Elecsys BRAHMS PCT

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REF		Σ	SYSTEM
09318747190	09318747500	300	**cobas e** 402 **cobas e** 801

English

System information

Short name	ACN (application code number)
PCTX	10241

Intended use

Immunoassay for the in vitro quantitative determination of procalcitonin (PCT) in human serum and plasma. PCT is a marker of host response to bacterial infection. The Elecsys BRAHMS PCT assay is indicated as an aid to be used in conjunction with clinical evaluation for:

- the early detection of clinically relevant bacterial infections
- the assessment of the degree of severity and the prognosis of the outcome of systemic bacterial infection, sepsis, and septic shock
- identifying patients that benefit from antibiotic treatment
- monitoring of antibiotic therapy
- assessing the success of antibiotic therapy

in patients with suspected or confirmed bacterial infection.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

Sepsis presents a tremendous challenge to the healthcare system with an in-hospital mortality rate of up to 26 %.[1] The treatment goal in sepsis is to administer effective antimicrobial therapy as soon as possible as earlier recognition of sepsis and intervention improve patient outcome.[2,3] Lower respiratory tract infections (LRTIs) are a leading cause of sepsis and account for approximately 16 % of global sepsis-related deaths.[4] Respiratory tract infections (RTIs) are a common cause of antibiotic overtreatment with antibiotics prescribed for approximately 50-60 % of patients with suspected acute RTIs[5,6,7] and up to 70 % of patients with suspected LRTIs, despite the vast majority having a viral etiology.[8,9,10] This inappropriate use of antibiotics is believed to be a primary cause of the spread of antibiotic-resistant bacteria.[11] Antibiotic stewardship programs, involving promotion of the appropriate administration of antibiotics, are essential to combat the increase of antibiotic-resistant microorganisms.

PCT is a precursor protein of the hormone calcitonin produced by parafollicular cells (C cells) of the thyroid and neuroendocrine cells of the lung and the intestine.[12,13] PCT is undetectable in the blood of healthy individuals, but is produced ubiquitously in response to endotoxin or mediators released following bacterial infections.[14,15]

PCT serum concentrations are elevated in clinically relevant bacterial infections and can further increase correlating to the severity of infection.[14,16,17,18] Successful control of the underlying bacterial infection by the host immune system or antibiotic therapy results in a decrease of PCT concentration, with a half-life of 24 hours.[14,16,17] The measurable decline of PCT levels can be used to guide the discontinuation of antibiotic therapy.[19]

Depending on the clinical setting, PCT cut-off values can be used to guide antibiotic therapy decisions alongside other clinical and laboratory parameters.[20] In the low and moderate acuity setting (primary care/emergency department/medical ward), PCT concentrations ≤ 0.25 µg/L aid in identification of patients in which bacterial infection is unlikely and antibiotic therapy should be discouraged.[19] PCT concentrations > 0.25 µg/L aid in identification of patients with a probable bacterial infection for which antibiotic therapy is recommended.

Several randomized controlled trials and meta-analyses have demonstrated that the use of PCT-guided initiation or discontinuation of antibiotic therapy in patients with acute RTIs significantly reduces antibiotic consumption without compromising patient outcome.[21,22,23,24,25,26] Safe reduction of antibiotic consumption through PCT guidance was confirmed in routine clinical practice without increased risk of complications.[27]

The utility of PCT for guiding antibiotic therapy decisions has similarly been shown for sepsis with beneficial patient outcome.[28,29,30,31,32,33] A patient-level meta-analysis confirmed that PCT guidance can also be used in patients with impaired kidney function, for which PCT use was associated with shorter antibiotic treatment duration and lower mortality rates.[33]

The use of PCT to guide antibiotic therapy duration is recommended in International guidelines. The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) 2018 guidelines support the use of diagnostic tests, such as PCT, as part of sepsis management to guide antibiotic duration and dosing.[34] The 2011 European Respiratory Society (ERS) support the use of PCT to guide shorter treatment duration in patients with community acquired pneumonia.[35] PCT is also listed in the World Health Organization Model List of Essential In Vitro Diagnostics to guide antibiotic therapy or discontinuation in sepsis and LRTI (for use only in tertiary care facilities and above).[36]

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: Antigen in the sample (18 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.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- 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 II 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 **cobas** link.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The **cobas e** pack (M, R1, R2) is labeled as PCTX.

