Lifotronic

CE

Instruction for Use

【Product Name】

Cancer Antigen 15-3 (eCLIA)

【Order Information】

REF NO.	Package Size
0320500701	50 T
0320500702	2×50 T
0320500703	100 T
0320500704	2×100 T

【Intended Use】

Immunoassay for in vitro quantitative determination of Cancer Antigen 15-3 (CA15-3) in human serum and plasma, and for clinical application in breast cancer treatment effect and prognosis observation.

Breast cancer is one of the most common malignant tumors in women with high incidence. Cancer antigen 15-3, Cancer Antigen 125, Carcinoembryonic Antigen (CEA), Tissue Polypeptide Antigen (TPA) and Tissue Polypeptide Specific Antigen (TPS) are all clinically used serum markers of breast cancer. Provably, CA15-3 has been widely recognized as the preferred marker of breast cancer, and the CA1 5-3 in other cancers such as metastatic ovarian cancer, colon cancer, liver cancer, bile duct cancer, pancreatic cancer and lung cancer will also show an increase of different degrees[1, 2]. CA15-3 is an antigen determinant cluster on a high-molecular weight glycoprotein encoded by MUC1 gene, with a molecular weight greater than 400,000 Daltons. CA15-3 antigen is identified by using mouse monoclonal antibody 115-D8 prepared with glycoprotein MAM-6 on human milk fat globule membrane and monoclonal antibody DF-3 prepared with cytomembrane of liver metastatic breast cancer[3, 4]. Studies have shown that CA15-3 is not sensitive in the early diagnosis of breast cancer, but widely used in the monitoring of preoperative prognosis and postoperative efficacy as well as the monitoring of metastasis and recurrence.

【Principles of the examination method】

Sandwich principle. Total duration of assay: 9 minutes.

Cancer Antigen 15-3 (CA15-3) Assay Kit adopts the double-site sandwich electrochemiluminescence method. The pre-diluted samples, biotinylated CA15-3 monoclonal antibody and ruthenium (Ru) complex-labeled CA15-3 monoclonal antibody form antigen-antibody sandwich complex, which is bound to streptavidin coated magnetic particles, and then transferred to the measuring cell where the magnetic particles are captured onto the surface of the electrode, while the unbound substances are washed away. Chemiluminescence is generated after the electrode is electrified, and the generated optical signal is measured by a photomultiplier, processed by an instrument, and the CA15-3 concentration in the sample is calculated based on the calibration curve.

【Main Components】

The reagent pack consists of MB, RA, RB, DS, calibrators and control materials , and different components and reagents of lot numbers should not be used interchangeably.

Components	Ingredients	Volume (2×50 T)	Volume (50 T)	Volume (100 T)	Volume (2×100 T)
(MB)	Streptavidin-coated microparticles,0.45 mg/mL; 100 mM PBS; ProClin™300	2×1.8 mL	1×1.8 mL	1×3.5 mL	2×3.5 mL
(RB)	Biotinylated CA15-3 antibody, 1.5 mg/L; 50 mM MES; ProClin™300	2×3.8 mL	1×3.8 mL	1×7.5 mL	2×7.5 mL
(RA)	Ru complex-labeled CA15-3 antibody, 2.0 mg/L; 50 mM MES; ProClin™300	2×3.8 mL	1×3.8 mL	1×7.5 mL	2×7.5 mL
DS	0.05 M PBS; ProClin™300;	2×4.5 mL	1×4.5 mL	1×9.0 mL	2×9.0 mL
Calibrator	CA15-3 antigen; 50 mM PBS; ProClin™ 300;	High: 2×1.0 mL Low: 2×1.0 mL	High: 1×1.0 mL Low: 1×1.0mL		
Control Material	CA15-3 antigen; 50 mM PBS; ProClin™ 300;	High: 2×1.0 mL Low: 2×1.0 mL	High: 1×1.0 mL Low: 1×1.0mL		

The assignment process of supporting calibrators in this pack is strictly implemented with reference to ISO 17511: 2020, which can be traced back to Roche Elecsys CA15-3.

Refer to the quality control card for the target value and range of the quality controls.

Additional materials for Automated ECL Immunoassay Analyzer eCL8000, eCL8000i, eCL8000p, eCL8000x:

Auffer, 480 mL, 6×480 mL

Buffer, 480 mL, 6×480 mL

Concentrated Washing Buffer

Assay Cup

Additional materials for Automated ECL Immunoassay Analyzer eCL9000, eCL9000i, eCL9600, eCL9900, eCL9900i:

Auffer, 2 L

Buffer, 2 L

Concentrated Washing Buffer

Assay Cup, reaction cup

Disposable Sampling Head, pipette tips

PreClean, system wash solution

Waste Bags, litter bags

【Storage and Shelf Life】

Unopened reagent rackpack, calibrators and control materials should be placed at 2~8ºC and will be valid for 18 months.

Once opened, they can be stored at 2~8ºC for 56 days, and reagent kit can also be stored in machine (4~15ºC).

