Infection

ichroma™ Anti-HBs

INTENDED USE

ichroma™ Anti-HBs is a fluorescence Immunoassay (FIA) for the qualitative determination of antibody to Hepatitis B surface antigen (anti-HBs) in human whole blood/serum/plasma. It is useful as an aid to diagnosis of HBV infection or following Hepatitis B virus vaccination.

For *in vitro* diagnostic use only.

INTRODUCTION

Viral hepatitis is a serious global health problem affecting over two billion people worldwide and approximately one million people die each year due to cirrhosis of the liver and hepatocellular carcinoma (HCC), which are commonly associated with chronic hepatitis. The majority of hepatitis viral infections are caused by three distinct virus types: Hepatitis A (HAV, Hepatitis B(HBV), Hepatitis C (HCV). [1,2] The risk of developing chronic infection by HBV varies inversely with age and is highest for infants infected at birth compared to older children and adults. Up to 90% of infants infected with HBV will develop chronic infection leading to cirrhosis of the liver or HCC compared to 6-10% of adults who acquire HBV infection.[3] Determination of antibodies directed against HBV surface antigen (anti-HBs) is used to evaluate a person's immune status to HBV infection or to aid in the laboratory diagnosis of HBV infection when used in conjunction with other laboratory methods. The test is performed to assess the need for vaccination (if anti-HBs is absent or below levels considered protective), following completion of vaccination against HBV in high risk groups (healthcare workers, chronic renal failure patients, HIV infected persons), or to monitor recovery from acute HBV infection. The presence of anti-HBs following acute infection generally indicates recovery and immunity from reinfection.

PRINCIPLE

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

More antibodies in the sample will form the 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 'Positive' / 'Negative' / 'Indeterminate' in the sample.

COMPONENTS

ichroma™ Anti-HBs consists of 'cartridges', 'detector tubes' and 'detector diluent'.

- The cartridge contains the membrane called a test strip which has recombinant HBsAg at the test line 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 anti human HBsAg-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative in Tris-HCl. All detector tubes are packed in a box.
- The detector diluent contains salt and bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative in Tris-HCl 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 'Instruction 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 the 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 one sample only. A detector tube should be used for processing of one sample only.
- 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 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 components contain NaN3 (sodium azide), may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure. Therefore, please avoid it contacts to eyes, skin, or clothing. If it happens, please wash with running water immediately.

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

Recommended anticoagulant
Na EDTA, K_2 EDTA, K_3 EDTA, Na-heparin, Li-heparin, Sodium citrate

STORAGE AND STABILITY

Component	Storage condition: Storage Temperature	Storage condition: Shelf life	Note
Cartridge	4 - 30 °C	20 months	Disposable
Detector tube	2 - 8 °C	20 months	Disposable
Detector diluent	2 – 8 °C	20 months	Unopened
			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 antigens.
- The test may yield false negative result(s) due to the non-responsiveness of the antigen 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 antigen with time and/or temperature may also cause false negative result as it makes antigen unrecognizable by the antibodies.
- 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-52

Components of **ichroma™ Anti-HBs**

- Cartridge Box:
  - Cartridge 25
  - ID Chip 1
  - Instruction for Use 1
- Buffer Box:
  - Detector tube 25
  - Detector diluent 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ Anti-HBs**.

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M2** REF FPRR031
- **Boditech Anti-HBs Control** REF CFPO-144

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ Anti-HBs** 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.
- Samples 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 should be frozen at -20 °C.
- Samples stored frozen at -20 °C for 2 months showed no performance difference.
- 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

- **ichroma™ Anti-HBs** should be performed at environment temperature 25 ± 3℃.
- Check the contents of **ichroma™ Anti-HBs**: Sealed cartridges, detector tubes, detect diluent, ID chip and Instruction for use.
- Ensure that the lot number of the cartridge matches that of 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.
- Turn on the Instrument for ichroma™ tests.
- Insert the ID Chip into the ID chip port of the instrument for ichroma™ tests**.**
  (Please refer to the 'Instrument for ichroma™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

