BERONI GROUP LIMITED

SARS-CoV-2 IgG/IgM Antibody Detection Kit

(Colloidal Gold)

(Serum/Plasma/Whole Blood)

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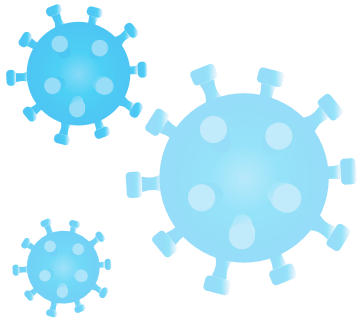
BACKGROUND

The SARS-CoV-2 IgG/IgM antibody detection kit

In response to the current global SARS-CoV-2 crisis, Beroni Group has developed and validated the SARS-CoV-2 IgG/IgM antibody detection kit (colloidal gold). This detection kit is a rapid in vitro diagnostic based on immunochromatographic detection techniques (lateral flow) developed for the qualitative and differential detection of a patient's IgG and the IgM antibody to SARS-CoV-2 in human whole blood (including 'fingerstick' blood), plasma and serum.

Advantages of Colloidal Gold assays

1. Quick - get results in 10 minutes.
2. Simple - reading the results directly.
3. Sampling – only a small amount (30 μL) of fingertip blood or venous blood needed fortest.
4. Self-contained – no need for additional diagnostic equipment.
5. High sensitivity and specificity.



Coronavirus disease (COVID-19) and SARS-CoV-2

Coronavirus disease (COVID-19) is an infectious disease caused by SARS-CoV-2, currently there are no specific vaccines or treatments for COIVD-19. According to the WHO, the majority of people infected with SARS-CoV-2 will develop mild to moderate symptoms and recover without requiring special treatment, however people with underlying medical conditions and those over 60 years of age have a greater risk of developing severe disease and death.

Common symptoms:

- Fever
- Tiredness
- Dry cough

Other symptoms

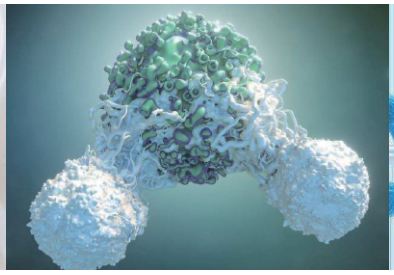
- Shortness of breath
- Aches and pains
- sore throat
- and very few people will report diarrhoea, nausea or a runny nose.

The COVID-19 virus spreads primarily through close contact with an infected person (within 6 feet) via droplets of saliva or discharge from the nose or mouth when an infected person coughs or sneezes and inhaled through the nose into the lungs.

ABOUT US

Beroni Group Limited (“Beroni Group”) is a global company integrating research and development (R&D), production and marketing. It was listed on National Stock Exchange of Australia (NSX) on 12th May 2017 and began trading on OTCQX in the U.S. market on 29th April 2019. It is the first company from the National Stock Exchange of Australia to be traded on OTCQX.

Beroni Group is committed to developing and manufacturing safe and reliable pharmaceutical and healthcare products, developing new products and latest technologies which improve quality of life for patients and consumer, creating value for shareholders and partners and contributing to the society by improving human health. It currently has four core businesses – cell therapies, developing new anti-cancer drugs, e-commerce platform for pharmaceutical and healthcare products, and detection & diagnosis of infectious diseases.



Beroni Group has emerged into an international enterprise with a world-class team of management and scientists that has the capability to become a leading global player in the biopharmaceutical sector. Through its collaboration with international research institutions, the company has embarked on a diagnostic kit (the CII-ArboViroPlex rRT-PCR assay) used to detect viruses such as Zika, Dengue, Chikungunya, and West Nile and a pipeline of new technologies in immune cell therapies and new cancer drug developments.

The CII-ArboViroPlex rRT-PCR assay can simultaneously test for Zika virus, all Dengue virus serotypes, Chikungunya virus and West Nile virus within a very short period of time. The US FDA has issued an emergency use authorization for emergency use of this diagnostic kit. Through its collaboration with Columbia University (USA), Beroni has secured the distribution rights to markets like Australia, Saudi Arabia, USA, China, Japan and India for the distribution of the CII-ArboViroPlex rRT-PCR assay.

