

Instructions for Use

Carcinoembryonic Antigen (CLIA)

[Product Name]

Carcinoembryonic Antigen (CLIA)

[Packing Size]

24×1 Tests/Pkg (Calibrators included);

60×1 Tests/Pkg (Calibrators included);

60×1 Tests/Pkg

[Intended Use]

Carcinoembryonic Antigen assay (CLIA) is used to quantitatively measure CEA concentration in human serum, plasma, and whole blood samples, and it is mainly used for curative effect observation, prognosis judgment, and recurrence monitoring of malignant tumors.

CEA is an acidic glycoprotein with the characteristics of human embryo antigen. It exists on the surface of cancer cells differentiated from endoderm cells, and is a structural protein of cell membrane with a molecular weight of 150-200 kDa containing 50-85% carbohydrates^[1,2]. The level of CEA in colorectal cancer, gastric cancer, lung adenocarcinoma, breast cancer is remarkably elevated^[1]. Measurement of CEA can provide clinical guidance for the prognosis of relevant patients, judgment of tumor recurrence, and treatment efficacy after surgical resection^[1-7]. The continuous rise of CEA level during treatment indicates ineffective therapy, poor prognosis, or possible tumor metastasis^[3,4]. In the trastuzumab antibody treatment of breast cancer patients, combined monitoring of CEA with CA15-3 can increase the sensitivity of efficacy monitoring^[5]. For some benign diseases such as colitis, pancreatitis, hepatitis, pulmonary and cardiovascular diseases, the level of serum CEA may also increase to different degrees^[6,7].

[Principle of the Assay]

CEA assay takes a double-antibody sandwich format. The detection principle is described below:

- (1) Mix the sample with magnetic microparticle coated with an anti-CEA antibody, add another acridinium labeled anti-CEA antibody and reaction diluent. After mixing and incubation, CEA in the sample will react with anti-CEA antibody coated on the microparticles, acridinium labeled anti-CEA antibody will react with another site on CEA, forming antigen-antibody complex;
- (2) A magnet captures microparticle, and then unbound substance is washed off. Add pre-trigger and trigger solution to the reaction mixture sequentially to initiate chemiluminescence reaction;
- (3) A photomultiplier tube is used to measure photons generated from the reaction. Signal is amplified exponentially. The count is proportional to CEA concentration in the sample. CEA concentration is determined by an internal calibration curve.

[Main Components]

Packing Size

Packing Size		Fill Volume		
		24×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg
CEA Reagent Cartridge	Microparticle (R1)	24×50μL	60×50μL	60×50μL
	Conjugate (R2)	24×100μL	60×100μL	60×100μL
	Reaction diluent (R3)	24×150μL	60×150μL	60×150μL

CEA Calibrator	CEA Calibrator C1	1×1.0mL	1×1.0mL	/
	CEA Calibrator C2	1×1.0mL	1×1.0mL	/
Calibration Card	Calibration curve and calibrator information	1 pcs	1 pcs	/

Main Composition

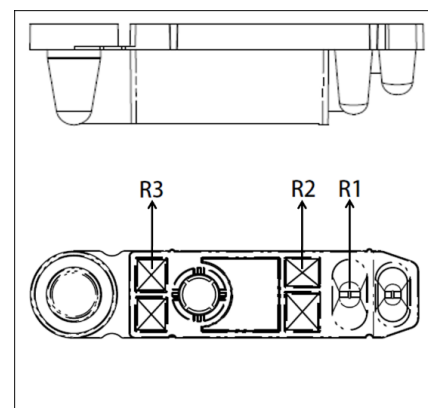
Component	Main Composition	
CEA Reagent Cartridge	Microparticle (R1)	Mouse anti-CEA monoclonal antibody coated microparticle, ~0.2g/L; Tris buffer, 50mmol/L; ProClin 300, 0.5g/L
	Conjugate (R2)	Acridinium labeled mouse anti-CEA monoclonal antibody, ~0.2μg/L; MES buffer, 50mmol/L; ProClin 300, 0.5g/L
	Reaction diluent (R3)	Tris buffer, 50mmol/L; ProClin 300, 0.5g/L
CEA Calibrator C1	CEA (Human); HEPES buffer, 50mmol/L; ProClin 300, 0.5g/L	
CEA Calibrator C2	CEA (Human); HEPES buffer, 50mmol/L; ProClin 300, 0.5g/L	
Calibration Card	Calibration curve and calibrator information	

Note: (1) Components in different lots of reagent cannot be mixed or exchanged for use.

(2) Traceability: This quantification method can be traced back to WHO Reference material, Code: 73/601 from NIBSC (National Institute for Biological Standard and control).

(3) Information about the calibrators (such as lot number and concentration etc.) can be found on the instrument interface after scanning the Calibrator Card.

The position of each component in the reagent pack is shown in the front view (Upper) and vertical view (Down) of the reagent cartridge.



Instruments and accessories needed but not supplied (available from Medcaptain)

- (1) Medcaptain Immu F6/F6S Automatic chemiluminescent immunoassay analyzers;
- (2) Pre-trigger solution;
- (3) Trigger solution;
- (4) Washing solution;
- (5) 500μL pipette tips;
- (6) Tumor Marker Controls.

[Storage and Shelf-life]

Storage: Store sealed reagent cartridges and calibrators at 2~8°C in upright position, and avoid freezing.

Shelf life: 14 months.

Stability of Calibrators: Sealed vial of calibrators can be kept at 2~8°C in dark for 14 months. After calibrator C1 and C2 is uncapped, it can be stored at 10~30°C for 5 days, and at 2~8°C for 60 days.

The dates of manufacturing and expiration can be found on the labels.

[Matched Instruments]

Medcaptain Immu F6/F6S automatic chemiluminescent immunoassay analyzers

[Specimen Types]

Serum, plasma, and whole blood (collected with EDTA-K₂, EDTA-K₃, lithium heparin, and sodium heparin as the anti-coagulants) can be used in the testing.

Sample volume for each test: 10μL.

The collected sample should be tested as soon as possible.

Whole blood should be tested within 4 hours after sample collection.

Serum and plasma can be kept at 10~30°C for 8 hours, at 2~8°C for 7 days, and at -20°C or below for 6 months. Frequent freeze-thaw cycle should be avoided, and only one freeze-thaw cycle is allowed. If the sample contains precipitate or frozen floccule, centrifugation is needed to clear the sample before testing.

Sample collection tubes from different manufacturers may lead to variation in testing results, due to the difference in tube material and additives in the tubes. Medcaptain has not evaluated all types of sample collection tubes from different manufacturers. Each laboratory should make its own judgment about the usability of sample collection tubes.

[Test Procedure]

Reagent Preparation

Reagent: CEA reagent cartridge (containing magnetic microparticle R1, acridinium labeled conjugate R2, reaction diluent R3) is ready for use. It can be loaded directly into the instrument after opening the package.

Calibrators: Calibrator C1 and C2 are ready for use. Each calibrator can be added to a sample cup, load the cups to a sample rack. The sample rack can be pushed directly into instrument for calibrator testing.

Calibration

Refer to the relevant chapter in the operation manual of each chemiluminescent immunoassay analyzer.

Calibration tests should be ordered before the first time use of CEA assay. Medcaptain provides CEA reagent pack and matched calibrators to calibrate the instrument.

Before calibration, scan the calibration card provided in the kit, and the calibration curve and calibrator information can be scanned into the system.

Before calibration, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

Put calibrators on a sample rack, load the sample rack into the instrument.

On the screen interface of "Reagent > Request Calibration", select test name and lot number to request a calibration.

Select the position of each calibrator on the sample rack, set the number of repeat tests, start calibration.

Automatic immunoassay analyzer makes use of calibration data to validate the calibration, and adjust the calibration curve automatically.

Instrument calibration is effective for 60 days.

A new calibration is needed in the following situation:

- (1) Change into a new lot of reagent;
- (2) Control test results are out of the target range;
- (3) The lot of reagent has been used on the same instrument for more than 60 days.