The manufacturing date is labeled on the box, kit and bottles, and the expiration time is 18 months after production.

Damaged, expired or contaminated reagents should be discarded.

【Applicable Instrument】

Automated ECL Immunoassay Analyzer: eCL8000, eCL8000i, eCL8000p, eCL8000x, eCL9000, eCL9000i, eCL9600, eCL9900, eCL9900i.

【Specimen collection, handlinhaodeg and storage】

It is recommended to use human serum samples or plasma samples collected with EDTA-K2, EDTA-K3, heparin lithium, heparin sodium blood collection tubes.

Blood samples should be collected in accordance with the standard operation of venipuncture. After the sample is completely coagulated, centrifugation should be performed to remove residual cellular substances. The sample should be free of air bubbles during testing. Lipid layer covering the sample after centrifugation should be removed. It is not recommended to use hemolyzed samples.

Samples can be stored for 48 hours at room temperature (18~28ºC), 5 days at 2~8ºC, and 3 months at -15ºC or below. Samples should avoid repeated freeze-thaw cycles. Do not use the samples after five freeze-thaw cycles.

【Testing Procedure】

Testing procedure and precautions

Before testing, the system operation manual of the measuring instrument should be carefully read, so as to obtain relevant information such as system operating procedures, sample management, safety precautions and maintenance, and materials required for testing should be prepared. CA15-3 testing procedures should be called and set up in accordance with the system operating procedures.

Before using the reagent, put it into the analyzer 30 minutes in advance to automatically stir the magnetic bead particles and keep them in suspension.

Recommended environment temperature for testing: 10~30ºC relative humidity: ≤ 80.0%.

The CA15-3 test adopts the double-site sandwich electrochemiluminescence method, with the total test time of 9 minutes, and the test method is as follows:

Step 1: After the user applies for testing, the system automatically aspirates 10 μL samples and 90 μL sample diluent into the first reaction cup for Pre-dilution.

Step 2: Then the system automatically aspirates 10 μL pre-diluted samples from the first reaction cup ,and aspirates 75 μL of biotinylated CA15-3 monoclonal antibody, 75 μL of Ru complex-labeled CA15-3 monoclonal antibody and 35 μL of streptavidin coated magnetic particles into the second reaction cup. They are automatically incubated at 37ºC for 9 min to form antigen-antibody sandwich complexes, and then the whole complexes are bound to the magnetic particles under the interaction of biotin and streptavidin.

Step 3: After incubation, the system automatically aspirates the reaction mixture into the measuring cell, the magnetic particles are captured onto the surface of electrode, while the unbound substances are washed away by buffer, and the electrodes is applied with voltage to generate chemiluminescence. The generated optical signals are measured by the photomultiplier, and the measured results are automatically determined via the calibration curve specifically generated by the instrument (this curve is obtained by performing two-point calibration for the master calibration curve obtained by reading the reagent RFID).

Calibration

Calibration should be performed using lot-matching reagent and calibrators.

The target value of the calibrator has been written into the Radio-Frequency Identification card (RFID card) of the kit.

1. Before calibration, the target value, reagent information and master calibration curve information of the calibrator in the RFID card (Radio Frequency Identification, inductive electronic chip or proximity card) of the kit should be imported into the test system by swiping the card.
2. The supporting calibrator is tested, and the analyzer adjusts the master calibration curve according to the test results of the supporting calibrator to obtain the calibration curve tested by the current system (the analyzer can automatically interpret the validity of the calibration curve according to the adjustment results).

The test system should re-perform the calibration operation under the following conditions:

(1) When different lots of reagents are used;

(2) When the same lot of reagents has been used on the analyzer for more than 28 days;

(3) According to requirements: e.g. if the quality control result exceeds the

defined limit;

(4) When changing the buffers of different lot numbers.

Quality Control procedure

In order to ensure the reliability of test results, it is recommended to test the control materials every 24 hours. It is recommended to test the control materials after each calibration, reagent lot replacement, maintenance or troubleshooting. The quality control results should all fall within the defined range. If they exceed the defined range, the reasons such as instrument status, reagents and calibrators should be investigated and the corrective measures should be taken.

Calculation

The system software can automatically calculate the analyte concentration, with the result in U/mL.

Specimen dilution

CA15-3 concentration in the sample higher than the upper limit of detection can be diluted manually with sample diluent.

The recommended dilution ratio is 1:9. (automatic dilution by instrument or manual dilution). If manual dilution, the result should be multiplied by the dilution ratio. If instrument automatic dilution, the instrument will automatically calculate the result.

【Biological Reference Interval】

By analyzing the serum samples of 157 healthy females in hospitals, it is calculated that the upper limit of the reference range of 95% is 25.31 U/mL.

Due to the differences in geography, race, gender and age, it is recommended that each laboratory determine the applicability of reference range through tests, and establish the reference range of this laboratory if necessary.

【Interpretation of results】

When interpreting the test results, it is necessary to refer to the patient's overall clinical situation, including: symptoms, medical history as well as other corresponding data and information.

