ichroma™ iFOB

INTENDED USE

ichroma™ iFOB is a fluorescence immunoassay for the quantitative determination of FOB in human Feces specimens. **ichroma™ iFOB** is used as an aid in the screening 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 standard FOB test uses the chemical Guaiac, which is sensitive to Hb peroxidase activity. However, the standard 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** uses specific monoclonal antibodies against human Hb as capture and detection buffer[7].

PRINCIPLE

The principle of **ichroma™ iFOB** uses a sandwich immunofluorescence assay. A fluorescence conjugated Anti-hemoglobin in a detection buffer binds to hemoglobin in a sample to form an antigen-antibody complex. These antigen-antibody complexes are then captured by another Anti-hemoglobin that has been immobilized on a test strip, as the sample mixture migrates through a nitrocellulose matrix. The more hemoglobin in a sample, the more antigen-antibody complexes are accumulated on a test strip, resulting in higher signal intensities of fluorescence. **ichroma™ Reader** analyzes and reads the fluorescence intensity, and shows the hemoglobin concentration in a sample.

COMPONENTS AND REAGENTS

ichroma™ iFOB consists of a 'Test Cartridges', an 'ID Chip' and 'Sample collection tubes including a detection buffer'.

- The Test Cartridge contains a test strip on which murine antibody against human hemoglobin and rabbit IgG have been immobilized in the test line and the control line, respectively.
- Each Test Cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed Test Cartridges are packed in a box which also contains the ID Chip.
- The Detection Buffer contains fluorochrome-labeled Anti-human hemoglobin, fluorescence-labeled anti-rabbit IgG, bovine serum albumin (BSA) as a stabilizer and sodium azide in PBS as a preservative.
- The Detection Buffer is dispensed in each sample collection tube. 25 sample collection tubes are packed in a separate box which is further packed in a Styrofoam box provided with ice packs for the purpose of shipment.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Carefully follow the instructions and procedures described in this insert.
- Lot numbers of all the test components (Test cartridge, ID Chip and Sample collection tube) must match each other.
- Do not interchange the test components from different lots or use the test components beyond the expiration date.
- Test performed by using any test component with mismatching lot number or that beyond the expiration date may yield misleading of test result (s).
- The Test Cartridge should remain sealed in its original pouch until use. Do not use the test cartridge if that is damaged or already opened.
- Allow a minimum of 30 minutes for the Test Cartridge to attain room temperature if it has been stored in a refrigerator.
- The detection buffer dispensed in a sample collection tube should attain room temperature prior to performing the test.
- **ichroma™ iFOB** as well as the **ichroma™ Reader** should be kept away from vibration exposure and/or magnetic fields. During normal usage, **ichroma™ Reader** may produce minor vibrations which should be regarded as normal.
- Used sample collection tube, pipette tips and Test Cartridge should be handled carefully and disposed of 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.

STORAGE AND STABILITY

- The Test Cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4 – 30 °C.
- The Detection Buffer Dispensed in a sample collection tube is stable for 20 months if stored at 2 – 8 °C.
- After the Test Cartridge pouch is opened, the test should be performed immediately.

LIMITATIONS OF THE TEST SYSTEM

ichroma™ iFOB provides accurate and reliable results subject to the following constraints:

- **ichroma™ iFOB** should be used only in conjunction with **ichroma™ Reader.**
- Use freshly collected samples for testing.
- If the test samples are shipped for the purpose of this test, appropriate precautions must be exercised.
- Effectiveness of the test is highly dependent on storage conditions of test components and samples at prescribed optimal conditions.
- Tests may yield false positive result (s) due to cross-reactions between some components of serum with the capture/detector antibodies and/or non-specific adhesion of certain components having similar epitopes to bind to these antibodies.
- The test may also yield false negative results; the most common factor being non-responsiveness of the antigen to the antibodies due to its epitopes being masked by some unknown components such that the antigen cannot be detected or captured by the antibodies. False negative results may also be obtained due to instability or degradation of the human hemoglobin with time and/or temperature making it unrecognizable by the antibodies.
- Other factors interfering with tests and causing erroneous results include technical/procedural errors, the degradation of the test components/reagents as well as the presence of interfering substances in samples.
- Any clinical diagnosis based on the test results must be supported by comprehensive judgment of a concerned physician, clinical symptoms and any other relevant test results.

SAMPLE COLLECTION AND PROCESSING

ichroma™ iFOB Tests can be performed using human feces.

- Collect random samples of feces in a clean, dry container or a receptacle, making sure to exclude.
- Loosen a cap on the upper part of a sample collection tubes and remove a sampling stick. Use with care not to spill or splatter solution from the tube.
- Collect random samples by using a sampling stick with the

proper method; insert the sampling stick and turn the stick into the fecal samples several times (5~6 times) at different sites so as to get a representative sampling.

