BIO TECHNOLOGY boditech

Tumor ichroma™ CEA

INTENDED USE

ichroma™ CEA is a fluorescence Immunoassay (FIA) for the quantitative determination of CEA in human serum/plasma. It is useful as an aid in management and monitoring of cancer patients.

For *in vitro* diagnostic use only.

INTRODUCTION

CEA is an oncofetal glycoprotein, which is found at high levels in the fetal colon and at lower levels in the normal adult colonic epithelium. CEA occurs at abnormally high levels in several benign disorders and in some malignant tumors, including those of the stomach, small intestine, colon, rectum, pancreas, liver, breast, ovary, cervix, and lung[1]. CEA is a 180-kD glycoprotein that occurs at high levels in colon epithelial cells during embryonic development. Levels of CEA are significantly lower in colon tissue of adults, but can become elevated when inflammation or tumors' arise in any endodermal tissue, including in the gastrointestinal tract, respiratory tract, pancreas and breast[2]. CEA is also expressed by epithelial cells in several non-malignant disorders, including diverticulitis, pancreatitis, inflammatory bowel disease, cirrhosis, hepatitis, bronchitis and renal failure and also in individuals who smoke[3]. This fact has made it difficult to use serum CEA determination as a sensitive method for cancer screening. However, serum CEA levels have been useful in monitoring individuals for the recurrence of cancer[4].

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 and lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for ichroma™ tests to show CEA concentration in the sample.

COMPONENTS

ichroma™ CEA consists of 'cartridges', 'detection buffer tubes', 'ID chip' and 'instruction for use'.

- The cartridge contains the membrane called a test strip which has anti human CEA 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 detection buffer contains anti human CEA-fluorescence conjugate, anti chicken IgY-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.
- The detection buffer is pre-dispensed in tubes. Detection buffer tubes are packaged in a box and further packed in a Styrofoam box with ice-pack for the shipment.

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.
- Lot numbers of all the test components (cartridge, detection 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 detection buffer tubes. A cartridge should be used for testing one sample only. A detection buffer 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 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, detection 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, detection 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™ CEA** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ CEA** should be used only in conjunction with instrument for ichroma™ tests.
  - Have to use recommended anticoagulant sample.

Recommended anticoagulant
K2 EDTA, K3 EDTA, sodium heparin

STORAGE AND STABILITY

Storage condition		
Component	Storage Temperature	Shelf life
Cartridge	4 - 30 °C	20 months
Detection buffer tube	2 - 8 °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 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 13013

Components of **ichroma™ CEA**

- Cartridge Box:
  - Cartridge 25
  - ID Chip 1
  - Instruction for Use 1
- Buffer Box
  - Detection buffer tube 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ CEA**.

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
- **Printer** REF FPRR007
- **Boditech Tumor marker Control** REF CFPO-94

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ CEA** is human 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.
- Once the sample was frozen, it should be used one time only for test, because repeated freezing and thawing can result in the change of test values.

TEST SETUP

- Check the contents of **ichroma™ CEA**: Sealed Cartridges, Detection buffer tubes, ID Chip and Instruction for use.
- Ensure that the lot number of the cartridge matches that of the detection buffer tube as well as the ID chip.
- If the sealed cartridge and the detection 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.
  (Please refer to the 'Instrument for ichroma™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

<Multi mode>

1) Transfer 150 µL (Human serum/plasma/control) of sample using a pipette to a tube containing the detection buffer.
2) Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
3) Pipette out 75 µL of a sample mixture and load it into the sample well on the test cartridge.
4) Leave the sample-loaded cartridge at room temperature for 12 minutes.
   ⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*
5) 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.
6) Tap the 'Start' button or press the 'Select' button on the instrument for ichroma™ tests to start the scanning process.
7) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
8) Read the test result on the display screen of the instrument for ichroma™ tests.

<Single mode>

1) Transfer 150 µL (Human serum/plasma/control) of sample using a pipette to a tube containing the detection buffer.
2) Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
3) Pipette out 75 µL of a sample mixture and load it into the sample well on the test cartridge.
4) Insert the cartridge into the holder of the instrument for ichroma™ test. 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.

5) Tap the 'Start' button or press the 'Select' button on the instrument for ichroma™ tests.
6) The Instrument for ichroma™ tests will automatically start scanning the sample-loaded cartridge after 12 minutes.
7) 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 CEA concentration of the test sample in terms of ng/mL.

	Cut-off (reference value)
Non-Smoker	4 ng/mL
Smoker	5 ng/mL (95 % of healthy subjects)

- Working range : 1-500 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 not provided with **ichroma™ CEA**. 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.)

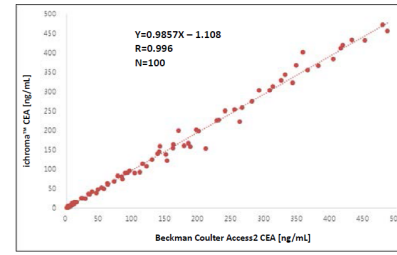
PERFORMANCE CHARACTERISTICS

- **Specificity**
  There, in test samples, are biomolecules such as bilirubin, lipid and hemoglobin for interference test, and disease related makers such as NCA in higher concentration than their normal physiological levels. But this doesn't interfere with the **ichroma™ CEA** test measurements, nor occurs any significant cross-reactivity.

- **Precision**
  The intra-assay precision was calculated by one evaluator, who tested different concentration of control standard ten times each with three different lots of **ichroma™ CEA.** The inter-assay precision was confirmed by 3 different evaluators with 3 different lots, testing five times each different concentration.

CEA [ng/mL]	Intra-assay		Inter-assay	
	Mean	CV (%)	Mean	CV (%)
6.5	6.86	8.66	6.81	7.76
65	68.54	3.81	67.13	4.49
130	131.67	5.12	129.23	5.60

- **Comparability**
  CEA concentrations of 100 clinical samples were quantified independently with **ichroma™ CEA** and Beckman Coulter Access2 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=0.9857X – 1.108 and R = 0.996 respectively.



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2. Benchimol, S., A. Fuks, S. Jothy, N. Beauchemin, K. Shirota, and C.P. Stanners. 1989. Carcinoembryonic antigen, a human tumor marker, functions as an intercellular adhesion molecule. Cell 57:327-334.
3. Oikawa, S., C. Inusuka, M. Kuroki, Y. Matsuoka, G. Kosaki, and H. Nakazato. 1989. Cell adhesion of non-specific cross-reacting antigen (NCA) and carcinoembryonic antigen (CEA) expressed on CHO cell surface: homophilic and heterophilic adhesion. Biochem. Biophys. Res. Commun. 164:39-45.
4. Averbach, A.M., and P.H. Sugarbaker. 1995. Use of Tumor Markers and Radiologic Tests in Follow-up. In Cancer of the Colon, Rectum and Anus.

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
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices