510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K173927

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Elecsys BRAHMS PCT.

C. Measurand:

Procalcitonin (PCT)

D. Type of Test:

Quantitative, Electrochemiluminescence Immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Elecsys BRAHMS PCT

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3215; Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis

2. Classification:

   Class II (Special Controls)

3. Product codes:

   PMT

4. Panel:

   83 - (Microbiology)

H. Intended Use/ Indications for Use:

1. **Intended Use/ Indications for Use**:

   Immunoassay for the in vitro quantitative determination of PCT (procalcitonin) in human serum and plasma (K2 –EDTA, K3-EDTA and Li-Heparin).

   The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immunoassay analyzers.

   Used in conjunction with other laboratory findings and clinical assessments, Elecsys BRAHMS PCT is intended for use as follows:

   - to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock,
   - to determine the change in PCT level 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,
   - to aid in decision making on antibiotic therapy, for inpatients or patients in the emergency department with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD),
   - to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

2. Special conditions for use statement(s):

   For prescription use only

   Warnings and Precautions:

   The Elecsys BRAHMS PCT assay should not be used as a sole basis for diagnosis for determining 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. There is no uniformly recognized interpretation of the change in PCT levels for the prediction of mortality, and overall mortality is strongly dependent on many factors, including pre-existing patient risk factors and clinical course. The need for continued ICU care at Day 4 and other covariates (e.g., age, sepsis-related organ failure assessment (SOFA score) are also significant predictors of 28-day cumulative mortality risk. Validation of the Elecsys BRAHMS PCT assay as an aid in predicting mortality was performed in a study population with an overall 28-day mortality of 22%.

3. Special instrument requirements:

The submission demonstrates performance on the cobas e411 immunoassay analyzer.

I. Device Description:

Reagents

Materials provided in Elecsys BRAHMS PCT:

The reagent working solutions include: Rackpack (kit placed on analyzer)

- M: Streptavidin-coated microparticles
- R1: Anti-PCT-Ab~biotin
- R2: Anti-PCT – Ab~Ru (bpy)

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BRAHMS PCT sensitive KRYPTOR

2. Predicate 510(k) number(s):

   K171338

4. Comparison with predicate:

Similarities		
Item	**Candidate Device: Elecsys BRAHMS PCT (K173927)**	**Predicate Device: BRAHMS PCT sensitive KRYPTOR (K171338)**
Intended Use	Immunoassay for the in vitro quantitative determination of PCT (procalcitonin) in human serum and plasma (K2 –EDTA, K3-EDTA and Li-Heparin). The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immunoassay analyzers. Used in conjunction with other laboratory findings and clinical assessments, Elecsys B·R·A·H·M·S PCT is intended for use as follows: • to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock, • to determine the change in PCT level 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, • to aid in decision making on antibiotic therapy, for inpatients or patients in the emergency department with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD), • to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.	The BRAHMS PCT sensitive KRYPTOR is an immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE) technology to determine the concentration of PCT (procalcitonin) in human serum and EDTA or heparin plasma. The BRAHMS PCT sensitive KRYPTOR is intended to be performed on the BRAHMS KRYPTOR analyzer family. Used in conjunction with other laboratory findings and clinical assessments, BRAHMS PCT sensitive KRYPTOR is intended for use as follows: • to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock, • to determine the change in PCT level 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, • to aid in decision making on antibiotic therapy, for inpatients or patients in the emergency department with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD), • to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

