Procalcitonin (PCT) - Plasma Technical Procedure 3285
Roche cobas® e411 Immunoanalyzer

Principle

Intended Use

The Elecsys BRAHMS PCT electrochemiluminescence immunoassay (“ECLIA”) is intended for use on Elecsys and **cobas e** immunoassay analyzers.

The Procalcitonin (PCT) assay is intended for use to determine the change of PCT over time 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 Intensive Care Unit (ICU) or when obtained in the emergency department or other medical wards prior to ICU admission, and for use in conjunction with other laboratory findings and clinical assessment, monitoring, and treatment of patients with severe sepsis and septic shock.

Summary and Explanation

PCT is the prohormone of the hormone calcitonin, but PCT and calcitonin are distinct proteins. Calcitonin is exclusively produced by C-cells of the thyroid gland in response to hormonal stimuli, whereas PCT can be produced by several cell types and many organs in response to pro-inflammatory stimuli, in particular by bacterial products. (1). In healthy people, plasma PCT concentrations are found to be below 0.1 µg/L.(2) Depending on the clinical background, a PCT concentration above 0.1 µg/L can indicate clinically relevant bacterial infection, requiring antibiotic treatment.(3) PCT levels rise rapidly (within 6-12 hours) after a bacterial infectious insult with systemic consequences. The magnitude of the increase in PCT concentration correlates with the severity of the bacterial infection.(4) At a PCT concentration > 0.5 µg/L, a patient should be considered at risk of developing severe sepsis or septic shock.(5,6) On the other hand, the relief of the septic infection is accompanied by a decrease in the PCT concentration which returns to normal with a half-life of 24 hours,(7,8) i.e., the continuous decline of PCT is indicative of effective source control measures and has been implicated in the safe de-escalation of antibiotic therapy.(9,10)

By evaluating PCT concentrations, the physician may use the findings to aid in the risk assessment of critically ill patients for progression to severe sepsis and septic shock. In addition, the change of PCT levels over time offers information about the risk of mortality after diagnosis of severe sepsis or septic shock.

Early after multiple traumas, major surgery, severe burns, or in neonates, PCT levels can be elevated independently of an infectious process, but the return to baseline is usually rapid. Viral infections, bacterial colonization, localized infections, allergic disorders, autoimmune diseases, and transplant rejection do not usually induce a significant PCT response (values < 0.5 µg/L). Therefore, PCT is an important marker enabling specific differentiation between a bacterial infection and other causes of inflammatory reactions.[3]

Sepsis is an excessive reaction of the immune system and coagulation system to an infection. The diagnosis and monitoring of infected patients are major problems for physicians. It has been proven that PCT levels increase precipitously, specifically in patients with a bacterial infection. For laboratory diagnosis, PCT is an important marker enabling specific differentiation between a bacterial infection and other causes of inflammatory reactions. Moreover, the resorption of the septic infection is accompanied by a decrease in the PCT concentration, which returns to normal with a half-life of 24 to 35 hours.

In certain situations (e.g., newborns, polytrauma, burns, major surgery, prolonged or severe cardiogenic shock, etc.), PCT elevation may be independent of any infectious aggression. The return to normal values is usually rapid. Viral infections, allergies, autoimmune diseases and graft rejection do not lead to a significant increase in PCT. However, a localized bacterial infection can lead to a moderate increase in PCT levels.

Procalcitonin (PCT) is a biomarker associated with the inflammatory response to bacterial infection that aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock. The percent change in PCT level over time aids in the prediction of cumulative 28-day mortality in patients with severe sepsis and septic shock.

A PCT level that declines ≤ 80 % from the day that severe sepsis or septic shock was clinically diagnosed (Day 0) to four days after clinical diagnosis (Day 4) is associated with higher cumulative 28-day risk of all-cause mortality than a decline > 80 %.

The combination of the first PCT level (≤ 2.0 ng/mL or > 2.0 ng/mL) at initial diagnosis of severe sepsis or septic shock with the patient's clinical course and the change in PCT level over time until Day 4 provides important additional information about the mortality risk.

The PCT level on Day 1 (the day after severe sepsis or septic shock is first clinically diagnosed) can be used to calculate the percent change in PCT level at Day 4 if the Day 0 measurement is unavailable.