※ Fill up the groove with fecal samples and please check whether the quantity is too much or not.

- Return the sampling stick into the Sample Collection Tube and screw the cap tightly.
- Shake the tube 10 times or more until the sample on the stick is dissolved.

★ Mixture can be kept for 3 days in a darkroom.

MATERIALS SUPPLIED

REF CFPC-15

Components of ichroma™ iFOB

- **Test Cartridge Box:**
  - Sealed Test Cartridges 25
  - ID Chip 1
  - Package Insert 1
- **Box Containing Detection Buffer Tube:**
  - Sample Collecion Tubes 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

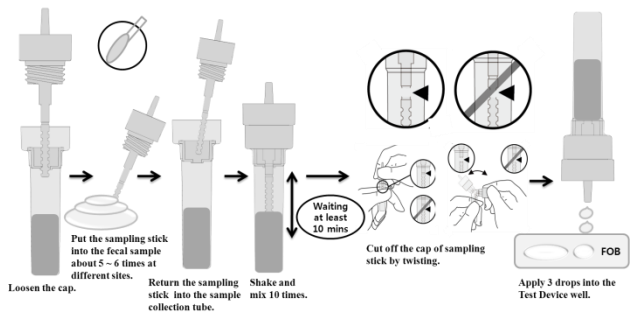
Following items can be purchased separately from **ichroma™ iFOB**. Please contact our sales division for more information.

- **ichroma™ Reader** REF FR203
- **ichroma™ Printer** REF FPRR007
- **ichroma™ iFOB Control L** REF CFPO-14-1
- **ichroma™ iFOB Control H** REF CFPO-14-2

TEST SETUP

1. Check the test components of **ichroma™ iFOB**: Sealed Test Cartridge, ID Chip and Sample collection tubes.
2. Ensure that the lot number of the Test Cartridge matches that of the ID Chip as well as the Sample collection tubes.
3. Keep the sealed Test Cartridge and the Sample collection tubes (if previously stored in the refrigerator) at room temperature for at least 30 minutes prior to testing. Place the Test Cartridge on a clean, dust-free and flat surface.
4. Turn on the **ichroma™ Reader**.
5. Insert the ID Chip into the ID Chip port of the **ichroma™ Reader**.
6. Press the "Select" button on the **ichroma™ Reader**. (Please refer to the **ichroma™ Reader** Operation Manual for complete information and operating instructions.)

TEST PROCEDURE



1. Take out one sample collection tube of Detection Buffer from refrigerator and leave it at room temperature.
2. Loosen and separate a sampling stick from a sample collection tube. (The socket between the stick and the tube should stay inside the tube).
3. Put a sampling stick into the fecal sample about 5 ~ 6 times at different sites and try to avoid obtaining clumps of fecal matter.
4. Return the fecal sampling stick into the Sample Collection Tube. (Tighten the cap).
5. Shake the tube 10 times or more until the sample on the stick is dissolved.
6. Mixture should be waiting at least 10 min. (It could be stored at darkness (4 - 28°C) for 3 days.)
7. Cut off the cap of sampling stick by twisting. (The tube must be vertical during this stick-cutting process.)
8. Apply 3 drops of the mixture onto the sample well of the Cartridge (refer to the picture above)
9. Leave the Cartridge at room temperature for 10 min before inserting the device into the holder.
10. For scanning the sample-loaded Test Cartridge, insert it into the Test Cartridge holder in the **ichroma™ Reader**. Ensure proper orientation of the Test Cartridge before pushing it all the way inside the test cartridge holder. An arrow has been marked on the test cartridge especially for this purpose.
11. Press "Select" button on the **ichroma™ Reader** to start the scanning process.
12. The **ichroma™ Reader** will immediately scan the sample-loaded Test Cartridge.
13. Read the test result on the display screen of the **ichroma™ Reader**.

INTERPRETATION OF TEST RESULT

- **ichroma™ Reader** automatically calculates the test results and displays the hemoglobin concentration of samples in terms of ng/mL.
- The cut-off (reference value) of **ichroma™ iFOB** is 50 ng/mL
- Working range of **ichroma™ iFOB** is 25 – 1,000 ng/mL.
- **ichroma™ iFOB** should be considered as a screening tool only. Please consult a physician to discuss the test results.

