PCT

Porrima

Procalcitonin (CLIA)

REF: PM037701 **100**

Intended use
The Porrima PCT assay is a Chemiluminescent Immunoassay (CLIA) for the quantitative determination of Procalcitonin (PCT) in **Human Serum**. For professional use only.

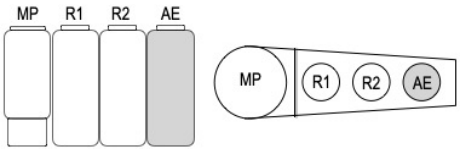
Summary
References[1-6]
Procalcitonin (PCT) is a 116 amino acid prohormone with a molecular weight of approximately 12.7 kD. PCT is expressed by neuroendocrine cells (C cells of the thyroid, pulmonary and pancreatic tissues) and successively enzymatically cleaved into (immature) calcitonin, katacalcin, and an N-terminal region. The blood of healthy individuals contains only low levels of PCT. It was discovered that PCT increases during bacterial infection. It is probable that multiple tissues express PCT throughout the body in 3 response to sepsis as was shown in an animal model. PCT circulating in septic patients consists of only 114 amino acids lacking the N-terminal dipeptide Ala-Pro. Increased PCT levels are often found in patients suffering from bacterial sepsis, especially severe sepsis and septic shock. PCT is considered as a prognostic marker to support outcome prediction in sepsis patients. In acute pancreatitis PCT was found to be a reliable indicator of severity and of major complications. In patients suffering from community-acquired respiratory tract infections or ventilator-induced pneumonia PCT has been proposed as a guide for the decision of antibiotic treatment necessity and to monitor treatment success.

Test principle
Two-step Sandwich principle. Total duration of assay: **25 minutes**
In the first incubation, sample and paramagnetic microparticles coated with monoclonal anti-PCT antibody are added into a reaction vessel. After incubation, microparticle is magnetically captured while other unbound substances are removed by washing.
In the second incubation, add monoclonal anti-PCT antibody-acridinium labeled conjugate to reaction mixture to form a sandwich complex, the complex becomes bound to the solid phase while other unbound Conjugate are removed by washing. Pre-Trigger and Trigger Solutions are then added to the reaction mixture, the resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of PCT in the sample and the RLUs detected by the Porrima system.

Materials provided

MP	1 x 5.0 mL, anti-PCT antibody (mouse, monoclonal) coated Microparticles in TRIS buffer with protein (bovine) stabilizers with preservative.
AE	1 x 10 mL, monoclonal anti-PCT antibody (mouse)-acridinium ester labeled conjugate in MES buffer containing BSA (bovine serum albumin). Contains 0.1% ProClin300 preservative.
C0	Calibrator, 1 vial, 1.0 mL, ready to use.
C1	Calibrator, 1 vial, 1.0 mL, ready to use.
C2	Calibrator, 1 vial, 1.0 mL, ready to use.

The position of each reagent component is shown in the figure below (front view on the left and top view on the right):



Materials required (but not provided)
- Porrima Chemiluminescent Immunoassay Analyzer
- CT2201 DiaSino ControlSet: 2 levels, L and H
- TR7701 Porrima TriggerPack: ①Pre-Trigger Solution, ②Trigger Solution
- WB7701 Porrima Wash Buffer (20X)
- RV7701 Porrima Reaction Vessels
- PW7701 Porrima Probe Wash Buffer
- SC7701 Porrima Sample Tubes (D13x75mm, D13x100mm or D16x100mm can be acceptable on Porrima system)