Differences		
Item	**Candidate Device: Elecsys BRAHMS PCT (K173927)**	**Predicate Device: BRAHMS PCT sensitive KRYPTOR (DEN150009)**
Assay Protocol	The Elecsys BRAHMS PCT assay is a two-step sandwich immunoassay with streptavidin microparticles and an electrochemiluminescence detection system. The test system reagents contain a biotinylated monoclonal PCT-specific antibody and a ruthenium labeled monoclonal PCT-specific antibody.	The BRAHMS PCT sensitive KRYPTOR assay is a homogeneous sandwich immunoassay for detection of PCT in human serum or plasma. The measuring principle is based on Time-Resolved Amplified Cryptate Emission (TRACE) technology, which measures the signal that is emitted from an immunocomplex with time delay.
Detection Protocol	Electrochemiluminescent Assay	Time-Resolved Amplified Cryptate Emission (TRACE)
Applications	18-minute application	19-minute incubation
Instrument Platform	cobas e 411 analyzer	BRAHMS KRYPTOR analyzer
Sample Volume	30 µL	50 µL
Sample Type	Human serum and plasma (Li- Heparin, K2/K3 EDTA)	Human serum and plasma (EDTA, heparin)
Reagents	• Streptavidin-coated microparticles: • Steptavidin-coated microparticles; preservative • Anti-PCT-Ab~biotin: Biotinylated monoclonal anti-PCT antibody (mouse), phosphate buffer, preservative • Anti-PCT – Ab~Ru(bpy) 2/3+ a monoclonal anti-PCT antibody (mouse) labeled with ruthenium complex, phosphate buffer, preservative	• Cryptate conjugate, cryptate labeled, anti-PCT antibody (polyclonal, sheep), 3.2mL after reconstitution with KRYPTOR Solution 2 • L665 conjugate, XL665 labeled, anti-PCT antibody (monoclonal, mouse), 3.95 mL after reconstitution with KRYPTOR Solution 1 and KRYPTOR Solution 2 • Defibrinated human plasma, for diluting samples above 50 µg/L, ready for use
Calibrator	Elecsys PCT CalSet	BRAHMS PCT sensitive KRYPTOR Calibrator
Calibration Interval	Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows: • after 8 weeks when using the same reagent lot after 7 days (when using the same reagent kit on the analyzer) as required: e.g. quality control findings outside the specified limits	Before first use of each new BRAHMS PCT sensitive KRYPTOR assay lot, then repeated on a regular basis automatically managed by the BRAHMS PCT sensitive KRYPTOR.

Differences		
Item	**Candidate Device: Elecsys BRAHMS PCT (K173927)**	**Predicate Device: BRAHMS PCT sensitive KRYPTOR (DEN150009)**
Controls	Precicontrol PCT	BRAHMS PCT sensitive KRYPTOR Controls
Traceability/ Standardization	This method has been standardized against the BRAHMS PCT LIA assay.	Not Provided
Reagent 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. Stability: • unopened at 2-8 °C: up to the stated expiration date • after opening at 2-8 °C: 12 weeks on the analyzers: 4 weeks	In original shipping containers unopened at 2-8 °C: up to the stated expiration date after opening, onboard at 2-8 °C: 29 days
Measuring Range	0.02 – 100ng/mL	0.02-50µg/L
LoB	0.015 ng/mL	Not Provided
LoD	0.02 ng/mL	Not Provided
LoQ	0.06 ng/mL	0.075 µg/L
Hook Effect	No hook effect up to 1000ng/mL	N/A

K. Standard/Guidance Documents Referenced (if applicable):

- CLSI Guideline EP05-A3 – Evaluation of Precision Performance of Quantitative Measurements and Methods; Approved Guideline; Third Edition.
- CLSI Guideline EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.
- CLSI EP17-A2 guideline, Protocol for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline; Second Edition.

L. Test Principle:

The Elecsys BRAHMS PCT assay is a two-step sandwich immunoassay with streptavidin microparticles and an electrochemiluminescence detection system. The test system reagents contain a biotinylated monoclonal PCT-specific antibody and a ruthenium labeled monoclonal PCT-specific antibody.

Total assay duration: 18 minutes.

- 1st incubation: Antigen in the sample (30 µL), a biotinylated monoclonal PCT-specific antibody, and a monoclonal PCT-specific antibody labeled with a ruthenium complex*) 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. 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 specific, generated by 2-point calibration and a master curve provided via the reagent barcode.

M. Performance Characteristics:

1. Analytical performance:

   a. Reproducibility/Precision:

   The repeatability and intermediate precision studies of the Elecsys BRAHMS PCT assay were conducted using the cobas e 411 analyzer. Studies were performed in accordance with CLSI guideline EP5-A3, "Evaluation of Precision Performance of Quantitative Measurement Methods". One reagent lot was evaluated.

