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 immunochromatography 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 a 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 the instrument for ichroma™ tests to show hemoglobin concentration in the sample.

COMPONENTS

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

- The cartridge contains the membrane called a test strip, which has anti-hemoglobin at the test line, anti-hemoglobin and 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, and they are further packaged in a box.
- The extraction buffer tube contains sodium azide as a preservative in HEPES buffer. It is pre-dispensed in extraction buffer tubes. All the 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 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- 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 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).
- 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 cartridge, if pouch is damaged or has already been opened.
- For shipping, samples must be packed in accordance with local regulations.
- If test components and/or sample are stored in refrigerator, then 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.
- The extraction buffer tube 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™ iFOB Neo** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ iFOB Neo** should be used only in conjunction with the instrument for ichroma™ tests.

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
Extraction buffer tube	2 - 30°C	20 months	Disposable

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

MATERIALS SUPPLIED

REF CFPC-15-1

Components of **ichroma™ iFOB Neo**

- Cartridge box:
  - Cartridge 25
  - Extraction buffer tube 25
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **ichroma™ iFOB Neo**.

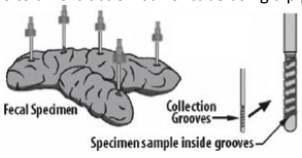
Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M3** REF FPRR035
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 PLUS** REF FPRR036
- **Printer** REF FPRR007
- **Boditech iFOB Neo Control** REF CFPO-14

SAMPLE COLLECTION AND PROCESSING

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

- Collect the sample feces in a clean and dry container.
- Invert an extraction buffer tube and loosen the cap where the sampling stick (yellow color) is attached.
- Poke the sampling stick into the fecal sample about 5 to 6 times at different sites. Whilst collecting the sample with the sampling stick, make sure to exclude large solid lumps. (In case the fecal matter is in liquid form, transfer 10 μL of the sample to an extraction buffer tube using a pipette.)



- Return the stick to the extraction buffer tube. Tighten the cap thoroughly and shake the tube vigorously around 10 times so as to disperse the specimen throughout the extraction buffer in the tube.

- Sample storage periods are as below:
  - Sample (feces) stored at room temperature showed no performance difference for 3 hours.
  - Sample (feces) stored at refrigerator (2~8°C) showed no performance difference for 3 days.
  - Sample (feces) stored at freezer (-20°C~-70°C) showed no performance difference for 8 weeks.
- The sample mixture storage periods in extraction buffer tube are as below:
  - The sample mixture in an extraction buffer tube stored at room temperature showed no performance difference for 3 hours.
  - The sample mixture in an extraction buffer tube stored at refrigerator (2~8°C) showed no performance difference for 7 days.
- However, it is recommended to use the sample mixture in the extraction buffer on the same day after sampling.
- The storage period may vary depending on the condition and type of feces.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen sample.

TEST SETUP

- Check the contents of **ichroma™ iFOB Neo**: Sealed cartridges, extraction buffer tubes, an ID chip and an instructions for use.
- Ensure that the lot number of the cartridges matches that of the extraction buffer tube as well as an ID chip.
- If the sealed cartridge and extraction buffer tube 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 complete information and operating instructions.**

TEST PROCEDURE

▶ **ichroma™ Reader, ichroma™ II, ichroma™ M3**

Multi test mode

1) Collect sample using a sampling stick according to the sample collection method described in the 'sample collection and processing'.
2) Shake the assembled extraction buffer tube about 10 to 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 tube upside down and apply 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 the 'Select' or tap the 'Start' button on the

instrument for ichroma™ tests.
(ichroma™ M3 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

1) The test procedure is same with 'Multi test mode 1)-5)'.
2) Insert the sample-loaded cartridge 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) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests.
(ichroma™ M3 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 10 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, ichroma™-50 PLUS**

