ichroma™ COVID-19 Ab

INTENDED USE

ichroma™ COVID-19 Ab in conjunction with ichroma™ II Reader is an *in vitro* diagnostic fluorescence Immunoassay intended for qualitative detection and differentiation of IgG/IgM antibodies to the novel coronavirus SARS-CoV-2 in human venous whole blood, serum or plasma samples.

ichroma™ COVID-19 Ab is indicated as an aid in the screening of asymptomatic individuals and patients with early, mild or acute symptoms suspected of COVID-19 disease at point-of-care sites and clinical laboratories.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease was first identified in 2019 in Wuhan, the capital of Hubei Province, China, and has since spread globally, resulting in the 2019–20 coronavirus pandemic.

The SARS-CoV-2 (2019-nCOV) 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).

As the disease could progress to life-threatening pneumonia and multi-organ failure, prevention and control of the infection has become very essential. Since the symptoms become rapidly severe after onset of illness in absence of specific treatment, early diagnosis of SARS-CoV-2 infection is quite crucial.

ichroma™ COVID-19 Ab test system is a rapid *in vitro* diagnostic test that qualitatively detects anti-SARS-CoV-2 IgG/IgM antibodies in venous whole blood, serum or plasma samples with high sensitivity.

The antibodies detected by the test indicate that a person had an immune response to SARS-CoV-2 irrespective of whether the individual developed any symptoms after the infection, or he/she was asymptomatic. The test results are important in detecting infections with few or no symptoms.

In case of COVID-19, time from exposure to onset of symptoms varies from two days to two weeks. IgM antibodies usually appear in the patient's blood within a week after infection while IgG antibodies appear within 2-4 weeks after infection.

Hence, detection of anti-SARS-Cov-2 antibodies in patient specimens has clinical significance for prevention or effective control of community spread of COVID-19.

Moreover, periodic serological tests after confirmation of SARS-CoV-2 infection in a patient, may help determine the course of treatment.

PRINCIPLE

ichroma™ COVID-19 Ab for use in conjunction with ichroma™ II Reader, is an in vitro diagnostic test system based on lateral flow sandwich detection immunofluorescence technology.

Lyophilized detection buffer in the detection buffer tube is reconstituted with the diluent/reconstitution buffer and patient specimen is mixed with the reconstituted detection buffer resulting in binding of the fluorochrome-antigen conjugates from the detection buffer with the anti-SARS-CoV-2 IgG/IgM antibodies present in the clinical sample.

When clinical sample-detection buffer mixture is added into the 'sample well' of the ichroma™ COVID-19 Ab test cartridge, the test mixture migrates through its test strip.

Complexes of fluorochrome-antigen conjugates with anti-SARS-CoV-2 IgG/IgM antibodies from the test mixture are further captured by the anti-human IgG and anti-human IgM antibodies immobilized respectively at the 'IgG test line' and the 'IgM test line' of the test cartridge.

The sample-loaded test cartridge is scanned/read by the ichroma™ II Reader after allowing the sample-loaded test cartridge to complete the incubation/reaction time of 10 minutes.

The laser light source illuminates the cartridge membrane thereby triggering fluorescence from the fluorochrome-labeled complexes accumulated at the test lines and the control line.

While computing the test result, ichroma™ II Reader takes into account ratio of fluorescence generated at the respective test line to that at the control line.

Intensity of the fluorescence is scanned and converted into an electric signal which correlates to the intensity of fluorescence generated at the respective test line and hence to the concentration of respective anti-SARS-CoV-2 antibodies in the test sample.

Ichroma™ II Reader computes respective anti-SARS-CoV-2 antibodies concentration and ultimately displays the ichroma™ COVID-19 Ab test result qualitatively as 'Negative' or 'Indeterminate' or 'Positive' based on pre-programed analytical equivocal zone and cut-offs.

TEST COMPONENTS

For performing ichroma™ COVID-19 Ab test on a clinical sample, following test components are required:

- **ichroma™ COVID-19 Ab Test Cartridge**
- **ichroma™ COVID-19 Ab Detection Buffer Tube** (containing a pellet of the lyophilized detection buffer)
- **ichroma™ COVID-19 Ab Reconstitution Buffer Tube** (150 µL of reconstitution buffer/diluent from the tube)
- **ichroma™ COVID-19 Ab Test ID Chip**
- **ichroma™ II Reader**

MATERIALS SUPPLIED

REF CFPC-114

Each box of ichroma™ COVID-19 Ab test cartridges contains the following items:

- 25 individually sealed ichroma COVID-19 Ab Test Cartridges

- 25 ichroma™ COVID-19 Ab Detection Buffer Tubes (Each containing a pellet of the lyophilized detection buffer)
- 1 ichroma™ COVID-19 Ab Reconstitution Buffer Tube (containing 4.5 mL of the reconstitution buffer/diluent)
- 1 ichroma™ COVID-19 Ab Test ID Chip
- 1 Package Insert of ichroma™ COVID-19 Ab Test

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from ichroma™ COVID-19 Ab Test Cartridge box.

