Instruction for Use

【Product Name】

Procalcitonin (Electrochemiluminescence Immunoassay)

【Order Information】

REF NO.	Package Size
689013	100T
689014	2×100T
689021	50T
689022	2×50T

【Intended Use】

Immunoassay for the in vitro quantitative determination of PCT (procalcitonin) in human serum and plasma. The results can be used to aid in the early detection of clinically relevant bacterial infections.

Procalcitonin is a 116 amino acid prohormone with a molecular weight of approx 12.7 kD. PCT is expressed by neuroendocrine cells (C cells of the thyroid, pulmonary and pancreatic tissues) and successively enzymatically cleaved into (immature) calcitonin, katacalcin, and an N-terminal region. The blood of healthy individuals contains only low levels of PCT[1,2]. It was discovered that PCT increases during bacterial infection. It is probable that multiple tissues express PCT throughout the body in response to sepsis as shown in an animal model[3]. PCT circulating in septic patients consists of only 114 amino acids lacking the N-terminal dipeptide Ala-Pro[4].

【Test Principle】

Sandwich principle.Total duration of assay:18 minutes

1st incubation: 30 µL of sample, a biotinylated monoclonal PCT-specific antibody, and a monoclonal PCT-specific antibody labeled with a ruthenium complex react to form a sandwich complex.

2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.

Measurement: 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 Buffer. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.

Results are determined via a calibration and a master curve provided via the reagent barcode.

【Main Components】

The reagent pack consist of MB, RA, RB, calibrators and control materials (Optional). Different lots can not used in the same time or mixed up together.

Components	Ingredients	Volume (100T)	Volume (2×100T)	Volume (50T)	Volume (2×50T)
(MB)	Streptavidin-coated microparticles, 0.75 mg/mL; 0.1 M PBS; ProClin™ 300	1×5.0 mL	2×5.0 mL	1×3.0 mL	2×3.0 mL
(RB)	Anti-PCT-Ab~biotin,1.5 mg/L; 0.1 M PBS; ProClin™ 300.	1×9.0 mL	2×9.0 mL	1×5.5 mL	2×5.5 mL
(RA)	Anti-PCT-Ab~Ru(bpy)$_3^{2+}$, 0.5 mg/L; 0.1 M PBS; ProClin™ 300.	1×9.0 mL	2×9.0 mL	1×5.5 mL	2×5.5 mL
Calibrators	Horse serum; ProClin™ 300; lyophilized.	High: 1×4.0 mL Low: 1×4.0 mL			
Control Materials (Optional)	Horse serum; ProClin™ 300; lyophilized.	High: 2×4.0 mL Low: 2×4.0 mL		High: 1×4.0 mL Low: 1×4.0 mL	

The calibration value assignment of calibrators can be traced back to the BRAHMS PCT LIA.

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

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, o REF 0320507503, PreClean, 4×800 mL
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, o REF 032120111, Assay Cup/Assay Tip, 12×2×105

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 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 store at 2℃~8℃	18 months
Store at 2℃~8℃ after opening	8 weeks
Store 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 resolution	8 hours
Store at -25℃~-15℃ after resolution	3 months (freeze-thawed only once)

Store calibrators and control materials upright in order to prevent the calibrators and control materials from adhering to the cap of the vial.

【Applicable Instrument】

Automated ECL Immunoassay Analyzer: 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, heparin sodium and EDTA-K_2 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 would better to be tested in 8 hours after collection, otherwise, stored at 2~8℃ for 3 days , or -20℃ for 90 days. Centrifuge samples containing precipitates before performing the assay. Freeze-thawed only once.

Because of possible evaporation effects, samples, calibrators, and control materials on the analyzers should be measured within 2 hours.

【Assay Procedure】

Testing procedures 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. PCT STAT 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: 10~30℃; relative humidity: ≤80%.

Handing of lyophilized calibrators and control materials

Carefully dissolve the contents of lyophilized calibrator by adding exactly 4.0 mL of distilled or deionized water and allow to stand closed at room temperature for at least 15 minutes to reconstitute. Mix carefully, avoiding foam formation. Transfer aliquots of the reconstituted calibrators to empty tubes after the tubes were marked. Aliquots intended for storage at -25℃~-15℃ should be frozen immediately.

Carefully dissolve the contents of lyophilized control material by adding exactly 4.0 mL of distilled or deionized water and allow to stand closed at room temperature for at least 15 minutes to reconstitute. Mix carefully, avoiding foam formation. Transfer aliquots of the reconstituted control materials to empty tubes after the tubes were marked. Aliquots intended for storage at -25℃~-15℃ should be frozen immediately.

