BIO TECHNOLOGY boditech

Tumor

ichroma™ iFOB Neo

INTENDED USE

ichroma™ iFOB Neo is a fluorescence Immunoassay (FIA) for the quantitative determination of hemoglobin in human feces. It is useful as an aid in management and monitoring of colorectal cancer.

For *in vitro* diagnostic use only.

INTRODUCTION

Colorectal cancer is the third most common cancer in the world[1], with about 1 million new cases and more than 500, 000 deaths per year. Screening method for colorectal cancer include the immuno chromatography fecal occult blood (iFOB) test, barium enema, sigmoidoscopy and colonoscopy[2]. Large randomized controlled trials have shown that iFOB screening can result in decreased colorectal cancer mortality[3,4]. The traditional FOB test uses the chemical Guaiac, which is sensitive to Hb peroxidase activity. However, the Guaiac-FOB test has low sensitivity to clinically significant colorectal neoplasis and has low specificity due to its non-specificity for human Hb[5,6]. To overcome these potential problems in immunochemical test, **ichroma™ iFOB Neo** uses specific monoclonal antibodies against human Hb.

PRINCIPLE

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

More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for ichroma™ tests to show hemoglobin concentration in the sample.

COMPONENTS

ichroma™ iFOB Neo consists of 'cartridges', 'extraction buffer tubes'.

- The cartridge contains the membrane called a test strip, which has anti human hemoglobin at the test line, anti-human hemoglobin, anti IgG fluorescence conjugate at the glazed line and rabbit IgG at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant in a box.
- The extraction buffer contains bovine serum albumin (BSA), sucrose, triton x-100 and sodium azide as a preservative in HEPES buffer.
- The extraction buffer is pre-dispensed in extraction tubes. Extraction buffer tubes are packed in a box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instruction for use'.
- Use only fresh samples and avoid direct sunlight.
- It is possible to use frozen samples. Please refer to "SAMPLE COLLECTION AND PROCESSING."
- There should be no contamination with urine or water in samples.
- Samples should not be taken during menstruation, hemorrhoids or when using rectal medications.
- Lot numbers of all the test components (cartridge, extraction buffer, 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 extraction buffer tubes. A cartridge should be used for testing one sample only. An extraction buffer tube should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use the cartridge, if is damaged or already opened.
- For shipping, samples must be packed in accordance with local regulations.
- Allow the cartridge, extraction buffer tube 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, extraction buffer tubes and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **ichroma™ iFOB Neo** will provide accurate and reliable results subject to the below conditions.
  - Use **ichroma™ iFOB Neo** should be used only in conjunction with the instrument for ichroma™ tests.

STORAGE AND STABILITY

Storage condition		
Component	Storage Temperature	Shelf life
Cartridge	4 - 30 °C	20 months
Extraction buffer tube	4 - 30 °C	20 months

- 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

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.

- 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-15-1

Components of **ichroma™ iFOB Neo**

- Cartridge Box:
  - Cartridge 25
  - Extraction buffer tube 25
  - ID chip 1
  - Instruction for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

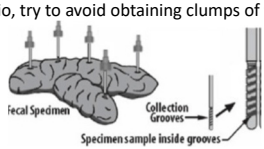
Following items can be purchased separately from **ichroma™ iFOB Neo**. Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
  - **ichroma™-50** REF FPRR022
- **Printer** REF FPRR007
- **Boditech iFOB Neo Control** REF CFPO-14

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ iFOB Neo** is human feces.

- Invert an extraction buffer tube and loosen the cap which is attached a sampling stick (yellow color).
- Introduce the sampling stick into the fecal sample six times at different sites. In order to get sampling even in the spirals of the stick and to ensure appropriate specimen to buffer ratio, try to avoid obtaining clumps of fecal matter.



- Return the stick to the extraction buffer tube. Tighten the cap thoroughly and shake the tube vigorously so as to disperse the specimen throughout the extraction buffer in the tube.

[Sample storage]

- Store the samples in an extraction solution tube.
- The sample storage period in the extraction solution is below.
  - Samples stored at the room temperature for 3 hours showed no performance difference.
  - Samples stored frozen at 2~8 °C for 7 days showed no performance difference.

TEST SETUP

- Check the contents of **ichroma™ iFOB Neo**: Sealed Cartridges, Extraction Buffers and ID Chip.
- Ensure that the lot number of the cartridge matches that of the extraction buffer 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.
  (Please refer to the 'Instrument for ichroma™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

▶ Instrument: ichroma™-50

1) Collect sample according to the sample collection method using a sampling stick in the 'sample collection and processing'. Then invert the extraction buffer tube again.
2) Insert pipette tips which are provided with ichroma™-50 (or purchased on demand) into the tip station of ichroma™-50.
3) Insert test cartridges into the cartridge magazine and insert the cartridge magazine into the magazine station of ichroma™-50.
4) Remove the cap(black) of the extraction buffer tube and insert the extraction buffer tube into the sample rack which is provided with ichroma™-50.
5) Input or set the number of tests what you want to perform and tap 'Start' button which is provided in the screen of ichroma™-50. (Please refer to ichroma™-50 operation manual for complete information.)
6) ichroma™-50 performs the tests automatically.
7) ichroma™-50 will display the test results 10 minutes after loading samples.

