COV-13C25

INTENDED USE

The Rapid Response™ 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 (including venous whole blood and capillary whole blood), serum, or plasma. At the Point of Care setting, this test is only authorized for use with fingerstick whole blood specimens. This test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. The Rapid Response™ COVID-19 IgG/IgM Rapid Test Device should not be used for screening patients or to diagnose or exclude acute SARS-CoV-2 infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. A negative or non-reactive result for an individual subject indicates absence of detectable COVID-19 virus antibodies. However, a negative or non-reactive rest result does not preclude the possibility of exposure to or infection with COVID-19 virus. False positive results 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 confirmed using a second, different IgG/IgM detection method. Laboratories are required to report all results to the appropriate public health authorities. The test is for use by trained laboratory or healthcare professionals. This assay is not intended for home testing (or self-testing).

The Rapid Response™ COVID-19 IgG/IgM Rapid Test Device may detect a response to vaccination.

PRINCIPLE

The Rapid Response™ 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
- Disposable pipettes
- Buffer
- Package insert

Materials Required but Not Provided

- Clock, timer, or stopwatch
- Lancet
- Specimen collection container
- Alcohol prep pad

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 STORAGE AND STABILITY).
- 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 Rapid Response™ COVID-19 IgG/IgM Rapid Test Device at 2~30°C 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 within 1 hour after specimen collection. 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 no more than 2 months. 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 (15-30°C) 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.

TEST PROCEDURE

Specimen Collection:

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

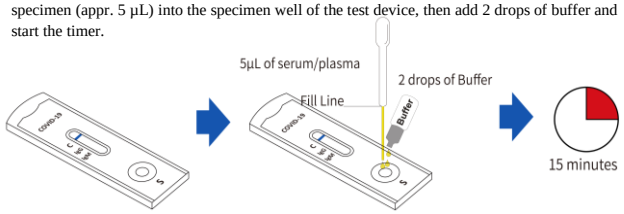
1. Bring the pouch to room temperature before opening. Remove the test device from the sealed pouch and use it as soon as possible.
2. Place the test device on a clean and level surface. Label the test with patient or control identification.

Note: There should be a blue line in the control region (next to "C"), discard the device if there is no blue line.

3. Add the specimens

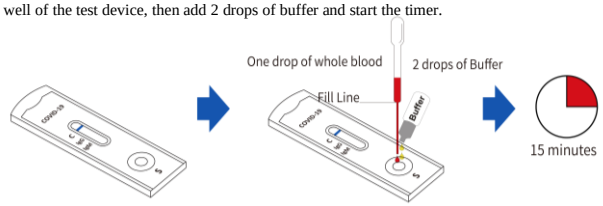
For Serum or Plasma Specimen

a) Using the provided disposable pipette, draw the specimen up to the Fill Line, and transfer all the specimen (appr. 5 µL) into the specimen well of the test device, then add 2 drops of buffer and start the timer.



For Venous Whole Blood Specimens

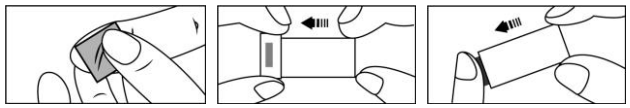
a) Using the provided disposable pipette, draw the specimen above the fill line (avoid the specimen entering the bubble of disposable pipette) and transfer one drop of the specimen into the specimen well of the test device, then add 2 drops of buffer and start the timer.



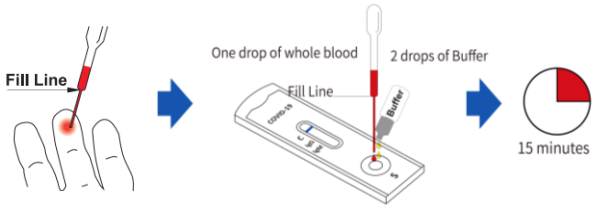
For Fingerstick Blood

a) Clean the puncture site with the alcohol prep pad

b) Carefully remove the cap from the safety lancet. Push the safety lancet firmly against the puncture site until it pricks the finger.



c) Using the provided disposable pipette, draw the specimen above the fill line (avoid the specimen entering the bubble of disposable pipette) and transfer one drop of the specimen into the specimen well of the test device, then add 2 drops of buffer and start the timer.



4. Wait for the blue line change to red line, read results at 15 minutes.
   Note: Specimens can also be applied using a micropipette.

RESULT INTERPRETATION

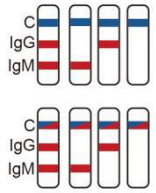
For COVID-19 IgG/IgM Test:

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 Rapid Response™ 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 blue band should be always located at the "C" region before testing, and the red band should be always present before result interpretation.