INSTRUCTIONS FOR USE

SARS-CoV-2 IgG/IgM antibody detection kit (colloidal gold) (serum/plasma/whole blood)

IINTRODUCTION

Before using the SARS-CoV-2 IgG/IgM antibody detection kit this package insert must be read carefully. All the instructions must be followed strictly. Assay reliability and results are not guaranteed in case of deviations from the instructions provided in this package insert.

INTENDED USE

The SARS-CoV-2 IgG/IgM detection kit is a rapid, single-use immunochromatographic test intended for the qualitative detection of IgG and IgM antibody from SARS-CoV-2 in capillary “fingerstick” whole blood, plasma, and serum.

The SARS-CoV-2 IgG/IgM detection kit is for the qualitative detection of SARS-CoV-2 in individuals with signs and symptoms of SARS-CoV-2. The SARS-CoV-2 IgG/IgM detection kit is not intended for use for general SARS-CoV-2 screening, such as airport screening or contact tracing of individuals without signs and symptoms of SARS-CoV-2. The SARS-CoV-2 IgG/IgM detection kit is intended for use in laboratories or facilities adequately equipped, trained and capable of such testing (including treatment centers and public health clinics).

Negative results do not preclude SARS-CoV-2 and should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status. The definitive identification of SARS-CoV-2 requires additional testing including RT-PCR and confirmation procedures in consultation with public health or other authorities for whom reporting is required.

The level of SARS-CoV-2 IgG and IgM antigens that would be present in the clinical specimen from individuals with early systemic infection is unknown. The SARS-CoV-2 was evaluated in a limited clinical study using retrospective clinical specimens from individuals with SARS-CoV-2 confirmed by RT-PCR.

FDA guidance for in vitro SARS-CoV-2 antigen detection diagnostics

Laboratories are obligated to include the following information on their test report:

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.

KIT CONTENTS

1. 25 individually sealed foil pouches each containing:
   - Disposable test cassette
   - Disposable plastic dropper
   - Desiccant pouch
2. 1 bottle of sample diluent (4 ml)
3. 1 product insert
4. 1 quick reference instructions

TECHNICAL PRINCIPLE

The SARS-CoV-2 IgG/IgM antibody detection kit is a qualitative test for the detection of SARS-CoV-2 virus in capillary “fingerstick” whole blood, serum and plasma. The SARS-CoV-2 IgG/IgM antibody detection kit employs a unique combination of antibodies to a patient’s IgG and IgM to SARS-CoV-2, which are conjugated to colloidal gold dye particles and bound to the fiberglass membrane solid phase. These antibodies consist of mouse anti-human IgG antibody for SARS-CoV-2 in test area (G), mouse anti-human IgM antibody for SARS-CoV-2 in test area (M) and goat anti-mouse IgG antibody for quality control in test area (C).

To perform the test, the device should be removed from its pouch and placed on a flat surface. At least 50 µL of sample is obtained from the patient and one drop of sample is added to the Sample + Diluent well (marked by S) of the device. Immediately following sample addition, 3 drops of sample diluent are added to the Sample + Diluent well (marked by S), upon sample/diluent migration along the test strip to the test site, to allow for the capture of SARS-CoV-2 IgG/IgM, if present in the sample and capture of human antibodies as an indicator of normal kit performance.

Test results are interpreted by the presence of a colored line next to the G, M and C markers. The presence of colored line at marker C indicates that the test is performing normally, and the results of the test can be used. The presence of marker G and M indicates the presence of SARS-CoV-2 IgG and IgM in the patient sample.

TEST PROCEDURE

1. Prior to use, allow the kit to equilibrate to room temperature.

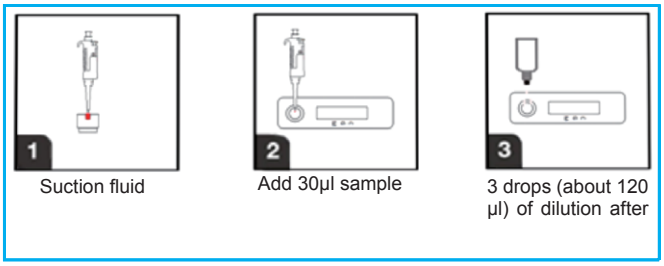
2. Remove the testing cassette and sample diluent from packaging and place on a clean and flat surface.

3. Specimen loading:
   a) For blood specimens already collected: place one drop (approximately 30µl) of blood from the specimen tube into the specimen collecting reservoir.
   b) For finger prick sampling: disinfect finger with alcohol wipes and then using a disposable lancet to pierce the skin and collect one drop of blood (approximately 30µl) into the specimen collecting reservoir.