   The precision study was conducted using the study design of 21 days x 2 runs per day x 2 replicates per sample. One (1) instrument was used for the study and calibration was performed according to the Instructions for Use. Aliquots of sixteen (16) human serum samples and two (2) QC samples (PC PCT 1 and PC PCT 2) distributed over the measuring range were assayed in duplicate and randomized order on the cobas e 411 analyzer using one lot of reagent.

   Summary of precision results are represented in the table below:

Table 1: Summary of Precision Results –cobas e 411 analyzer

Sample	Mean (ng/mL)	Repeatability (CV%)		Intermediate Precision (CV%)		% Total Error
		Within Run		Within Lab		
		SD (ng/mL)	CV%	SD (ng/mL)	CV%	
1	0.036	0.008	21.2	0.009	24.5	60.33
2	0.037	0.006	16.7	0.009	24.3	57.02
10	0.085	0.005	6.4	0.008	9.2	22.49
11	0.121	0.005	4.2	0.007	6.2	14.95
12	0.183	0.006	3.1	0.008	4.2	10.18
13	0.242	0.005	2.2	0.009	3.6	8.67
14	0.300	0.006	2.1	0.008	2.8	6.75
3	0.400	0.008	2.0	0.013	3.2	7.68
15	0.415	0.008	1.9	0.010	2.3	5.56
4	1.52	0.024	1.6	0.034	2.2	5.36
16	2.12	0.032	1.5	0.047	2.2	5.38
5	2.93	0.042	1.4	0.071	2.4	5.76
6	26.1	0.392	1.5	0.725	2.8	6.81
7	44.6	0.723	1.6	1.25	2.8	6.69
8	64.5	1.24	1.9	1.96	3.0	7.33
9	97.6	1.67	1.7	2.31	2.4	5.79
Control 1	0.466	0.007	1.5	0.010	2.2	N/A
Control 2	9.53	0.101	1.1	0.207	2.2	N/A

Reproducibility/Precision results are acceptable.

b. Linearity/Assay Reportable Range:

Linearity:

See K160729 for study design and data.

Linearity was confirmed in the range of 0.02 ng/mL to 100 ng/mL, which fulfills the defined specifications. The measuring-range claim for the Elecsys BRAHMS PCT assay is 0.02–100 ng/mL.

Linearity results are acceptable.

Dilution Tests:

See K160729 for study design and data.
The data shown demonstrate consistent accuracy of recovery with all dilution steps.
The recommended dilution in the Method sheet is 1:4 using PCT-negative human serum or plasma.

c. *Traceability, Stability, Expected Values (controls, calibrators, or methods)*:

See K160729 for study design and data.

d. *Limit of Blank:*

See K160729 for study design and data.

Based on testing, the highest LoB value is 0.011 ng/mL, which fulfills the specification of LoB: ≤0.015 ng/mL. The claim for LoB is 0.015 ng/mL

e. *Limit of Detection:*

See K160729 for study design and data.

Based on testing, the highest LoD value was determined to be 0.0181 ng/mL, which fulfills the specification of LoD: ≤0.02 ng/mL. The claim for LoD is 0.02 ng/mL

f. *Limit of Quantitation:*

See K160729 for study design and data.

Based on testing, the highest LoQ value (meeting the CV% specification) was determined to be 0.045 ng/mL. The claim for LoQ is 0.06 ng/mL.

Table 2: Total Error

Expected value ng/mL	Elecsys BRAHMS PCT		
	% CV	% BIAS	% TE
2.00	2.37	1.94	5.85
0.50	2.40	2.17	6.13
0.30	3.00	2.50	7.44
0.25	3.41	2.70	8.32
0.15	5.38	3.7	12.57
0.10	8.11	5.35	18.73
0.05	16.65	12.45	39.92

g. *Analytical Specificity/Cross-Reactivity:*

See K160729 for study design and data.

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

Table 3: Analytical Specificity/Cross-Reactivity

Substances	Non-interfering concentration (ng/mL)
Human katacalcin	30
Human calcitonin	10
Human alpha-CGRP*	10000
Human beta-CGRP	10000

* Calcitonin Gene-Related Peptide

h. *Interfering Substances:*
Endogenous Interference:

The effect on quantitation of PCT in the presence of five endogenous interfering substances (Hemoglobin, Biotin, Intralipid, Bilirubin, and Rheumatoid Factor) was tested using one cobas e 411 analyzer. Spiked serum pools were used for testing. For each potential interferent, three human serum samples (containing low, mid, and high concentrations of PCT) were tested.

