careUS™ COVID-19 IgM/IgG

Intended use

The careUS™ COVID-19 IgM/IgG is an *in vitro* rapid immunochromatographic diagnostic test for the qualitative detection of IgM/IgG antibodies against SARS-CoV-2 directly from human whole blood, serum or plasma.

Summary

There are outbreaks of a respiratory disease caused by a novel coronavirus that was first found in Wuhan City, Hubei Province, China. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). SARS-CoV-2 has been designated as a pandemic by the World Health Organization (WHO) and has been detected worldwide. SARS-CoV-2 is highly contagious and has devastating impacts on healthcare systems and economy in the United States and globally. To effectively control the spread of SARS-CoV-2, rapid detection of the cases and exposure to the virus that may be subclinical but contagious, is critical.

Principle

careUS™ COVID-19 IgM/IgG test is an immunochromatographic assay for the detection of SARS-CoV-2 IgM/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, IgG, and IgM test line. The nitrocellulose membrane is attached onto a plastic backing card and combined with other reagents and pads to construct a test strip. The test strip is encased inside a plastic cassette. Blood samples, including whole blood, serum, or plasma, can be added to the sample well of the test cassette to start a test. The sample specimens are migrating sequentially through filter pad, conjugate pad, nitrocellulose membrane, and absorbent pad. The SARS-CoV-2 antibodies in sample specimens interact with the recombinant SARS-CoV-2 antigen that is conjugated to colloidal gold nanoparticles to form an immune complex while it migrates through the conjugate pad. IgM reacts with the gold-conjugated SARS-CoV-2 antigen and biotinylated anti-human IgM. IgG also reacts 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 streptavidin region ("M" test line) on a membrane to generate a purple-colored line for IgM positive. The IgG immune complexes bind to anti-human IgG region ("G" test line) on a membrane to generate a purple-colored line for IgG positive. The control line will appear as gold-conjugated chicken IgY binds to the control antibody in the control region. The test results should be interpreted 10 -15 minutes after starting the test. Some specimens possibly with low titers of IgM and/or IgG antibodies may result in a faint line, but visible lines including faint ones should be read as a positive result.

Precautions

1. *in vitro* diagnostic use only.
2. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
3. Immediately use after opening the cassette.
4. In order to obtain accurate results, the test must follow this instruction for use.
5. Do not interpret the test result after 15 minutes starting the test.
6. Do not use if the test cassette package is damaged.
7. Do not use the kit contents beyond the expiration date.
8. Use appropriate precautions in the collection, handling, storage, and disposal of patient samples and used kit contents.
9. Do not eat, drink, or smoke in the area where the specimens and kit contents are handled.
10. Dispose of used contents as biohazardous wastes in accordance with federal, state and local requirements.
11. Nitrile or latex gloves should be worn when performing this test.
12. If the assay buffer contacts the skin or eye, flush with copious amounts of water.
13. Handle all specimens as though they contain infectious agents.
14. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens.
15. 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.
16. Do not interchange kit contents from different lots.
17. Do not re-use the tested cassette.

Limitation

1. 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 test should be considered to rule out infection in these individuals.
2. Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to determine infection status.
3. This test may complement the diagnostic accuracy of quantitative polymerase chain reaction (qPCR) tests, but it is not meant to compare this test's clinical sensitivity and specificity with those of a molecular test since the performance of these tests are affected by virus titers and patient's immunity against SARS-CoV-2.
4. This test will only indicate the presence of SARS-CoV-2 IgM and/or IgG antibodies in the specimen from both viable and non-viable SARS-CoV-2 virus.
5. The detection of SARS-CoV-2 IgM/IgG antibodies is dependent upon proper specimen collection, handling, transportation, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results.
6. Results from the cassette should be correlated with the clinical history, epidemiological data and other data available to the clinician evaluating the patient.
7. This cassette has been evaluated for use with human specimen material only.
8. The possibility of false positive or false negative results cannot be excluded due to various factors.
9. This cassette is a qualitative test and does not provide information on the viral load present in the specimen.
10. This test cannot rule out diseases caused by other bacterial or viral pathogens.
11. The prevalence of infection will affect the test's predictive values.
12. Positive and negative predictive values are highly dependent on prevalence. False-negative test results are more likely during peak activity when the prevalence of the disease is high. False-positive test results are more likely during the periods of low SARS-CoV-2 activity when prevalence is moderate to low.
13. This cassette should not be used for the screening of blood donated by individuals.

