Procalcitonin FS*

Order Information

Cat. No.	Kit size		
1 7318 99 43 018	R1 2 x 18 mL	+	R2 2 x 6 mL

Intended Use

Diagnostic reagent for quantitative in vitro determination of procalcitonin (PCT) in human serum or lithium heparin plasma on automated Abbott ARCHITECT cSystem analyzers (c4000, c8000, c16000) and Beckman Coulter (AU480, AU680, AU5800, DxC 700 AU,DxC 500 AU and DxC 500i) analyzers.

Indications for Use

DiaSys Procalcitonin FS assay is a particle enhanced immunoturbidimetric test intended for quantitative in vitro determination of procalcitonin (PCT) levels in human serum and lithium heparin plasma on automated Abbott ARCHITECT c8000 analyzer. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock.

Summary

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host immune response to infection. It is a global health concern and a leading cause of death worldwide, affecting an estimate of 48.9 million people each year [1-3]. Early diagnosis and treatment of sepsis still remains a big challenge in the intensive care units. PCT, the thyroid precursor of calcitonin, is a 116 amino acid polypeptide with a molecular weight of approximately 13 kDa. Under normal physiological conditions, PCT is exclusively synthesized by thyroid C cells and undergoes successive cleavages into three fragments, N-terminus, calcitonin and katacalcin [4-8]. PCT serum levels in healthy individuals are very low (< 0.05 ng/mL). In response to microbial systemic infections and sepsis, PCT is ubiquitously expressed in multiple tissues via stimulation by inflammatory cytokines or bacterial endotoxins and may increase up to 1000 ng/mL [5-8]. However, in order to correctly interpret PCT results, they should be placed into clinical context. Clinical findings, evaluation of severity of illness and of patient's characteristics should be taken into account. Thus, decisions should not be based solely on PCT serum levels [9].

Method and Principle

Particle enhanced immunoturbidimetric test

Determination of PCT concentration by photometric measurement of antigen antibody reaction between antibodies against human PCT bound to polystyrene particles and PCT present in the sample.

Reagents

Components and Concentrations

R1:	TRIS	pH 6.5	0.1 mol/L
R2:	TRIS	pH 9.0	0.1 mol/L
	Polyclonal antibodies (goat) against human PCT covalently bound to polystyrene particles.		

Storage and Reagent Stability

Reagents are stable until expiration date on the respective labeling, if stored at 2° – 8°C. Keep protected from light. Once opened, contamination must be avoided. Do not freeze. Discard if contamination, turbidity or any change in appearance occurs.

The open-vial stability of the reagent is 24 months until expiry date.

Warnings and Precautions

1. For in vitro diagnostic use only.
2. Caution: Federal law (USA) restricts this device to sale by or on the order of a licensed physician.
3. Reagent 1 contains sodium azide (0.9 g/L) as preservative. Do not swallow! Avoid contact with skin and mucous membranes.
4. Reagent 2 contains sodium azide (0.95 g/L) as preservative. Do not swallow! Avoid contact with skin and mucous membranes.
5. The reagents contain material of biological origin from regulated, certified sources. Handle the product as potentially infectious according to universal precautions and good laboratory practice.
6. In very rare cases, samples from patients with gammopathy may artificially lower or elevate PCT levels [10].
7. This assay is not intended for use as an independent diagnostic test and should be used in conjunction with clinical signs and symptoms of infection and other diagnostic evidences.
8. The assay is not intended to be used as an aid in the decision making process regarding antibiotic therapy for patients.
9. Patient characteristics, such as severity of renal insufficiency or failure, may influence procalcitonin levels and should be considered as potential clinical confounders when interpreting PCT values.
10. Please refer to the safety data sheets (SDS) and take the necessary precautions for the use of laboratory reagents.
11. For professional use only.

