Snibe Diagnostic

CE

REF 130216001M: 100 tests
130616001M: 50 tests

MAGLUMI® PCT (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of PCT in human serum and plasma with the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer (including Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 1000 Plus, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X8, MAGLUMI X3 and MAGLUMI X6) and Biolumi series Integrated System (including Biolumi CX8).

SUMMARY AND EXPLANATION OF THE TEST

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin, the latter being involved with calcium homeostasis. It arises from the once preprocalcitonin is cleaved by endopeptidase[1]. It was first identified by Leonard J. Deftos and Bernard A. Roos in the 1970s[2]. Procalcitonin is produced by the neuroendocrine cells of the lung and intestine and is released as an acute-phase reactant in response to inflammatory stimuli, especially those of bacterial origin[1]. This raised procalcitonin level during inflammation is associated with bacterial endotoxin and inflammatory cytokines[3]. Increased levels of serum procalcitonin in response to viral infections and noninfectious inflammatory stimuli such as autoimmune disease and chronic inflammatory processes are much less pronounced[4].PCT is located on the CALC-1 gene on chromosome 11. Bacterial infections induce a universal increase in the CALC-1 gene expression and a release of PCT[5]. Expression of this hormone occurs in a site specific manner[5]. In healthy and non-infected individuals, transcription of PCT only occurs in neuroendocrine tissue, except for the C cells in the thyroid[5]. The formed PCT then undergoes post-translational modifications, resulting in the production small peptides and mature CT by removal of the C-terminal glycine from the immature CT by peptidylglycine α-amidating monooxygenase (PAM)[5]. A bacterial infection induces a substantial increase in the expression of CALC-1, leading to the production of PCT in all differentiated cell types[5-6].Due to PCT's variance between bacterial infections and healthy individuals, it has become a marker to improve bacterial infections identification[7].

PRINCIPLE OF THE TEST

The PCT assay is a sandwich chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), ABEI labeled with anti-PCT monoclonal antibody, magnetic microbeads coated with another anti-PCT monoclonal antibody are mixed thoroughly and incubated, forming sandwich complexes. After precipitation in a magnetic field, decant the supernatant, and then perform a wash cycle. Subsequently, the Starter 1+2 are added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light unit (RLUs), which is proportional to the concentration of PCT present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Components	Contents	100 tests (REF: 130216001M)	50 tests (REF: 130616001M)
Magnetic Microbeads	Magnetic microbeads coated with anti- PCT monoclonal antibody, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Containing BSA and PCT antigen, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	Containing BSA and PCT antigen, NaN_3 (<0.1%).	2.5 mL	2.0 mL
ABEI Label	Anti-PCT monoclonal antibody labeled with ABEI, containing BSA, NaN_3 (<0.1%).	10.5 mL	7.0 mL
Diluent	Containing bovine serum, NaN_3 (<0.1%).	25.0 mL	15.0 mL
Internal Quality Control 1	Containing BSA and PCT antigen, NaN_3 (<0.1%).	2.0 mL	2.0 mL
Internal Quality Control 2	Containing BSA and PCT antigen, NaN_3 (<0.1%).	2.0 mL	2.0 mL
All reagents are provided ready-to-use.			

Accessories Required But Not Provided

MAGLUMI and Biolumi Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M, 130299027M
Wash Concentrate	REF: 130299005M
Light Check	REF: 130299006M
Reaction Cup	REF: 130105000101

Please order accessories from Shenzhen New Industries Biomedical Engineering Co., Ltd. (SNIBE) or our authorized representatives.

CALIBRATION

Traceability: This method has been standardized against the SNIBE internal reference substance.

Test of assay specific calibrators allows the RLU values to adjust the assigned master curve. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (10 calibrations) provided via the reagent Radio Frequency Identification (RFID) CHIP.

Recalibration is recommended if any of the following conditions occurs:

- After each change of lots (Reagent or Starter 1+2).
- Every 2 weeks and/or each time a new reagent kit is used (recommended).
- After instrument service is required.
- If control results lie outside the expected range.

QUALITY CONTROL

Follow government regulations or accreditation requirements for quality control frequency.

Internal quality control is only applicable with MAGLUMI and Biolumi systems. For instructions for use and target value refer to ***PCT (CLIA) Quality Control Information***. User needs to judge results with their own standards and knowledge.

For detailed information about entering quality control values, refer to the corresponding Analyzer Operating Instructions.