The Elecsys BRAHMS PCT is not indicated to be used as a stand-alone diagnostic assay to determine the risk of 28-day all-cause mortality. Changes in PCT should always be interpreted in the context of the clinical status of the patient and other laboratory results. Validation of the Elecsys BRAHMS PCT test as an aid in predicting mortality was performed in a study population with an overall 28-day mortality of 22 %. There is no uniformly recognized interpretation of the change in PCT concentration levels for the prediction of mortality, and overall mortality is strongly dependent on many factors, including pre-existing patient risk factors and clinical course.

Methodology

The Elecsys BRAHMS PCT assay utilizes a sandwich principle. Total duration of the PCT assay is 18 minutes with two incubations.

During the first incubation, antigen in the sample (30 µL), a biotinylated monoclonal PCT-specific antibody, and a monoclonal PCT-specific antibody labeled with a ruthenium complex[a] react to form a sandwich complex.

Streptavidin-coated microparticles are added to the mixture, and incubated a second time.

During the second incubation, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. At the end of the second incubation, 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 ProCell/ProCell M.

Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

a Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)(2,3)

Specimen

Acceptable Sample Containers

13 x 75 PST BD tubes
PST BD microtainers

Type of Specimen

Biological fluid samples should be collected in the same manner routinely used for any laboratory test. Freshly drawn plasma is the only acceptable specimen. Whole blood or urine is not acceptable.

Specimen Storage and Stability

Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the plasma be physically separated from contact with cells within two hours from the time of collection.

Separated plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the

separated sample is to be stored beyond 48 hours, samples should be frozen at -20°C ± 5 °C. Frozen samples are stable for up to 3 months. Frozen samples should be thawed only once. After thawing, mix plasma thoroughly and re-centrifuge if necessary. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.

Ensure residual fibrin and/or cellular matter has been removed from plasma prior to analysis.

Due to possible evaporation effects, open samples, calibrators and controls on the analyzers should be analyzed/measured and recapped within 2 hours, then stored appropriately.

Use laboratory posted settings for sample centrifugation of sample tubes.

Reagents

The reagent rackpack in the kit (containing reagents M, R1, and R2) is ready-for-use and is supplied in bottles compatible with the system.

Reagent rackpack

Ref 05053888-200 tests

The reagent rackpack is labeled as PCT.

M	Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL	Streptavidin-coated microparticles 0.72 mg/mL; preservative
R1	Anti-PCT-Ab~biotin (gray cap), 1 bottle, 9 mL	Biotinylated monoclonal anti-PCT antibody (mouse) 2.0 µg/mL; phosphate buffer 95 mmol/L, pH 7.5; preservative
R2	Anti-PCT-Ab~Ru(bpy) (black cap), 1 bottle, 9 mL	Monoclonal anti-PCT antibody (mouse) labeled with ruthenium complex 5.6 µg/mL; phosphate buffer 95 mmol/L, pH 7.5; preservative

PCT Calibrators

M PCT Cal1	PCT Calibrator Level 1 (white cap), 1 bottle (lyophilized) to make 4 mL	PCT (recombinant) approximately 0.10 ng/mL in a human serum matrix; preservative
PCT Cal2	PCT Calibrator Level 2 (black cap), 1 bottle (lyophilized) to make 4 mL	PCT (recombinant) approximately 54 ng/mL in a human serum matrix; preservative

The exact lot-specific calibrator values are encoded in the barcoded labels of the test-specific reagent.

PCT Controls

PC PCT1	PreciControl PCT 1 (beige cap), 2 bottles (lyophilized) each to make 4 mL	PCT (recombinant) approximately 0.50 ng/mL in a human serum matrix; preservative
PC PCT2	PreciControl PCT 2 (brown cap), 2 bottles (lyophilized) each to make 4 mL	PCT (recombinant) approximately 10 ng/mL in a human serum matrix; preservative

The exact lot-specific target values and ranges are encoded in the barcodes as well as printed on the enclosed (or electronically available) value sheet.