Limitations

1. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce human anti-animal antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other antibodies such as human anti-goat antibodies may be present in patient samples [11, 12]. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.
2. Other potential interferences in the patient sample could be present and may cause erroneous results in immunoassays. Some examples that have been documented in literature include rheumatoid factor, endogenous alkaline phosphatase, fibrin, and proteins capable of binding to alkaline phosphatase [13]. Carefully evaluate results if the sample is suspected of having these types of interferences.
3. The DiaSys Procalcitonin FS assay is not intended to be used in isolation. The DiaSys Procalcitonin FS assay results should be interpreted in consideration of the total clinical presentation of the patient, including symptoms, clinical history, data from additional tests, and other appropriate information. In cases where the laboratory results do not agree with the clinical picture or history, additional tests should be performed.
4. Not indicated to be used as an aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time.
5. Not indicated to be used as an aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary diseases (AECOPD) in an inpatient setting or an emergency department.
6. Not indicated to be used as an aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis or other conditions.
7. Elevated PCT levels may be seen in conditions other than systemic bacterial infection. These may include but are not limited to polytrauma, burns, major surgery, and prolonged or cardiogenic shock. In addition, certain patient characteristics including, renal insufficiency or failure, may impact procalcitonin levels and should be considered as potentially confounding clinical factors when evaluating PCT results.
8. PCT levels may not be elevated in patients infected by certain atypical pathogens, such as *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*.
9. Values obtained by different PCT assay methods may differ and should not be used interchangeably.
10. The DiaSys Procalcitonin FS Assay is only to be used on validated Abbott ARCHITECT cSystem (c4000, c8000, c16000) and Beckman Coulter (AU480, AU680, AU5800, DxC 700 AU, DxC 500 AU and DxC 500i) chemistry analyzers.

Waste Management

Please refer to local institutional requirements.

Warning: Handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Reagent Preparation

The reagents are provided ready to use.

Materials Required

General laboratory equipment.

Abbott ARCHITECT cSystem chemistry analyzers (c4000, c8000, c16000), Beckman Coulter (AU480, AU680, AU5800, DxC 700 AU, DxC 500 AU and, DxC 500i) chemistry analyzers.

DiaSys TruCal Procalcitonin Calibrator Set
(Cat. No. 1 7310 99 43 082) and
DiaSys TruLab Procalcitonin Bi-Level Controls
(Cat. No. 5 9980 99 43 086) are sold separately.

Specimen

Human serum and lithium heparin plasma can be used in the assay. Please collect blood by standard venipuncture and fill the blood collection tube according to manufacturer specifications. Avoid hemolysis.

Stability:

24 hours	at	20 – 25°C
5 days	at	2 – 8°C
14 days	at	-20°C

Only freeze once. Discard contaminated specimens.

Assay Procedure

Basic settings for ARCHITECT cSystem chemistry analyzers

Wavelength	660 nm
Temperature	37°C
Measurement	Endpoint
Sample/Calibrator	10 µL
Reagent 1	120 µL
Reagent 2	40 µL
Main read points	33 – 33 (576 s – 576 s)
Blank read points	19 – 20 (324 s – 342 s)
Calibration	Spline

Note: Refer to the appropriate system manuals and/or help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting. As well as information on managing samples, configuring tests, requesting tests, and reviewing test results.

Calculation

The PCT concentration of unknown samples is derived from the calibration curve using an appropriate mathematical model such as RCM or spline. The calibration curve is obtained with six calibrators at different levels, including a matrix-based zero-value.

Calibrator Traceability

TruCal Procalcitonin Calibrator Set is recommended for calibration. Due to the fact that no international reference material is available, DiaSys Procalcitonin FS is traceable to a commercially available assay whose measuring principle is based on an enzyme linked fluorescent test, which is a commonly used method in the market.

	Cat. No.	Kit size
TruCal Procalcitonin Calibrator Set	1 7310 99 43 082	6 x 1 mL

Calibration Frequency

An active calibration is required for all tests. Calibration is required every 21 days. See calibrator Instructions For Use (IFU) for additional calibration information.

Controls

Use TruLab Procalcitonin Bi-Level Controls for internal quality control. Controls should be run daily on the instrument prior to reporting patient results respecting the established ranges. Recovered control values outside of the established ranges may require the following corrective actions:

a) Repeat the same control but do not report patient results unless the control results are within the established limits.

b) If the repeated control results are still outside of established limits, use a fresh control and repeat the test. If the results are within range, report patient results.

c) If the results from the fresh controls are still out of range, recalibrate and repeat the controls. If the controls are within range, repeat test with patient specimens.

d) If recalibrating on the existing reagent show control results still out of range, recalibrate on fresh reagent and repeat the controls. If the control results are in range, repeat test with patient specimens.

e) If none of the preceding produces acceptable QC results,contact technical service. Contact details are listed below.

	Cat. No.	Kit size	
TruLab Procalcitonin Bi-Level Controls	5 9980 99 43 086	low Level high Level	6 x 1 mL 6 x 1 mL

Performance Characteristics

Data evaluated on ARCHITECT c8000 analyzer

Linearity per the method of CLSI EP06-A:
Linearity in human serum and plasma is evaluated by assaying dilutions of stock solutions at least in quadruplicate. Mean values (y-axis) versus target values (x-axis) are plotted and linear regression is applied.