The following substances evaluated with the Elecsys BRAHMS PCT assay were found not to affect the test performance at concentrations reasonably and consistently found in clinical situations.

Table 4: Endogenous Interference

Interfering substance	Claim	Maximum Value with No Interference Observed
Hemoglobin	900 mg/dL	1000 mg/dL
Biotin	30 ng/mL	42 ng/mL
Intralipid	1,500 mg/dL	2,000 mg/dL
Bilirubin	25 mg/dL	66 mg/dL
Rheumatoid Factor	1,500 IU/mL	1,500 IU/mL

Table 5: Endogenous Interference: Biotin

% Bias for samples containing various concentrations of biotin										
Samples PCT concentrations (ng/mL)	**Biotin concentration (ng/mL)**									
	9.6	**20.4**	**30.0**	**39.6**	**80.4**	**99.6**	**150**	**300**	**600**	**1200**
0.04	2.3	2.8	0.2	-17.0	*	-65.7	*	*	*	*
0.10	4.5	-2.8	-6.6	-13.2	-26.8	-55.2	-83.3	*	*	*
0.13	0.5	-2.8	-3.1	-4.8	-25.1	-45.8	-68.4	*	*	*
0.20	1.5	0.3	-8.6	-11.5	-38.4	-50.9	-75.8	*	*	*
0.48	0.9	0.5	-0.03	-0.5	-9.1	-15.5	-26.8	-60.5	-97.7	*
1.96	3.9	3.6	1.4	0.5	-8.0	-12.7	-24.1	-60.5	-92.0	-97.5

* = value below measurable range

Exogenous Interference:

Fifteen pharmaceutical compounds were spiked into two human serum sample pools of different PCT concentrations. Each serum sample was evaluated both with and without the potential interference substances and tested with the Elecsys BRAHMS PCT assay on the Elecsys 2010 analyzer.

The following substances evaluated with the Elecsys BRAHMS PCT assay were found not to affect the test performance at concentrations reasonably and consistently found in clinical situations.

Table 6: Exogenous Interference

Interfering substance	Concentration tested (mg/L)	Result
Cromolyn	24	No interference observed
Acetaminophen	200	No interference observed
Acetylsalicylic acid	652	No interference observed
Alcohol	4000	No interference observed
Azithromycin	11.5	No interference observed
Cetirizine HCL	3.6	No interference observed
Dextromethorphan	1.4	No interference observed
Ibuprofen	500	No interference observed
Imipenem	1180	No interference observed
Levofloxacin	17.5	No interference observed
Loratadine	0.3	No interference observed

Interfering substance	Concentration tested (mg/L)	Result
Nicotine	1	No interference observed
Oxymetazoline HCL	0.09	No interference observed
Phenylephrine	0.18	No interference observed
Tiotropium	0.0216	No interference observed

See K160729 for additional interference studies.

HAMA Effect:

See K160729 for study design and data.

There was no HAMA interference observed.

i. High-Dose Hook Effect:

There was no observed high-dose hook effect at PCT concentrations up to 1,000 ng/mL PCT.

j. Assay Cut-off:

28-day mortality:

- **ΔPCT ≤ 80%**

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

NOTE: 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.

Progression Risk:

- **PCT > 2 µg/L**

  A PCT level above 2.0 µg/L on the first day of ICU admission is associated with a high risk for progression to severe sepsis and/or septic shock.

- **PCT < 0.5 µg/L**

  A PCT level below 0.5 µg/L on the first day of ICU admission is associated with a low

risk for progression to severe sepsis and/or septic shock.

LRTI Antibiotic Decision Making:

- **PCT < 0.10 ng/mL**

  Antibiotic therapy strongly discouraged.

- **PCT 0.10-0.25 ng/mL**

  Antibiotic therapy discouraged.

- **PCT 0.26-0.50 ng/mL**

  Antibiotic therapy encouraged.

- **PCT >0.50 ng/mL**

  Antibiotic therapy strongly encouraged.