Storage and Stability

1. Store the test kit as packaged between 1 ~ 30°C.
2. The careUS™ COVID-19 IgM/IgG kit reagents and materials are stable until the expiration date printed on the outer packaging (12 months).
3. The test cassette must remain in the sealed pouch until use.
4. Do not freeze any contents of the kit.

Test kit contents

1. Test cassette 25 each
2. Assay buffer vial 1 each
3. Disposable capillary pipette 25 each
4. Instructions for use (Package insert) 1 each

* Materials not supplied

- Pair of gloves
- Biohazard or sharps container
- Alcohol pad
- Micropipette
- Timer / Pen
- Sterile gauze or cotton
- Lancet

Specimen Type

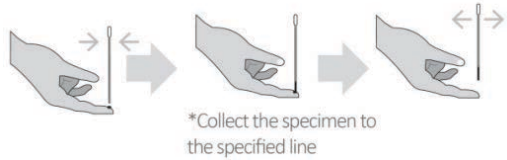
Acceptable specimen types for testing with the careUS™ COVID-19 IgM/IgG are human whole blood, serum, or plasma (venous, capillary blood). Proper specimen collection methods must be followed. Inadequate specimen collection, improper specimen handling and/or transport may yield a false negative result; therefore, specimen collection requires specific training and guidance due to the importance of specimen quality to obtain accurate test results.

Specimen Collection and Test Procedures

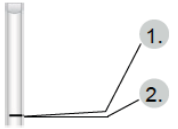
Specimen Collection Procedure

Procedural Notes

- Use only provided disposable capillary pipette for specimen collection.
- Collect the specimen wearing safety gloves to avoid contact and contamination.
- Process the test of the sample immediately after collection.
- Only those samples that are clean, clear, and with good fluidity can be used for the assay.



***Collect the specimen to the marked line**



1. Fill whole blood, serum or plasma up to the marked line (10 µL)
2. Do not overfill the pipette beyond the marked line.

1. Capillary Blood Collection

a. Clean the fingertip to be pierced with an alcohol swab.	b. Gently squeeze the end of the fingertip and pierce the cleaned area using the lancet. Discard the lancet in a sharps container.	c. Wipe out the first drop of blood with sterile gauze or cotton.	d. Collect 10 µL of whole blood using the provided disposable capillary pipette or micropipette. Then follow the test procedure.
			

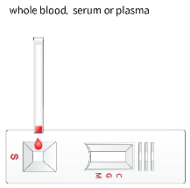
2. Venipuncture Whole Blood or Serum/Plasma Collection

a. Human whole blood, serum or plasma is collected using a collection tube containing anticoagulants (EDTA, heparin, or sodium citrate).
b. Serum and plasma samples are stored at 2-8℃ for 5 days. For long-term storage, store at -20℃. However, avoid multiple freeze-thaw cycles.
c. Whole blood samples with anticoagulants are stored at 2-8℃ and must be tested within 3 days.
d. If possible, collect and test the fresh samples immediately.
e. For testing, transfer 10 µL of a sample using the provided disposable capillary pipette or micropipette. Then follow the test procedure.

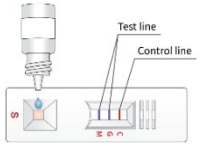
Procedural Notes

- Allow test cassettes, reagents, and specimens to warm up to room temperature (15~30°C) before testing.
- Remove the careUS™ COVID-19 IgM/IgG test cassette from its foil pouch immediately before testing.
- The careUS™ COVID-19 IgM/IgG kit IS INTENDED to be used only with human whole blood, serum or plasma specimens.

1. Place cassette on a clean, flat surface after removing from the pouch.
2. Write the patient's ID on the cassette
3. Add 10 µL of the sample collected using the provided disposable capillary pipette to the sample well "S".



4. Add 1 drop of Assay Buffer solution to the sample well "S" immediately after sample loading.



5. Start a timer.
6. Read and interpret the test results after 10 minutes. Do not interpret the test result before 10 minutes and after 15 minutes.

Interpretation of Results

NOTE: The test result should not be read and interpreted after 15 minutes. Do not interpret the result using any instruments.