Measuring range from 0.23 ng/mL up to 50 ng/mL, depending on the concentration of the highest calibrator.
Linearity < 0.5 ng/mL is given with ± 0.1 ng/mL, between 0.5 ng/mL to 5 ng/mL within ± 20%, at > 5 ng/mL within ± 10%.

LOD and LOQ per the method of CLSI EP17-A2:
LOD and LOQ were evaluated in human serum and plasma. Nine samples with different value are assayed on twenty consecutive days. On each day two replicates are measured nonconsecutively. For each sample mean, standard deviation and coefficient of variation are calculated. Acceptance criteria were; LoQ/LoD ≤ 0.5 ng/mL

Limit of detection	0.23 ng/mL
Limit of quantitation	0.23 ng/mL

Calibration Stability per the method of CLSI EP25-A:
Open reagent bottles are placed on the analyzer and an initial calibration is performed at the beginning of testing period. Two controls and human serum (one level) are measured several times during the period. Recovery of controls and human serum has to be within defined limits without any recalibration.

Onboard Stability per the method of CLSI EP25-A:
The reagent is placed on the analyzer for an intended period in open bottles. Calibration is made at the beginning of the period and repeated if necessary (depending on calibration stability). Two controls and human serum (one level) are measured several times during the period. Recovery of controls and human serum has to be within defined limits.

Onboard stability	63 days
Calibration stability	21 days

Prozone Effect per the method of DiaSys internal protocol:
Absorbances of the highest calibrator and of several samples with concentrations above the one of the highest calibrator are measured.

No prozone effect up to 1000 ng/mL.

Interference per the method of CLSI EP07-A3:
Sequential dilutions of the interfering substances are mixed in equal parts with aliquots of human samples at approximate PCT concentrations of 0.5 and 2.0 ng/mL, and each mixture is tested in five replicates. The mean measured PCT values (y-axis) are plotted against the concentration of the interfering substance (x-axis). No significant interference was observed, defined as a shift in PCT concentration greater than ±15%, when the following substances were tested at the concentrations indicated in the table below.

Interferent Evaluated	Interferent concentration tested
Ascorbic acid	151 mg/dL
α-CGRP	12 µg/mL
Azithromycin	1.44 mg/dL
β-CGRP	12 µg/mL
Bilirubin (conjugated)	72.5 mg/dL
Bilirubin (unconjugated)	71.4 mg/dL
Calcitonin	10.8 ng/mL
Cefotaxime	189 mg/dL
Cromolyn	28.8 mg/L
Dobutamine	22.9 µg/mL
Dopamine	27.3 mg/dL
Doxycycline	6.61 mg/dL
Enoxaparin	24000 U/L
Ethanol	720 mg/dL
Furosemide	4.2 mg/dL
HAMA	480 ng/mL
Hemolysis	1200 mg/dL
Ibuprofen	63.1 mg/dL
Imipenem	2.52 mg/mL
Katacalcin	6 ng/mL
Lipemia (triglycerides)	1910 mg/dL
Noradrenalin	4.2 µg/mL
Pantoprazole	4.32 mg/dL
Rheumatoid factor	1020 IU/mL
Salmeterol Xinafoate	104 ng/mL
Scopolamine-N-butyl bromide	72 mg/L
Total Protein	139 g/L
Vancomycin	3.78 mg/mL
N-Terminus interferes.	
There is the possibility that other substances (e.g. ingestion, drugs or during specimen preparation) and medical conditions may lead to deviating results. Detailed information on every possible interfering substance or medical condition is beyond the scope of this script.	

Precision/Reproducibility per the method(s) of CLSI EP05-A3 and EP15-A3:

Repeatability

Five samples with different values over the measuring range assayed 20 times each.

Within-laboratory

Five samples with different values over the measuring range assayed in duplicate over 20 days.

Precision					
Repeatability (n=20)	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 4**	**Sample 5**
Mean [ng/mL]	0.252	0.555	2.02	9.68	18.8
CV [%]	16.6	3.89	2.78	2.24	2.16
Within-laboratory (n=80)	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 4**	**Sample 5**
Mean [ng/mL]	0.285	0.571	2.23	10.5	20.8
CV [%]	11.5	5.64	2.34	1.93	2.00

Method Comparison per the method of CLSI EP09-A3:

Two method comparison studies were performed with predicate device – VIDAS Brahms PCT Assay (K071146) and the Abbott ARCHITECT c8000 analyzer.

1.) Method comparison study

At least 100 native patient samples were measured two times with each method. Analysis of the mean patient recovery measured by validated method (x-axis) against mean patient recovery measured by evaluation method (y-axis) by Passing/Bablok.