M Streptavidin-coated microparticles, 1 bottle, 12.4 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-PCT-Ab~biotin, 1 bottle, 18.8 mL:
Biotinylated monoclonal anti-PCT antibody (mouse) 2.0 µg/mL; phosphate buffer 95 mmol/L, pH 7.5; preservative.

R2 Anti-PCT-Ab~$Ru(bpy)_3^{2+}$, 1 bottle, 18.8 mL:
Monoclonal anti-PCT antibody (mouse) labeled with ruthenium complex 5.6 µg/mL; phosphate buffer 95 mmol/L, pH 7.5; preservative.

PCT Cal1 PCT calibrator 1 (lyophilized), 1 bottle for 4 mL:
PCT (recombinant) approximately 0.10 ng/mL in a human serum matrix; preservative.

PCT Cal2 PCT calibrator 2 (lyophilized), 1 bottle for 4 mL:
PCT (recombinant) approximately 54 ng/mL in a human serum matrix; preservative.

PC PCT1 PreciControl PCT 1 (lyophilized), 2 bottles each for 4 mL:
PCT (recombinant) approximately 0.50 ng/mL in a human serum matrix; preservative.

PC PCT2 PreciControl PCT 2 (lyophilized), 2 bottles each for 4 mL:
PCT (recombinant) approximately 10 ng/mL in a human serum matrix; preservative.

Calibrators: The exact lot-specific calibrator values are available via the **cobas** link.

Controls: The exact lot-specific target values and ranges are available via the **cobas** link.

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Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing dust/fume/gas/mist/vapours/spray.
P273	Avoid release to the environment.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

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 use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
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.[37,38]

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

Reagent handling

The reagents (M, R1, R2) in the kit are ready-for-use and are supplied in **cobas e** packs.

Calibrators and controls:

Carefully dissolve the contents of 1 bottle by adding exactly 4.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation. Transfer the reconstituted calibrators/controls into empty labeled snap-cap bottles.

Unless the entire volume is necessary for calibration and quality control on the analyzer, transfer aliquots of the freshly reconstituted calibrators and controls into empty snap-cap bottles (CalSet Vials/ControlSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at -20 °C (± 5 °C) for later use. Perform **only one** calibration or control procedure per aliquot.

Note: Do not combine bottles from different lots. Use only control bottles out of one lot with each other.

All information required for correct operation is available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the **cobas e** pack:	
unopened at 2-8 °C	up to the stated expiration date
on the analyzers	16 weeks

The lyophilized calibrators and controls are stable up to the stated expiration date.

Stability of the reconstituted calibrators/controls:	
at -20 °C (± 5 °C)	3 months (freeze only once)
on the analyzers at 20-25 °C	2 hours (use only once)

Store the calibrators and controls **upright** in order to prevent the solution from adhering to the snap-cap.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, K_2-EDTA and K_3-EDTA plasma.

Plasma tubes containing separating gel can be used.

Criterion: Slope 0.9-1.1 + intercept within ≤ ± 0.06 ng/mL + coefficient of correlation ≥ 0.95.

Stable for 24 hours at 20-25 °C, 48 hours at 2-8 °C, 13 months at -20 °C (± 5 °C). Freeze only once.

Frozen samples can lead to a lower recovery of up to 8 %.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not use samples and controls stabilized with azide.

Ensure the samples and calibrators are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators on the analyzers should be analyzed/measured within 2 hours.

Materials provided

See “Reagents – working solutions” section for reagents.

- 2 x 8 bottle labels (calibrators)
- 2 x 14 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
- General laboratory equipment
- **cobas e** analyzer

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M

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- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibrators:

Place the reconstituted calibrators (in the system-compatible bottles with barcoded labels) in the sample zone.

Read in all the information necessary for calibrating the assay.

After calibration has been performed, discard the calibrators.

Controls:

Place the reconstituted controls in the sample zone.
After the control procedure has been performed, discard the controls.

