PROCALCITONIN (PCT)

Diagnostic reagent for determination of PCT concentration.
Liquid. Dual reagents. Store at +2/+8°C. For in Vitro Diagnostic Use (IVD). **Do not freeze.**

Ref No	Package	Ref No	Package	Ref No	Package	Ref No	Package
At2292	250,4 mL	LM069	104 mL	M2293	200 mL	ZA55	100 mL
HN294	240 mL	L2167	80 mL	RC2603	58,3 mL	8A114	200 mL
LB122	80 mL	L2168	80 mL	T2302	180 mL		

Changes made in the instructions for use are marked as grey.

INTENDED USE
The test is applied for the quantitative determination of procalcitonin in serum and plasma.

GENERAL INFORMATION
Procalcitonin (PCT) is a precursor of the hormone calcitonin, which is secreted in high concentrations by non-endocrine parenchymal cells in numerous tissues in response to inflammatory cytokines such as TNF-α and IL-1β as well as bacterial toxins such as lipopolysaccharide, and thus functions as a marker of inflammatory states.[1-3] PCT release in response to inflammatory cytokines is weakened by interferon-γ, which is hypothesized to produce lower PCT levels in viral response compared to bacterial infections.[2] Although severe infection is one of the most common causes of elevated serum PCT, it is also released in non-infectious inflammatory conditions, such as following pancreatitis, severe ischemia, respiratory injury, major burns, heat stroke, severe trauma and extensive surgical procedures, and may also be chronically elevated in patients with advanced kidney disease.[3,4] There is widespread interest in the use of PCT in the diagnosis and treatment of infection, although it is not fully specific for infection.[5] Numerous studies have shown that in the context of infection, PCT levels begin to rise within 4 to 6 hours of the onset of the inflammatory state, but may also have a delayed peak and tend to be higher in severe, systemic bacterial infection than in viral or localized bacterial infections by comparison.[3,6-8] Levels decline rapidly in response to appropriate antimicrobial therapy and infection management, and kinetics, particularly within the first 72 hours after hospitalization, are associated with patient outcomes.[6,9,10] These extensive properties have led to the use of PCT levels to differentiate between infectious and non-infectious conditions, bacterial and viral infections, especially in syndromes such as community-acquired pneumonia, and also to the use of serial PCT levels to determine when antibiotics can be stopped.[5]

Numerous studies have concluded that although PCT levels are positively correlated with the presence of invasive bacterial infection, a single PCT value is insufficient to determine whether an individual patient has an infection and should receive antibiotics and should be used to complement clinical evaluation.[8,11-15]

TEST PRINCIPLE
Immunoturbidimetric method

Serum PCT causes agglutination of latex particles coated with anti-human PCT protein. Agglutination of latex particles is proportional to PCT concentration and can be measured turbidimetrically.

The clinical diagnosis should not be based solely on the findings of the test results; the integration of laboratory data should also be included in the clinical diagnosis.

REAGENT COMPONENTS

Reagent 1:

Glycine buffer	: ≤ 0.8 mol/L
Sodium azide	: ≤ %0.1

Reagent 2:
Latex particle suspension coated with anti-human procalcitonin antibodies

Sodium azide	: ≤ %0.1

REAGENT PREPARATION
Reagents are ready for use.

REAGENT STABILITY AND STORAGE
Reagents are stable at +2/+8°C till the expiration date stated on the label which is only for closed vials.

Once opened vials are stable for 30 days at +2/+8°C in optimum conditions. On board stability is strongly related to auto analyzers' cooling specification and carry-over values.

Reagent stability and storage data have been verified by using Clinical and Laboratory Standards Institute (CLSI) EP25-A protocol.[16]

SAMPLE REQUIREMENTS
Serum or plasma collected by standard procedure can be used. Li-heparin, K_2-EDTA or K_3-EDTA must be used as anticoagulants for plasma. Multiple sample freezing and thawing should be avoided.