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.
- Before testing a clinical sample using a new test lot, control reagents should be tested to confirm the test procedures, and to verify whether the test produces expected results.
- Quality control testing should also be performed whenever there is any question concerning the validity of the test results.
- Control reagents are not provided with **ichroma™ iFOB**. For more information, contact Boditech Med Inc.'s Sales Division for assistance.
- **ichroma™ iFOB** has a built-in internal control that satisfies the routine quality control requirements. This internal control test is performed automatically each time a clinical sample is tested. An invalid result from the internal control leads to displaying an error message on the **ichroma™ Reader** indicating that the test should be repeated.

PERFORMANCE CHARACTERISTICS

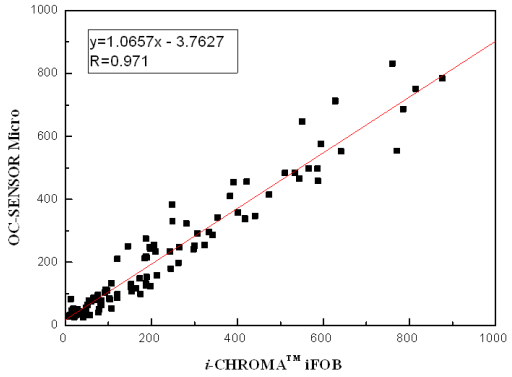
1. **Specificity/Interference:** Other bio-molecules, such as bovine Hb, swine Hb, chicken Hb, bilirubin, albumin for interference test, and disease related makers such as PSA, AFP, CEA, CA15-3 and vitamin C were added to test specimen with much higher level than their physiological level in normal sample. There was no significant interference with the FOB measurement, nor was there any significant assay cross-reactivity with other disease-related biomarkers in sample.

2. **Imprecision:** For intra-assay precision, one person tested three different lots of **ichroma™ iFOB**, ten times per concentration by controls. For inter-assay precision, three persons under the

same conditions tested three different lots of test devices, 10 times per concentration with known controls.

FOB	Intra-assay			Inter-assay		
[ng/mL]	Mean	S.D	CV (%)	Mean	S.D	CV (%)
20	31.0	1.6	5.2	30.7	2.0	6.6
50	51.2	3.0	5.9	50.0	2.9	5.8
250	250.8	18.4	7.3	245.7	14.8	6.0
700	695.6	32.3	4.6	692.2	31.0	4.8

3. **Comparability:** The FOB concentrations of 100 samples were quantified by using **ichroma™ iFOB** and a Eiken OC-SENSOR Micro automatic analyzer as per the prescribed test procedures. The test results were compared and their comparability was investigated with linear regression and coefficient of correlation (R). The correlation value of coefficient was 0.971 between two methods.



REFERENCES

1. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2020: Cancer incidence, motality and Prevalence worldwide. IARC CancerBase no. 5, version 2.0. Lyon, France: IARC Pr; 2004.
2. Arnold CN, Goel A, Blum HE, Boland CR. Molecular pathogenesis of colorectal cancer: implications for molecular diagnosis. Cancer 2005;104:2035-2047.
3. Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, et al. Reducing mortality from colorectal cancer by scrrning for fecal occult blood. Minnesota Colon Cancer Control study. N Engl J Med 1993;328:1365-1371
4. Kronborg O, Fenger C, Olden J, Jorgensen OD, Sondergaard O. Randomised study of screening for colorectal cancer with fecal occult blood test. Lancet 1996;384:1467-1471.
5. Hardcastle JD, Chamberlain J, Robinson MH, Moss SM, Amar SS, Balfour TW, et al. Randomised controlled trial of fecal occult blood screening for colorectal cancer. Lancet 1996;348:1472-1477.
6. Rozen P, Waked A, Vilkin A, et al. Evaluation of a desk top instrument for the automated development and immunochemical quantification of fecal occult blood. Med Sci Moint 2006;12(6):MT27-32.
7. Oh SW, Moon JD, Park SY, et al. Evaluation of fluorescence hsCRP immunoassay for point of care testing. Clin Chim Acta 2005;356:172-177.

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

	Read instructions for use
	Use by
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:
Boditech Med Inc.'s Technical Services
Tel.: +82-33-243-1400
E-mail: sales@boditech.co.kr

Boditech Med Incorporated
43, Geodudanji 1-gil, Dongnae-myeon,
Chuncheon-si, Gang-won-do, 200-883
Republic of Korea
Tel.: +82 -33-243-1400
Fax.: +82 -33-243-9373
www.boditech.co.kr

EC REP Boditech Med Europe.
25a Hampstead Hill Gardens
London NW32PJ, United Kingdom
Tel.: +44-207-947-5400
Fax.: +44-207-947-5401
E-Mail: jfnewsome@googlemail.com

Revision No: 05
Date of last revision: October 22, 2014

CE