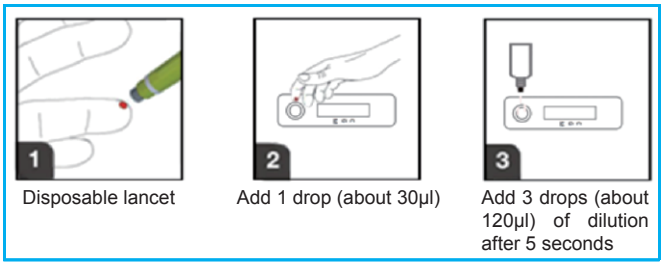
4. After 5 seconds, add 3 droplets (approximately 120µl) of diluent provided in the specimen collecting reservoir.

5. Place test card on a flat surface and wait ten minutes.

6. Observe results in the test window:
   a) A colored line at marker C (control) indicates the test card is working normally, if a colored line at C is not present, disregard the results of the kit.
   b) A color line at marker G and/or at marker M indicates a positive test for COVID-19, as the presence of IgG and/or IgM antibodies were detected.



Schematic of serum, plasma and whole blood sampling in a clinical laboratory



Schematic of peripheral whole blood sampling

INTERPRETATION OF THE RESULTS

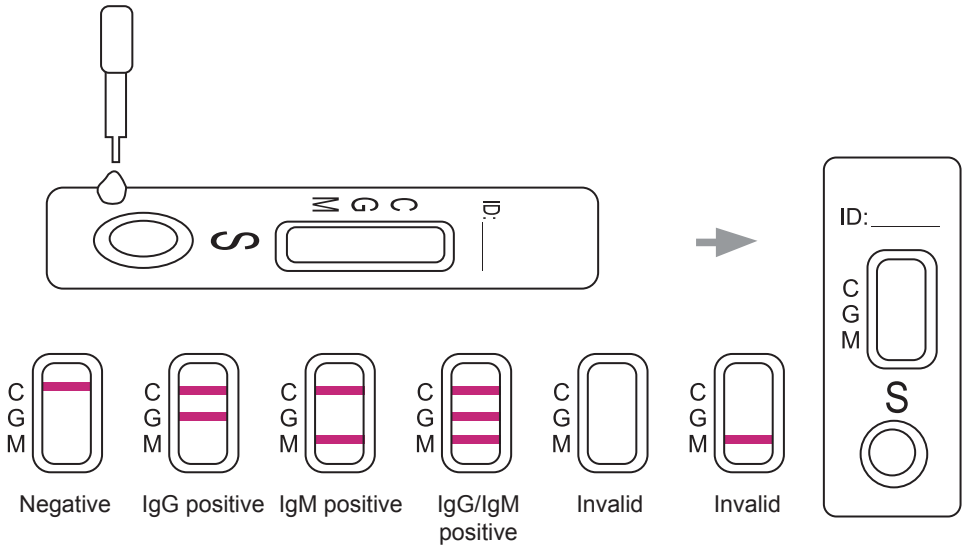
IgG positive: control line C and IgG line are visible on the test cassette. The results showed that IgG antibody was positive. This indicates that the patient is in the recovery stage of infection.

IgM positive: control line C and IgM line are visible on the test cassette. IgM antibody was positive, indicating that the patient was in the acute stage of Infection.

IgM and IgG positive: control line, IgM line and IgG line are clearly visible on the test cassette. IgM and IgG antibody were positive. It indicates that the patient is in the acute late stage of infection.

Negative: the control line is the only visible line in the test cassette. No IgG or IgM antibody was detected. The results do not exclude infection. If symptoms persist, a new specimen should be taken from the patient within 3-5 days and retested.

Invalid test results: if the control C line is not visible in the test cassette, the test is invalid, therefore disregard any results. Dispose of test and retest with a new cassette.



PERFORMANCE CHARACTERISTICS

Clinical agreement

In the absence of a standardized SARS-CoV-2 IgG or IgM references, the studies to evaluate the SARS-CoV-2 IgG/IgM antibody detection kit was conducted on 148 archived whole blood, plasma and serum samples from 148 healthy volunteers and 35 patient samples with confirmed SARS-CoV-2 infection confirmed by RT-PCR collected in Wuhan, Hubei, China.