PCT activity stability in serum and plasma:
24 hours at +20/+25ºC
48 hours at +2/+8ºC
13 months at -20°C

CALIBRATION AND QUALITY CONTROL

Calibration: The assay requires the use of an Procalcitonin Calibrator Set.

Procalcitonin Calibrator Set (1-5 Levels)
Ref.No: ZA95

Calibration stability is 15 days. Calibration stability depends on the application characteristics and cooling capacity of the autoanalyzer used.

Control: Commercially available control material with established values determined by this method can be used. We recommend:

Procalcitonin Control Set (1.- 2. Levels)
Ref.No: ZA94
Ref.No: ZA94-1

At least two level controls must be run once in every 24 hours. Each laboratory should determine its own quality control scheme and procedures. If quality control results are not within acceptable limits, calibration is required.

REFERENCE INTERVALS / MEDICAL DECISION LEVELS

Adult Serum : Up to 0.5 ng/mL

1. **PCT < 0.3 ng/mL:** Recommending not to use antibiotic
2. **0.3 ng/mL ≦ PCT < 0.5 ng/mL:** Suspected to be mild local bacterial infection or early stage of bacterial infection, or viral infection, autoimmune disease, chronic nonspecific inflammation; suggested to use antibiotic for emergency
3. **0.5 ng/mL ≦ PCT < 2 ng/mL:** Quite possible to be general bacterial infection, unless it is one of the clinical status such as baby born in 48 hours, serious trauma, burns, major surgery, and severe cardiac shock.
4. **2 ng/mL ≦ PCT < 10 ng/mL:** General bacterial infection (sepsis) and quite possible to develop into severe sepsis.
5. **10 ng/mL ≦ PCT:** Severe sepsis or septic shock.

Annotation:

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- A PCT concentration >0.1 ng/mL may indicate clinically significant bacterial infection requiring antibiotic treatment.[18]
- When the PCT concentration is >0.5 ng/mL, the patient should be considered at risk of developing severe sepsis or septic shock.[19] Although there is heterogeneity in the literature due to the variety of specific PCT assays used, a systemic review and meta-analysis for bacteremia have estimated that PCT has a sensitivity of 76% and specificity of 69% at the most common cut-off value of 0.5 ng/mL.[20]

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

Reference interval has been verified by using CLSI EP28-A3c protocol.[21]

PERFORMANCE CHARACTERISTICS

Measuring Interval

According to CLSI EP34-ED1:2018, "Measuring Interval" refers to the interval where the analyte concentration is measured with intended accuracy in terms of medical and laboratory requirements without dilution, concentrating or any kind of pre-treatment that is between the analyte's lower limit of quantitation (LLoQ) and upper limit of quantitation (ULoQ).[22]

The determined analytic measuring interval for Procalcitonin is 0.31 – 22 ng/mL.

Detection Capability

Limit of Detection (LoD): 0.1 ng/mL

Limit of Quantitation (LoQ): 0.31 ng/mL

Note: LoQ values are based on Coefficient of Variation Percentage (CV) ≤ 20%.

LoD and LoQ values have been verified by using CLSI EP17-A2:2012 protocol.[23]

Linearity

This method shows measurement linearity in the activities up to 22 ng/mL. Autoanalyzer's auto-dilution system can be used if the concentrations have higher values. See device manual for further information.

For the manual dilution procedure, dilute the sample 1:5 using 0.90% isotonic. After this process, multiply the result of the reworked sample by the dilution factor. Do not report the sample result after dilution if it is marked as lower than the linear lower limit. Rerun with a suitable dilution.

Linearity Studies data have been verified by using CLSI EP06-A:2003 protocol.[24]

Precision

Running system has been developed according to 20x2x2 "The Single Site" protocol. Repeatability and Within-Laboratory Precision/Within-Device values have been obtained according to the running results.

According to the protocol in use, 2 separate runs per day have been made for 20 days (no obligation for being consecutive days). This protocol has been applied to each low and high samples separately and 80 results have been obtained for each one. Statistically, the results have been obtained using 2-factor Nested-ANOVA model.[25]

Repeatability (Within Run) and Repeatability (Day to Day) CV% values of PCT have been given in the table 1 and 2 respectively.