1) Collect sample using a sampling stick according to the sample collection method described in the 'sample collection and processing'.
2) Insert the tip array in the tip station.
3) Insert the cartridges in the cartridge magazine and put the cartridge magazine into the magazine station.
4) Open the black cap of the extraction buffer tube and insert the opened extraction buffer tube into the tube rack.
5) Tap the button located in the upper side of the No. of reagent and select ID chip you want to use.
6) Confirm the number of cartridges and extraction buffer tubes inserted into the instrument for ichroma™ tests.
7) When the selected slot is activated, set the number of inserted cartridges and extraction buffer tubes in the main menu of instrument for ichroma™ tests.
8) Set the number of pipette tips by tapping.
9) Tap the 'Start' button on the main screen.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays hemoglobin concentration of the test sample in terms of ng/mL.
- Cut-off: 100 ng/mL (10 μg Hb/g Stool)
- 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.
- 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 instructions 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 Quantitation (LoQ) 25.0 ng/mL

- **Analytical specificity**
  - Cross reactivity
    Biomolecules listed in the following table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the feces. **ichroma™ iFOB Neo** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactants	Concentration
Bovine hemoglobin	2,000 μg/mL
Chicken hemoglobin	500 μg/mL
Fish hemoglobin	100 μg/mL
Horse (Equine) hemoglobin	500 μg/mL
Goat hemoglobin	500 μg/mL
Pig (Swine) hemoglobin	500 μg/mL
Rabbit hemoglobin	500 μg/mL
Sheep hemoglobin	500 μg/mL

  - Interference
    Interferents listed in the following table were added to the test sample(s) at the concentration mentioned below. **ichroma™ iFOB Neo** test results did not show any significant interference with these materials.

Interferents	Concentration
Ascorbic acid	350 μmol/L
Bilirubin	350 μmol/L
Albumin	60 g/L
Myoglobin	2,000 μg/mL
Glucose	120 mg/dL
triglyceride mixture	500 mg/dL

- **Precision**
  - Single-site study
    Repeatability (within-run precision)
    within-laboratory precision (Total precision)
    Lot to lot precision
    3 Lots of **ichroma™ iFOB Neo** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

Single-site study						
FOB [ng/ml]	Repeatability		Within-laboratory precision		Lot to lot precision	
	Mean [ng/ml]	CV (%)	Mean [ng/ml]	CV (%)	Mean [ng/ml]	CV (%)
50	50.18	4.3	50.49	4.2	50.47	4.1
100	101.05	3.7	101.12	3.8	100.87	3.8
500	502.75	4.0	502.41	4.0	504.67	4.1

- Multi-site study

  Reproducibility

  1 Lot of **ichroma™ iFOB Neo** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per run and 5 replicates per day.

Multi-site study		
Conc. [ng/ml]	Reproducibility	
	Mean [ng/ml]	CV (%)
50	50.21	4.3
100	100.67	4.3
500	505.66	3.4

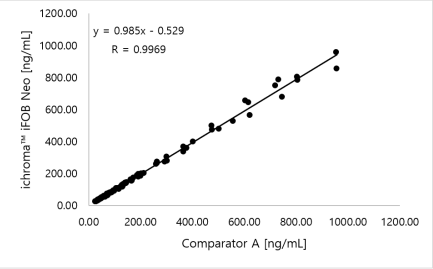
■ **Accuracy**

The accuracy was confirmed by testing with three different lots of **ichroma™ iFOB Neo**. The tests were repeated 10 times at each concentration of the control standard.

FOB [ng/mL]	Lot 1	Lot 2	Lot 3	AVG [ng/mL]	Recovery (%)
500.0	511.89	452.78	503.02	489.23	98
406.0	398.36	386.03	410.92	398.44	98
312.0	306.50	277.30	321.60	301.80	97
218.0	215.78	196.72	219.91	210.81	97
124.0	123.09	112.14	128.52	121.25	98
30.0	30.06	27.26	30.01	29.11	97

■ **Comparability**

Hemoglobin concentration of 100 clinical samples were quantified independently with **ichroma™ iFOB Neo (ichroma™ II)** and **Comparator A** as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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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

For technical assistance, please contact:
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