Miscellaneous required items also included in the kit:
- 2 barcode cards
- Control barcode sheet
- 2 x8 bottle labels (calibrators)
- 2x14 bottle labels (controls)
- 6 empty labeled snap-cap bottles

Materials required (but not provided)

REF 11776576322	CalSet Vials, 2 x 56 empty snap-cap bottles
REF 03142949122	ControlSet Vials, 2 x 56 empty snap-cap bottles
REF 11662970122	CleanCell, 6 x 380 mL measuring cell cleaning solution
REF 11930346122	Elecsys SysWash, 1 x 500 mL washwater additive
REF 11662988122	ProCell, 6 x 380 mL system buffer
REF 11933159001	Adapter for SysClean
REF 11706802001	AssayCup, 60 x 60 reaction vessels
REF 11706799001	AssayTip, 30 x 120 pipette tips
REF 11298500160	ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Reagent Preparation

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Reagent pack should sit at room temperature at least 1 hour, but no longer than 24 hours prior to loading on the instrument. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles while on the instrument.

Reagent Storage and Stability

Store at 2-8 °C. Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

If microparticles are present on the lid, gently mix the cartridge without producing bubbles to remove them from the lid.

If microparticles are dried around rim or on the lid, do not use the reagent pack.

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	4 weeks

Warnings and precautions

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.(11,12)

Do not use reagents after the expiration date indicated on the label.

Do not mix reagents or disposables from different lots.

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Equipment

This test is performed on the Roche cobas e 411; Roche Diagnostics, Indianapolis, IN. For technical assistance, call US Customer Technical Support 1-800-428-2336.

Refer to the *Roche cobas e 411 Operators Manual* for detailed instructions.

Calibration

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using PCT Cal1 and PCT Cal2. The exact lot-specific calibrator values are encoded on the barcoded labels of the PCT reagent pack.

Note: Calibrator sequence on all systems: **Always measure PCT Cal2 before PCT Cal1.**

Calibrator	Storage and Stability
VIDAS PCT CaL 1	Lyophilized calibrators are stable until the expiration date at +2°C to +8°C. Stable after reconstitution for 2 hours on the analyzer or at room temperature. Stable after reconstitution for 3 months at -20 ± 5°C. Freeze only once.*
VIDAS PCT Cal 2	Lyophilized calibrators are stable until the expiration date at +2°C to +8°C. Stable after reconstitution for 2 hours on the analyzer or at room temperature. Stable after reconstitution for 3 months at -20 ± 5°C. Freeze only once.*

Calibrator Preparation

1. Add 4.0 mL of deionized water into each calibrator vial using a volumetric pipet.
2. Allow the calibrators to stand closed and undisturbed for 15 to 20 minutes at room temperature (15 - 25°C) to allow the lyophilized material to dissolve.
3. Mix carefully, avoiding foam formation. Use immediately.
4. Transfer 1 mL aliquots of the remaining reconstituted calibrators into empty labeled aliquot vials. Freeze the aliquots upright at -20 ± 5°C. Thaw and use only once.
5. Allow frozen calibrator aliquots to sit 15-30 minutes at room temperature to ensure they have reached 15 - 25°C before use.

NOTE: Do not combine calibrator bottles from different lots. Use only calibrator bottles that come with the reagent kit box.

The system must have valid calibration factors in memory before controls or patient samples can be run.

Under typical operating conditions the PCT reagent must be calibrated every 8 weeks or with each new lot of reagent, when quality control is outside the defined limits, and also with certain parts replacements or maintenance procedures, as defined in the *Roche cobas e 411 Operators Manual* (IFU).

If the same reagent pack remains on the analyzer more than 7 days, recalibration is required for that pack.

Verify that the calibration has not exceeded the recommended calibration date prior to running controls or patients, and recalibrate as necessary.

For detailed calibration instructions, refer to the *Roche cobas e 411 Operators Manual*.

The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will print out with error codes and the system will alert the operator of the failure. The explanation of these error codes can be found in the *Roche cobas e 411 Operators Manual*.

Quality Control

A minimum of two levels of control material will be analyzed each day of patient testing. Controls from one kit box should not be used with a different kit box. The exact lot-specific target values and ranges are encoded in the barcodes as well as printed on the enclosed value sheet.

In addition, controls should be run under the following circumstances:

Upon loading a new reagent cartridge.
Following each new calibration.
Following specific maintenance or troubleshooting procedures as detailed in the *Roche cobas e 411 Operators Manual*.

More frequent use of controls or the use of additional controls is left to the discretion of the user based on workload and workflow.

The following controls should be used in accordance with the package instructions for use inserts. Quality control results should be evaluated and handled with respect to the Clinical Chemistry Quality Control Procedure #3000.T. Controls are compiled statistically in the LIS and reagent lot changes are documented on the e411 Reagent Log sheets.

