Instruction For Use

【Product Name】

Anti-CCP (eCLIA)

【Order Information】

REF NO.	Package Size
0320510801	50T
0320510803	100T
0320510802	2×50T
0320510804	2×100T

【Intended Use】

Immunoassay for the in vitro quantitative determination of Autoantibodies to cyclic citrullinated peptides (Anti-CCP) in human serum and plasma.

Anti-cyclic citrullinated peptide (CCP) antibodies are polypeptide fragments o f ringed polymelon protein, mainly IgG antibodies, spontaneously secreted b y B lymphocytes of rheumatoid arthritis (RA) patients[1]. Rheumatoid arthriti s (RA) is a common systemic autoimmune disease, with an incidence of ap proximately 0.5% of the globalpopulation[2-3]. Its main characteristics are syno vial joint inflammation and progressive joint destruction. It can cause joint s welling, stiffness, and pain, leading to decreased quality of life and, in sever e cases, disability[4]. Prior to the onset of rheumatoid arthritis, rheumatoid fac tor (RF), anti-cyclic citrullinated peptide antibodies (Anti-CCP), and cytokine s are elevated[5-7]. Among them, anti-cyclic citrullinated peptide antibodies (A nti-CCP) can be detected in 60-70% of rheumatoid arthritis patients and hav e a high correlation with rheumatoid arthritis[8-9]. In 2007, the European Leag ue Against Rheumatism (EULAR) published guidelines for the early diagnosi s of rheumatoid arthritis, in which the detection of anti-cyclic citrullinated p eptide antibodies was included as a serological marker[10].

Determination of Anti-CCP is used for auxiliary diagnosis of Rheumatoid arthritis.

【Test Principle】

IgG-capture principle. Total duration of assay: 9 minutes

15 μL of sample, biotinylated cyclic citrullinated peptides, and monoclonal antibody labeled with ruthenium react to form a sandwich complex. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with system reagent. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument specifically generated by 2-point calibration and a master curve provided via the RFID.

【Main Components】

The reagent pack consists of MB, RA, RB, calibrators and control materials (Optional). Different lots cannot be used at the same time or mixed up together.

Components	Ingredients	Volume (2×50T)	Volume (50T)	Volume (100T)	Volume (2×100T)
MB	Streptavidin-coated microparticles 0.45 mg/mL; 0.05% ProClin300	2×1.8 mL	1×1.8 mL	1×3.5 mL	2×3.5 mL
RB	CCP~biotin;Tris; 0.05% ProClin300	2×3.8 mL	1×3.8 mL	1×7.5 mL	2×7.5 mL
RA	Anti-human IgG~Ru; Tris; 0.05% ProClin300	2×3.8 mL	1×3.8 mL	1×7.5 mL	2×7.5 mL
Calibrators	Anti-CCP antibody; Tris; 0.05% ProClin300	High: 1×1.0 mL Low: 1×1.0 mL			
Control Materials (Optional)	Anti-CCP antibody; Tris; 0.05% ProClin300	High: 1×1.0 mL Low: 1×1.0 mL			

The calibration process of this kit is traceable to the measurement procedures selected by the enterprise.

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 Analyzer 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, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p:

- 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 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 0320510002, Assay Cup/Assay Tip, 1×6×105

【Storage and Shelf Life】

Store at 2℃-8℃.

Do not freeze.

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

Damaged, expired or contaminated reagents should be discarded.

Stability of the reagents	
Unopened at 2℃~8℃	18 months
Store at 2℃~8℃ after opening	8 weeks
Stored on the analyzers at 2℃~15℃	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 2℃~8℃	18 months
Store at 2℃~8℃ 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, handling and storage】

Human serum and plasma added with heparin lithium, EDTA-K3 and EDTA-K2 anti-coagulants are recommended. Blood samples should be collected by standard operation of venous puncture, after complete coagulation, the tangible component should be removed by centrifugation. The sample should avoid bubbling during testing. Lipid layer floating on the upper of the sample should be removed. Samples with severe hemolysis are not recommended.

Samples can be stored for 3 day at 18-28℃, 8 day at 2-8℃, and 3 months at -15℃ or below. The samples may be frozen three times.

Ensure the samples are at 18℃-28℃ prior to measurement.

