BERONI GROUP LIMITED

SARS-CoV-2 IgG/IgM Antibody Detection Kit

(Colloidal Gold)

(Serum/Plasma/Venous Whole Blood/Fingerstick Whole Blood)

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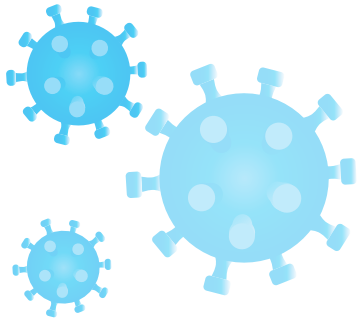
BACKGROUND

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 detection of a patient's antibodies to SARS-CoV-2 in human whole blood (including 'fingerstick' whole 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

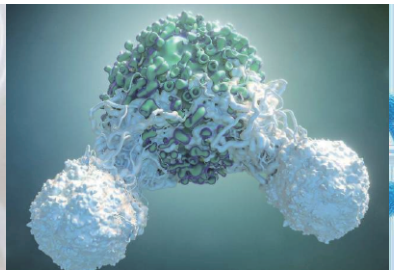
The novel coronavirus belongs to the β genus. COVID-19 is an acute respiratory infectious disease. People are generally susceptible. Currently, the patients infected by the novel coronavirus are the main source of infection; asymptomatic infected people can also be an infectious source. Based on the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

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/Venous Whole Blood/Fingerstick 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 antibody detection kit is an in vitro diagnostic test for the qualitative detection of IgM and IgG antibodies to the SARS-CoV-2 virus in capillary “fingerstick” whole blood, venous whole blood, plasma (EDTA, citrate), and serum. The Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit is an aid in the diagnosis of patients with suspected SARS-CoV-2 infection in conjunction with clinical presentation and the results of other laboratory tests. IgM antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although levels over the course of infection are not well characterized. IgG antibodies to SARS-CoV-2 become detectable later following infection.

The SARS-CoV-2 IgG/IgM antibody detection kit is intended for use in laboratories equipped to perform moderate or high complexity tests, including at the point of care.

Negative results do not preclude SARS-CoV-2 and should not be used as the sole basis to diagnose. 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.
False positive results for SARS-CoV-2 antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
At this time, it is unknown for how long IgM or IgG antibodies may persist following infection.
The SARS-CoV-2 IgG/IgM antibody detection kit is for in vitro diagnostic use only.

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 Instructions for user

TECHNICAL PRINCIPLE

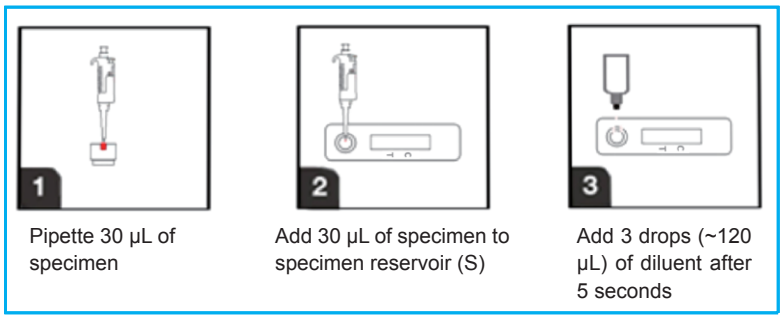
The SARS-CoV-2 IgG/IgM antibody detection kit is a lateral flow, immunochromatographic test for the presence of anti-SARS-CoV-2 antibodies in venous whole blood, “fingerstick” whole blood, plasma and serum in persons suspected of being currently or previously infected with SARS-CoV-2.
It is generally accepted that IgM antibodies are typically produced during the initial phase of an immune response with a typical half-life of 5-6 days, which can indicate a recent or still active infection, while IgG antibodies increase during the later phase of an immune response. In many infections (such as measles, chickenpox, hepatitis B and more) the presence of IgG antibodies can indicate that the patient may be sufficiently immune to re-infection. The Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit test cassette consists of: 1) a purple colored conjugate pad containing recombinant antigens to the SARS-CoV-2 S1 region (which contains the RBD domain) conjugated with colloidal gold (SARS-CoV-2 gold conjugates) and mouse IgG-colloidal gold conjugates; 2) a nitrocellulose membrane strip containing both mouse anti-human IgG and mouse anti-human IgM (T line), and the control line (C Line) coated with goat anti-mouse IgG, all contained in a plastic housing. The IgG/IgM test line, and the control line are indicated with a “T” and “C” printed on the plastic housing.
An adequate volume of specimen is dispensed into the sample well of the test cassette, followed by the diluent supplied with the kit. The specimen migrates by capillary action along the nitrocellulose membrane strip and dissolves the gold conjugates into solution with the sample. The anti-SARS-CoV-2 virus IgG or IgM antibodies if present in the specimen, will bind to the SARS-CoV-2 gold conjugates. The IgG or IgM -gold immunocomplexes will continue to migrate along the nitrocellulose membrane to the test line, and then be captured by the anti-human IgG and IgM antibody printed on the “T” test line. Binding of these immunocomplexes concentrates them on the nitrocellulose, forming a purple colored T Line, indicating the presence of SARS-CoV-2 virus IgG and/or IgM antibodies.
Test results are interpreted by the presence of a colored line next to the T 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 T indicates the presence of IgG and/or IgM antibodies to SARS-CoV-2 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:

