July 6, 2018

Roche Diagnostics
Wes Gerbig
Regulatory Affairs Principal
9115 Hague Road
Indianapolis, Indiana 46250

Re: K173927
Trade/Device Name: Elecsys BRAHMS PCT
Regulation Number: 21 CFR 866.3215
Regulation Name: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis
Regulatory Class: Class II
Product Code: PMT
Dated: December 22, 2017
Received: December 26, 2017

Dear Wes Gerbig:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR

803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven R. Gitterman -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K173927

Device Name
Elecsys BRAHMS PCT

Indications for Use *(Describe)*
Elecsys BRAHMS PCT

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Elecsys BRAHMS PCT
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the Elecsys BRAHMS PCT Test System.

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Wes Gerbig Phone: (317) 521-3743 FAX: (317) 521-2324 Email: wes.gerbig@roche.com Secondary Contact Name Michael Leuther Phone: (317) 521-3930 FAX: (317) 521-2324 Email: michael.leuther@roche.com
Date Prepared	December 22, 2017
Proprietary Name	Elecsys BRAHMS PCT
Common Name	Procalcitonin
Classification Name	Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis
Product Codes, Regulation Numbers	PRI, PMT, NTM, 866.3215
Predicate Devices	B.R.A.H.M.S. PCT sensitive KRYPTOR® cleared under K171338.
Establishment Registration	For the Elecsys BRAHMS PCT Test System the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany is 9610126, and for Penzberg, Germany, 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260.

1. DEVICE DESCRIPTION

The Elecsys BRAHMS PCT assay is a two-step sandwich immunoassay with streptavidin microparticles and an electrochemiluminescence detection system. PCT in the sample reacts with these labeled antibodies to form a sandwich complex. This complex binds to streptavidin coated magnetic microparticles, which are magnetically captured onto an electrode. Application of voltage to the electrode induces chemiluminescence which is measured by a photomultiplier tube. 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. An optional Procalcitonin CalCheck product is also available.

1.1. Reagents

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) $\frac{2}{3}^{+}$

2. 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 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.

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3. TECHNOLOGICAL CHARACTERISTICS

Table 1: Assay Comparison

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
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 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 B·R·A·H·M·S 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 B·R·A·H·M·S PCT sensitive KRYPTOR® is intended to be performed on the B·R·A·H·M·S KRYPTOR® analyzer family. Used in conjunction with other laboratory findings and clinical assessments, B·R·A·H·M·S 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,
Intended Use/		• to aid in decision making on antibiotic therapy, for

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
Indications for Use Continued		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.
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)

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
Reagents	M: Streptavidin-coated microparticles: Steptavidin-coated microparticles; preservative R1: Anti-PCT-Ab~biotin: Biotinylated monoclonal anti-PCT antibody (mouse), phosphate buffer, preservative R2: Anti-PCT – Ab~Ru(bpy) 2/3+ a monoclonal anti-PCT antibody (mouse) labeled with reuthenium complex, phosphate buffer, preservative	Cryptate conjugate, cryptate labeled, anti-PCT antibody (polyclonal, sheep), 3.2mL after reconstitution with KRYPTOR® Solution 2 XL665 conjugate, XL665 labeled, anti-PCT antipody (monoclonal, mouse), 3.95 mL after reconstitution with KRYPTOR® Solution 1 and KRYPTOR® Solution 2 Defibrinated human plasma, for diluting samples above 50µg/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® lot, then repeated on a regular basis automatically managed by the BRAHMS PCT sensitive KRYPTOR®.
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	N/P
LoD	0.02 ng/mL	N/P

