Infection

ichroma™ CHIKV IgG/IgM

INTENDED USE

ichroma™ CHIKV IgG/IgM is a fluorescence immunoassay (FIA) for the qualitative determination of IgG/IgM antibodies against chikungunya virus in human whole blood/serum/plasma. It is useful as an aid in screening of chikungunya virus infection.

For *in vitro* diagnostic use only.

INTRODUCTION

Chikungunya virus (CHIKV), a mosquito-borne virus, phylogenetically belongs to the genus Alphavirus. According to reports of the epidemiology, chikungunya virus is highly prevalent in tropical/subtropical area worldwide, likely to Flavivirus. Chikungunya virus infection causes clinically a wide range of human diseases from fever to severe arthralgia[1]. Several lines of evidences show that clinical symptoms of CHIKV infection are more prolonged for 1 year than it of dengue virus[2], which means it is not only crucial to detect CHIKV-specific IgM but CHIKV-specific IgG simultaneously. Although there are many types of serological diagnostic reagents including enzyme-linked immunosorbent assay (ELISA) or gold rapid test (RDT), development of simultaneous and accurate kit of IgG and IgM detection is required.[3]

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antigens in buffer bind to antibodies in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized antibodies on a test strip.

More antibodies in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal which is processed by the instrument for ichroma™ tests to show the 'CHIKV IgG/IgM positive/negative/indeterminate' in the sample.

COMPONENTS

ichroma™ CHIKV IgG/IgM consists of 'cartridge', 'detector tube' and 'detector diluent'.

- The cartridge contains the membrane called a test strip which has anti-IgM and anti-IgG at each test lines respectively, with chicken IgY at the control line.
- The detector tube has 2 granules containing CHIKV antigen fluorescence conjugate, anti-chicken IgY fluorescence conjugate. All detector tubes are packed in a pouch.
- The detector diluent contains sodium azide as a preservative in potassium phosphate 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 instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detector tube, detector diluent and ID chip) must match each other.
- Do not interchange the test components between different lots or use test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges or detector tubes. A cartridge should be used for testing of one sample only. A detector tube should be used for processing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use 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.
- If test components and/or sample are stored in refrigerator, then allow cartridge, detector tube, detector diluent and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests 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 relevant local regulations.
- The detector diluent contains sodium azide (NaN_3), and it may cause certain health issues like convulsions, low blood pressure, low heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- **ichroma™ CHIKV IgG/IgM** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ CHIKV IgG/IgM** should be used only in conjunction with instrument for ichroma™ tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
Na_2EDTA, K_2-EDTA, Sodium Heparin, Lithium Heparin, Sodium citrate

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 antigens to the antibodies which is the 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 antigens with time and/or temperature may also cause false negative result as it makes the antigens 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 in conjunction with clinical symptoms and other relevant test results.

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.

MATERIALS SUPPLIED

REF CFPC-95

Components of **ichroma™ CHIKV IgG/IgM**

- Cartridge box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 1
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **ichroma™ CHIKV IgG/IgM**.

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M2** REF FPRR031
  - **ichroma™ -50 PLUS** REF FPRR036
- **Boditech CHIKV IgG/IgM Control** REF CFPO-392

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ CHIKV IgG/IgM** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection when collected sample is stored at room temperature.
- The samples (serum, plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (whole blood, serum, plasma) may be stored for up to a week at 2-8 °C prior to being tested. If testing will be delayed more than a week, samples (serum, plasma) should be frozen at -20 °C.
- The samples (serum, plasma) stored frozen at -20 °C for 8 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the contents of **ichroma™ CHIKV IgG/IgM**: Sealed cartridges, detector tubes, a detector diluent, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the detector tube, the 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.
- Turn on the instrument for ichroma™ tests.
- Insert the ID chip into the 'ID chip port'.

※ Please refer to the instrument for ichroma™ tests operation manual for the complete information and operating instructions.

TEST PROCEDURE

▶ ichroma™ II, ichroma™ M2

Multi test mode/Read now mode

1) Select the sample type (whole blood or serum/plasma) on the screen.
2) Take 150 µL of detector diluent using a pipette and dispense it to the detector tube containing granules. When the granule form is completely dissolved in the tube, it becomes detection buffer.
   (The detection buffer must be used immediately. Do not exceed 30 seconds.)
3) Take 30 µL of sample (whole blood/serum/plasma/control) using a pipette and dispense it to the detector tube.
4) Close the lid of the detector tube and mix the sample thoroughly by shaking about 10 times.
   (The sample mixture must be used immediately. Do not exceed 30 seconds.)
5) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
6) Leave the cartridge at room temperature for 12 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inexact test result.*
7) 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 has been marked on the cartridge especially for this purpose.
8) Tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
   (ichroma™ M2 will start the test automatically after inserting.)
9) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.

10) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode/Walk away mode

1) The test procedure is same with the 'Multi test mode 1) – 5)'.
2) Insert the sample-loaded cartridges into the 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.
3) Tap the 'Start' button on the instrument for ichroma™ tests.
(ichroma™ M2 will start the test automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 12 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ ichroma™ III

1) The test procedure is same with the 'Single test mode'.