Sepsis Antibiotic Discontinuation:

- **ΔPCT > 80%**

  Antibiotic therapy may be discontinued

- **PCT ≤ 0.50 ng/mL**

  Antibiotic therapy may be discontinued

Recommendations for Laboratory Reports for Initiation and Discontinuation**:**

The Change in Procalcitonin Calculator is available at http://www.brahms-pct-calculator.com. The Change in Procalcitonin Calculator can be used to determine ΔPCT results. 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 package insert for a guided interpretation of the test results.

k. Specimen Stability:

Refer to K160729 for stability data.

l. Sample Matrix Comparison:

See K160729 for study design and data.

SST is an acceptable sample type for use with the Elecsys PCT assay

Li-Heparin plasma is an acceptable sample type for use with the Elecsys BRAHMS PCT assay

K2-EDTA plasma is an acceptable sample type for use with the Elecsys BRAHMS PCT assay.

K3-EDTA plasma is an acceptable sample type for use with the Elecsys BRAHMS PCT assay.

2. Clinical Studies:

The clinical performance of the Elecsys BRAHMS PCT assay was establishing with multicenter testing of retrospective specimens available as frozen samples from adult patients (i.e., >18 years of age) diagnosed with severe sepsis or septic shock who were enrolled in the BRAHMS MOSES study from the Intensive Care Unit, the emergency department, other wards or directly from out of hospital and subsequently admitted to the ICU.

The clinical concordance analysis in this report was performed with all available valid test results obtained in the Elecsys BRAHMS PCT clinical performance study. The line listings of the Elecsys BRAHMS PCT clinical performance study were included in K160729.

The clinical concordance analysis of the Elecsys BRAHMS PCT clinical performance study shows more than 97% total agreement between the Elecsys BRAHMS PCT and the BRAHMS PCT sensitive Kryptor (predicate device) at the medical decision points 0.1, 0.25, 0.5 and 2.0 ng/mL. The regression slopes are within +/- 10% of identity in Passing-Bablok and Weighted Deming Analysis. This demonstrates equivalence to the predicate device.

Table 7: Elecsys BRAHMS PCT vs Predicate at 0.5 ng/mL

Elecsys BRAHMS PCT on cobas e 411	**BRAHMS PCT sensitive Kryptor**		**Total**
	≤ 0.5 ng/mL	**> 0.5 ng/mL**	
≤ 0.5 ng/mL	667	50	717
> 0.5 ng/mL	18	1882	1900
Total	685	1932	2617

Table 8: Elecsys BRAHMS PCT vs Predicate at 2.0 ng/mL

Elecsys BRAHMS PCT on cobas e 411	**BRAHMS PCT sensitive Kryptor**		**Total**
	≤ 2.0 ng/mL	**> 2.0 ng/mL**	
≤ 2.0 ng/mL	1223	56	1279
> 2.0 ng/mL	13	1325	1338
Total	1236	1381	2617

Table 9: 3 x 3 Table Elecsys BRAHMS PCT vs Predicate

Elecsys BRAHMS PCT on cobas e 411	**BRAHMS PCT sensitive Kryptor**			**Total**
	≤ 0.5 ng/mL	**0.5 ng/mL < PCT ≤ 2.0 ng/mL**	**> 2.0 ng/mL**	
≤ 0.5 ng/mL	667	48	2	717
0.5 ng/mL < PCT ≤ 2.0	18	490	54	562
> 2.0 ng/mL	0	13	1325	1338
Total	685	551	1381	2617

Table 10: 5 x 5 Table Elecsys BRAHMS PCT vs Predicate

Elecsys BRAHMS PCT on cobas e 411	BRAHMS PCT sensitive Kryptor					Total
	≤ 0.1 ng/mL	0.1 ng/mL < PCT≤ 0.25 ng/mL	0.25 ng/mL < PCT≤ 0.5 ng/mL	0.5 ng/mL < PCT ≤ 2.0 ng/mL	> 2.0 ng/mL	
≤ 0.1 ng/mL	97	47	1	1	1	147
0.1 ng/mL < PCT≤ 0.25 ng/mL	6	240	42	1	1	290
0.25 ng/mL < PCT≤ 0.5 ng/mL	0	16	218	46	0	280
0.5 ng/mL < PCT≤ 2.0 ng/mL	1	1	16	490	54	562
> 2.0 ng/mL	0	0	0	13	1325	1338
Total	104	304	277	551	1381	2617