Quality Control Material

Control	Storage and Stability
VIDAS PCT Control 1	Lyophilized controls are stable until the expiration date at +2°C to +8°C. Stable after reconstitution for 2 hours on the analyzer or at room temperature. Stable after reconstitution for 3 months at -20 ± 5°C. Freeze only once.*
VIDAS PCT Control 2	Lyophilized controls are stable until the expiration date at +2°C to +8°C. Stable after reconstitution for 2 hours on the analyzer or at room temperature. Stable after reconstitution for 3 months at -20 ± 5°C. Freeze only once.*

* Freeze 1 mL aliquots of reconstituted controls at –20 ± 5°C.

Control Preparation

6. Add 4.0 mL of deionized water into each control vial using a volumetric pipet.
7. Allow the controls stand closed and undisturbed for 15 to 20 minutes at room temperature (15 - 25°C) to allow the lyophilized material to dissolve.
8. Mix carefully, avoiding foam formation. Use immediately.

9. Transfer 1 mL aliquots of the remaining reconstituted calibrators/controls into empty labeled ControlSet snap-cap bottles. Freeze the aliquots upright at -20 ± 5°C. Thaw and use only once.
10. Allow frozen control aliquots to sit 15-30 minutes at room temperature to ensure they have reached 15 - 25°C before use.

NOTE: Do not combine control bottles from different lots. Use only control bottles that come with the reagent kit box.

Both the vial labels and the additional labes contain two different barcodes. The e 411 uses the longer barcodes without the yellow marks at the ends. Be sure the vial cap and the correct barcode are both oriented properly in the rack.

Lot-to-Lot Check

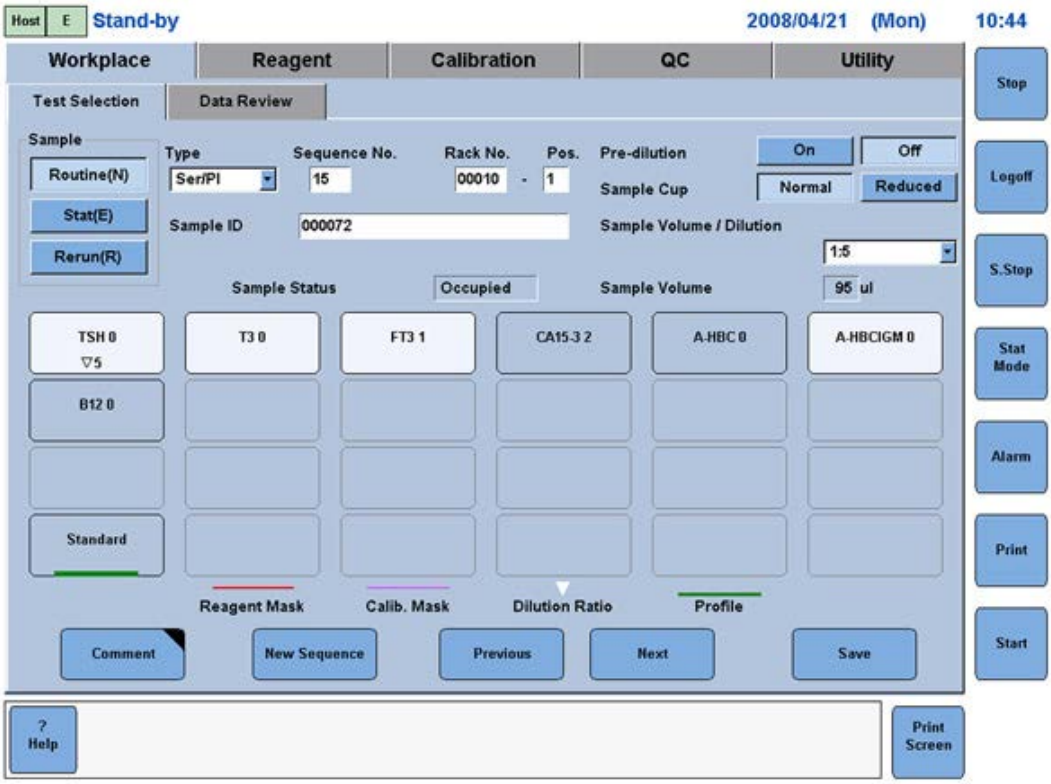
In addition, for new shipments and reagent lot changes, patient comparisons should be run and evaluated for acceptability. Two patient samples that were run on the current lot should be retrieved with previous results of 0.15ng/mL and 2.0 ng/mL. After the new lot is calibrated and controls have been run, the patient samples should be run with the new lot. Results should agree within ±2 SD of a control range, or 20%, whichever is greater.