【Assay Procedure】

Testing procedures and precautions

Previous to operation, one should read the operational manual carefully to obtain system operation procedure, sample processing, security precaution, maintenance and other related information.

Set up Anti-CCP test according to the operational manual.

Put the Anti-CCP rackpack into the correct analyzer slot to automatically suspend magnetic beads at least 30 minutes before testing.

Recommended ambient temperature:10~30°C; Relative humidity: ≤ 80%.

Calibration

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

Before calibration, the reagent 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 lots are used;

(2) The same reagent lot was used on the analyzer beyond 28 days;

(3) Quality control is beyond the defined limits;

(4) The Buffer of different lots are used.

Quality control

For quality control, use Anti-CCP 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 automatically calculates the analyte concentration using particular algorithm, and the result unit is U/mL.

Specimen dilution

Samples with Anti-CCP concentrations above the test range can be diluted with sample diluent. The recommended dilution is 1:5 (automatic dilution by instrument or manual dilution). If manually diluted, the result should be multiplied by the dilution. If the instrument is automatic dilution, the instrument will automatically calculate the result.

【Biological reference interval】

According to serum test results of 255 healthy human serum samples , the upper limit of the 95% reference interval is calculated to be 17.52 U/mL.

Due to differences in the region, race, gender and age, laboratories are recommended to set up their own reference ranges.

【Interpretation of results】

For explaining the result, the patient's overall clinical manifestation should be referred to, including symptoms, medical history and other relevant data and information.

【Limitations】

Test results are used only for clinical reference and cannot be used as the basis for diagnosis or rule-out of diseases alone. For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

The measuring range of the kit is 1 ~500 U/mL. Values below the lower detection limit are reported as <1 U/mL. valves above the measuring range are reported as > 500 U/mL(or >2500 U/mL for 5 times diluted samples).

When the sample containing bilirubin ≤ 25 mg/dL ,triglyceride ≤ 1500 mg/dL, total protein ≤ 10 g/dL, biotin ≤ 30 ng/mL, hemoglobin ≤ 500 mg/dL, HAMA ≤100 ng/mL, interference deviation to the test result lies within ±10%. When the concentration of rheumatoid factor in the sample ≤ 150 IU/mL, the relative recovery of the test results is between 90%- 110%.

When the samples containing 0.4 g/dL immunoglobulin A (IgA) and 0.23 g/dL immunoglobulin M (IgM) were detected, the relative deviation of the results was within ±10%.

When the Anti-CCP concentration reached 2000 U/mL, there was no high-dose hook effect. When the Anti-CCP concentration reached 7000 U/mL, the test result is not affected by hooked effect.

【Analytical Performance】

Lower limits of measurement

Limit of Blank = 1 U/mL

Limit of Detection = 8 U/mL.

Accuracy

The relative deviation shall not exceed ±10%.

Linearity

The correlation coefficient is not less than 0.9900 in the interval of 8～500 U/mL.

Within-run precision (repeatability)

The coefficient of variation (CV) ≤ 5.0%.

Between-lot precision

The coefficient of variation (CV) ≤ 10.0%.

Homogeneity of calibrators and control materials

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

Method comparison

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

Number of serum samples measured: 120

Linear regression:

Y=0.4152+0.997X

r = 0.998

The sample concentrations were between 12.6 and 488.6 U/mL.

【Precaution and Warning】

The kit is only used for in vitro diagnostics.

When using the kit, it's necessary to exercise the normal precautions in the laboratory.

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

Test results of the kit are for clinical reference only, and clinical evaluation of patients should be combined with their symptoms and signs, medical history, other laboratory examination results and treatment responses.

Due to factors such as methodology or antibody specificity, testing identical samples with reagents from different manufacturers may get different results, and the results from different kits should not compare directly, lest cause the wrong medical explanation,It's suggested that laboratorians should point out the characteristics of used reagent in the test report to the clinician. In serial monitoring, if the reagent type is changed, a continuous parallel test should be performed and comparison of the results to the former should be to determine new baseline value.

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.

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		In vitro diagnostic medical device
	Batch code		Sufficient for <n> tests
	Serial number		Biological risks
	Temperature limit		This way up
	Authorized representative in the European Community		Indicates this device is in compliance with Europe Directive
	Catalogue number	P/N	Material code
	Warning		Date of manufacture
	Unique device identifier		

【Literature References】

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