External Positive and Negative Controls

Good laboratory practice suggests that positive and negative external controls are run routinely to ensure that the test is correctly performed. External positive and negative controls should be used in accordance with applicable accrediting organizations, or your lab's standard Quality Control procedures, as applicable.

LIMITATIONS OF THE TEST

1. The Rapid Response™ 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 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.
6. 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.
7. Negative results do not preclude COVID-19 and should be confirmed via other methods such us molecular assay.
8. The Rapid Response™ COVID-19 IgG/IgM Rapid Test Device is not for the screening of donated blood.
9. Positive results may be due to past or present infection with non SARS CoV2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.
10. Patients on intravenous IgG may give false positive results with IgG-based assays.
11. The performance of this device has not been assessed in a population vaccinated against COVID-19.
12. This test identifies antibodies to the spike protein of the SARS-CoV-2 virus and is therefore unable to distinguish between previously infected individuals and vaccinated individuals.
13. The assay is not intended for home testing (or self-testing).
14. False negatives can occur in elderly and immunocompromised patients.
15. The performance of the device has not been assessed on specimens from individuals who have been infected with emerging variants of SARS-CoV-2 of public health concern.

PERFORMANCE CHARACTERISTICS

Clinical Evaluation:

Study 1

Total of 56 positive and 105 negative samples were collected and tested at 4 different sites. These samples which were either venous whole blood or serum from patients confirmed by RT-PCR method for SARS-CoV-2 infection were tested with the Rapid Response™ COVID-19 IgG/IgM Rapid Test device for antibodies. The PPA/sensitivity and NPA/specificity results are summarized in following tables:

IgG PPA and IgM PPA for Rapid Response™ COVID-19 IgG/IgM Rapid Test Device

Site	Days from symptom onset	# PCR Positive	IgG Test Results			IgM Test Results		
			Antibody Positive	PPA	95%CI	Antibody Positive	PPA	95%CI
(Site 1 + 4)Serum	≤7	8	7	87.5%	52.9%-97.8%	8	100%	67.6%-100%
	8-14	15	13	86.7%	62.1%-96.3%	13	86.7%	62.1%-96.3%
	≥15	20	20	100%	79.9%-100%	18	90.0%	66.9%-98.2%
(Site 2) Venous Whole Blood	≤7	1	1	100%	20.7%-100%	1	100%	20.7%-100%
	8-14	3	3	100%	43.9%-100%	3	100%	43.9%-100%
	≥15	9	9	100%	70.1%-100%	9	100%	70.1%-100%
Sites combined	-	56	53	94.6%	84.2%-98.6%	52	92.9%	81.9%-97.6%

IgG NPA and IgM NPA for Rapid Response™ COVID-19 IgG/IgM Rapid Test Device

Site	# PCR Negative	IgG Test Results			IgM Test Results		
		Negative Results	NPA	95%CI	Negative Results	NPA	95%CI
(Site 1 + 3+ 4) Serum	96	96	100%	96.2%-100%	94	97.9%	92.7%-99.4%
(Site 2) Venous Whole Blood	9	9	100%	70.1%-100%	9	100%	70.1%-100%
Sites combined	105	105	100%	96.5%-100%	103	98.1%	93.3%-99.5%

Study 2

Total of 42 positive and 113 negative fingerstick whole blood samples were collected and tested at 3 different POC sites. These samples were tested with both RT-PCR method for SARS-CoV-2 infection and Rapid Response™ COVID-19 IgG/IgM Rapid Test device for antibodies. The PPA/sensitivity and NPA/specificity results are summarized in following tables.

IgG PPA and IgM PPA for Rapid Response™ COVID-19 IgG/IgM Rapid Test Device

Site	Days from symptom onset	# PCR Positive	IgG Test Results			IgM Test Results		
			Antibody Positive	PPA	95%CI	Antibody Positive	PPA	95%CI
(Site 1+2+3)	0-7 days	2	0	0%	0%-57.5%	2	100%	42.5%-100%
	8-14 days	12	10	83.3%	55.2%-95.3%	10	83.3%	55.2%-95.3%
	≥15 days	28	28	100%	91.2%-100%	25	89.3%	72.8%-96.3%

IgG NPA and IgM NPA for Rapid Response™ COVID-19 IgG/IgM Rapid Test Device

(Site 1+2+3)	PCR Negativ	IgG Test Results			IgM Test Results		
		Antibody Negativ	NPA	95%CI	Antibody Negative	NPA	95%CI
Combined Site	113	113	100%	97.7% -100%	113	100%	97.7%-100%

The NPA/specificity of the Rapid Response™ COVID-19 IgG/IgM Rapid Test Device for IgG/IgM in fingerstick whole blood samples is 100%.