Testing Procedure

Samples must be at room temperature prior to analysis.

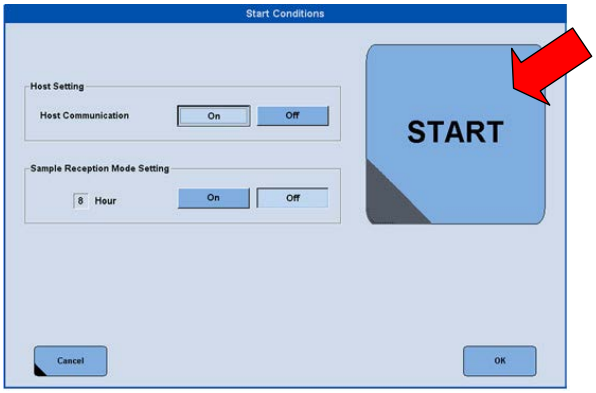
Without LIS Interface/LIS down

1. Choose [**Workplace**] > [**Test Selection**]. Use the Tab key on the software keyboard or touch the required field to move the cursor to the appropriate fields.



2. Select the **Routine** option from the Sample area on the top left of the screen. A sequence number is assigned atomically.
3. It is not necessary to program a rack ID and position with bar-coded samples.
4. Select the sample type using the **Type** drop-down list.
5. Choose the **Sample ID** field to open the software keyboard. Type in the sample ID (barcode number) of the sample in the Sample ID text box.
6. Select the **Normal** option, or **Reduced** option if you are using the e411Sample Cup.
7. Select the test.
8. Choose **Save** to save the test selection.
9. Place the barcoded samples on the racks. Make sure the barcodes are visible through the openings on the rack.
10. Load the racks on the tray present on the A-Line. (See image.)

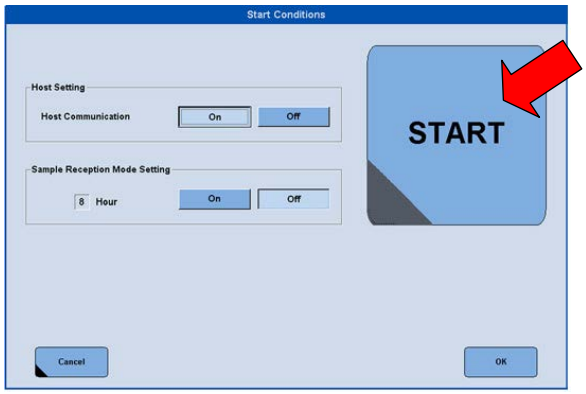
11. Select Start (global button on the right), verify the settings on the Start Conditions screen and adjust if necessary, then press the large START button.



With LIS Interface

1. Place barcoded samples on the rack. Make sure the barcodes are visible through the openings on the rack.
2. Load the racks on the tray present on the A-Line. (See image.)

3. Select Start (global button on the right), verify the settings on the Start Conditions screen and adjust if necessary, then press the large START button.



Results and Interpretation

Once the assay is completed, results are automatically calculated; the concentrations are expressed in ng/mL.

Procedural Notes

High Dose Hook Effect

There is no high-dose hook effect at PCT concentrations up to 1000 ng/mL.

Limitations

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Increased PCT levels may not always be related to systemic infection.(4,13,14,15) These include, but are not limited to:

Patients experiencing major trauma and/or recent surgical procedure including extracorporeal circulation or burns.

Patients undergoing treatment with OKT3 antibodies, OK-432, interleukins, TNF-alpha and other drugs that stimulate the release of pro-inflammatory cytokines or result in anaphylaxis.

Patients diagnosed with active medullary C-cell carcinoma, small cell lung carcinoma, or bronchial carcinoid.

Patients with acute or chronic viral hepatitis and/or decompensated severe liver cirrhosis (Child-Pugh Class C).

Patients with prolonged or severe cardiogenic shock, prolonged severe organ perfusion anomalies, or after resuscitation from cardiac arrest.

Patients receiving peritoneal dialysis or hemodialysis treatment.