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
LoQ	0.06 ng/mL	0.075 µg/L
Lower Detection Limit	0.015 ng/mL	N/P
Hook Effect	No hook effect up to 1000ng/mL	N/A
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. 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.	B·R·A·H·M·S PCT sensitive KRYPTOR® is not indicated to be used as a stand-alone diagnostic assay and should be used in conjunction with clinical signs and symptoms of infection and other diagnostic evidence. In cases where the laboratory results do not agree with the clinical picture or history, additional tests should be performed Decisions regarding antibiotic therapy should NOT be based solely on procalcitonin concentrations. PCT results should always be interpreted in the context of the clinical status of the patient and other laboratory results. Changes in PCT levels for the prediction of mortality, and overall mortality, are strongly dependent on many factors, including pre-existing patient risk factors and clinical course. The need to continue ICU care at Day 4 and other covariates (e.g., age and SOFA score) are also significant predictors of 28-day cumulative mortality risk. The safety and performance of PCT-guided therapy for individuals younger than age 18 years, pregnant women, immunocompromised individuals or those on immunomodulatory agents, was not formally analyzed in the supportive clinical trials performed.

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
Limitations Continued		PCT levels may not be elevated in patients infected by certain atypical pathogens, such as Chlamydophila pneumoniae and Mycoplasma pneumoniae.1 Severity of renal failure or insufficiency, may influence procalcitonin values and should be considered as potentially confounding clinical factors when interpreting PCT values.2 Increased PCT levels may not always be related to systemic infection 2-5. These conditions include, but are not limited to: Patients experiencing major trauma and/or recent surgical procedure including extracorporeal circulation or burns; • Patients under treatment with OKT3 antibodies, OK-432, interleukins, TNF-alpha and other drugs stimulating the release of pro-inflammatory cytokines or resulting 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;

Feature	Candidate Device: Elecsys BRAHMS PCT	Predicate Device: B.R.A.H.M.S. PCT sensitive KRYPTOR® (K171338).
Limitations Continued		• Patients with invasive fungal infections (e.g. candidiasis, aspergillosis) or acute attacks of plasmodium falciparum malaria; and • Neonates during the first 2 days of life.
Method Comparison	2617 samples were run on the **cobas e** 411 and the predicate device (BRAHMS PCT sensitive KRYPTOR®). Passing Bablok 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)	

4. PERFORMANCE EVALUATION

The following data was requested by the FDA in Q171237 to support the updated Indications for Use statement and is listed below:

- Precision according to CLSI EP5-A3
- Interferences – Endogenous
- Interferences – Exogenous (Drugs)
- Clinical Performance Evaluation - Method Comparison to Predicate

The remaining data required to support the updated Indications for Use was supplied in the previous submission K160729:

- Analytical Sensitivity: LoB, LoD and LoQ according to CLSI EP17-A2
- Linearity according to CLSI EP6-A
- High Dose Hook Affect
- Human Anti-Mouse Antibodies (HAMA)

- Analytical Specificity
- Serum/Plasma Comparison
- Sample Stability
- Reagent Stability

4.1. Precision

The repeatability and intermediate precision of the Elecsys BRAHMS PCT assay was 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. Data is acceptable and is summarized below. An analysis was also performed to calculate % Total Error across the measuring range.

Table 2: Summary of Precision Results – Elecsys BRAHMS PCT Repeatability and Intermediate Precision

Mean (ng/mL)	Repeatability (CV%)	Intermediate Precision (CV%)	%Total Error
0.037	16.7	24.3	57.02
0.085	6.4	9.2	22.49
0.121	4.2	6.2	14.95
0.183	3.1	4.2	10.18
0.242	2.2	3.6	8.67
0.300	2.1	2.8	6.75
0.400	2.0	3.2	7.68
0.415	1.9	2.3	5.56
1.52	1.6	2.2	5.36
2.12	1.5	2.2	5.38
2.93	1.4	2.4	5.76
26.1	1.5	2.8	6.81
44.6	1.6	2.8	6.69
64.5	1.9	3.0	7.33
97.6	1.7	2.4	5.79

4.2. Endogenous Interferences

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. The substances were found not to affect test performance at clinically relevant concentrations. Recovery was within ± 15 % of the initial value. See K160729 for additional interference data.

