ichroma™ COVID-19 Ab

INTENDED USE

ichroma™ COVID-19 Ab is a fluorescence Immunoassay (FIA) for the qualitative determination of IgG/IgM antibodies against of novel corona virus (SARS-CoV-2) in human whole blood/serum/plasma. It is helpful as an aid in the screening of early mild, asymptomatic or acute patients for identification of 'Novel Coronavirus (eg. SARS-CoV-2)' infection.

For *in vitro* diagnostic use only.

INTRODUCTION

The third zoonotic human coronavirus (CoV) of the century emerged in December 2019, with a cluster of patients connected to Wuhan, Hubei Province, China. This virus, the newly identified coronavirus SARS-CoV-2, could cause risky pneumonia so that prevention and control of the infection has become highly required. The SARS-CoV-2 is a member of the Betacoronavirus Genus, that also includes Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV). Since it is identified that symptoms become rapidly severe without a proper treatment after onset of illness, early diagnosis of the virus infection is quite crucial. Currently, the spread of the viral transmission become fast so that the prevention of local transmission requires a point-of care test (POCT), which shows quick outcome within 20 minutes.

ichroma™ COVID-19 Ab test is an *in vitro* diagnostic medical device that helps you to diagnose Novel Coronavirus infections quickly and accurately by measuring the IgG or IgM antibody for the SARS-CoV-2.

* The benefits of using this product are;

1) To prevent the spread (secondary infection) and recovery of CoV infections, the most important serological test results, determined between the first two weeks after infection, can increase the confidence of confirmatory testing with RT-PCR.
2) Periodic serological tests after an infection is confirmed can help determine when to end treatment by analyzing the formation of protective antibodies through seroconversion and recovery of infection through treatment.

PRINCIPLE

This test uses a sandwich immunodetection method; the detector in buffer binds to antibody in sample, forming antibody-antigen complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-anti-human IgG & anti-human IgM on test strip.

More antibodies in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antigen, which is processed by the instrument for ichroma™ tests to display the COVID IgG & IgM 'Positive' / 'Negative' / 'Indeterminate' in the sample.

COMPONENTS

ichroma™ COVID-19 Ab consists of 'cartridges', 'detector tubes', 'detector diluent', 'ID chip' and 'Instruction for use'.

- The cartridge part contains the membrane called a test strip which has anti-human IgM at the test line 1, anti-human IgG at the test line 2 and chicken IgY at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant in a box.
- The detector tube has a granule containing antigen-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative. All detector tubes are packed in a pouch.
- The detector diluent contains salt, detergent and sodium azide as a preservative in Tris buffer and it is pre-dispensed in a vial. The detector diluent is packed in a box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instruction for use'.
- Do not reuse cartridges or detector tubes. A cartridge should be used for testing one sample only. A detector tube should be used for processing of one sample only.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detector tube and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- The cartridge should remain sealed in its original pouch until just before use. Do not use the cartridge, if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- Allow the cartridge, detector tube, detector diluent and sample to be at room temperature for approximately 30 minutes before use.
- The ichroma™ instruments may generate slight vibration during use.
- Used cartridges, detector tubes, detector diluent and pipette tips should be handled carefully and discarded by an appropriate method in accordance with the relevant local regulations.
- The detector diluent contains NaN_3 as preservatives, of which the contact to eyes, skin or clothing should be avoided. If it happens, please wash with running water immediately.
- An exposure to larger quantities of sodium azide may cause specific health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.

- **ichroma™ COVID-19 Ab** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ COVID-19 Ab** should be used only in conjunction with the instrument for ichroma™ tests.
  - Have to use recommended anticoagulant sample.

Recommended anticoagulant
Sodium EDTA, K_2 EDTA, Sodium Heparin, Lithium heparin, Sodium citrate

STORAGE AND STABILITY

Storage condition			
Component	Storage Temperature	Shelf life	Note
Cartridge	2 - 30 °C	20 months	Disposable
Detector tube	2 - 30 °C	20 months	Disposable
Detector diluent	2 - 30 °C	20 months	Unopened
		12 months	Opened

- After the cartridge pouch is opened, the test should be performed immediately.

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigen to the antibodies which is most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may also cause the false negative result as it makes antigen unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.

MATERIALS SUPPLIED

REF CFPC-114

Components of **ichroma™ COVID-19 Ab**

- Cartridge Box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 1
  - ID chip 1
  - Instruction for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ COVID-19 Ab.**

Please contact our sales division for more information.