Table 11: Comparison Elecsys BRAHMS PCT vs Predicate
N = 2617 (104 ≤ 0.1 ng/mL, 408 ≤ 0.25 ng/mL; 685 ≤ 0.5 ng/mL; 1236 ≤ 2.0 ng/mL)

Cutoff (> vs. ≤)	PositiveAgreement (95% CI)	NegativeAgreement(95% CI)	TotalAgreement	Cohen'sKappa
0.10 ng/mL	93.3%	98.0%	97.8%	0.762
	(86.6 - 97.3)	(97.4 - 97.3)		
0.25 ng/mL	95.6%	97.9%	97.5%	0.908
	(93.1 - 97.4)	(97.2 - 98.4)		
0.50 ng/mL	97.4%	97.4%	97.4%	0.934
	(95.9 - 98.4)	(96.6 - 98.1)		
2.00 ng/mL	98.9%	95.9%	97.4%	0.947
	(98.2 - 99.4)	(94.8 - 96.9)		

Table 12: Weighted Deming and Passing Bablok Regression Analysis

Parameter	Passing Bablok Regression	Weighted Deming (λ=1) Regression Analysis
n	2617	2617
Slope	0.959	0.949
95% CI	[0.947; 0.972]	[0.937; 0.961]
Intercept	-0.023	-0.008
95% CI	[-0.028; -0.018]	[-0.013; -0.004]
Pearson Correlation Coefficient (R)	0.989	0.989
Spearman Correlation Coefficient (R)	0.990	0.990
Sample Range	[0.02; 662.86]	[0.02; 662.86]

Figure 1: Weighted Deming Regression plots of Elecsys BRAHMS PCT versus Predicate