▶ Instrument: ichroma™ Reader/ichroma™ II

<Multi mode>

1) Collect sample according to the sample collection method using a sampling stick in the 'sample collection and processing'.
2) Assemble the sample collector and the extraction buffer into one and shake it about 10~15 times.
3) Break off the black tip on the outside of the black cap.
4) Discard 3 drops of reagent onto the paper towel before applying to the cartridge.
5) Hold the vial upside down and transfer 3 drops of the sample mixture and load it into the sample well on the cartridge.
6) Leave the sample-loaded cartridge at room temperature for 10 minutes.
   ⚠*Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate 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 is marked on the cartridge especially for this purpose.

8) Press 'Select' button or Tap the 'START' button on the instrument for ichroma™ tests to start the scanning process.
9) 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 Mode>

1) The test procedure is same with "Multi test 1)-5)".
2) 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.
3) Press 'Select' button or Tap the 'START' button on the instrument for ichroma™ tests to start the scanning process.
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.

INTERPRETATION OF TEST RESULT

- Instrument for ichroma™ tests calculates the test result automatically and displays hemoglobin concentration of the test sample in terms of ng/mL.
- The cut-off (reference value): 100 ng/mL(10 μg Hb/g Stool)
- The cut-off(reference value) may depend on the test method and the test object. It is recommended to set a cut-off(reference value) for each laboratory.
- In case of a positive result (above 100 ng/mL), consult a physician to discuss the test result. The physician may decide further course of action.
- Working range : 25-1,000 ng/mL

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 provided on demand with **ichroma™ iFOB Neo**. 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) 0.91 ng/ml
  - Limit of Detection (LoD) 1.34 ng/ml
  - Limit of Quantification (LoQ) 25.0 ng/ml

- **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™ iFOB Neo** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactivity materials	Concentration (ng/mL)		
	25	100	500
	Cross-reactivity (%)		
Bovine hemoglobin (2,000 μg/mL)	1.22	-0.84	1.12
Chicken hemoglobin (500 μg/mL)	-2.55	0.09	1.11
Fish hemoglobin (100 μg/mL)	0.83	3.35	-1.43
Horse(Equine) hemoglobin (500 μg/mL)	-1.25	-1.17	0.81
Goat hemoglobin (500 μg/mL)	0.15	1.46	1.50
Pig(Swine) hemoglobin (500 μg/mL)	0.62	-0.24	-0.87
Rabbit hemoglobin (500 μg/mL)	-0.53	-0.48	-2.02
Sheep hemoglobin (500 μg/mL)	1.91	0.17	-0.58

  - **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™ iFOB Neo** test results did not show any significant interference with these materials.

Interference materials	Concentration (ng/mL)		
	25	100	500
	Interference (%)		
Ascorbic acid (350 μmol/L)	0.37	-1.66	0.92
Bilirubin (350 μmol/L)	-4.03	0.01	1.41
Albumin (60 g/L)	-1.99	-3.27	1.47
Glucose (120 mg/dL)	1.47	-1.07	0.78
Triglyceride mixture (500 mg/dL)	0.72	-2.65	-2.40

- **Precision**
  - Between Lot
    One person tested three different lots of **ichroma™ iFOB Neo**, five times at each concentration of the control standard.
  - Between person
    Three different persons tested one lot of **ichroma™ iFOB Neo**, five times at each concentration of the control standard.
  - Between day
    One person tested **ichroma™ iFOB Neo** during five days; five times at each concentration of the control standard.
  - Between site
    One person tested one lot of **ichroma™ iFOB Neo** at three different sites, five times at each concentration of the control standard.

Hb (ng/mL)	Between-lot		Between-person		Between-day		Between-site	
	AVG	CV(%)	AVG	CV(%)	AVG	CV(%)	AVG	CV(%)
25	24.90	6.03	24.68	6.06	25.12	6.84	24.11	7.88
100	99.84	3.32	100.78	4.20	98.52	3.60	100.15	3.50
500	501.36	1.99	506.49	1.76	499.48	2.45	496.16	2.22

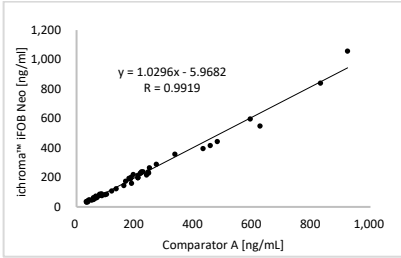
■ **Accuracy**

The accuracy was confirmed by testing 3 different lots, ten times at each concentration of the control standard.

Hb(ng/mL)	Lot 1	Lot 2	Lot 3	AVG	Recovery
25	24.89	24.26	24.73	24.62	98%
100	100.18	101.32	99.84	100.44	100%
500	503.76	496.10	507.90	502.59	101%

■ **Comparability**

Hemoglobin concentrations of 50 feces samples were quantified independently with **ichroma™ iFOB Neo** and Comparator A as per prescribed test procedures. Test results were compared and their comparability was investigated with linear regression and coefficient of correlation (R). Linear regression and coefficient of correlation between the two tests were Y= 1.0296X – 5.9682 and R = 0.9919 respectively.



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

	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

For technical assistance; please contact:
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