Tumor AFIAS CEA

INTENDED USE

AFIAS CEA is a fluorescence immunoassay (FIA) for the quantitative determination of CEA (carcinoembryonic antigen) in human whole blood/ 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 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 AFIAS tests to show CEA concentration in the sample.

COMPONENTS

AFIAS CEA consists of 'Cartridges'.

- Each sealed aluminum pouch contains two cartridges.
- Each cartridge packaged in an aluminum pouch has three components including a cartridge part, a detector part, and a diluent part.
- The cartridge part contains the membrane called a test strip which has anti-CEA at the test line, while rabbit IgG at the control line.
- The detector part has a granule containing anti-CEA-fluorescence conjugate, anti-rabbit IgG-fluorescence conjugate and sodium azide as a preservative in phosphate buffered saline (PBS).
- The diluent part contains tween 20 as a detergent and sodium azide as a preservative in Tris-HCl.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow 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 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 cartridge. A cartridge should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use a cartridge if the 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.
- If test components and/or sample are stored in refrigerator, then allow cartridge and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for AFIAS tests may generate slight vibration during use.
- Used cartridges and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The cartridge contains soium 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.
- No Biotin interference was observed in **AFIAS CEA** when biotin concentration in the sample was below 100 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **AFIAS CEA** will provide accurate and reliable results subject to the below conditions.
  - **AFIAS CEA** should be used only in conjunction with the instrument for AFIAS tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2 EDTA, K_3 EDTA, Sodium heparin

LIMITATIONS 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	Unopened
		1 month	Resealed

- Return an unused cartridge to the spare cartridge zipper bag containing the desiccant pack. Reseal along entire edge of zip-seal.

MATERIALS SUPPLIED

REF SMFP-21

Components of **AFIAS CEA**

- Cartridge box:
  - Cartridge 24
  - Pipette tip (zipper bag) 24
  - Spare cartridge zipper bag 1
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately with **AFIAS CEA**. Please contact our sales division for more information.

- **AFIAS-1** REF FPRR019
- **AFIAS-3** REF FPRR040
- **AFIAS-6** REF FPRR020
- **AFIAS-10** REF FPRR038
- **Boditech Tumor marker Control** REF CFPO-94
- **Boditech Tumor marker Calibrator** REF CFPO-106
- **Boditech CEA Control** REF CFPO-246
- **Boditech CEA Calibrator** REF CFPO-272

SAMPLE COLLECTION AND PROCESSING

The sample type for **AFIAS CEA** is human whole blood/serum/plasma.

- It is recommended to test the sample within 18 hours after collection.
- The samples (serum, plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (whole blood, serum, plasma) may be stored for a week at 2-8°C prior to being tested. If testing will be delayed more than a week, samples (serum, plasma) should be frozen at -20℃.
- The samples (serum, plasma) stored frozen at -20°C for 3 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the components of the **AFIAS CEA** as described below. : Cartridges, pipette tips, an ID chip, a spare cartridge zipper bag and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the ID chip.
- If the sealed cartridge has 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 AFIAS tests.
- Empty the tip box.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for AFIAS tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

▶ **AFIAS-1, AFIAS-3, AFIAS-6**

General mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Select the 'General mode' in the instrument for AFIAS tests.
4) Take 100 µL of the sample (whole blood/serum/plasma/ control) using a pipette and dispense it into the sample well of the cartridge.
5) Tap the 'Start' button on the screen.
6) The test results will be displayed on the screen after 15 minutes.

▶ **AFIAS-10**

Normal mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Tap the 'Load' button of the bay that holds the cartridge with the tip to read the barcode of the cartridge and please confirm the item name written on the cartridge.
4) Insert the sample tube into the tube rack.
5) Insert the tube rack into the loading part of the sampling station.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 15 minutes.

Emergency mode – General tip

1) The test procedure is same with the 'Normal mode 1) – 3)'.
2) Convert the 'Emergency mode' in AFIAS-10.
3) Select the tip type (general tip) on the screen.
4) Select the sample type (whole blood/serum/plasma) on the screen.
5) Take 100 µL of the sample using a pipette and dispense it into the sample well of the cartridge.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 15 minutes.

INTERPRETATION OF TEST RESULT

- The instrument for AFIAS tests calculates the test result automatically and displays CEA concentration of the test sample in terms of ng/mL.
- Working range: 1 - 500 ng/mL
- Reference range: < 4.7 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 **AFIAS CEA**. 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) 0.32 ng/mL
  - Limit of Detection (LoD) 0.45 ng/mL
  - Limit of Quantitation (LoQ) 1.00 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. **AFIAS CEA** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactants	Concentration
PSA	400 ng/mL
AFP	1,000 ng/mL
CA 125	3,500 U/mL

  - Interference

    Interferents listed in the following table were added to the test sample at the concentration mentioned below. **AFIAS CEA** test results did not show any significant interference with these materials.

Interferents	Concentration
Hemoglobin	10 g/L
Bilirubin, unconjugated	684 µmol/L
Triglycerides	1500 mg/dL
Ascorbic acid	5.25 mg/dL
Glucose	1000 mg/dL
Cholesterol	400 mg/dL

- **Precision**

Single-site study

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision

3 Lots of **AFIAS CEA** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

Single-site study						
CEA [ng/mL]	Repeatability		Within-laboratory precision		Lot to lot precision	
	AVG [ng/mL]	CV (%)	AVG [ng/mL]	CV (%)	AVG [ng/mL]	CV (%)
5.00	5.02	5.75	5.04	5.75	5.01	5.84
15.00	14.95	5.87	14.84	5.74	14.92	5.96
300.00	304.51	5.73	298.45	6.12	299.44	5.97

Multi-site study

- Reproducibility

1 Lot of **AFIAS CEA** 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 and 5 replicates per day.

Multi-site study		
CEA [ng/mL]	Reproducibility	
	AVG [ng/mL]	CV (%)
5.00	5.00	5.90
15.00	14.93	5.47
300.00	300.60	5.68

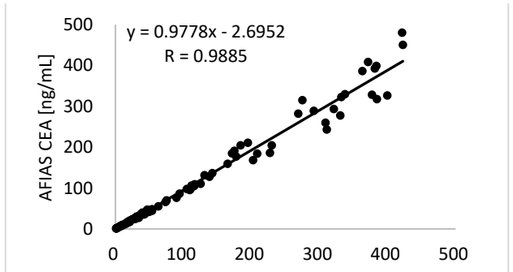
- **Accuracy**

The accuracy was confirmed by testing with 3 different lots of **AFIAS CEA**. The tests were repeated 10 times at each concentration of the control standard.

CEA [ng/mL]	Lot 1	Lot 2	Lot 3	AVG [ng/mL]	Recovery
300.00	298.55	308.10	289.20	298.61	100
225.75	223.08	227.30	227.33	225.90	100
151.50	143.29	154.06	150.38	149.24	99
77.25	76.54	77.30	74.53	76.12	99
30.00	29.60	30.01	30.23	29.95	100
8.82	8.60	8.73	8.76	8.69	99

- **Comparability**

CEA concentration of 100 clinical samples were quantified independently with **AFIAS CEA (AFIAS-6)** 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 follow.



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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

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