Patients with biliary pancreatitis, chemical pneumonitis or heat stroke.

Patients with invasive fungal infections (e.g., candidiasis, aspergillosis) or acute attacks of plasmodium falciparum malaria.

Neonates during the first 2 days of life.

The results of the Elecsys BRAHMS PCT assay should be evaluated in the context of all laboratory findings and the total clinical status of the patient. In cases where laboratory results do not agree with the clinical picture or history, additional tests should be performed.

Interference study

Human Anti-Mouse Antibody (HAMA) interference testing was completed with three PCT analyte concentrations using a high HAMA human serum pool. No interference was detected.

Samples from patients routinely exposed to animals or animal serum products may contain heterophilic antibodies causing an atypical result. This assay has been formulated to mitigate the risk of this type of interference. However, potential interactions between rare sera and test components can occur.

No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

The following endogenous substances were added to human-based samples at the concentrations listed and evaluated for potential interference in the Elecsys BRAHMS PCT assay. Recovery was within ± 15 % of the reference value.

Hemolysis	< 900 mg/dL of hemoglobin
Lipemia	< 1500 mg/dL of Intralipid
Icterus	< 25 mg/dL
Biotin*	< 30 ng/mL

*Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

In vitro tests were performed on 27 commonly used pharmaceuticals. No interference with the assay was found. The specific drugs were tested with concentrations shown in the table below. Recovery was within ± 10 % of the reference value.

Active agent	**Concentration mg/L**
Acetylcysteine	150
Ampicillin	1000
Ascorbic acid	300
Ca-Dobesilate	200
Cyclosporine	5
Cefoxitin	2500
Heparin	8000 U
Levodopa	20
Methyldopa	20
Metronidazole	200
Phenylbutazone	400
Doxycycline	50
Acetylsalicylic acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100
Imipenem	1180
Cefotaxin	900
Vancomycin	3500
Dopamine	130

Active agent	Concentration mg/L
Noradrenaline	2
Dobutamine	11.2
Furosemide	200000
Calcitonin Eel	30
Calcitonin Salmon	30
Fentanyl	10

Performance Characteristics

Analytical Measurement Range

The Elecsys BRAHMS PCT measurement range is 0.02 to 100 ng/mL.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation:

Limit of Blank = 0.015 ng/mL

Limit of Detection = 0.02 ng/mL

Limit of Quantitation = 0.060 ng/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

Clinical Reportable Range

The Elecsys BRAHMS PCT assay reportable range is **0.02 - 100 ng/mL**.

Samples with procalcitonin concentrations less than 0.02 ng/mL shall be reported as "**< 0.02 ng/mL**".

Samples with procalcitonin concentrations greater than 100 ng/mL shall be reported as "**> 100 ng/mL**".

Reference Interval

<0.08 ng/mL

NOTE: Procalcitonin levels should be used along with other clinical information for sepsis and antimicrobial stewardship. The reference intervals are not validated for neonates and patients with burn injury.

Studies evaluating various populations (e.g., emergency, surgery, community acquired pneumonia, intensive care unit, endotoxin challenged) without sepsis corresponded with reference interval of < 0.15 ng/mL. The reference range does not apply to neonates or patients with burn injury.

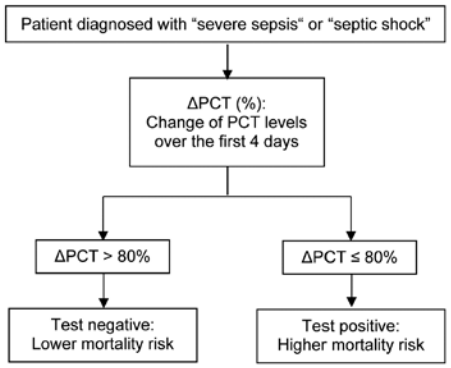
This assay is also intended for use to determine the change of PCT over time as an aid in assessing the cumulative 28-day risk of all cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU, or when obtained in the emergency department or other medical wards prior to ICU admission.

SIRS (Systemic Inflammatory Response Syndrome), sepsis, severe sepsis, and septic shock were categorized according to the criteria of the consensus conference of the American College of Chest Physicians/Society of Critical Care Medicine.(16)

PCT should always be interpreted in the clinical context of the patient. Therefore, clinicians should use the PCT results in conjunction with other laboratory findings and clinical signs of the patient.