Table 3: Potentially Interfering Endogenous Substances and Test Concentrations

Potential Interferent	Maximum Value With No Interference Observed
Intralipid	2000 mg/dL
Bilirubin	66 mg/dL
Hemoglobin	1000 mg/dL
Rheumatic Factor	1500 IU/mL

Table 4: Biotin Interference

% 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
0.04	2.3	2.8	0.2	-17.0	*
0.10	4.5	-2.8	-6.6	-13.2	-26.8
0.13	0.5	-2.8	-3.1	-4.8	-25.1
0.20	1.5	0.3	-8.6	-11.5	-38.4
0.48	0.9	0.5	-0.03	-0.5	-9.1
1.96	3.9	3.6	1.4	0.5	-8.0

% Bias for samples containing various concentrations of biotin					
Samples PCT concentrations (ng/mL)	Biotin concentration (ng/mL)				
	99.6	150	300	600	1200
0.04	-65.7	*	*	*	*
0.10	-55.2	-83.3	*	*	*
0.13	-45.8	-68.4	*	*	*
0.20	-50.9	-75.8	*	*	*
0.48	-15.5	-26.8	-60.5	-97.7	*
1.96	-12.7	-24.1	-60.5	-92.0	-97.5

* = value below measurable range

** Specimens with biotin concentrations up to 30 ng/mL demonstrated ≤ 13 % bias in results. Biotin concentrations greater than 30 ng/mL can lead to higher negative bias for PCT results. The recommended daily intake for biotin is 30 µg. Higher doses of biotin (> 10 mg per day) may be taken as a dietary supplement aimed at reducing hair loss or improving nail or skin condition.13

Some pharmacokinetic studies have shown that serum concentrations of biotin can reach 355 ng/mL for subjects taking supplements containing at least 20 mg of biotin14 or 1160 ng/mL

for subjects taking doses of biotin up to 300 mg.13 These studies were performed in healthy subjects, and some patients may be taking supplements with biotin at levels greater than 20 mg per day. Clearance of biotin could be different in patients tested with this device, which may lead to higher than expected concentrations of biotin in serum.

4.3. Exogenous Interferences – Drugs

The effect on quantitation of analyte in the presence of drugs was determined by comparing values obtained from samples spiked with 38 pharmaceutical compounds into two human serum samples at differing analyte concentrations and tested on the **cobas e** 411 analyzer. The substances were found not to affect test performance at clinically relevant concentrations. Recovery was within ± 10 % of the reference value. See K160729 for additional interference data.

Table 5: Potentially Interfering Drugs and Test Concentrations

Potential Interferent	Drug Level Tested (mg/L)
Cromolyn	**24**
Acetaminophen	**200**
Acetylsalicylic acid	**652**
Alcohol	**4000**
Azithromycin	**11.5**
Cetirizine HCL	**3.6**
Dextromethorphan	**1.4**
Ibuprofen	**500**
Imipenem	**1180**
Levofloxacin	**17.5**
Loratadine	**0.3**
Nicotine	**1**
Oxymetazoline HCL	**0.09**
Phenylephrine	**0.18**
Tiotropium	**0.0216**

4.4. Clinical Performance Evaluation - Method Comparison to Predicate

The Elecsys® B•R•A•H•M•S PCT clinical performance study was conducted by retrospective multicenter testing of PCT from available frozen samples of 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 or 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® B·R·A·H·M·S PCT clinical performance study. The clinical line data of the BRAHMS MOSES study is available via MAF2386 (Amendment 9 – Clinical Line Data). The line listings of the Elecsys B·R·A·H·M·S PCT clinical performance study was included in K160729.

The clinical concordance analysis of the Elecsys B·R·A·H·M·S PCT clinical performance study shows more than 97% total agreement between the Elecsys B·R·A·H·M·S PCT and the B•R•A•H•M•S 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 to include all currently cleared claims of the predicate device in the labeling of the candidate device.