Precautions and warnings
- For in vitro diagnostic use only.
- Exercise the normal precautions required for handling all laboratory reagents.
- Disposal of all waste material should be in accordance with local guidelines.
- Do not use reagents beyond the labeled expiry date.
- Do not mix or use components from kits with different batch codes.
- All the specimen and reaction wastes should be considered potentially biohazard. The handling of specimens and reaction wastes should be in accordance with the local regulations and guidelines.
- Neutralized acids and other liquid waste should be decontaminated by adding a sufficient volume of sodium hypochlorite to obtain a final concentration of at least 1.0%. Exposure to 1.0% sodium hypochlorite for 30 minutes may be necessary to ensure effective decontamination.
- Some reagents contain 0.05% or 0.1% ProClin 300 which may cause sensitization by skin contact, which must therefore be avoided. Reagents and their containers must be disposed of safely. If swallowed, seek medical advice immediately and show this container or label.
- For information on hazardous substances included in the kit please refer to the Materials Safety Data Sheet (MSDS), which is available on request.
- Do not smoke, drink, eat or apply cosmetics in the work area.
- Do not pipette by mouth. Wear protective clothing, disposable gloves and eye/ face protection when handling samples and reagents. Wash hands after use.
- If any of the reagents comes into contact with the skin or eyes, wash the area extensively with water.

Reagent handling
The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.
All information required for correct operation is read in from the respective reagent barcodes.

Incident report
Any suspected serious incidents related to this assay shall be immediately reported to DiaSino, DiaSino's Authorized Representative in the EU, and the national competent authorities of the Member States where the users and/or patients are located.

Storage and stability
- Store at 2-8°C. Do not freeze.
- Store the Porrima reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use.
- The Porrima PCT reagent kit can be stored onboard and used for a maximum of 28 days after opening at 2-8°C.

Specimen collection and preparation
- Human serum is recommended for this assay.
- Centrifuge the specimens after clot formation is complete. Transfer the supernatants into tubes for storage or test within two hours after centrifugation.
- Specimens should be tested as soon as possible after sample collection. If testing is not completed within 8 hours, specimens should be tightly capped and refrigerated at 2-8°C. If testing will be delayed for more than 72 hours, specimens should be frozen at -20°C or below.
- Avoid repeated freeze and thaw cycles.

Assay procedure
- For optimal performance of this assay, operators should read the Porrima CLIA system operation manual carefully, to get sufficient information such as operation instructions, sample preservation and management, safety precaution, and maintenance. Prepare all required materials for the assay as well.
- Before loading the reagent kit on the machine for the first time, unopened reagent bottle should be inverted gently for at least 30 times to resuspend the microparticles that have settled during shipment or storage.
- Visually inspect the bottle to ensure the microparticles have been resuspended. If the microparticles remain adhered to the bottle, continue inverting until the microparticles have been completely resuspended.
- If the microparticles cannot be resuspended, **DO NOT USE**. Contact DiaSino Technical Support for help. Do not invert opened reagent bottle.
- This assay requires 50 µL of sample for a single test. This volume does not include the dead volume of the sample container. Additional volume is required when performing additional tests from the same sample. Operators should refer to the system operation manual and specific requirement of the assay to determine the minimum sample volume.

Calibration
Traceability: The Porrima PCT CLIA has been standardized against the BRAHMS PCT assay.
The specific information of master calibration curve of PCT CLIA reagent kit is stored in the barcode attached in the reagent pack. It's used together with calibrators for the calibration of the specific reagent lot. When performing the calibration, scan the information of master calibration curve from the barcode into the system first, and then

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use the calibrators at two levels. Valid calibration curve is required before any PCT test. Recalibration is recommended every 28 days, or when a new reagent lot is used, or the quality controls are out of specified range. For detailed instruction of calibration, refer to the system operations manual.

Quality control
For quality control, use DiaSino ControlSet. In addition, other suitable control material can be used.
Controls 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.
Quality control results should be within the acceptable ranges. If a control is out of its specified range, the associated test results are invalid and the samples must be retested. Recalibration may be required. Examine the assay system referring to the system operation manual. If the quality control results are still out of the specified range, please contact DiaSino Technical Support for help.

Calculation
The analyzer automatically calculates the analyte concentration of each sample.