Calibration

Traceability: This method has been standardized against the BRAHMS PCT LIA assay.

The predefined master curve is adapted to the analyzer using PCT Cal1 and PCT Cal2.

Calibrator sequence: Always measure PCT Cal2 before PCT Cal1.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the **cobas e** pack was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PC PCT 1 and PC PCT 2.

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 **cobas e** pack, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note: When using two reagent kits with different lots in the same run, the controls will be measured with both reagent lots. Use only control values measured with the corresponding lots.

Calculation

The analyzer automatically calculates the analyte concentration of each sample in ng/mL.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 685 µmol/L or ≤ 40 mg/dL
Hemoglobin	≤ 0.559 mmol/L or ≤ 900 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL

Criterion: For concentrations ≤ 0.1 ng/mL the deviation is ≤ 0.015 ng/mL. For concentrations > 0.1 ng/mL the deviation is ≤ 15 %.

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

Pharmaceutical substances
In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special therapeutic substances were tested. No interference with the assay was found.

Special therapeutic substances

Drug	Concentration tested mg/L
Cefotaxime	≤ 900
Dobutamine	≤ 11.2
Dopamine	≤ 130
Furosemide	≤ 20
Imipenem	≤ 1180
Noradrenaline	≤ 2.0
Vancomycin	≤ 3500

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.

PCT levels can be increased in certain situations without infectious origin. These include, but are not limited to:[39]

- 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
- neonates (< 48 hours after birth)[40]

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

Limits and ranges

Measuring range

0.02-100 ng/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 0.02 ng/mL. Values above the measuring range are reported as > 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 = 0.06 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.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 %.

Dilution

Samples with PCT concentrations above the measuring range can be diluted manually with PCT negative human serum or plasma. The recommended dilution is 1:4. The concentration of the diluted sample must be ≥ 20 ng/mL. After manual dilution, multiply the result by the dilution factor.

Expected values

Reference range

A study performed with the Elecsys BRAHMS PCT assay using 492 samples from apparently healthy males (245) and females (247) revealed the following normal value: 0.046 ng/mL (95th percentile).

Clinical cutoff

Note: The cutoffs indicated below may vary according to the clinical situation.

PCT serum concentrations are elevated in clinically relevant bacterial infections and continue to rise with the increasing severity of the disease. However, as an expression of individually different immune responses and different clinical situations, the same focus of infection may be associated with varying individual elevations in PCT concentrations. Therefore, clinicians should use the PCT results in conjunction with the patient's other laboratory findings and clinical signs, and interpret the concrete values in the context of the patient's clinical situation. The reference ranges are therefore given for orientational purpose only.

Diagnosis of systemic bacterial infection/sepsis*[17,18,41]

*SIRS, 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[42]

ng/mL PCT	Analysis
< 0.5	Local bacterial infection is possible. Systemic infection (sepsis) is unlikely. Low risk for progression to severe systemic infection (severe sepsis). **IMPORTANT:** PCT levels < 0.5 ng/mL do not exclude an infection, because localized infections (without systemic signs) may be associated with such low levels. If the PCT measurement is done very early after bacterial insult (< 6 hours), values may still be low. In this case, PCT should be re-assessed 6-24 hours later.
≥ 0.5 to < 2	Systemic infection (sepsis) is possible, but various conditions are known to induce PCT as well (see below). Moderate risk for progression to severe systemic infection (severe sepsis). The patient should be closely monitored both clinically and by re-assessing PCT within 6-24 hours.
≥ 2 to < 10	Systemic infection (sepsis) is likely, unless other causes are known. High risk for progression to severe systemic infection (severe sepsis).
≥ 10	Important systemic inflammatory response, almost exclusively due to severe bacterial sepsis or septic shock. High likelihood of severe sepsis or septic shock.

Differential diagnosis of Lower Respiratory Tract Infections[21]

ng/mL PCT	Analysis
< 0.1	Indicates absence of bacterial infection. Use of antibiotics strongly discouraged, also in the presence of impaired pulmonary reserve in AECOPD.
0.1 to 0.25	Bacterial infection unlikely. The use of antibiotics is discouraged.
> 0.25 to 0.5	Bacterial infection is likely. Antibiotic treatment is encouraged.
> 0.5	Suggestive of the presence of bacterial infection. Antibiotic treatment is strongly encouraged.