Table 6: Elecsys BRAHMS PCT vs Predicate at 0.5 ng/mL

Elecsys BRAHMS PCT on cobas e 411	B•R•A•H•M•S 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 7: Elecsys BRAHMS PCT vs Predicate at 2.0 ng/mL

Elecsys BRAHMS PCT on cobas e 411	B•R•A•H•M•S 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

Elecsys BRAHMS PCT on cobas e 411	B•R•A•H•M•S PCT sensitive Kryptor®		Total
	≤ 2.0 ng/mL	> 2.0 ng/mL	
Total	1236	1381	2617

Table 8: 3 x 3 Table Elecsys BRAHMS PCT vs Predicate

Elecsys BRAHMS PCT on cobas e 411	B•R•A•H•M•S 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 ng/mL	18	490	54	562
> 2.0 ng/mL	0	13	1325	1338
Total	685	551	1381	2617

Table 9: 5 x 5 Table Elecsys BRAHMS PCT vs Predicate

Elecsys BRAHMS PCT on cobas e 411	B•R•A•H•M•S 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 10: 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. ≤)	Positive Agreement (95% CI)	Negative Agreement (95% CI)	Total Agreement	Cohen's Kappa
0.10 ng/mL	93.3% (86.6 - 97.3)	98.0% (97.4 - 97.3)	97.8%	0.762
0.25 ng/mL	95.6% (93.1 - 97.4)	97.9% (97.2 - 98.4)	97.5%	0.908
0.50 ng/mL	97.4% (95.9 - 98.4)	97.4% (96.6 - 98.1)	97.4%	0.934
2.00 ng/mL	98.9% (98.2 - 99.4)	95.9% (94.8 - 96.9)	97.4%	0.947

Table 11: 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	0.989	0.989
Spearman Correlation Coefficient	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