To monitor system performance and chart trends, commercially available quality control materials are required. Treat all quality control samples the same as patient samples. A satisfactory level of performance is achieved when analyte values obtained are within the acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical supporters or distributors for assistance.

SPECIMEN COLLECTION AND PREPARATION

Serum

- Use standard sampling tubes or tubes containing separating gel. Collect blood aseptically followeing the universal precautions for venipuncture.
- Avoid repeated freezing and thawing. The serum sample can be frozen and thawed for only two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer).
- Serum was stable at 2-8 °C for 24 hours. If preserved more than 12 hours, please packed, -20°C can be stored for 2 months.

Plasma

- For plasma samples, the anticoagulant including EDTA-2K has been tested and may be used with this assay. (Note: recommended EDTA-2K as an anticoagulant, heparin cannot be used as anticoagulant).
- Avoid repeated freezing and thawing. The plasma sample can be frozen and thawed for only two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer).
- Plasma was stable at 2-8 °C for 24 hours. If preserved more than 12 hours, please packed, -20°C can be stored for 2 months.
- Ensure that complete clot formation in serum and plasma specimens has taken place prior to centrifugation. Some serum specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time.
- If the serum and plasma specimen is centrifuged before a complete clotting, the presence of fibrin may cause erroneous results. Serum and plasma samples must be free of fibrin and other particulate matter.
- For serum and plasma, do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate matter or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Centrifuged serum and plasma specimens with a lipid layer on the top must be transferred to a sample cup or a secondary tube. Care should be taken to transfer only the clarified specimen without the lipemic material.
- All samples (patient specimens and controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more details of onboard sample storage constraints.
- Before shipping serum or plasma specimens, it is recommended that specimens be removed from the serum or plasma separator, red blood cells or clot. When shipped, specimens should be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Serum and plasma specimens should be shipped frozen.
- The sample volume required for a single determination of PCT is 40 µL.

WARNING AND PRECAUTIONS FOR USERS

- **IVD**
- For *In Vitro* Diagnostic Use.
- Follow the package insert carefully. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION**: This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the 29 CFR 1910.1030 Occupational exposure to bloodborne pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- All samples, biological reagents and materials used in the assay should be considered potentially able to transmit infectious agents. They should therefore be disposed in accordance with the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.
- This product contains Sodium Azide. Dispose of contents and containers must be in accordance with all local, regional and national regulations.
- Refer to safety data sheets which are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not interchange reagent components from different reagents or lots.
- Prior to loading the reagent kit on the system for the first time, the reagent kit requires mixing to re-suspend magnetic microbeads that have settled during shipment.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and samples.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

STORAGE AND STABILITY

- Sealed: Stored at 2-8°C until the expiration date.
- Opened at 2-8°C: Minimum stability is 4 weeks.
- On-board: Stable for 4 weeks.
- To ensure the best kit performance, it is recommended to place opened kits in the refrigerator after the end of the intraday test work.
- Keep upright for storage to facilitate later proper resuspension of magnetic microbeads.
- Keep away from sunlight.

TEST PROCEDURE

Preparation of the Reagent

- Resuspension of the magnetic microbeads takes place automatically when the kit is loaded successfully, ensuring the magnetic microbeads are totally resuspended homogenous prior to use.
- To ensure proper test performance, strictly adhere to the corresponding Analyzer Operating Instructions. Each test parameter is identified via a RFID CHIP on the Reagent kit. For further information please refer to the corresponding Analyzer Operating Instructions.

DILUTION

Samples with concentrations above the measuring range can be diluted.
After manual dilution, multiply the result by the dilution factor. After dilution by the analyzers, the analyzer software automatically takes the dilution into account when calculating the sample concentration.
Availability of sample dilution by analyzer please refers to the MAGLUMI and Biolumi series Fully-auto chemiluminescence immunoassay analyzer user software program. Dilution settings please refer to the corresponding Analyzer Operating Instructions.

High-Dose Hook

No high-dose hook effect was seen for PCT concentrations up to 10,000 ng/mL.

LIMITATIONS

- A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.
- A result within the expected range does not rule out the presence of disease and should be interpreted together with other diagnostic procedures.
- Test results are reported quantitatively. However, diagnosis of a disease should not be based on the result of a single test, but should be determined in conjunction with clinical findings in association with medical judgement.
- Any therapeutical decision should also be taken on a case-by-case basis.
- Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

RESULTS

Calculation of Results

The analyzer automatically calculates the PCT concentration of each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are reported in the unit of ng/mL. For further information please refer to the corresponding Analyzer Operating Instructions.