【Limitations】

The test results are only for clinical reference and cannot be used alone as the basis for diagnosis or exclusion of cases.

The detection range of the kit is 0.15~300 U/mL. If the CA15-3 concentration in the sample is lower than the lower limit of detection, the result is reported as < 0.15 U/mL; if the CA15-3 concentration in the sample is higher than the upper limit of detection, the result is reported as > 300 U/mL (10x diluted sample is reported as > 3000 U/mL).

When jaundice (bilirubin) is ≤ 65 mg/dL, hemolysis (hemoglobin) is ≤ 1000 mg/dL, lipid (triglyceride) is ≤ 1500 mg/dL, biotin is ≤ 50 ng/mL, total protein is ≤ 10 g/dL, and HAMA is ≤ 100 ng/mL in the sample, the interference deviation of the measured results is within ±10.0%. When the concentration of rheumatoid factor in the sample is ≤ 1500 IU/mL, the relative recovery of the test results is between 90.0% and 110.0%.

When the sample contains methotrexate (15 μg/mL), acetaminophen (200 μg/mL), cyclophosphamide (350 μg/mL), 5-fluorouracil (300 μg/mL), cisplatin (70 μg/mL), aspirin (500 μg/mL), doxorubicin hydrochloride (6.6 μg/mL), adriamycin (6.6 μg/mL), paclitaxel(5 μg/mL), ibuprofen (400 μg/mL), megestrol acetate (40 μg/mL), tamoxifen (5 μg/mL), the interference deviation of the measured results is within ±10.0%.

Samples of other tumor markers containing 1000 ng/mL AFP, 1000 U/mL CA125, 1000 ng/mL CEA, 1000 U/mL CA19-9, 100 ng/mL PSA, and 1000 ng/mL Ferritin are tested, and the CA15-3 measured results are not greater than 10 U/mL.

When the CA5-3 concentration reaches 4000 U/mL, there is no high-dose hook effect; when the CA5-3 concentration reaches 20000 U/mL, the test results are not be affected by the hook effect.

【Analytical Performance】

Limit of detection (LoD)

Not greater than 0.5 U/mL.

Accuracy

The accuracy control subject to standardized traceability is tested, and the relative deviation of its test results is within ±10.0%.

Linearity

Within the range of 0.5 U/mL~300 U/mL, the correlation coefficient (r) of the kit should not be less than 0.9900.

In-batch imprecision (repeatability)

The coefficient of variation (CV) ≤ 5.0%.

Inter-batch imprecision

The coefficient of variation (CV) ≤ 10.0%.

Homogeneity of calibrators and control materials

In-bottle homogeneity: coefficient of variation (CV) ≤ 5.0%.

Between-bottle homogeneity: coefficient of variation (CV) ≤ 10.0%.

Accuracy of calibrators

The supporting calibrators of the kit are tested, the relative deviation of their test results is within ±10.0%.

Measured values of quality control

The measured results of supporting assigned quality control of the kit should be within the quality control range.

【Precaution and Warning】

This kit is only used for in vitro diagnosis;

When using this kit, the relevant operation precautions of the laboratory must be observed;

The test results of this kit can only be used as clinical reference, the patient's clinical evaluation should be based on the patient's clinical symptoms/signs, medical history, other laboratory test results and treatment response, etc.

Due to methodological reasons or antibody specificity, the results of the same sample tested with reagents of different manufacturers may be different. Therefore, results obtained with different kits should not be directly compared, so as to prevent wrong medical interpretation; it is recommended that the Laboratory Department indicate the characteristics of the reagents in the test report issued to the clinician. If the reagent type is changed during series monitoring, continuous testing should be conducted, and the results should be compared with the original reagent results in parallel to re-determine the baseline value;

This product contains animal-derived substances, and may have potential biological risks. All samples and reaction wastes should be treated as the source of infection, and all wastes must be disposed of in accordance with local regulations.

【Symbol】

Symbol	Title of Symbol	Symbol	Title of Symbol
	Manufacturer		Consult instructions for use
	Authorized representative in the European		In vitro diagnostic medical device
	Use-by date		Indicates this device is in compliance with Europe
	Batch code		Contains sufficient for<*n*>tests
	Serial number		Biological risks
	Temperature limitation		This way up
	Catalogue number		

【Bibliography】

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3. Hilkens J, et al. Monoclonal antibodies against human miikfat globule membranes detecting differentiation antigens of the mammary gland. Prot Biol Fluids 1982; 29: 813-816.
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【Manufacturer】

Shenzhen Lifotronic Technology Co., Ltd.

Unit A, 4th Floor, Building 15, Yijing Estate, No.1008 Songbai Road, Nanshan District, Shenzhen City, Guangdong Province, 518055, P.R.China

E-mail: inter-service@lifotronic.com

【European Representative】

Shanghai International Holding Corp. GmbH (Europe)

Eiffestrasse 80, 20537 Hamburg, Germany

Tel: +49-40-2513175 Fax: +49-40-255726

【Version and Revision】

Version: A0

Issue Date: 2020-12-17