NOTE: The color intensity in the test region will vary depending on the amount of IgM and IgG present in the sample. Any faint colored line(s) in the test region(s) should be considered as positive.

IgM Positive: Two distinct lines appear.
One line next to "C" and the other line next to "M" indicates an IgM positive result.

IgG Positive: Two distinct lines appear.
One line next to "C" and the other line next to "G" indicates an IgG positive result.

IgM/IgG Positive: Three distinct lines appear.
One line next to "C", one line next to "G" and the remaining line next to "M" indicates an IgM/IgG positive result.

Negative: Only one line appears.
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. It is recommended that the specimen be re-tested. If the same invalid result persist, contact the manufacturer or distributor before continuing the test.

Quality Control

Internal Quality Control: The careUS™ COVID-19 IgM/IgG test contains a built-in internal procedural control included in the test cassette. A colored line appearing in the control region ("C") is designed as an internal procedural control. The appearance of a procedural control line indicates sufficient flow has occurred and the functional integrity of the test cassette was maintained. If the reddish purple procedural control line does not develop at 10 minutes, the test result is considered invalid. If the internal procedural control line did not appear, please contact the manufacturer or distributor before testing patient specimens.

Reproducibility

The reproducibility of this kit was evaluated by testing total 1,800 cassettes of careUS™ COVID-19 IgM/IgG with three different lots at two different sites for five different days, 2runs per day in triplicate with 5 test sample panels by two operators. The test results showed 100% confirmation of the expected results.

Repeatability

The Repeatability of this kit was evaluated by testing total 600 cassettes of careUS™ COVID-19 IgM/IgG with one lot for 20 different days in triplicate, 2runs per day with 5 test sample panels. The test results showed 100% confirmation of the expected results.

Performance Characteristics

Cross-Reactivity/Class Specificity

Cross-Reactivity of the careUS™ COVID-19 IgM/IgG was evaluated by testing each disease or infectious agent listed below and did not show any cross-reactivity.

- Anti-Influenza A total antibodies
- Anti-Influenza B total antibodies
- Anti-Dengue virus total antibodies
- Anti-HIV total antibodies
- Anti-HCV total antibodies
- Anti-HBV total antibodies
- Anti-Syphilis total antibodies
- Anti-respiratory syncytial virus

Interference Substances

The impact of potentially interfering substances on the careUS™ COVID-19 IgM/IgG Serological Test was be evaluated. The interfering substances for testing are listed below and did not interfere with careUS™ COVID-19 IgM/IgG at the following levels:

- 10 mg/mL Hemoglobin
- 15 mg/mL Triglycerides
- 5.0 mg/mL Albumin human
- 0.5 mg/mL Biotin
- 0.4 mg/mL Bilirubin
- 60 IU/mL Sodium heparin
- 2.0 mg/mL EDTA
- 3.2% Sodium citrate

Clinical Performance

Out of 47 SARS-CoV-2 positive samples confirmed by the RT-PCR, the careUS™ COVID-19 IgM/IgG detected 44 positive samples (93.6%)

- Percentage of SARS-CoV-2 IgM or IgG from 44 positive samples
  - SARS-CoV-2 IgG 41/44 (93.2%)
  - SARS-CoV-2 IgM 38/44 (86.4%)

Out of 50 SARS-CoV-2 negative samples confirmed by the RT-PCR, the careUS™ COVID-19 IgM/IgG showed the specificity of 98.0%.

careUS™ COVID-19 IgM/IgG kit		Comparator (RT-PCR)		
		Positive	Negative	Total
Positive	IgG+/IgM+	35	0	35
	IgG+/IgM-	6	0	6
	IgG-/IgM+	3	1	4
Negative	IgG-/IgM-	3	49	52
Subtotal		47	50	97
Positive Percent Agreement (PPA)		93.6% (95% CI: 82.8% – 97.8%)		
Negative Percent Agreement (NPA)		98.0% (95% CI: 89.5% – 99.6%)		

Description of Symbol Used

REF	Catalogue number	Σ	Contains sufficient for <n> tests
LOT	Batch code		Temperature limitation
	Manufacturer		Consult instructions for use
	Use by		Do not use if package is damaged
	Single use	IVD	*In-Vitro* diagnostic medical device
	Keep away from sunlight		Keep dry
	Date of manufacture	EC REP	Authorized representative in EU
CE	CE mark		

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