Interpretation of Results

The expected ranges for the PCT assay were obtained by testing 474 apparently healthy individuals in China, and gave the following expected values:
Serum and plasma: <0.05 ng/mL (95^{th} percentile).
Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory should establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the PCT assay was determined as described in the CLSI EP5-A2. 3 human serum pools and 2 controls containing different concentration of analyte were assayed in duplicate at two independent runs per day for 20 testing days. The results are summarized in the following table:

Sample	Mean(ng/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(ng/mL)	%CV	SD(ng/mL)	%CV	SD(ng/mL)	%CV
Serum Pool 1	0.835	0.049	5.87	0.053	6.35	0.072	8.62
Serum Pool 2	10.411	0.375	3.60	0.547	5.25	0.663	6.37
Serum Pool 3	52.082	0.615	1.18	2.841	5.45	2.907	5.58
Control 1	0.576	0.033	5.73	0.045	7.81	0.059	9.69
Control 2	8.734	0.263	3.01	0.549	6.29	0.609	6.97

Limit of Blank (LoB)

The LoB for the PCT assay is 0.01 ng/mL.

Limit of Detection (LoD)

The LoD for the PCT assay is 0.04 ng/mL.

Limit of Quantitation (LoQ)

The LoQ for the PCT assay is 0.05 ng/mL. Limit of Quantitation is defined as the concentration of PCT that can be measured with an interassay CV of 20%.

Measuring range

0.04-100 ng/mL (defined by the limit of detection and the maximum of the master curve).

Linearity

The assay is linear between 0.05 ng/mL and 100 ng/mL based on a study performed with guidance from CLSI EP6-A. Nine equally distributed levels of samples were prepared by blending a serum sample containing PCT 107 ng/mL with a serum sample depleted of PCT (0.0 ng/mL).The mean sample recovery ranged from 90% to 110%.

Method Comparison

A total of 100 samples in the range of 0.02 to 97.45 ng/mL were tested using the PCT assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: y=0.987x-0.005, r^2=0.996.

Analytical Specificity
The specificity of the assay was obtained by adding Calcitonin (20 ng/mL) to two serum samples at the indicated concentrations. No interference was found.

Endogenous Interference
Substances up to the following concentrations did not interfere with the assay:
- Bilirubin 25 mg/dL
- Hemoglobin 1500 mg/dL
- Triglyceride 900 mg/dL

REFERENCES

1. Procalcitonin: Reference Range, Interpretation, Collection and Panels. 2017-03-09.
2. Deftos, L J; Roos, B A; Parthemore, J G (1975-12-01). "Calcium and skeletal metabolism..." Western Journal of Medicine. 123 (6): 447–458.
3. Dandona P, Nix D, Wilson MF, Aljada A, Love J, Assicot M(1994 Dec). Procalcitonin increase after endotoxin injection in normal subjects. J Clin Endocrinol Metab. 79(6):1605-8.
4. Meili M, Müller B, Kulkarni P, Schütz P (2015 Oct). Management of patients with respiratory infections in primary care: procalcitonin, C-reactive protein or both?. Expert Rev Respir Med. 9 (5):587-601.
5. Ming, Jin,; I., Khan, Adil (2010-03-01). "Procalcitonin: Uses in the Clinical Laboratory for the Diagnosis of Sepsis". Laboratory Medicine. 41 (3): 173–177.
6. Linscheid, Philippe; Seboek, Dalma; Nylen, Eric S.; Langer, Igor; Schlatter, Mirjam; Becker, Kenneth L.; Keller, Ulrich; Müller, Beat (December 2003). "In vitro and in vivo calcitonin I gene expression in parenchymal cells: a novel product of human adipose tissue". Endocrinology. 144 (12): 5578–5584.
7. Schuetz, Philipp; Albrich, Werner; Mueller, Beat (2011-09-22). "Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future". BMC Medicine. 9: 107.

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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
2°C 8°C	Temperature limit (Store at 2-8 °C)		Use-by date
Σ	Contains sufficient for		Keep away from sunlight
	This way up	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device	CONTENTS	Kit components
REF	Catalogue number	LOT	Batch code