Of the 148 negative samples, none of the samples were detected by the assay. The SARS-CoV-2 IgG/IgM detection kit found 148 negative samples non-reactive (148/148 = 100%). Of the 35 positive samples, 31 of the samples were detected by the assay. The SARS-CoV-2 IgG/IgM detection kit found 31 positive samples reactive (31/35 = 88.57%) (Table 1).

Table 1: Clinical agreement study summary				
SARS-COV-2 status (confirmation by RT-PCR or CT scan)	#Samples tested	SARS-COV-2 IgG/IgM antibody detection kit results (# reactive/ # tested)		Percentage agreement
		IgM reactive	IgG reactive	
Negative	148	0/148	0/148	100%
Positive	35	19/35	28/35	88.57%

Cross-reactivity

Cross-reactivity of the SARS-CoV-2 IgG/IgM antibody detection kit was evaluated by testing additional viral or bacterial pathogens. In this study three (3) replicates were tested with the pathogens spiked into serum. Additionally, the cross-reactivity of this kit for whole blood components was also evaluated in three (3) replicated with serum spiked with mucin, bilirubin, triglycerides, hemoglobin, Hematocrit, IFN-α and the cross-reactivity for commonly used antibiotics were also assessed in three (3) replicates.

Pathogens

Other Coronaviruses

The SARS-CoV-2 IgG and IgM antibody detection kit demonstrated no cross-reactivty when evaluated against HCoV-HKU1, HCoV-OC43, HCoV- NL63 and HCoV-229E antigens and antibodies.

Other viruses and bacteria

This study found H1N1 (new H1N1 influenza virus (2009)), seasonal H1N1 influenza virus, H3N2, H5N1, H7N9, influenza B Yamagata, Victoria virus, respiratory syncytial virus, rhinovirus A, B, C groups, adenovirus 1,2, 3, 4, 5, 7, 55 types , Enterovirus A, B, C, D groups, EB virus, measles virus, human cytomegalovirus, rotavirus, norovirus, mumps virus, chickenpox, Herpesvirus antigens, viral antibodies, Mycoplasma pneumoniae antigen or antibody spiked into serum, did not demonstrated cross-reactivity with the SARS-CoV-2 IgG/IgM antibody detection kit.

Interfering substances:

This study found that purified mucin, bilirubin, triglycerides, hemoglobin, Hematocrit, IFN-α, Rheumatoid factor, antinuclear antibodies, antimitochondrial antibodies, heterophilic antibodies (HAMA), spiked into serum did not demonstrated interference with the SARS-CoV-2 IgG/IgM antibody detection kit.

Commonly used chemicals including antibiotics, zanamivir, ribavirin, oseltamivir, paramivir, lopinavir, ritonavir, arbidol, levofloxacin,Azithromycin, Ceftriaxone, Meropenem, tobramycin, histamine hydrochloride, phenylephrine, oxymetazoline, sodium chloride (with preservatives) (0.8%, 0.9%), beclomethasone, dexamethasone, flunisolone, Triamcinolone, budesonide, mometasone, fluticasone did not interfere with the SARS-CoV-2 IgG/IgM antibody detection kit.

REPRODUCIBILITY STUDY

Repeated measurements:

The reproducibility of reading the SARS-CoV-2 IgG/IgM antibody detection kit was evaluated using a single positive and negative reference. A total of 10 measurements per sample were obtained. The calculated reproducibility rate for both positive and negative SARS-CoV-2 sample was 100% in serum.

Reading equivalence in serum, plasma and whole blood:

25 matched serum, plasma and whole blood samples from SARS-CoV-2 negative volunteers and 25 matched serum, plasma and whole blood samples from SARS-CoV-2 positive patients were tested on three (3) SARS-CoV-2 IgG/IgM antibody detection kit batches (8420200204, 8420200205, 8420200206) to determine the reproducibility of IgG and IgM readings across sample types, serum, plasma and whole blood. The agreement across sample types for IgG and IgM in SARS-CoV-2 negative volunteers and in SARS-CoV-2 positive patient samples was 25/25 (100% agreement) respectively.

Stability Studies

Sample and kit component stability studies were conducted in order to determine appropriate sample handling and storage conditions.