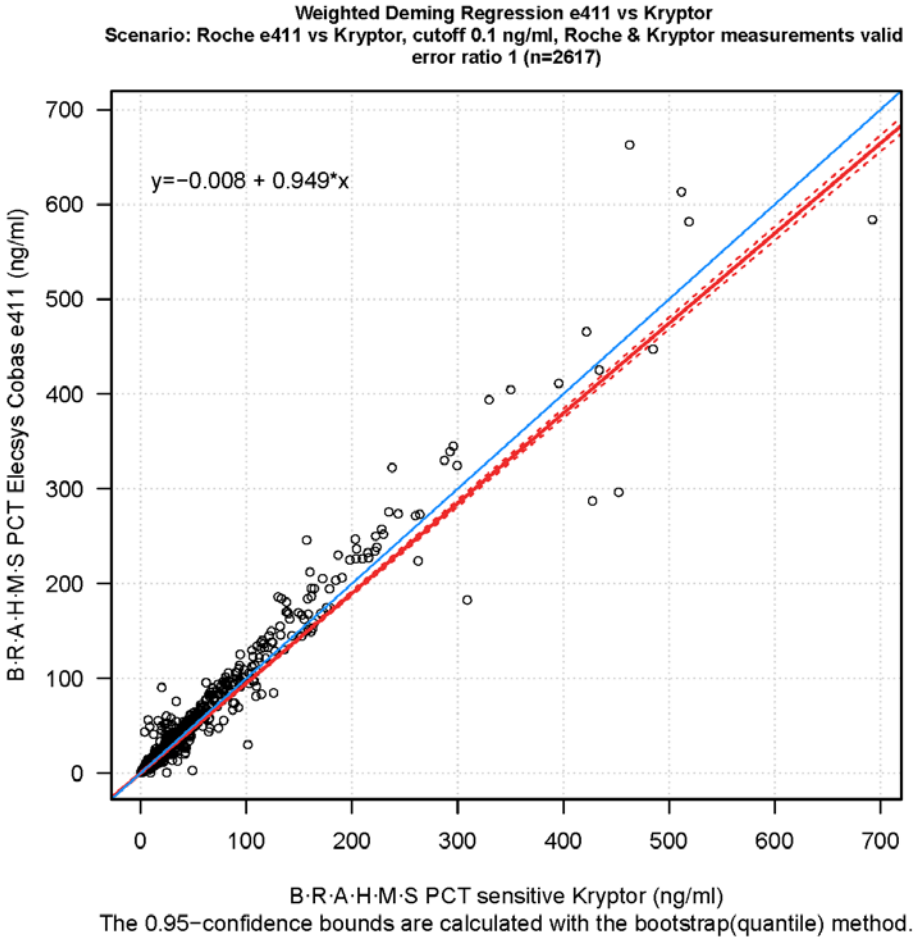
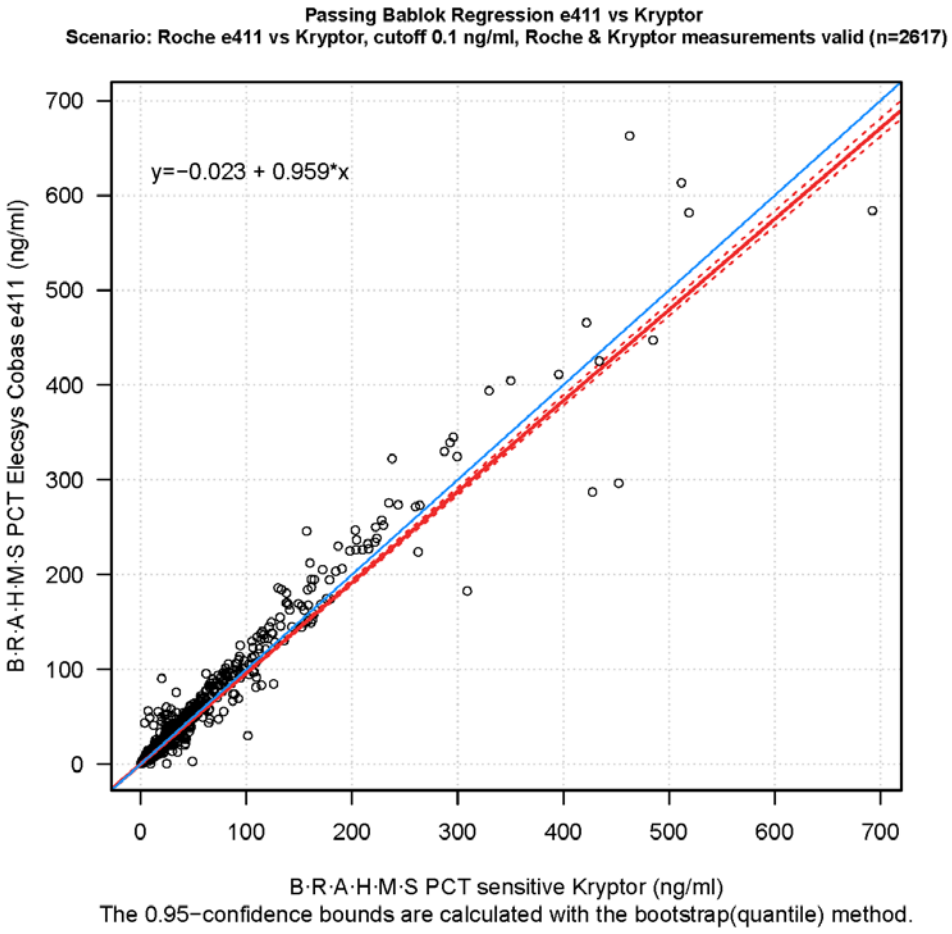


Figure 2: Passing Bablok Regression plots of Elecsys BRAHMS PCT versus Predicate



5. ADDITIONAL INFORMATION

The calibration materials PCT Cal1 and PCT Cal2 as well as the control material PreciControl PCT1 and PreciControl PCT2 are in the Elecsys BRAHMS PCT kit and are not changed as a result of the new claims. The Elecsys BRAHMS PCT CalCheck 5 is also not changed as a result of the change. See K160729 for additional information.

6. CONCLUSIONS

The information provided in this 510(k) Premarket Notification will support a determination of substantial equivalence for the Elecsys BRAHMS PCT test system. The data supports a safe, effective device which performs as well as or better than the predicate device.