Table 1. PCT Repeatability (Within Run) results obtained from samples in two different concentrations

Mean Concentration	SD	CV%	n
0.80 ng/mL	0.044	5.50	80
7.30 ng/mL	0.263	3.60	80

Note: This working system has been named "Within-Run Precision" in the previous CLSI - EP05-A2 manual.[26]

Table 2. PCT Repeatability (Day to Day) results obtained from samples in two different concentrations

Mean Concentration	SD	CV%	n
0.80 ng/mL	0.053	6.60	80
7.30 ng/mL	0.343	4.70	80

Note: This working system has been named "Total Precision" in the previous CLSI - EP05-A2 manual.[26]

Interference

Endogenous interferant and analyte concentrations that have been used in the PCT scanning tests has been determined according to "CLSI EP37-ED1:2018" and "CLSI EP07-ED3:2018" manuals.[27,28]

The total acceptable error rate, which is going to be used to detect whether the observed differential value obtained from PCT interference scanning test is appropriate, is determined as ±10%.[17]

In PCT test results, no significant interaction has been observed in the determined endogenous interferant and analyte concentrations or between interferants and analyte.

Hemoglobin	: ≤ 40 g/L
Bilirubin	: ≤ 40 mg/dL
Lipemia	: ≤ 1000 mg/dL

Annotation:

- Samples from patients routinely exposed to animals or animal serum products may contain heterophilic antibodies that cause atypical results.

It should be noted that endogenous interferants, as well as various medicines and metabolites, anticoagulants (e.g. Heparin, EDTA, citrate, oxalate) and preservatives (e.g. sodium floride, iodoacetate, hydrochloride acide) such as additives, materials that may contact with samples during collection and processing (serum separator devices, sample collection containers and contents, catheters, catheter wash solutions, skin disinfectants, hand cleaners and lotions, glass washing detergents, powder gloves), dietary substances known to affect some specific tests (caffeine, beta-carotene, poppy seeds, etc.), or some substances present in a sample that cause foreign proteins (heterophilic antibodies, etc.), autoimmune response (autoantibodies, etc.), or due to malignancy (for example, interference by paraproteins with phosphate testing and indirect ion selective electrode methods) may show some negative effects that will cause various attempts and some misjudgements.[28]

These performance characteristics have been obtained using an autoanalyzer. Results may vary slightly when using different equipment or manual procedures.

WARNINGS AND PRECAUTIONS

IVD: For in Vitro Diagnostic use only.
Do not use expired reagents.
Reagents with two different lot numbers should not be interchanged.
For professional use.
Follow Good Laboratory Practice (GLP) guidelines.
Contains sodium azide.

CAUTION: Human source samples are processed with this product. All human source samples must be treated as potentially infectious materials and must be handled in accordance with OSHA (Occupational Safety and Health Administration) standards.

Danger

EUH032	:Releases a very toxic gas if contacts with acid.
H317	:May cause allergic skin reaction.

Precaution

P280	:Use protective gloves / clothes / glasses / mask.
P264	:Wash your hands properly after using.
P272	:Contaminated work clothes should not be allowed to be used outside of the workplace.

Intervention

P302+P352	:Wash with plenty of water and soap if it contacts with skin.
P333+P313	:Seek medical help if it irritates your skin or develops rash.
P362+P364	:Remove contaminated clothes and wash properly before using.

Disposal

P501	:Dispose the vials and contents according to the local regulations.

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SYMBOLS

IVD	In Vitro Diagnostic Medical Device
LOT	Lot Number
R1	Reagent 1
R2	Reagent 2
GTIN	Global Trade Item Number
REF	Reference Number
GLP	Good Laboratory Practices
FOR USE WITH	Identifies Products to Be Used Together
PRODUCT OF TURKEY	Product of Turkey
	Manufacturer
	Expiration Date
	Temperature Limits
	Consult Instructions for Use
	Caution
	Number of Tests