Antibiotic guidance in sepsis[43] and LRTI[22]

Antibiotic therapy should be considered regardless of PCT result if the patient is clinically unstable, is at high risk for adverse outcome, has strong evidence of bacterial pathogen, or the clinical context indicates antibiotic therapy is warranted. If antibiotics are withheld, reassess if symptoms persist/worsen and/or repeat PCT measurement within 6-24 hours.

In order to assess treatment success and to support a decision to discontinue antibiotic therapy, follow up samples should be tested once every 1-2 days, based upon physician discretion taking into account the patients' evolution and progress. Antibiotic therapy may be adjusted using the discontinuation formula below:

- PCT_{Peak}: Highest observed PCT concentration
- $PCT_{Current}$: Most recent PCT concentration
- ΔPCT: Change in PCT concentration

ΔPCT: Calculate by using the following equation:

$$\Delta PCT = \frac{PCT_{Peak} - PCT_{Current}}{PCT_{Peak}} \times 100$$

Antibiotic therapy may be discontinued if the ΔPCT > 80 % or if the $PCT_{Current}$ is:

- ≤ 0.25 ng/mL for LRTI patients
- ≤ 0.5 ng/mL for suspected or confirmed septic patients

Antibiotic therapy may be continued based upon other clinical findings, such as:

- apparent progression on chest x-ray or ongoing/increasing toxicity for LRTI patients or
- failure to control a local infection, or ongoing physiologic instability for patients with suspected or confirmed sepsis.

If clinical picture has not improved and PCT remains high, re-evaluate and consider treatment failure or other causes.

Recomendations for laboratory reports

It is suggested to report the numerical PCT values (individual or paired). For paired PCT values the report should also indicate if the ΔPCT(%) was ≤ 80 % or > 80 %. The laboratory report should include a reference or a link to the Elecsys BRAHMS PCT assay Method Sheet for a guided interpretation of the test results.

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

Clinical performance

Clinical studies were conducted on samples from 283 ICU patients. The patients were classified into categories based on the ACCP/SCCM (American College of Chest Physicians/Society of Critical Care Medicine) consensus criteria on their first day of ICU admission: SIRS (systemic inflammatory response syndrome), sepsis, severe sepsis and septic shock.[44]

The PCT values of the patients with SIRS (n = 95) or sepsis (n = 71) compared to patients with severe sepsis (n = 60) or septic shock (n = 57) were as follows:

Results with a cutoff at 0.5 ng/mL

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	Clinical classification		
Elecsys BRAHMS PCT	SIRS	Severe sepsis/ septic shock	Total
< 0.5 ng/mL	63	5	68
≥ 0.5 ng/mL	32	112	144
Total	95	117	212

Based on the above data the sensitivity was 96 %, the specificity 66 %, the positive predictive value 78 % and the negative predictive value 93 %.

	Clinical classification		
Elecsys BRAHMS PCT	SIRS	Sepsis	Total
< 0.5 ng/mL	63	25	88
≥ 0.5 ng/mL	32	46	78
Total	95	71	166

Based on the above data the sensitivity was 65 %, the specificity 66 %, the positive predictive value 59 % and the negative predictive value 72 %.

Results with a cut-off at 2 ng/mL

	Clinical classification		
Elecsys BRAHMS PCT	SIRS	Severe sepsis/ septic shock	Total
< 2 ng/mL	88	18	106
≥ 2 ng/mL	7	99	106
Total	95	117	212

Based on the above data the sensitivity was 85 %, the specificity 93 %, the positive predictive value 93 % and the negative predictive value 82 %.