Limitations - interference
- The assay is unaffected by icterus (bilirubin < 428 µmol/L or < 25 mg/dL), hemolysis (Hb < 0.559 mmol/L or < 0.900 g/dL), lipemia (Intralipid < 1500 mg/dL).
- No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.
- There is no high-dose hook effect at PCT concentrations up to 1000 ng/mL.
- In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies. These effects are minimized by suitable test design.
- PCT levels can be increased in certain situations without infectious origin. These include, but are not limited to:[6]
  - Prolonged or severe cardiogenic shock
  - Prolonged severe organ perfusion anomalies
  - Small cell lung cancer or medullary C-cell carcinoma of the thyroid
  - Early after major trauma, major surgical intervention, severe burns
  - Treatments which stimulate the release of pro-inflammatory cytokines
- For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Measuring range
0.02-300 ng/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.02 ng/mL. Values above the measuring range are reported as
> 300 ng/mL.

Lower detection limit
0.02 ng/mL
The detection limit represents the lowest analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1+2 SD, repeatability study, n = 21).

Expected values
A study performed with Porrima PCT assay using 216 samples from apparently healthy males (105) and females (111) revealed the following normal value: 0.05 ng/mL (95th percentile).

Clinical cut-off
Results obtained with the Porrima PCT assay are in agreement with the literature. A study performed on samples from patients admitted to an ICU (intensive care unit) showed that PCT values:
- < 0.5 ng/mL represent a low risk of severe sepsis and/or septic shock
- > 2.0 ng/mL represent a high risk of severe sepsis and/or septic shock

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data
Representative performance data are given below. Results obtained in individual laboratories may differ.

Precision
Precision was determined using DiaSino reagents, pooled human sera, and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 2 times daily for 20 days (n = 40). The following results were obtained:

		Repeatability		Intermediate precision	
Sample	Mean ng/mL	SD ng/mL	CV %	SD ng/mL	CV %
Human Serum 1	0.017	0.0037	21.43	0.0038	22.13
Human Serum 2	1.34	0.111	8.32	0.126	9.41
Human Serum 3	24.89	1.454	5.84	1.561	6.27
PC Universal 1	1.27	0.094	7.38	0.101	7.92
PC Universal 2	16.93	0.884	5.22	1.046	6.18

Method comparison
A comparison of the Porrima PCT assay (y) with the bioMerieux BRAHMS PCT (x) using clinical samples gave the following correlations:
Number of samples measured: 98
Linear regression
y = 1.026x - 1.005
r = 0.9682

Analytical specificity
The Porrima PCT assay does not show any significant cross-reactivity with the following substances, tested with PCT concentrations of approximately 0.1 ng/mL and 1.1 ng/mL (maximum tested concentration):

Substances	Non-interfering concentrations (ng/mL)
Human katacalcin	30
Human calcitonin	20

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References

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, et al. 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.ugs on Clinical Laboratory Tests", *Clinical Chemistry*, 21, 3660 (1975)
3. Müller B, White JC, Nylén ES, et al. Ubiquitous Expression of the Calcitonin-I Gene in Multiple Tissues in Response to Sepsis. J Clin Endocrinol Metab 2001;86(1):396-404.
4. Weglöhner W, Struck J, Fischer-Schulz C, et al. Isolation and characterization of serum procalcitonin from patients with sepsis. Peptides 2001;22:2099-2103.
5. Gaïni S, Koldkjær OG, Møller HJ, et al. 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.
6. Castelli GP, Pognani C, Cita M, et al. Procalcitonin, C-reactive protein, white blood cells and SOFA score in ICU: diagnosis and monitoring of sepsis. Minerva Anestesiol 2006;72:69-80.

Symbols

IVD In vitro diagnostic medical device	8°C / 2°C Temperature limit	Consult instructions for use	REF Catalog number
LOT Batch code	Date of manufacture	Use-by date	Σ Contains sufficient for <n> tests
Manufacturer	This side up	CE European Conformity	EC REP Authorized representative in the European Community

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