For blood/ serum/ plasma specimens already collected: place one drop (approximately 30 µL) of blood from the specimen tube into the specimen collecting reservoir (S).

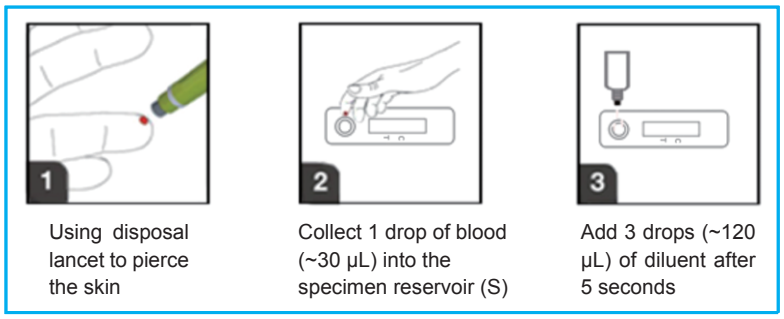


Pipette 30 µL of specimen

Add 30 µL of specimen to specimen reservoir (S)

Add 3 drops (~120 µL) of diluent after 5 seconds

For fingerstick sampling: disinfect finger with alcohol wipes and then using a disposable lancet to pierce the skin and collect one drop of blood (approximately 30 µL) into the specimen collecting reservoir (S).



Using disposal lancet to pierce the skin

Collect 1 drop of blood (~30 µL) into the specimen reservoir (S)

Add 3 drops (~120 µL) of diluent after 5 seconds

4. After 5 seconds, add 3 droplets (approximately 120 µL) of diluent into the specimen collecting reservoir.
5. Place test card on a flat surface and wait ten minutes.
6. Observe results in the test window:

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.

A color line at marker T indicates a positive test for COVID-19, as the presence of IgG and/or IgM antibodies were detected.

INTERPRETATION OF THE RESULTS

The possible results and their interpretations are listed below in both text and graphical representation (Fig 1).

Positive result:
T line positive: Control line C and test T line are visible on the test cassette. This indicates that the IgG/IgM antibodies against SARS-CoV-2 were present in the sample, indicating that the patient has been exposed to the SARS-CoV-2 virus.

Negative result:
The control line C is the only visible line in the test cassette. This indicates that no IgG or IgM antibodies against SARS-CoV-2 were detected in the sample.

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

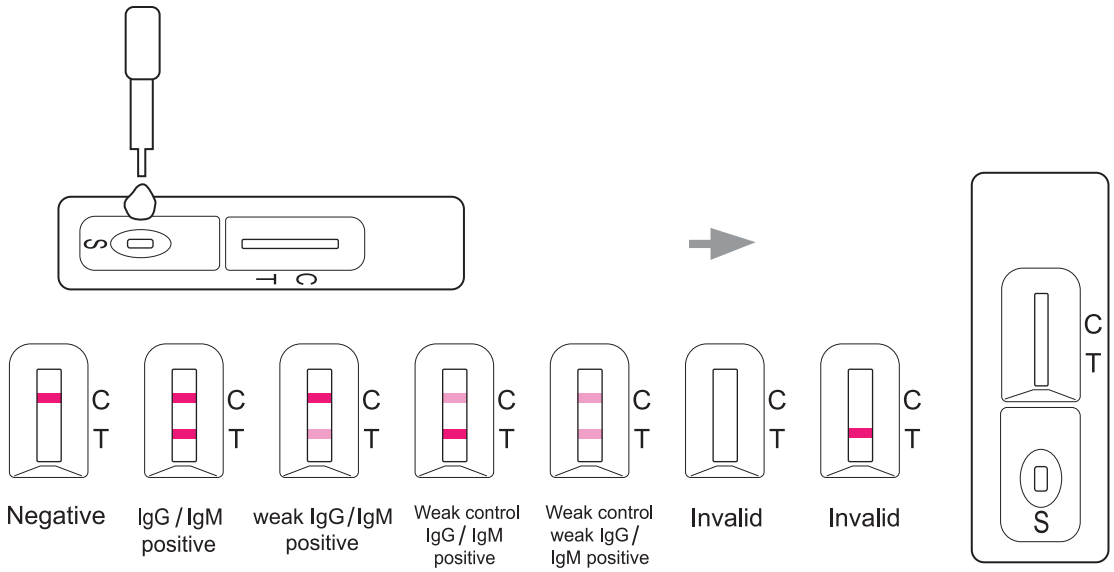


Fig 1. Graphical representation of possible results from the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit

PERFORMANCE CHARACTERISTICS

Clinical sample

In the absence of standardized SARS-CoV-2 IgG or IgM references, the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit was evaluated using prospective samples collected from 55 patients with confirmed COVID-19 and 148 volunteer venous whole blood (from all 203 participants), fingerstick whole blood (from 183 participants), plasma and serum (generated from venous whole blood of the 203 participants). The COVID-19 status of all participants was confirmed by RT-PCR methodology using respiratory samples, with the 'New Coronavirus (2019-nCoV) Nucleic Acid Detection Kit (Fluorescence PCR probing) (CE certified, NMPA registration no. 202003400065) from Shanghai BioGerm Medical Technology Co. Ltd. on an Applied Biosystems 7500 Real-Time PCR System (A summary of the participants clinical characteristics can be found in Table 1).

Table 1. Clinical data						
SARS-CoV-2 status (confirmed by RT-PCR)	n	Sex	Average age (yrs)	Age Range	Average in-patient days	Disease clinical classification
Negative	148	M = 26	35.8	23 - 48	-	-
		F = 122	32.3	22 - 51	-	
Positive	55	M = 13	61.6	32 - 80	27.38	Critically severe type = 8 Severe type = 20 Mild type = 27
		F = 42	42.9	26 - 75	26.65	

Cross-reactivity

Cross-reactivity of the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit was evaluated by "spiking" – the separate addition of exogenous viral or bacterial antigen, the addition of anti-pathogen IgG, and IgM – into seronegative serum.

This study found no cross-reactivity with Beroni Group SARS-CoV-2 IgG/IgM for any of the antibodies to the pathogens or to the pathogen antigens tested, or with interfering substances or commonly used chemicals including antibiotics tested. Moreover, we have tested venous whole blood, fingerstick whole blood, plasma and serum samples from 148 known COVID-19 negative volunteers and did not detect any false positive readings, suggesting that the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit has low cross-reactivity (Table 2).

Table 2. Cross-reactivity study		
Pathogens: Viruses and bacteria	Interfering substances	Commonly used chemicals including antibiotics:
HKU1	Purified Mucin	Zanamivir
OC43	Bilirubin	Ribavirin
NL63	Triglycerides	Oseltamivir
229E	Hemoglobin	Peramivir
H1N1 (New H1N1 Influenza Virus (2009)	IFN-α	Lopinavir
Seasonal H1N1 Influenza Virus, H3N2, H5N1	Rheumatoid Factor	Ritonavir
Influenza B Yamagata Virus	Antinuclear Antibodies	Arbidol
Influenza B Victoria Virus	Antimitochondrial Antibodies	Levofloxacin
Respiratory Syncytial Virus	Heterophilic Antibodies	Azithromycin
Rhinovirus A		Ceftriaxone
Adenovirus 1, 2, 3, 4, 5, 7 types		Meropenem
Enterovirus A		Tobramycin
EB virus		Histamine hydrochloride
Measles virus		Phenylephrine
Human Cytomegalovirus		Oxymetazoline
Rotavirus		Beclomethasone
Norovirus		Dexamethasone
Mumps		Flunisolide
Varicella-Zoster Virus		Triamcinolone acetonide
Mycoplasma Pneumoniae		Budesonide

Clinical agreement

SARS-CoV-2 IgG/IgM antibody detection kit predic- tive agreement.

The clinical agreement of the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit was assessed against known COVID-19 negative and positive venous whole blood participant samples, as confirmed by RT-PCR (n=203).

Of the 148 negative samples, none of the samples were detected for SARS-CoV-2 by the assay. The SARS-CoV-2 IgG/IgM antibody detection kit found 148 negative samples non-reactive, thus the negative predictive agreement is 100%. Of the 55 positive samples, 48 of the samples tested positive using the Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit, thus the positive percentage agreement is 87.27% (95% CI: 78.46 – 96.08%) and negative percentage agreement is 100% (95% CI: 100 – 100%) (Table 3).

Table 3. 2x2 table for the SARS-CoV-2 IgG/IgM antibody detection kit

		SARS-CoV-2 Status (by RT-PCR)	
		Positive	Negative
Beroni Group SARS-CoV-2 IgG/IgM antibody detection kit	Positive	48	0
	Negative	7	148

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.

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%).

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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