Cross Reactivity

The Rapid Response™ COVID-19 IgG/IgM Rapid Test Device has been evaluated for cross-reactivity for the following potentially cross-reactive substances. It has been noted that there is potential cross-reactivity with HSV-1 and Toxoplasma IgM+.

Potential Cross-reactive substances	IgM Agreement	IgG Agreement	Potential Cross-reactive substances	IgM Agreement	IgG Agreement
Anti-HAV IgM +	5/5	5/5	Anti-Haemophilus influenza+	5/5	5/5
Anti-HEV IgM +	5/5	5/5	Anti-Adenovirus +	5/5	5/5
HBsAg +	10/10	10/10	Anti-Mycoplasma pneumonia+	5/5	5/5
Anti-HCV +	10/10	10/10	Anti-Chlamydia pneumonia+	5/5	5/5
Anti-HIV+	10/10	10/10	Toxoplasmosis +	5/5	5/5
Anti-Rubella IgM +	5/5	5/5	Toxoplasma IgM+	5/5	4/5
Anti-CMV IgM +	5/5	5/5	HAMA +	5/5	5/5
Anti-HSV-I IgM +	5/5	5/5	RF +	5/5	5/5
HSV-1	0/1	0/1	ANA+	5/5	5/5
Anti-HSV-II IgM +	5/5	5/5	HCoV-HKU1+	7/7	20/20
EBV IgG +	5/5	5/5	HCoV-0C43+	8/8	14/14
Anti-Dengue virus +	5/5	5/5	HCoV-NL63+	13/13	19/19
Anti-Yellow fever +	5/5	5/5	HCoV-229E+	8/8	10/10
Anti-Zika virus +	5/5	5/5	MERS-CoV+	5/5	5/5
Anti-Chikungunya +	5/5	5/5	SARS-CoV+	5/5	5/5
Chagas IgG+	5/5	5/5	Mouse Anti-human Metapneumovirus IgG	5/5	5/5
Anti-Syphilis +	10/10	10/10	Anti-Parainfluenza Type 1 IgG	5/5	5/5
Anti-Chlamydia +	5/5	5/5	Anti-Parainfluenza Type 2 IgG	5/5	5/5
Anti-Tuberculosis +	5/5	5/5	Anti-Parainfluenza Type 3 IgG	5/5	5/5
Typhoid IgM +	5/5	5/5	Enterovirus IgM+	5/5	5/5
Lyme disease+	5/5	5/5	Enterovirus IgG+	5/5	5/5
P. falciparum +	5/5	5/5	Mouse Anti-Norovirus IgG	5/5	5/5
P. vivax +	5/5	5/5	Enterovirus+	2/2	2/2
Anti-Influenza A +	5/5	5/5	Rhinovirus+	2/2	2/2
Anti-Influenza B +	5/5	5/5	Rhinovirus IgM+	3/3	3/3
Anti-RSV+	5/5	5/5	Rhinovirus IgG+	2/2	2/2
CoV OC43 IgM	4/4	4/4	CoV NL63 IgM	2/2	2/2
CoV OC43 IgG	4/4	4/4	CoV NL63 IgG	2/2	2/2
CoV HKU1 IgM	1/1	1/1	CoV 229E IgM	3/3	3/3
CoV HKU1 IgG	1/1	1/1	CoV 229E IgG	3/3	3/3

Interfering Substances

The assay performance of the Rapid Response™ COVID-19 IgG/IgM Rapid Test Device is not affected by substances at concentrations 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
Common medicines	
Acetylsalicylic acid	3.62 mmol/L
Ascorbic acid (Vitamin C)	342 µmol/L
Amoxicillin	206 µmol/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. Ithete, N. L. et al. Close relative of human Middle East respiratory syndrome coronavirus in bat, South Africa. Emerg. Infect. Dis. 19, 1697–1699 (2013).

GLOSSARY OF SYMBOLS

	Consult instructions for use	Σ	Test per Kit	REF	Catalogue number
2°C 30°C	Store between 2°C and 30°C		Use by		Do Not Reuse
EC REP	EC Authorized Representative	LOT	Lot Number	IVD	For *in-vitro* Diagnostic Use Only

BTNX, Inc.
570 Hood Rd, Unit 23
Markham, ON, L3R 4G7, Canada
Technical Support: 1-888-339-9964

EC REP
MDSS GmbH
Schiffgraben 41
30175 Hannover, Germany