- **ichroma™ II** REF FPRR021
- **ichroma™ M2** REF FPRR031
- **Boditech COVID-19 Ab Control** REF CFPO-292

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ COVID-19 Ab** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood. If longer storage is required, e.g. if the test could not be performed within 24 hours, serum or plasma should be immediately frozen below -20 °C. The freezing storage of sample up to 3 months does not affect the quality of results.
- However, the whole blood sample should not be kept in a freezer in any case.
- Once the sample was frozen, it should be thawed one time and only for test, because repeated freezing and thawing can result in the changed test values.

TEST SETUP

- Check the contents of **ichroma™ COVID-19 Ab**: Sealed cartridges, detector tubes, detector diluent, ID chip and Instruction for use.
- Ensure that the lot number of the cartridge matches that of the detector tubes, detector diluent as well as an ID chip.
- If the sealed cartridge, the detector tube and the detector diluent have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Avoid directly windy place. The air flow can affect the flow of samples.
- Turn on the instrument for ichroma™ test.
  (Please refer to the 'Instrument for ichroma™ tests Operation Manual for the complete information and operating instructions).

TEST PROCEDURE

- **ichroma™ II**

< Multi test mode >

1) Transfer 150 µL of detector diluent using a pipette to detector tube containing a granule. When the granule form is completely dissolved in the tube, it becomes detection buffer.
2) Transfer 10 µL of sample (Human whole blood/serum/plasma/control) using a pipette to a detector tube(①).
3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
4) Pipette out 75µL of a sample mixture and load it into the sample well on the cartridge.
5) Leave the cartridge at room temperature for 10 minutes before inserting the device into the holder.
   ⚠ *Scan the sample loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*
6) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.

7) Tap the "START" button on the instrument for ichroma™ test to start the scanning process.
8) The instrument for ichroma™ tests will start scanning the sample loaded cartridge immediately.
9) Read the test result on the display screen of the instrument for ichroma™ tests.

< Single test mode >

1) The test procedure is same with "Multi test mode". (Multi Test mode ① – ④)
2) Insert the cartridge into the holder immediately of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
3) Tap the "START" button on the instrument for ichroma™ test.
4) Cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 10 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

■ **ichroma™ M2**

< Read Now mode >

1) Check the display "Read Now" on the ichroma™ M2 screen and set the sample type.
2) The test procedure is same with "ichroma™ II Multi test mode ① – ④".
3) Leave the cartridge at room temperature for 10 minutes before inserting the device into the cartridge holder of ichroma™ M2.
   ⚠ *Scan the sample loaded cartridge immediately when the incubation time is over. If not, it will cause inexact test result.*
4) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
5) The instrument will automatically start scanning the cartridge. Do not remove the cartridge or touch the reader during scanning.
6) Read the test result on the display screen of the instrument.
7) When the cartridge is removed from cartridge holder, the display will show "Read Now" as a standby state.

< Walk Away mode >

1) Check the display "Walk Away" on the ichroma™ M2 screen and set the sample type.
2) The test procedure is same with "ichroma™ II Multi test mode ① – ④".
3) After loading the sample mixture, insert the mixture loaded cartridge into the holder. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
4) The instrument will automatically start scanning the cartridge after reaction time. When the cartridge is inserted, reaction time is displayed.
5) Read the test result on the display screen of the instrument.
6) When the cartridge is removed from cartridge holder, the display will show "Walk Away" as a standby state.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays 'Positive' / 'Negative' /'Indeterminate' with ancillary value, cut-off index (COI).

Cut-off index	Result	Note
< 0.9	Negative for IgG	No need to retest
0.9 ≤ COI< 1.1	Indeterminate	Need to retest
≥1.1	Positive for IgG	Need to confirmation test

Cut-off index	Result	Note
< 0.9	Negative for IgM	No need to retest
0.9 ≤ COI< 1.1	Indeterminate	Need to retest
≥1.1	Positive for IgM	Need to confirmation test

- If the test result is "Negative" even though the patient has significant infectious symptoms, it should be recommended to conduct additional test including PCR or culture test.
- The accurate determination of test result as "Positive" should be confirmed by additional clinical evaluation.
- "Negative" result should be considered with possibilities of other infections. Positive result should be considered with additional infections by another pathogenic bacterium.

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are not provided with **ichroma™ COVID-19 Ab**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instruction for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical Sensitivity**
  - **Cut-off**

The **ichroma™ COVID-19 Ab** test result indicates 'positive' or 'negative' of a sample defined by the algorithm of ichroma™ reader based on COI (cut-off index).

Cut-off index (COI)	Result
< 0.9	Negative for IgG / IgM
0.9 ≤ COI< 1.1	Indeterminate
≥1.1	Positive for IgG / IgM

- **Analytical specificity**
  - **Cross-reactivity**

Biomolecules such as below the ones in the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood.

ichroma™ COVID-19 Ab test results did not show any significant cross-reactivity with these biomolecules.