The change of PCT concentration over time provides prognostic information about the risk of mortality(17) within 28 days for patients diagnosed with severe sepsis or septic shock coming from the emergency department, ICU, other medical wards, or directly from outside the hospital. Data support the use of PCT determinations from the day severe sepsis or septic shock is first diagnosed (Day 0) or the day thereafter (Day 1) and the fourth day after diagnosis (Day 4) for the classification of patients into higher and lower risk for mortality within 28 days according to the workflow below:

$$\Delta PCT = \frac{PCT_{\text{Day0 (or Day1)}} - PCT_{Day4}}{PCT_{Day0\ (or\ Day1)}} \times 100\%$$



ΔPCT ≤ 80%
A decrease of PCT levels below or equal to 80% defines a positive ΔPCT test result representing a higher risk for 28-day all-cause mortality of patients diagnosed with severe sepsis or septic shock.

ΔPCT > 80%
A decrease of PCT levels of more than 80% defines a negative ΔPCT result representing a lower risk for 28-day all-cause mortality of patients diagnosed with severe sepsis or septic shock.

Methods Comparison

2617 samples were run on the **cobas e** 411 analyzer and the predicate device (BRAHMS PCT sensitive KRYPTOR). Sample concentrations covered the measuring range of 0.02 - 100 ng/mL.

Passing Bablok[19]

Slope: 0.959 (95% CI: 0.947; 0.972)

Intercept: -0.023 (95% CI: -0.028; -0.018)

Coefficient: 0.989 (95% CI: 0.988; 0.990)

As determined by UCDMC:

A comparison study was performed at UCDMC comparing samples drawn from patients with suspected sepsis. Clinical conditions included respiratory tract, bloodstream, urinary tract, and wound infections. Procalcitonin was measured on the Roche cobas e411 and compared to the B·R·A·H·M·S PCT assay on the BioMerieux miniVIDAS immunoanalyzer at UCDMC..

Plasma (in the range of 0.05 – 132.28 ng/mL)

Y (cobas e411)	= 0.77x – 0.55
N	= 60
MEAN (cobas e411)	= 16.98
MEAN (miniVIDAS)	= 23.01
CORRELATION COEFFICIENT (r)	= 0.99
Mean (SD) Bias	= -5.75
P-value	= 0.002

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplication each for 21 days (n = 84). The following results were obtained:

cobas e 411 and Elecsys 2010 analyzers					
		Repeatability		**Intermediate precision**	
Sample	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**	**SD (ng/mL)**	**CV (%)**
Human serum 1	0.079	0.004	5.03	0.005	6.44
Human serum 2	0.442	0.008	1.71	0.013	3.14
Human serum 3	1.49	0.035	2.35	0.051	3.40
Human serum 4	27.5	0.381	1.38	0.891	3.24
Human serum 5	71.4	1.59	2.23	2.61	3.66
Human serum 6	88.1	1.19	1.35	2.80	3.18
PreciControl PCT1	0.456	0.009	1.91	0.015	3.21
PreciControl PCT2	9.07	0.166	1.83	0.303	3.35

Precision established at UCDMC

Type of Precision	**Sample Type**	**n**	**Mean (ng/mL)**	**1 SD**	**%CV**
cobas e411 Within-run	PCT Low Control	20	0.451	0.006	1.406
	PCT High Control	20	8.939	0.087	0.971

Type of Imprecision	**Sample Type**	**n**	**Mean (ng/mL)**	**1 SD**	**%CV**
cobas e411 Day to Day	PCT Low Control	23	0.486	0.024	0.049
	PCT High Control	23	9.021	0.199	0.022

Analytical Specificity

The Elecsys BRAHMS PCT assay on Elecsys and **cobas e** analyzers does not show any significant cross-reactions with the following substances, tested with PCT concentrations of approximately 0.4 ng/mL and 1.5 ng/mL (maximum tested concentration):

Substances	Non-interfering concentrations (ng/mL)
Human katacalcin	30
Human calcitonin	10
Human alpha-CGRP[a]	10000
Human beta-CGRP	10000

a Calcitonin Gene-Related Peptide

References

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Prepared By	Date Adopted	Supersedes Procedure #
kdagang	08/01/2017	bioMérieux miniVIDAS® #3280

Revision Date	Type of Revision	Revised by	Review/Annual Review Date	Reviewed By
New	Replaces testing on the miniVIDAS			