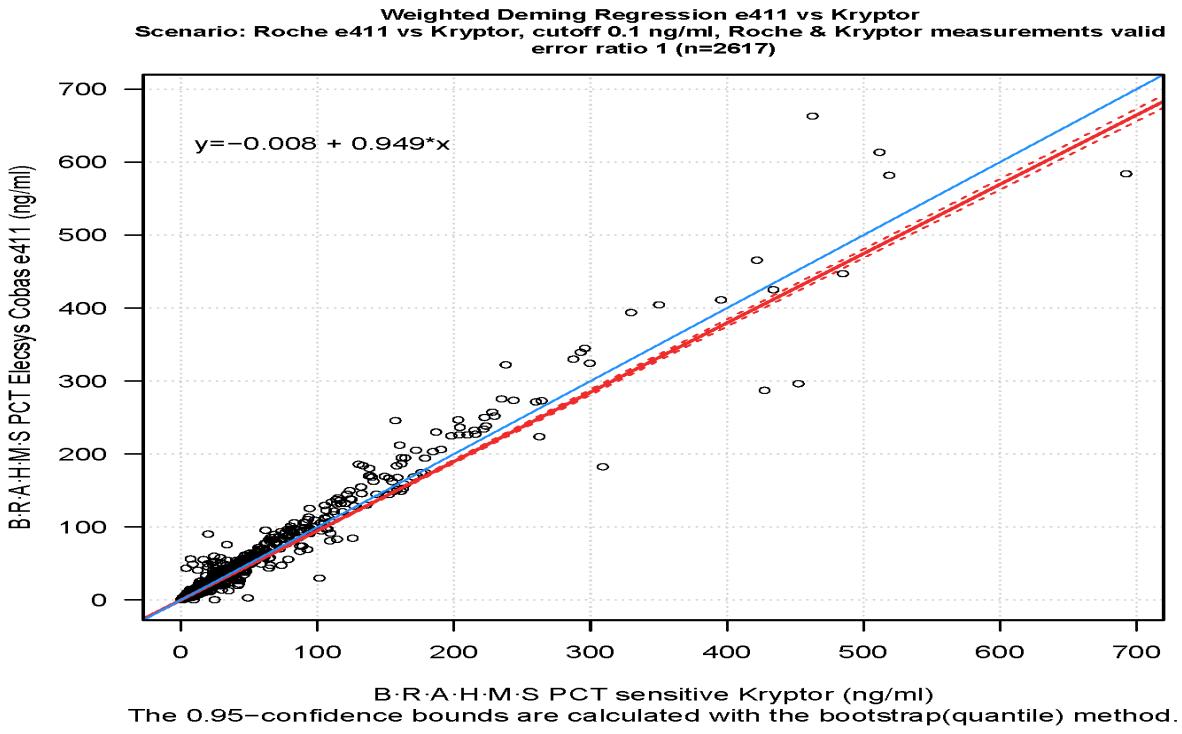
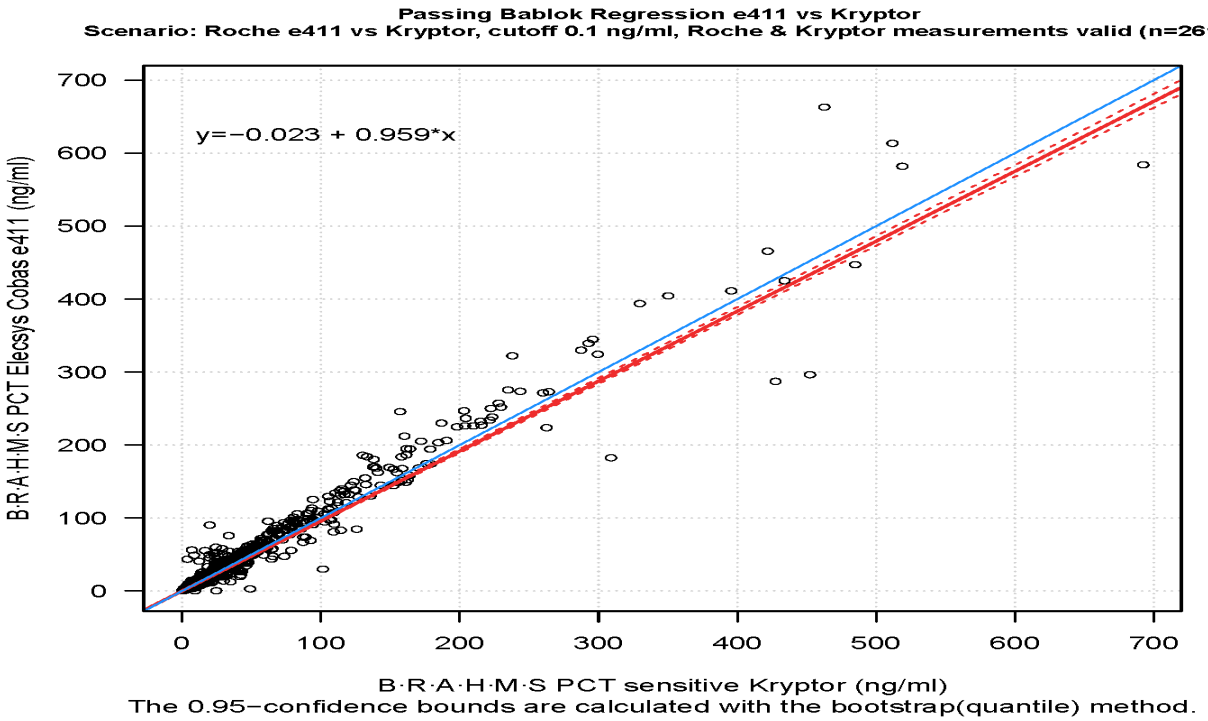


Figure 2: Passing Bablok Regression plots of Elecsys BRAHMS PCT versus Predicate



3. Clinical Cut-off:

   See assay cut-off M.1.j above.

N. Instrument Name:

The cobas e411 immunoassay analyzer

O. System Descriptions:

1. Modes of Operation:

   See Device Description (Section I) above

2. Software

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

4. Specimen Identification:

A barcode reader reads the barcodes on each tube for positive identification.

4. Specimen Sampling and Handling:

   See Sample Stability (M.1.k) above.

5. Calibration:

   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.

   Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows:

   - after 8 weeks when using the same reagent lot
   - after 7 days (when using the same reagent kit on the analyzer)
   - as required: e.g. quality control findings outside the defined limits

6. Quality Control:

   See "Traceability, Stability, Expected Values (controls, calibrators, or methods)" Section (M.1.c) above.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In the "Performance Characteristics" Section above:

N/A

Q. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.