No.	Name	Sample type
1	Cytomegalovirus(CMV)	Positive serum
2	Epstein-Barr virus(EBV)	Positive serum
3	Hepatitis A virus(HAV)	Positive serum
4	Hepatitis C virus(HCV)	Positive serum
5	Hepatitis B virus(HBV)	Positive serum
6	Herpes simplex virus(HSV)	Positive serum
7	Rubella virus	Positive serum
8	Varicella-zoster virus(VZV)	Positive serum
9	Treponema pallidum	Positive serum
10	Anti Nuclear Antibody(ANA)	Positive serum
11	Rheumatoid factor(RF)	Positive serum
12	Early stage of pregnancy	Pregnant women sample
13	Middle stage of pregnancy	Pregnant women sample
14	Hepatitis B antibody (anti-HBs)	Hepatitis B (HBsAg) Ab positive sample
15	Influenza A	Positive serum
16	Influenza B	Positive serum
17	RSV	Positive serum
18	Mycoplasma pneumoniae	Positive serum

- **Interference**

Interference materials such as below the ones in the table were added to the test sample(s) the same as the below concentrations. **ichroma™ COVID-19 Ab** test results did not show any significant interference with these materials.

No.	Interference material	Concentration
1	Li-Heparin	100,000 U/L
2	Na-Heparin	100,000 U/L
3	Na-EDTA	1.6 mg/mL (4 μM)
4	K_2-EDTA	1.6 mg/mL (4 μM)
5	Sodium citrate	25 mg/mL (0.085 μM)
6	Hemoglobin	2 mg/ml
7	BSA	60 mg/ml
8	Bilirubin	0.24 mg/mL (400 μM)
9	Triglycerides	1.5 mg/ml
10	Cholesterol	7.7 mg/mL (20 mM)

■ **Precision**

- Between lots

One person tested three different lots of **ichroma™ COVID-19 Ab**, ten times at each concentration of the control standard.

- Between persons

Three different persons tested one lot of **ichroma™ COVID-19 Ab**, ten times at each concentration of the control standard.

- Between days

One person tested one lot of **ichroma™ COVID-19 Ab** during three days, ten times at each concentration of the control standard.

- Between sites

One person tested **ichroma™ COVID-19 Ab** at three different site, ten times at each concentration of the control standard.

[IgG result]

Cal No.	Between lot		Between person	
	Positive/No.	Positive rate	Positive/No.	Positive rate
1	0/30	0%	0/30	0%
2	30/30	100%	30/30	100%
3	30/30	100%	30/30	100%
Cal No.	Between day		Between site	
	Positive/No.	Positive rate	Positive/No.	Positive rate
1	0/30	0%	0/30	0%
2	30/30	100%	30/30	100%
3	30/30	100%	30/30	100%

[IgM result]

Cal No.	Between lot		Between person	
	Positive / No.	Positive rate	Positive / No.	Positive rate
1	0/30	0%	0/30	0%
2	30/30	100%	30/30	100%
3	30/30	100%	30/30	100%
Cal No.	Between day		Between site	
	Positive / No.	Positive rate	Positive / No.	Positive rate
1	0/30	0%	0/30	0%
2	30/30	100%	30/30	100%
3	30/30	100%	30/30	100%

■ **Clinical performance evaluation**

ichroma™ COVID-19 Ab has demonstrated the following clinical performance results.

		RT-PCR		
		Positive	Negative	Total
ichroma™ COVID-19 Ab	Positive	46	0	46
	Negative	0	131	131
	Indeterminate	2	4	6
	Total	48	135	183

- Clinical sensitivity: 95.8%
- Clinical specificity: 97.0%

REFERENCES

1. Huang LR *et al.* Evaluation of Antibody Responses Against SARS Coronaviral Nucleocapsid or Spike Proteins by Immunoblotting or ELISA (2004) J Med Virol. 73: 33.
2. Woo PC et al. Longitudinal profile of immunoglobulin G (IgG), IgM, and IgA antibodies against the (SARS) coronavirus nucleocapsid protein in patients with pneumonia (2004) Clin Diagn Lab Immunol. 11: 665.
3. Wu HS et al. SARS-Associated Coronavirus Diagnostic kit_ development of an ELISA-based antibody detection test with a cocktail of nucleocapsid and spike SARS-CoV proteins (2008) J Clin Microbiol. 43: 3054.
4. Trivedi SU et al. Development and Evaluation of a Multiplexed Immunoassay for Simultaneous Detection of Serum IgG Antibodies to Six Human Coronaviruses (2019) Sci Rep. 9: 1390

Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
	Batch code
	Catalog number
	Caution
	Manufacturer
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

For technical assistance; please contact:
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