STORAGE CONDITIONS AND SHELF LIFE

- Keep away from direct sunlight.
- Keep dry.
- The SARS-CoV-2 IgG/IgM detection kit should be stored unopened at 2 ℃ ~ 30 ℃ (36 °F to 86 °F). **Do not freeze.**
- The SARS-CoV-2 IgG/IgM detection kit sample diluent bottle should be stored at 2 °C to 30 °C (36 °F to 86 °F) in the original vial.
- **Do not** use beyond the indicated expiration date. Test devices are stable until the expiration date marked on the pouch, when stored as indicated.
- **Do not** open the pouch until ready to perform the test and must be used within 1 hour after opening (where humidity <60%).

KIT LIMITATIONS

1. This product is only applicable for qualitative testing.
2. SARS-CoV-2 IgG and IgM antibodies in the body are not produced or titers at very high concentrations during the initial stage of infection, which may result in negative results.
3. The testing capabilities of this kit in patients with impaired immune function or taking immunosuppressive agents is limited.

4. All results should be interpreted by a trained professional in conjunction with the patient's history and clinical signs and symptoms, and epidemiological risk factors.
5. Interpretation of results from the SARS-CoV-2 IgG/IgM detection kit must account for the possibility of false-negative and false-positive results.
6. Negative results do not preclude infection with SARS-CoV-2 and should not be the sole basis of a patient treatment/management or public health decision.
7. False positive results may occur from cross-contamination by target organisms or other pathogens.
8. Failure to follow the assay procedures may lead to false negative results.
9. Improper collection, storage, or transport of specimens may lead to false negative results.
10. Inhibitors present in the samples may lead to false negative results.
11. Reading test results earlier than 10 minutes or later than 15 minutes after the addition of sample diluent into well S may yield erroneous results.
12. **Do not** open the sealed foil pouch until just prior to use.
13. **Do not** use kit contents beyond labeled expiration date.
14. Performing fingerstick sample collection when the finger is not completely dry could result in the contamination or dilution of the sample.
15. The test is not validated as a quantitative test for treatment monitoring.
16. Performance of this assay has only been established for whole blood and Fingerstick whole blood, serum or plasma. Performance with other specimen types has not been evaluated.
17. This test should not be used to test specimens from asymptomatic individuals.
18. The definitive identification of SARS-CoV-2 requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required.
19. The diagnosis of SARS-CoV-2 must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of SARS-CoV-2.
20. Cross-reactivity with organisms other than those tested in the Cross-reactivity Study has not been assessed and may lead to erroneous results.

WARNINGS AND PRECAUTIONS

- For best results, use fresh specimen from patients without bacterial infection, hemolysis, jaundice or excessive blood lipid.
- The results should be read 10 minutes after the addition of the testing reagent.
- Any and all results read 15 minutes after addition of testing reagents should be disregarded.
- Use of this assay should be limited to designated, trained personnel.
- All personnel who are involved in collecting, processing, handling, or transporting specimens from a patient with suspected SARS-CoV-2 should take appropriate precautions following the procedures recommended by Centers for Disease Control and Prevention (CDC).
- All persons entering the patient room should wear at least: Gloves, Gown (fluid resistant or impermeable), Eye Protection (goggles or face shield) and Facemask. Additional PPE might be required in certain situations (e.g., copious amounts of blood, other body fluids, vomit, or feces present in the environment), including but not limited to: double gloving, disposable shoe covers and leg coverings.

• **Do not** eat, drink or smoke in the area where specimens and kit reagents are handled. Avoid any contact between hands, eyes or mouth during specimen collection and testing.

• Dispose of all specimens and materials used in the test procedure in a biohazard waste container. The recommended method of disposal of biohazard waste is autoclaving for a minimum of 1 hour at 121 ºC. Disposable materials may be incinerated. Liquid wastes may be mixed with appropriate chemical disinfectants. A freshly prepared solution of 10% bleach (0.5% solution of sodium hypochlorite) is recommended. Allow 60 minutes for effective decontamination (preferably overnight). Use 10% bleach or other appropriate disinfectant to wipe all spills. The bleach solution should be made fresh daily. **NOTE: Do not autoclave solutions that contain bleach.**

• Avoid Aerosol Generating Procedures (AGPs) for patients with SARS-CoV-2.

• **Do not** use any device if the pouch has been perforated.

• Each device is for single use only.

• Always check expiration date prior to testing. **Do not** use the test beyond the expiration date printed on the pouch.

• If desiccant packet is missing, **Do not** use, discard and use a new test device.

• **Do not** mix reagents from different lot numbers of kits.

CONTACT INFORMATION

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