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 CA15-3 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.

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. 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 (optional), 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; ProClin300	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; ProClin300	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; ProClin300	2×3.8 mL	1×3.8 mL	1×7.5 mL	2×7.5 mL
DS	0.05 M PBS; ProClin300;	2×4.5 mL	1×4.5 mL	1×9.0 mL	2×9.0 mL
Calibrators	CA15-3 antigen; 50 mM PBS; ProClin 300;	High:1×1.0 mL Low:1×1.0 mL			
Control Materials (Optional)	CA15-3 antigen; 50 mM PBS; ProClin 300;	High:1×1.0 mL Low:1×1.0 mL			

Traceability:This method can be traceable to Roche Elecsys CA15-3.

See the control material value sheet for the target values and ranges of control materials.

Supporting instruments and materials required but not provided in this pack (provided by Lifotronic).

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

- REF 679005, Auffer, 480 mL, or REF 679004, Auffer, 6×480 mL
- REF 679007, Buffer, 480 mL, or REF 679006, Buffer, 6×480 mL
- REF 679009, Concentrated Washing Buffer, 1 L, or REF 679008, Concentrated Washing Buffer, 6×1 L
- REF 679011, Assay Cup, 300 T, or REF 679012, Assay Cup, 3000 T

Additional materials for Automated ECL Immunoassay Analyzer eCL8600,

- REF 0320501804, Auffer, 2×1 L, or REF 0320501805, Auffer, 4×1 L
- REF 0320501904, Buffer, 2×1 L, or REF 0320501905, Buffer, 4×1 L
- REF 0320507502, PreClean, 2×800 mL, or REF 0320507503, PreClean, 4×800 mL
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 032120111, Assay Cup/Assay Tip, 12×2×105

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

- REF 0320501801, Auffer, 2×2 L, or REF 0320501806, Auffer, 4×2 L
- REF 0320501901, Buffer, 2×2 L, or REF 0320501906, Buffer, 4×2 L
- REF 0320507501, PreClean, 2×2 L, or REF 0320507504, PreClean, 4×2 L
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 0320510002, Assay Cup/Assay Tip, 1×6×105

【Storage and Shelf Life】

Store at 2ºC~8ºC.

Do not freeze.

Store the reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagents	
Unopened store at 2ºC~8ºC	18 months
Store at 2ºC~8ºC after opening	8 weeks
Stored on the analyzers at 2ºC~15ºC	8 weeks

The Calibrators and Control Materials are stable up to the stated expiration date.

Stability of the Calibrators and Control Materials	
Unopened store at 2ºC~8ºC	18 months
Store at 2ºC~8ºC after opening	8 weeks

【Applicable Instrument】

Automated ECL Immunoassay Analyzers: eCL8000, eCL8000i, eCL8000p, eCL8000x, eCL8600, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p, eCL9000, 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 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%.

Calibration

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

Before calibration, the reagent and main curve information should be imported into the analyzer via radio frequency identification reagent card (refer to instrument user manual). The analyzer adjusts the main curve to produce working curve according to the calibrator results, and identifies validity of the working curve automatically.

Recalibration is recommended when:

(1) The reagents of different lot are used;

(2) The same lot of reagents were used on the analyzer beyond 28 days;

(3) Quality control findings outside the defined limits.

(4) The Buffer of different lots are used.

Quality Control procedure

For quality control, use CA15-3 control materials.

In addition, other suitable control material can be used.

Control materials for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Please make sure that the correct values are used.

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 CA15-3 concentration reaches 4000 U/mL, there is no high-dose hook effect; when the CA15-3 concentration reaches 20000 U/mL, the test results are not be affected by the hook effect.

【Analytical Performance】

Lower limit of measurement

Limit of Blank = 0.15 U/mL.

Limit of Detection = 0.5 U/mL.

Accuracy

The recovery sample added with an appropriate concentration of CA15-3 is tested, and the recovery is between 90.0% and 110.0%.

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.

Within-run imprecision (repeatability)

The coefficient of variation (CV) ≤ 5.0%.

Between-lot 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.

Method comparison

A comparison of the Lifotronic CA15-3 assay (y) with the Roche Elecsys CA15-3 Method (x) using clinical samples gave the following correlations:

Number of samples measured: 107

Linear regression:

y=0.9855x+1.282

r=0.992

The sample concentrations were between approx 2.98 and 281.7 U/mL.

【Precaution and Warning】

The kit is only used for in vitro diagnostics.

Exercise the normal precautions required for handling all laboratory reagents.

All reagents and samples including specimen, reagents, calibrators and control materials should avoid foaming before and during test.

Disposal of all waste material should be in accordance with local guidelines.

Safety data sheet available for professional user on request.

This product contains animal-sourced materials and may have potential biological risk. All samples and test wastes should be treated as the source of infection, and all wastes must be disposed according to local regulations.

Any serious incident that would be occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

The preservative ProClin™300 which contain Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-Methyl-2H-isothiazol-3-one (3:1): May cause an allergic skin reaction. thus, proper personal protection should be adopt while handling the reagent: avoid breathing dust/fume/gas/mist/vapours/ spray, wear protective gloves and contaminated work clothing should not be allowed out of the workplace. If skin irritation or rash occurs: get medical advice/attention, take off contaminated clothing and wash it before reuse, and dispose of contents/container to an approved waste disposal plant.

.**【Symbols Explanation】**

Symbol	Title of Symbol	Symbol	Title of Symbol
	Manufacturer		Consult instructions for use
	Use-by date	IVD	In vitro diagnostic medical device
LOT	Batch code	Σ	Sufficient for <n> tests
SN	Serial number		Biological risks
	Temperature limit		This way up
EC REP	Authorized representative in the European Community	CE	Indicates this device is in compliance with Europe Directive.
REF	Catalogue number	P/N	Material code
	Warning		Date of manufacture
UDI	Unique device identifier		

【Bibliography】

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2. Colomer R, Ruibal A, Genollá J, et al. Circulating CA15-3 Antigen Levels in Non-mammary Malignancies. Br J Cancer 1989; 59: 283-6.
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.
4. Hilkens J, et al. Monoclonal antibodies against human miikfat globule membranes detecting differentiation antigens of the mammary gland and its tumors. Int J Cancer 1984; 34: 197-206.

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