System 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 Buffers of different lot are used.

Quality control

For quality control, use PCT 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.

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.

Calculations

The system software automatically calculates the analyte concentration using particular algorithm, and the result unit is ng/mL or µg/L: 1 ng/mL=1 µg/L.

Specimen dilution

Samples that exceed the measuring range can be manually diluted with PCT-negative serum.
The recommended dilution ratio is 1:5, the concentration of the diluted sample must be >1.0 ng/mL or µg/L, and the diluted sample test results need to be multiplied by the dilution factor.

【Reference Interval】

According to serum test results of 330 cases of healthy human serum samples (male 172, female 158) in Guangdong Province, P. R. China, the reference range drawed by 95th percentile method is <0.052 ng/mL.
A study performed on samples from patients admitted to an ICU (intensive care unit) showed that PCT values:

- PCT <0.5 ng/mL represents a low risk of severe sepsis and/or septic shock
- PCT >2.0 ng/mL represents a high risk of severe sepsis and/or septic shock

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

【Result Interpretation】

In interpreting the results, the patient's overall clinical situations 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 confirmation or exclusion of diseases alone.
There's no high-dose hook effect at PCT concentrations up to 1000 ng/mL.
When the sample containing bilirubin <300 µg/mL, triglyceride <2000 mg/dL, biotin <15 ng/mL, hemoglobin <7 mg/mL, total protein is ≤20mg/mL, or HAMA is ≤ 289.44 ng/mL, interference deviation to the test result lies within ±10%. No interference was observed from rheumatoid factors up to a concentration of 2000 IU/mL.
When patients in the therapy with high-dose biotin (i.e. >5 mg/day), samples shouldn't be taken until at least 8 hours after last biotin administration.

【Measuring Range】

The measuring range of the kit is 0.02~100 ng/mL. Values below lower detection limit are reported as <0.02 ng/mL; values above the measuring range are reported as >100 ng/mL, then the sample is diluted and re-tested, the results are reported after multiplying with the dilution factor.

【Analytical Performance】

Lower limit of measurement

Limit of detection: 0.02 ng/mL

Accuracy

When measuring the metrologically traceable trueness control materials, the ratio between resulting value and target value lies between 0.900 and 1.100.

Linearity

The correlation coefficient (r) was not less than 0.9900 in the interval of 0.02~100 ng/mL.

Repeatability

The coefficient of variation (CV) ≤ 7.5%

Between-lot imprecision

The coefficient of variation (CV) ≤ 10%

Homogeneity of calibrators and control materials

Within-bottle homogeneity: coefficient of variation (CV) ≤ 7.5%.
Between-bottle homogeneity: coefficient of variation (CV) ≤ 10%.

Analytical specificity

The PCT assay doesn't show any significant cross-reactions with the following substances:

Substances	Concentration (ng/ml)
Human katacalcin	50
Human calcitonin	20
Human α-CGRP*	20000
Human β-CGRP	20000

*CGRP = Calcitonin Gene-Related Peptide

【Method Comparison】

A comparison of the Lifotronic PCT assay (y) with the Roche Elecsys BRAHMS PCT Method (x) using clinical samples gave the following correlations:
Number of samples measured: 143
Passing-Bablok regression:
y=-0.000407+1.017x
The sample concentrations were between approx 0.021ng/mL to 91.35 ng/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		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		

【Reference】

1. Gendrel D, Bohuon C. Procalcitonin as a marker of bacterial infection. Pediatr Infect Dis J 2000;19:679-688.
2. Becker KL, Nylén ES, White JC, Müller B, Snider RH. Procalcitonin and the Calcitonin Gene Family of Peptides in Inflammation, Infection, and Sepsis: A Journey from Calcitonin Back to Its Precursors. J Clin Endocrinol Metab 2004;89(4):1512-1525.
3. Gaïni S, Koldkjær OG, Møller HJ, Pedersen C, Pedersen SS. A comparison of high-mobility group-box 1 protein, lipopolysaccharide-binding protein and procalcitonin in severe community-aquired infections and bacteraemia: a prospective study. Crit Care 2007;11(4):77-87.
4. Castelli GP, Pognani C, Cita M, Stuani A, Sgarbi L, Paladini R. Procalcitonin, C-reactive protein, white blood cells and SOFA score in ICU: diagnosis and monitoring of sepsis. Minerva Anestesiol 2006;72:69-80.

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