Please contact the manufacturer or its authorized distributor for more information.

- **ichroma™ Reader** REF FPRR021
- **ichroma™ COVID-19 Ab Controls**
- **Micropipette and pipette tips**

STABILITY, STORAGE AND HANDLING OF TEST ITEMS

- ichroma™ COVID-19 Ab test cartridges, detection buffer tubes and the reconstitution buffer tube have a shelf-life of 20 months if stored in sealed/unopened conditions at 2-30 °C.
- If stored in cold conditions, allow the sealed test cartridges, detection buffer tubes, reconstitution buffer tube and controls to attain room temperature (15-30°C) for 15-30 minutes prior to using for the test.
- ichroma™ COVID-19 Ab test cartridge pouch and detection buffer tube should not be opened until just prior to actual use of these items for performing the test.
- ichroma™ COVID-19 Ab reconstitution buffer should not be used after 12 months once the reconstitution buffer tube is opened for the first time.
- Expiration date is printed on the label of the test cartridge box as well as on each test cartridge pouch.
- Never freeze any of the test items.

INSTRUCTIONS, PRECAUTIONS AND WARNINGS

- This test has not been reviewed by the FDA.
- For *in vitro* diagnostic use only.
- For prescription use only
- Carefully follow the instructions, precautions, warnings and procedures described in this package insert.
- Please refer to the operation manual of ichroma™ II Reader for operating instructions and complete information.
- Only the test cartridges, detection buffer tubes and the reconstitution buffer tube included in the ichroma™ COVID-19 Ab test cartridge box should be used for performing ichroma™ COVID-19 Ab test.
- Never interchange the test components between ichroma™ COVID-19 Ab test cartridge boxes of different lot numbers. Otherwise, the test results may be erroneous or misleading.
- Never use the test cartridge or any reagent of any other marketed COVID-19/SARS-CoV-2/2019-nCoV IVD test product/kit for performing ichroma™ COVID-19 Ab test. Otherwise, test results may be erroneous or misleading.
- For performing ichroma™ COVID-19 Ab test using test cartridge of given lot number, ichroma™ COVID-19 Ab ID chip of matching lot number must be currently or previously inserted into the ID Chip port of ichroma™ II Reader.
- Do not use any ichroma™ COVID-19 Ab test cartridge or detection buffer tube if it is found already unsealed/ opened or damaged.
- Never use any test component past the expiration date printed on the label of test cartridge box and cartridge pouch.
- Do not use the reconstitution buffer if 12 months have passed since the ichroma™ COVID-19 Ab reconstitution buffer tube was opened for the first time.
- Never reuse any test cartridge or detection buffer tube. Discard these test components after single use.
- ichroma™ COVID-19 Ab Controls which are supplied on demand separately from the test cartridge box, must be tested as recommended in this package insert.
- Wear protective clothing such as laboratory coats, masks, disposable gloves and eye protection when specimens are collected, processed and tested.
- The reconstitution buffer diluent contains sodium azide as preservative, contact of which with eyes, skin or clothing should be avoided. If it happens, please wash the affected part immediately under running water.
- 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.
- Used test cartridges, detection buffer tubes, reconstitution buffer tube, pipette tips etc. should be handled carefully and must be disposed in accordance with relevant local regulations.

SAMPLE COLLECTION, PROCESSING AND HANDLING

- ichroma™ COVID-19 Ab test should be performed only on following sample types:

Sample type	Recommended anticoagulant
Venous whole blood and plasma	Na-Heparin Li-Heparin, K_2 EDTA, Sodium Citrate
Serum	*Not applicable*

- Serum or plasma should be obtained within 3 hours after the collection of venous whole blood.
- It is recommended to test venous whole blood, serum and plasma sample within 24 hours after collection/ processing.
- Anti-coagulated venous whole blood samples should be tested within 4 hours after collection from patients if stored at room temperature (~25°C) and within 24 hours if stored at 2~8°C in a refrigerator.
- Venous whole blood samples should not be frozen in any case.
- Serum/plasma samples should be tested within 4 hours after collection from patients if stored at room

temperature (15-30°C) and within 48 hours if stored at 2~8°C in a refrigerator. For longer storage, serum or plasma samples should be immediately frozen at <-20 °C.

- Once frozen, serum/plasma samples should be thawed one time only for performing the test, because repeated freezing and thawing may result in erroneous/ misleading test results.
- Never test hemolyzed, lipemic or icteric clinical samples.
- If required to be shipped, clinical samples must be packed in accordance with relevant regulations.

TEST SETUP

- Arrange the following test items:
- **1 sealed ichroma™ COVID-19 Ab Test Cartridge**
- **1 ichroma™ COVID-19 Ab Detection Buffer Tube**
- **ichroma™ COVID-19 Ab Reconstitution Buffer Tube** (containing the reconstitution buffer/diluent)
- **ichroma™ COVID-19 Ab ID Chip** of lot number matching with that of the test cartridge, detection buffer tube and reconstitution buffer tube
- **Micropipette and ordinary pipette tips**
- **ichroma™ II Reader**

(**Note:** If stored in cold conditions, allow the sealed test cartridges, detection buffer tubes, reconstitution buffer tube and controls to attain room temperature (15-30°C) for 15-30 minutes prior to using for the test.

- Switch on the ichroma™ II Reader at least 15 minutes before running ichroma™ COVID-19 Ab test.

(Please refer to the operation manual of ichroma™ II Reader for operating instructions and complete information.)

- After completion of automatic self-test, ichroma™ II Reader should display the home screen thereby indicating that it is ready for running a test.
- Tap the 'QC test' icon on the screen if you need to perform the system check (using ichroma™ System Check Cartridge and System Check ID Chip and/or test ichroma™ COVID-19 Ab Controls.

(Please refer to the section 'System Check and External Control Testing' of this package insert.)

TEST PROCEDURE

- Tap 'Single Test' or 'Multi Test' icon on the home screen depending on under which mode you want to operate the ichroma™ II Reader for performing the test.

(**Note:** Under the 'Single Test' mode of operation, sample-loaded test cartridge is inserted in the cartridge holder of ichroma™ II Reader immediately after loading the test sample-detection buffer mixture into the sample well of the test cartridge but ichroma™ II Reader scans the inserted test cartridge and displays the test result after completion of the reaction time of 10 minutes after the test run is initiated.

Under the 'Multi Test' mode of operation, sample-loaded test cartridge is inserted in the cartridge holder of ichroma™ II Reader after completion of the reaction time of 10 minutes after loading the test sample-detection buffer mixture into the sample well of the test cartridge and ichroma™ II Reader scans the inserted test cartridge immediately after the sample-loaded test cartridge is inserted and test run is initiated.

Multi-mode is suitable for high-work load conditions as up to 100 ichroma™ COVID-19 Ab tests can be performed per hour).

- Log-in by inputting your registered User ID and password.
- Remove the ichroma™ COVID-19 Ab test cartridge from its aluminum foil and place it on a clean, dust-free, dry and flat surface.
- Insert the ichroma™ COVID-19 Ab Test ID Chip having exactly same lot number as that of the ichroma™ COVID-19 Ab test cartridge, detection buffer tube and reconstitution buffer tube if information of the same ID chip is not currently stored in the memory of ichroma™ II Reader.
- Reconstitute/dissolve the pellet of the lyophilized detection buffer in an ichroma™ COVID-19 Ab Detection Buffer by transferring 150 µL of the reconstitution buffer form the ichroma™ COVID-19 Ab Reconstitution Buffer Tube using a micropipette.
- Transfer 10 µL of the clinical sample (human venous whole blood, serum or plasma) to the ichroma™ COVID-19 Ab Detection Buffer Tube containing the reconstituted detection buffer.
- Close the lid of the detection buffer tube and shake it 10 times or more to mix its content well.
- Immediately pipette out 75µL of the clinical sample-detection buffer mixture and load it into the sample well on the ichroma™ COVID-19 Ab test cartridge.

(**Note:** Do not load the sample mixture into the 'scanning window' of the test cartridge. Otherwise the test result will be erroneous or misleading.)