2.) Method comparison study

At least 200 native patient samples were measured two times with each method. Analysis of the mean patient recovery measured by validated method (x-axis) against mean patient recovery measured by evaluation method (y-axis) by Passing/Bablok.

1.) Method comparison (n=120)	
Test x	Competitor Procalcitonin (VIDAS®)
Test y	DiaSys Procalcitonin FS (ARCHITECT c8000)
Slope	1.08
Slope 95% CI	1.05 – 1.12
Intercept	0.105 ng/mL
Intercept 95% CI	0.073 – 0.119
Coefficient of correlation	0.991

Concordance at 0.5 ng/mL cutoff			
	Competitor Procalcitonin VIDAS®		
Procalcitonin FS DiaSys	PCT < 0.5 ng/mL	PCT ≥ 0.5 ng/mL	Total
PCT < 0.5 ng/mL	31	0	31
PCT ≥ 0.5 ng/mL	2	87	89
Total	33	87	120

Negative percent agreement (NPA) = 93.9% (31/33),
95% CI: 79.7% to 99.3%
Positive percent agreement (PPA) = 100% (87/87),
95% CI: 95.8% to 100.0%

Concordance at 2.0 ng/mL cutoff			
	Competitor Procalcitonin VIDAS®		
Procalcitonin FS DiaSys	PCT < 2.0 ng/mL	PCT ≥ 2.0 ng/mL	Total
PCT < 2.0 ng/mL	70	1	71
PCT ≥ 2.0 ng/mL	5	44	49
Total	75	45	120

Negative percent agreement (NPA) = 93.3% (70/75),
95% CI: 85.1% to 97.8%
Positive percent agreement (PPA) = 97.8% (44/45),
95% CI: 88.2% to 99.9%

2.) Method comparison (n=210)	
Test x	Competitor Procalcitonin (VIDAS®)
Test y	DiaSys Procalcitonin FS (ARCHITECT c8000)
Slope	0.940
Slope 95% CI	0.903 – 0.988
Intercept	0.017 ng/mL
Intercept 95% CI	-0.007 – 0.047
Coefficient of correlation	0.965

Concordance at 0.5 ng/mL cutoff			
	Competitor Procalcitonin VIDAS®		
Procalcitonin FS DiaSys	PCT < 0.5 ng/mL	PCT ≥ 0.5 ng/mL	Total
PCT < 0.5 ng/mL	97	0	97
PCT ≥ 0.5 ng/mL	2	111	113
Total	99	111	120

Negative percent agreement (NPA) = 98.0% (97/99),
95% CI: 92.9% to 99.8%
Positive percent agreement (PPA) = 100% (111/111),
95% CI: 96.7% to 100.0%

Concordance at 2.0 ng/mL cutoff			
	Competitor Procalcitonin VIDAS®		
Procalcitonin FS DiaSys	PCT < 2.0 ng/mL	PCT ≥ 2.0 ng/mL	Total
PCT < 2.0 ng/mL	143	4	147
PCT ≥ 2.0 ng/mL	0	63	63
Total	143	67	210

Negative percent agreement (NPA) = 100.0% (143/143),
95% CI: 97.5% to 100.0%
Positive percent agreement (PPA) = 94.0% (63/67),
95% CI: 85.4% to 98.4%

Results Interpretation

Serum and Plasma [14, 15]:

< 0.5 ng/mL	Low risk of severe sepsis and/or septic shock.
≥ 2 ng/mL	High risk of severe sepsis and/or septic shock.

Concentrations under 0.5 ng/mL do not exclude local infections or systemic infections in their initial stages (e.g. under six hours from onset of illness) [15]. PCT concentrations between 0.5 and 2.0 ng/mL should be interpreted with consideration of the patient's history. In this range, it is recommended to retest PCT within 6 to 24 hours.

Test results are determined automatically by the system software. Test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

Reporting Results

Measuring Interval: 0.23 – 50 ng/mL
Samples can be accurately measured within the measuring interval of 0.23 ng/mL and the highest calibrator value.

1. If a sample contains less than the lower limit for the assay, report the result as less than that value.
2. If a sample contains more than the stated value of the highest calibrator, report the result as greater than that value. Alternatively, the sample may be diluted to obtain a result.

Laboratories and other users should establish their own reference intervals for their patient populations using the DiaSys Procalcitonin FS assay to reflect potential sources of variability, such as patient gender, race, and age.

Literature

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Additions and/or changes in the document are highlighted in grey. Deletions are communicated via customer info by stating the edition no. of the package insert/instruction for use.

Symbols

The symbol list is enclosed in the kit.

Rx ONLY

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