Refer to the Chapter of "Calibration" in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about

calibration.

Control Testing

Tumor Marker Controls are matched with CEA reagent pack. There are two levels of controls: Low Control (L) and High Control (H).

These two-level controls should be tested in accordance with any local applicable regulations. Control testing is highly recommended every time the lot of reagent has been changed, the instrument has been re-calibrated, or after trouble shooting/maintenance service.

Before the control testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

Put controls on a sample rack, and load the sample rack into the instrument;

Select "Control" on the interface of test menu, select test name and control lot;

Click on "Start" and begin the testing. Check the results after control test is finished.

Control test results should fall into a specific range. If it is out of the target range, the user should check the system, such as expiration date of the controls, storage condition, instrument performance and status. After root cause analysis and correction, the user should test controls again. If the same problem exists, please contact customer service of Medcaptain.

Each laboratory should set up its own control range and frequency of control testing, based on its own practice.

Refer to the Chapter of "Control Testing" in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about control testing.

Sample Testing

Before sample testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

If a sample collection tube is directly loaded to the instrument for testing, the sample volume should be at least 1.0mL;

Uncap sample collection tubes, put samples on a sample rack, and push the sample rack into the instrument;

Select "Sample" on the interface of test menu, enter information of samples, select test name;

Click on "Start" and begin the testing. Check the results after sample test is finished.

The reagent usage for each test is: R1 50μL, R2 100μL, and R3 150μL; The instrument aspirates and mixes each component in the reagent cartridge, and incubates at 37°C. Time duration from sampling to result is about 15 min.

Refer to the Chapter of "Sample Testing" in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about sample testing.

Result Calculation

Based on the built-in calibration curve, the instrument automatically calculate CEA concentration of each sample, in a unit of ng/mL.

[Reference Intervals]

Samples for the study of reference intervals come from local area in Guangdong Province. A total of 63 healthy and normal people have been recruited (Male: 32; Female: 31), age distribution: 18~70^[8]. Serum tests give a reference interval of 95% population at 5.00 ng/mL.

Due to the differences in geography, race, sex, and age of tested population, the reference interval may vary in different laboratories. It is highly recommended for each clinical lab to establish its own reference intervals.

[Interpretation of Test Results]

The test data is for clinical reference only. It cannot be used as the only confirmatory evidence nor to eliminate the possibility of diseases. Clinical diagnosis of patients should take clinical symptoms, body sign, disease history, other lab test results, and treatment response into comprehensive consideration.

The measurement range of this assay is: 0.50~1500.00 ng/mL. If CEA concentration is lower than LoD, it will be reported as < 0.50 ng/mL; if CEA concentration is over the upper limit, it will be reported as >1500.00 ng/mL.

For a sample with CEA concentration of >1500.00 ng/mL, sample diluent can be used to dilute the sample manually (a dilution factor of 1:100 is recommended). Test the diluted sample in duplicate to obtain more accurate results.

When the instrument shows a warning sign of "SMPL", it means there is insufficient sample volume. Make sure enough sample is added for repeating the test. When the instrument shows a warning sign of "SMPJ", it means the sample probe has been blocked. Clean sample clot in the probe before repeating the test.

Some results are tagged with other signs. Refer to the Chapter of "Result Signs" in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about results tagged with signs.

[Limitation of the Test Method]

The test data is for clinical reference only. It cannot be used individually as the evidence to confirm or eliminate the possibility of diseases.

There is no Hook effect for samples with CEA concentration ≤ 60000.00 ng/mL.

For endogenous interference substances with concentration less than the value shown in the table below, measurement error caused by the interference is within ±10%.

Endogenous interference substance	Concentration of interference substance
Total Protein	≤ 13.2 g/dL
Bilirubin	≤ 22 mg/dL
Hemoglobin	≤ 550 mg/dL
Triglyceride	≤ 3300 mg/dL

Heterophilic antibodies in human serum may react with immunoglobulin in the reagent or sample, and interfere with immunoassay in vitro. More clinical or diagnostic information is needed to confirm disease status of patients.