- **For testing under 'Single Test' mode**, insert the sample-loaded test cartridge in the cartridge holder of ichroma™ II Reader immediately after loading the test sample mixture.
- Initiate the test run by tapping the 'Start' button on the display screen immediately after inserting the sample-loaded test cartridge.
- ichroma™ II Reader scans the inserted test cartridge and displays the test result after completion of the reaction time of 10 minutes.
- **For testing under 'Multi Test' mode**, leave the sample-loaded test cartridge for precisely 10 minutes before inserting it in the cartridge holder of ichroma™ II Reader.
- Initiate the test run by tapping the 'Start' button on the display screen immediately after inserting the sample-loaded test cartridge.
- ichroma™ II Reader scans the inserted test cartridge and displays the test result immediately after the test run is initiated.

DISPLAY AND INTERPRETATION OF TEST RESULT

- ichroma™ II Reader displays the ichroma™ COVID-19 Ab test result qualitatively as 'Negative' or 'Indeterminate' or 'Positive' while also displaying test result numerically in terms of cut-off index (COI) value as follows:

ichroma™ COVID-19 Ab test result displayed by ichroma™ II Reader
COVID-19 Ab IgM *COI Negative or Indeterminate or Positive COVID-19 Ab IgG *COI Negative or Indeterminate or Positive
*Test result is negative if COI is < 0.9, indeterminate if COI is 0.9-1.1 and positive if COI is >1.1-200.

- If ichroma™ COVID-19 Ab test result is 'Negative' for IgG as well as for IgM, the patient may not be infected with anti-SARS-CoV-2 but follow-up testing with a molecular diagnostic test should be considered to rule out infection in these individuals.
- If the test result is 'Indeterminate' for IgG and/or for IgM, the patient may be infected with anti-SARS-CoV-2 and hence there is need to retest another sample from the patient.
- If the test result is 'Positive' for IgG and/or for IgM, the patient is most likely to be infected with anti-SARS-CoV-2.
- If the test result is 'Invalid', there must have been some procedural error or malfunction of test cartridge and/or ichroma™ II Reader.

  Retest another sample from the patient and if the test result continues to be displayed as 'Invalid', contact the manufacturer or its authorized service provider.

PERFORMING SYSTEM CHECK AND TESTING EXRERNAL CONTROLS

- System check and external control testing are to be carried out under the 'QC Test' mode of ichroma™ II Reader.

  (Refer to the operation manual of ichroma™ II Reader for details of system check and control testing procedures.)
- System check is additional tool to ascertain whether the optical system of ichroma™ II Reader is functioning as per pre-programmed specifications and whether the reader would provide accurate and reliable test results.
- System check needs to be performed using the set of ichroma™ System Check Cartridge and matching System Check ID Chip which is included in the commercial package of ichroma™ II Reader.
- ichroma™ COVID-19 Ab Controls are meant for monitoring the performance of ichroma™ COVID-19 Ab test system.
- ichroma™ COVID-19 Ab test results of clinical samples tested using a given lot of ichroma™ COVID-19 Ab test cartridges should not be considered valid and reliable/acceptable unless corroborated with valid/ acceptable results of 'system check' of ichroma™ II Reader as well as expected/valid/acceptable results of both of ichroma™ COVID-19 Ab Controls tested using the same test system.
- Following external controls are provided on demand separately from ichroma™ COVID-19 Ab test cartridge box:

ichroma™ COVID-19 Ab Controls	**Expected/valid/acceptable control result**
ichroma™ COVID-19 Ab Negative Control	COVID-19 Ab IgM *COI Negative COVID-19 Ab IgG *COI Negative
ichroma™ COVID-19 Ab Positive Control	COVID-19 Ab IgM *COI Positive COVID-19 Ab IgG *COI Positive
*Control result is negative if COI is < 0.9, indeterminate if COI is 0.9-1.1 and positive if COI is >1.1. *If either control result is 'Indeterminate', it should be considered invalid/unacceptable and the same control should be retested.	

- **The user laboratory should perform system check of ichroma™ II Reader and test both ichroma™ COVID-19 Ab Controls whenever any of the following situations is encountered:**

- Before testing clinical samples with any new lot of ichroma™ COVID-19 Ab test cartridges
- Before testing clinical samples with any new shipment of ichroma™ COVID-19 Ab test cartridges even if it belongs to a previously tested lot
- If a newly registered operator is operating the ichroma™ COVID-19 Ab test system for the first time
- If the operator is already registered but he/she has not performed any testing within last two weeks
- If there is any question concerning validity/accuracy of ichroma™ COVID-19 Ab test results of clinical samples
- If there is any concern regarding physical and/or functional integrity of ichroma™ II Reader
- Immediately after the 'System administrator' has changed the date/time setting of ichroma™ II Reader
- After ichroma™ II Reader software/firmware upgrade by any authorized person
- After any servicing of ichroma™ II Reader by the manufacturer's technical services or its authorized service provider
- As per requirements of local, state and/or federal regulations, accrediting organizations, or laboratory operating procedures

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive results due to cross-reactions and/or non-specific adhesion of certain components of the clinical samples to the capture/detector antibodies of the test cartridge.
- Positive results may also be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.
- The test may yield false negative results. Non-responsiveness of the antigen to the antibodies is common when the epitope is masked by some unknown components, so as not to be detected or captured by the antibodies.