< Multi test mode - ichroma™ II >
< Read now mode - ichroma™ M2 >

1) Transfer 100 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 50 µL of sample (Human whole blood/serum/plasma/control) using a pipette to a detector tube.
3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 10-20 times. (The sample mixture must be used immediately.)
4) Pipette out 100 µL of a sample mixture and load it into the sample well on the cartridge.
5) Leave the cartridge at room temperature for 15 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 - ichroma™ II >
< Walk away mode - ichroma™ M2 >
1) Transfer 100 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 50 µL of sample (Human whole blood/serum/plasma/control) using a pipette to a detector tube.
3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 10-20 times. (The sample mixture must be used immediately.)
4) Pipette out 100 µL of a sample mixture and load it into the sample well on the cartridge.
5) 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.
6) Tap the "START" button on the instrument for ichroma™ test.
7) Cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 15 minutes.
8) Read the test result on the display screen of the instrument for ichroma™ tests.

< ichroma™ III >
1) The test procedure is same with "Single test 1) – 8)".

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays "Positive" / "Negative" / "Indeterminate".

Result (mIU/mL)	Result	Note
≤ 5	Negative for anti-HBs.	No need to additional test.
5 < Titer < 15	Indeterminate.	Need to retest.
≥ 15	Positive for anti-HBs.	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.
- 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™ Anti-HBs**. 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**
  - Limit of Blank (LOB): 3.60 mIU/mL
  - Limit of Detection (LOD): 4.55 mIU/mL
  - Cut-off: 15 mIU/mL
- **Analytical Specificity**
  - Cross-reactivity
    There was no significant cross-reactions in the **ichroma™ Anti-HBs** test measurement.

No.	Cross-reactivity materials
1	Cytomegalovirus (CMV)
2	Epstein-Barr virus (EBV)
3	Hepatitis A virus(HAV)
4	Hepatitis C virus(HCV)
5	Herpes simplex virus(HSV)
6	Rubella virus
7	Varicella-zoster virus(VZV)
8	Treponema pallidum
9	Anti Nuclear Antibody(ANA)
10	Rheumatoid factor(RF)
11	Early stage of pregnancy
12	Middle stage of pregnancy

  - Interference
    There was no significant interference from these material with the **ichroma™ Anti-HBs** test.

No.	Interference materials	Conc.
1	Heparin	100,000 U/L
2	EDTA	4 µM
3	Sodium citrate	0.085 M
4	Hemoglobin	2 mg/mL
5	BSA	60 mg/mL
6	Bilirubin	400 µM
7	Triglycerides	1.5 mg/mL
8	Cholesterol	20 mM

- **Precision**
  - Between lot
    One person tested three different lots of **ichroma™ Anti-HBs**, ten times at each concentration of the control standard.
  - Between person
    Three different persons tested same lot of **ichroma™ Anti-HBs**, five times at each concentration of the control standard.
  - Between day
    One person tested one lot of **ichroma™ Anti-HBs** during three days, five times at each concentration of the control standard.
  - Between site
    One person tested one lot of **ichroma™ Anti-HBs** in three different site, five times at each concentration of the control standard.

Cal	Between lot		Between person	
	Positive/ Number of tests	Positive rate	Positive/ Number of tests	Positive rate
Negative	0/30	0%	0/15	0%
High	30/30	100%	15/15	100%
Mid	30/30	100%	15/15	100%
Low	30/30	100%	15/15	100%
Cal	Between day		Between site	
	Positive/ Number of tests	Positive rate	Positive/ Number of tests	Positive rate
Negative	0/15	0%	0/15	0%
High	15/15	100%	15/15	100%
Mid	15/15	100%	15/15	100%
Low	15/15	100%	15/15	100%

■ **Comparability with reference product**

		Reference product		
		Positive	Negative	Total
ichroma™ Anti-HBs	Positive	112	5	117
	Negative	10	679	689
	Total	122	684	806

- Positive Comparability: 91.8 %
- Negative Comparability: 99.3 %
- Total Comparability: 98.1 %

REFERENCES

1. The Global Burden of Liver Disease: The Major Impact of China. Hepatology. 2014, 60:2099-2108
2. Viral hepatitis in resource-limited countries and access to antiviral therapies: current and future challenges. Future Virol. 2013, 8:371-380
3. Mahoney FJ, et al. Update on diagnosis, management and prevention of hepatitis B virus infection, 1999, Clin Microbiol Rev, 12:351-366.

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
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse

For technical assistance; please contact:
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