Some patients have frequent contact with animals, or have been treated or diagnosed with mouse monoclonal antibodies. They may have generated heterophilic antibodies. For example, some patients under monoclonal antibody treatment may have human anti-mouse antibodies (HAMA) in blood circulation, leading to false positive or false negative results. Anti-interference components are added to this reagent formulation to minimize the impact of HAMA, but the problem may not be totally eliminated, and some sample testing may still be impacted. More clinical and diagnostic information is needed to make a solid conclusion.

For RF at a concentration of less than 1500 IU/mL, and for HAMA at a concentration of less than 120 ng/mL, the impact on measurement value is minimal, and the measurement error caused by the interference is within ±10%.

[Property and Performance]

1 Limit of Blank

LoB ≤ 0.20 ng/mL.

2 Limit of Detection

LoD ≤ 0.50 ng/mL.

3 Accuracy

Accuracy should meet at least one of the following criteria:

a) Take International reference material which can be used to prepare reference samples for routine evaluation. The relative error between the measured result and the target concentration is less than ±10.0 %.

b) Test the accuracy samples at two concentration levels multiple times. The relative deviation between the measurement result and the target value must not exceed 10.0%.

c) Spike CEA of a known concentration into real samples at different CEA levels. Spiked recovery should be 100.0±15.0%.

4 Linearity

Test CEA samples with concentration in the range of 0.50~1500.00 ng/mL, the linearity correlation coefficient $r \geq 0.9900$.

5 Repeatability

Coefficient of variation (CV) for the test results of low (10.00±2.00 ng/mL) and high (100.00±20.00 ng/mL) corporate reference sample is less than 8.0 %.

6 Lot-to-lot Variation

Coefficient of variation (CV) for the test results of low (10.00±2.00 ng/mL) and high (100.00±20.00 ng/mL) corporate reference sample with three batches of reagent is less than 10.0 %.

7 Accuracy of Calibrator Value Assignment

Use primary calibrators with assigned values from higher level measurement procedure, calibrate the immunoassay analyzer, and use the same lot of reagent to measure the value of each product calibrator. The measured value of Calibrator C1 and C2 has a relative deviation within ±10.0 % from its assigned value.

8 Homogeneity of Calibrators

8.1 Within-vial Homogeneity

Within-vial homogeneity of Calibrator C1 or C2 is represented with coefficient of variation, and $CV \leq 8.0 \%$.





8.2 Between-vial Homogeneity










Between-vial homogeneity of calibrator C1 or C2 is represented with coefficient of variation, and $CV \leq 5.0 \%$.

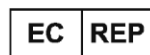
[Attention Notes]

- It is for in-vitro diagnosis only.
- It can only be used by professionals.
- Never use expired reagent kit.
- Never mix components from different kits, or from different reagent lots.
- Do not put the reagent cartridges upside down.
- Measurement of CEA in a sample using different detection systems may yield different results, due to the difference in test methods, assay specificity, and factors of interference. The measured values from different systems should not be directly compared to avoid inappropriate clinical interpretation.
- Strictly follow the protocol in the package insert, and operate according to the lab guidelines.
- The test results can only be used for clinical reference. Clinical diagnosis of patients should take symptoms, body sign, disease history, other laboratory test results, and response to treatment for comprehensive assessment.
- User should wear gloves and lab coat. Rinse with water if the skin is in contact with the reagent. Flush eyes with copious of water if eyes are in touch with the reagent, and see a doctor immediately.
- Take all samples and reaction waste as potential biohazards. All waste must be handled following the local government regulation.
- This product is a single-use cartridge. Reagent cartridge should be put back into refrigerator and stored at 2~8°C if they have been placed at room temperature but not opened yet.

[Interpretation of Signs]

	Temperature limit.		Date of manufacturing
	In vitro diagnostic medical device		Catalogue number

	Batch Code		Consult instruction for use
	Use-by Date		Authorized representative in the European Community
	This way up		CE marking of conformity
	Manufacturer		Unique device identifier
	Biological risks		



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[Issued on]

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[Basic Information]



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