Also, instability or degradation of the antigen with time and/or temperature may cause false negative result as it makes the antigen unrecognizable by the antibodies.

- 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.
- Other factors such as technical/procedural errors, degradation of the test components/reagents, presence of interfering substances in the specimens, etc. may cause erroneous or misleading results.
- 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.
- 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.

SUMMARY OF PERFORMANCE CHARACTERISTICS

(**Note:** *Though the analytical performance characteristics of ichroma™ COVID-19 Ab test have been validated, additional analytical and clinical performance studies are still ongoing and hence, following section will be updated as more data become available in coming days.*)

■ Analytical sensitivity:

- ichroma™ II Reader computes respective anti-SARS-CoV-2 antibodies concentration and ultimately displays the ichroma™ COVID-19 Ab test result qualitatively as 'Negative' or 'Indeterminate' or 'Positive' based on pre-programed analytical equivocal zone and cut-offs while also displaying test result numerically in terms of cut-off index (COI) value
- Test result is negative if cut-of-index (COI) is < 0.9, indeterminate if COI is 0.9-1.1 and positive if COI is >1.1-200.
- Cut-off index of ichroma™ COVID-19 Ab has been determined and validated using 60 samples confirmed as negative by a molecular test.

■ Analytical specificity

- **Cross-reactivity**

ichroma™ COVID-19 Ab test has not shown any significant cross-reactivity when clinical samples obtained from patients with following infections and physiological conditions were tested:

Clinical sample	Sample type
Cytomegalovirus(CMV)	Positive serum
Epstein-Barr virus (EBV)	Positive serum
Hepatitis A virus (HAV)	Positive serum
Hepatitis C virus (HCV)	Positive serum
Hepatitis B virus (HBV)	Positive serum
Herpes simplex virus (HSV)	Positive serum
Rubella virus	Positive serum
Varicella-zoster virus (VZV)	Positive serum
Treponema pallidum	Positive serum
Anti-nuclear Antibody (ANA)	Positive serum
Rheumatoid factor (RF)	Positive serum
Early stage of pregnancy	Pregnant woman's serum
Middle stage of pregnancy	Pregnant woman's serum
Hepatitis B antibody (anti-HBs)	Hepatitis B Antibodies sample
Influenza A	Positive serum
Influenza B	Positive serum
RSV	Positive serum
Mycoplasma pneumoniae	Positive serum

- **Interference**

ichroma™ COVID-19 Ab test did not show significant interference when test samples spiked with following endogenous substances and chemicals at a concentration much higher than their normal physiological level in human blood, were tested.

Interferent	Interferent concentration tested
Lithium heparin	100,000 U/L
Sodium heparin	100,000 U/L
Sodium EDTA	1.6 mg/mL (4 μM)
Potassium EDTA	1.6 mg/mL (4 μM)
Sodium citrate	25 mg/mL (0.085 μM)
Hemoglobin	2 mg/ml
BSA	60 mg/ml
Bilirubin	0.24 mg/mL (400 μM)
Triglycerides	1.5 mg/ml
Cholesterol	7.7 mg/mL (20 mM)

■ Clinical performance evaluation

ichroma™ COVID-19 Ab has demonstrated following clinical performance results when clinical samples collected from various asymptomatic individuals and patients suspected of COVID-19 disease were tested with ichroma™ COVID-19 Ab test and confirmed by testing with Allplex™ 2019-nCoV Assay (Seegene Inc., South Korea)

		2019-nCOV RT-PCR assay		
		Positive	Negative	Total
ichroma™ COVID-19 Ab	Positive	46	0	46
	Negative	0	131	131
	Indeterminate	2	4	6
	Total	48	135	183

- Positive Percent Agreement: 95.8%
- Negative Percent Agreement: 97.0%

Note: Please refer to the table below to know the meaning of various symbols which may be printed on the labels of various components of ichroma™ COVID-19 test system.

	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

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