▶ ichroma™ -50 PLUS

1) Insert the tip array in the tip station.
2) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
6) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip that you want to use.
7) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
8) Set the number of pipette tips by tapping.
9) Select the sample type (whole blood or serum/plasma) on the screen.
10) Tap the 'Start' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays "G (COI value): P / N / I", "M (COI value): P / N / I".
- Ancillary value is served in the form of a cut-off index (COI).

Cut-off index (COI)	Result	Note
< 0.9	Negative for CHIKV IgG / IgM	No need to additional test.
≥ 0.9, < 1.1	Indeterminate	Need to retest.
≥ 1.1	Positive for CHIKV IgG / IgM	Need to confirmation test.

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.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ichroma™ CHIKV IgG/IgM**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
(Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical Sensitivity**
  - **Cut-off**
  The **ichroma™ CHIKV IgG/IgM** 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
COI ≥ 1.1	Positive
0.9 ≤ COI < 1.1	Indeterminate
COI < 0.9	Negative

- **Analytical specificity**
  - **Cross-reactivity**
  There was no significant cross-reactivity from these materials the **ichroma™ CHIKV IgG/IgM** test measurement.

Cross-reactivity Materials	
#1	Cytomegalovirus (CMV)
#2	Epstein-Barr virus (EBV)
#3	Hepatitis A virus(HAV)
#4	Hepatitis C virus(HCV)
#5	Hepatitis B virus(HBV)
#6	Herpes simplex virus(HSV)
#7	Rubella virus
#8	Varicella-zoster virus(VZV)
#9	Treponema pallidum
#10	Anti Nuclear antibody(ANA)
#11	Rheumatoid factor(RF)
#12	Early stage of pregnancy
#13	Middle stage of pregnancy
#14	Hepatitis B antibody(anti-HBs)
#15	Influenza A
#16	Influenza B
#17	Yellow fever virus
#18	Lyme disease
#19	Leptospirosis
#20	Eastern equine encephalitis virus
#21	West Nile virus
#22	Japanese encephalitis virus
#23	Saint Louis encephalitis virus
#24	Dengue virus
#25	Zika virus

- **Interference**
  There was no significant interference from these materials with the **ichroma™ CHIKV IgG/IgM** test measurements.

	Interferents	Concentration
1	Sodium Heparin	100,000 U/L
2	Lithium heparin	100,000 U/L
3	K_2 EDTA	2 mg/mL, (5 μM)
4	Na_2 EDTA	2 mg/mL, (5 μM)
5	Sodium citrate	25 mg/mL, (0.085 M)
6	Bilirubin (conjugated)	0.24 mg/mL, (400 μM)
7	Hemoglobin	2 mg/mL
8	Triglycerides	1.5 mg/mL
9	Cholesterol	7.7 mg/mL, (20 mM)
10	BSA	60 g/L
11	DMSO	solvent
12	DMF	solvent
13	DDW	solvent

- **Precision**
  - Between Lot
    One person tested three different lots of **ichroma™ CHIKV IgG/IgM**, five times at each concentration of the control standard.
  - Between person
    Three different persons tested same lot of **ichroma™ CHIKV IgG/IgM**, five times at each concentration of the control standard.
  - Between day
    One person tested same lot of **ichroma™ CHIKV IgG/IgM** for three days, five times at each concentration of the control standard.
  - Between site
    One person tested same lot of **ichroma™ CHIKV IgG/IgM** at three different sites, five times at each concentration of the control standard.

Standard material	Between lot	Between person	Between day	Between site
	Positive ratio	Positive ratio	Positive ratio	Positive ratio
Negative	0 %	0 %	0 %	0 %
High	100 %	100 %	100 %	100 %
Mid	100 %	100 %	100 %	100 %
Low	100 %	100 %	100 %	100 %

- **Comparability**

CHIKV IgG		Reference reagent 1		
		Positive	Negative	Total
ichroma™ CHIKV IgG/IgM	Positive	60	0	60
	Negative	1	21	22
	Total	22	61	21
Percent positive agreement		98.4 %		
Percent negative agreement		100.0 %		
Overall percent agreement		98.8 %		

CHIKV IgM		Reference reagent 2		
		Positive	Negative	Total
ichroma™ CHIKV IgG/IgM	Positive	18	1	19
	Negative	2	32	34
	Total	22	20	33
Percent positive agreement		90.0 %		
Percent negative agreement		97.0 %		
Overall percent agreement		94.3 %		

REFERENCES

1. Chikungunya Fact sheet. WHO, April 2016
2. Chikungunya virus infection: an overview. Caglioti et. al., The New Microbiologica. 2013
3. Chikungunya fever: Epidemiology, clinical syndrome, pathogenesis and therapy. Thiberville et. al., Antiviral research., 2013
4. Chikungunya: a re-emerging virus: Burt et. al., The Lancet., 2012

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

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

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