	Clinical classification		
Elecsys BRAHMS PCT	SIRS	Sepsis	Total
< 2 ng/mL	88	55	143
≥ 2 ng/mL	7	16	23
Total	95	71	166

Based on the above data the sensitivity was 23 %, the specificity 93 %, the positive predictive value 70 % and the negative predictive value 62 %.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

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

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		Repeatability		**Intermediate precision**	
Sample	Mean ng/mL	SD ng/mL	CV %	SD ng/mL	CV %
Human serum 1	0.0557	0.00209	3.8	0.00253	4.5
Human serum 2	0.490	0.00783	1.6	0.0120	2.4
Human serum 3	1.69	0.0245	1.5	0.0424	2.5
Human serum 4	31.4	0.421	1.3	0.952	3.0
Human serum 5	91.4	1.56	1.7	2.47	2.7
PreciControl PCT1	0.469	0.00674	1.4	0.0113	2.4
PreciControl PCT2	9.68	0.134	1.4	0.245	2.5

Method comparison

a) A comparison of the Elecsys BRAHMS PCT assay, REF 08828679190 / 08828679200 / 09318747190 / 09318747200 (**cobas e** 801 analyzer; y), with the Elecsys BRAHMS PCT assay, REF 07301715190 / 07301715200 (**cobas e** 801 analyzer; x), using humannative serum gave the following correlations (ng/mL):

Number of samples measured: 153

Passing/Bablok[45]	Linear regression
y = 1.010x - 0.000418	y = 1.000x + 0.0622
τ = 0.994	r = 1.00

The sample concentrations were between 0.0368 and 93.6 ng/mL.

b) A comparison of the Elecsys BRAHMS PCT assay, REF 08828679190, 08828679200, 09318747190, 09318747200 (**cobas e** 402 analyzer; y), with the Elecsys BRAHMS PCT assay, REF 08828679190 / 08828679200 (**cobas e** 801 analyzer; x), gave the following correlations (ng/mL):

Number of samples measured: 135

Passing/Bablok[45]	Linear regression
y = 0.989x - 0.00304	y = 0.990x - 0.0191
τ = 0.992	r = 1.00

The sample concentrations were between 0.104 and 99.1 ng/mL.

Analytical specificity

The Elecsys BRAHMS PCT assay did not show any significant cross reactions with the following substances, when tested with PCT concentrations of approximately 0.4 ng/mL and 1.5 ng/mL:

Substances	**Maximum tested concentration ng/mL**
Human katacalcin	30
Human calcitonin	10
Salmon calcitonin	30000
Eel calcitonin	30000
Human alpha-CGRP[b)]	10000
Human beta-CGRP	10000

b) Calcitonin Gene-Related Peptide

Concordance with BRAHMS PCT LIA/BRAHMS PCT sensitive KRYPTOR

A comparison study was performed with the Elecsys BRAHMS PCT assay and the BRAHMS PCT LIA. Cutoff values of 0.5 ng/mL and 2 ng/mL have been evaluated.

	BRAHMS PCT LIA		
Elecsys BRAHMS PCT	< 0.5 ng/mL	≥ 0.5 ng/mL	Total
< 0.5 ng/mL	104	49	153
≥ 0.5 ng/mL	6	370	376
Total	110	419	529

	BRAHMS PCT LIA		
Elecsys BRAHMS PCT	< 2 ng/mL	≥ 2 ng/mL	Total
< 2 ng/mL	266	10	276
≥ 2 ng/mL	11	242	253
Total	277	252	529

The concordance between both assays was 90 % at the cutoff value of 0.5 ng/mL and 96 % at the cutoff-value of 2 ng/mL.

The Elecsys BRAHMS PCT assay was also compared to the BRAHMS PCT sensitive KRYPTOR. Cutoff values of 0.5 ng/mL and 2 ng/mL have been evaluated.

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	BRAHMS PCT sensitive KRYPTOR		
Elecsys BRAHMS PCT	< 0.5 ng/mL	≥ 0.5 ng/mL	Total
< 0.5 ng/mL	183	20	203
≥ 0.5 ng/mL	2	392	394
Total	185	412	597

	BRAHMS PCT sensitive KRYPTOR		
Elecsys BRAHMS PCT	< 2 ng/mL	≥ 2 ng/mL	Total
< 2 ng/mL	312	24	336
≥ 2 ng/mL	1	260	261
Total	313	284	597

The concordance between both assays was 96 % at the cutoff value of 0.5 ng/mL and 96 % at the cutoff-value of 2 ng/mL.

References

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