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March 9, 2020

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

Re: K192815
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: PRI, PMT, NTM
Dated: September 27, 2019
Received: October 1, 2019

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kristian Roth, Ph.D.
Chief
Bacterial Multiplex and Medical Counter Measures Branch
Division of Microbiology
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
K192815

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 Tammy Dean Phone: 317-521-3978 FAX: (317) 521-2324 Email: tammy.dean@roche.com
Date Prepared	September 30, 2019
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	Elecsys BRAHMS PCT cleared under K173927.
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, biotinylated antibody and antibody labeled with ruthenium as well as an electrochemiluminescence detection system. Procalcitonin (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~$Ru(bpy)_3^{2+}$

The following change is proposed to block the interference of biotin with the Elecsys BRAHMS PCT assay. Briefly, Roche is taking a one-step approach by adding an antibody to bind free biotin in the sample. For the neutralization of free biotin in serum and plasma, Roche developed an antibody which binds to free biotin. The antibodies are specific for free biotin and do not bind to, or interact with, the biotin-linker conjugates.

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 **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.

3. TECHNOLOGICAL CHARACTERISTICS

Table 1: Assay Comparison

Feature	Predicate Device: Elecsys BRAHMS PCT (K173927)	Candidate Device: Elecsys BRAHMS PCT with biotin update
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.	Same with the exception of intended analyzers, Elecsys BRAHMS PCT with biotin update is only intended for use on **cobas e** innunoassay analyzers.

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.	Same
Detection Protocol	Electrochemiluminescent immunoassay	Same
Applications	18-minute application	Same
Instrument Platform	**cobas e** 411 analyzer	**cobas e** 601 analyzer
Sample Volume	30 µL	Same
Sample Type	Human serum and plasma (Li-Heparin, K2/K3 EDTA)	Same
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)$_3^{2+}$ a monoclonal anti-PCT antibody (mouse) labeled with ruthenium complex, phosphate buffer, preservative	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)$_3^{2+}$ a monoclonal anti-PCT antibody (mouse) labeled with ruthenium complex, Biotin Scavenger Antii-body, phosphate buffer, preservative Roche is taking a one-step approach by adding an antibody to bind free biotin in the sample. For the neutralization of free biotin in serum and plasma, Roche developed an antibody which binds to free biotin. The antibodies are specific for free biotin and do not bind to, or interact with, the biotin-linker conjugates.
Calibrator	PCT Cal1 and PCT Cal2	Same
Calibration Interval	Calibration must be performed once per reagent lot using PCT Cal1, PCT Cal2 and 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	Same
Controls	PC PCT1 and PC PCT2	Same
Traceability/ Standardization	This method has been standardized against the BRAHMS PCT LIA assay.	Same

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	Same
Measuring Range	0.02 – 100 ng/mL	Same
LoB	0.015 ng/mL	Same
LoD	0.02 ng/mL	Same
LoQ	0.06 ng/mL	Same
Hook Effect	No hook effect up to 1000 ng/mL	Same
Biotin Limitations	Biotin interference can produce either falsely high or low results. Though the risk of misclassifying a test result due to biotin interference is lower than the risks from average assay imprecision, biological variability, or other known interference, patient biotin intake and the resulting % bias should be taken into account when interpreting PCT assay values. (See Interference study below). Do not test samples from patients who have indicated or whose clinical status or history would indicate they are currently taking high doses of biotin (> 10 mg per day). If biotin interference is suspected, follow your established internal procedures to investigate the interference per CLIA and GLP recommendations. Serial draws are indicated for procalcitonin measurements. Biotin will metabolize and clear, serum levels will reduce over time.	Specimens with biotin concentrations up to 1200 ng/mL did not demonstrate bias in measured PCT values. Specimens with biotin concentrations > 1200 ng/mL and ≤ 2600 ng/mL demonstrated ≤ 10 % negative bias in measured PCT levels. Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.
Method Comparison	474 samples were run on the **cobas e** 601 and the predicate device (Elecsys BRAHMS PCT K173927) **Passing Bablok** Slope: 0.990 (95% CI: 0.984; 0.994) Intercept: -0.003 ng/mL (95% CI: -0.004; -0.001) Pearson's r Coefficient: 1.000	

4. PERFORMANCE EVALUATION

The following data was requested by the FDA in Q171237/S0001 to support the updated Indications for Use statement and is listed below:

- Precision according to CLSI EP5-A3
- Serum/Plasma Comparison
- Interferences – Endogenous
- Interferences – Exogenous (Drugs)
- Analytical Specificity/Cross-reactivity
- Calibration Lot and On-board Stability
- Analytical Sensitivity: LoQ according to CLSI EP17-A2
- Clinical Performance Evaluation - Method Comparison to Predicate

The remaining data required to support the updated Indications for Use was supplied in the previous submissions K160729 and K173927:

- Analytical Sensitivity: LoB and LoD
- Linearity according to CLSI EP6-A
- High Dose Hook Effect
- Human Anti-Mouse Antibodies (HAMA)
- Sample Stability

4.1. Precision

The repeatability and intermediate precision of the Elecsys BRAHMS PCT assay was conducted using the **cobas e** 601 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 seven (7) 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** 601 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. The total error was calculated using the one sided Westgard-Model as:

TE = 1.65* CV + %bias

The %CV used corresponds to the intermediate precision.

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

Sample	Mean (ng/mL)	Repeatability (CV%)		Intermediate Precision (CV%)		% Total Error
		Within Run		Within Lab		
		SD (ng/mL)	CV%	SD (ng/mL)	CV%	
Control1	0.478	0.012	2.5	0.020	4.3	10.6
Control2	10.0	0.119	1.2	0.306	3.1	7.44
Sample1	0.045	0.006	13.2	0.007	16.1	39.9
Sample2	0.112	0.007	6.3	0.010	8.6	21.3
Sample3	0.249	0.008	3.0	0.011	4.3	10.4
Sample4	0.495	0.013	2.7	0.021	4.2	10.3
Sample5	1.71	0.031	1.8	0.058	3.4	8.09
Sample6	31.4	0.326	1.0	0.985	3.1	7.38
Sample7	93.0	1.52	1.6	3.40	3.7	8.71

4.2. Sample Matrix Comparison

The effect on quantitation of analyte in the presence of anticoagulants with the Elecsys BRAHMS PCT immunoassay was determined by comparing values obtained from samples (native human serum samples, single donors as well as pools) drawn into serum and Li-Heparin, K2-EDTA, K3-EDTA plasma tubes. A minimum of 40 serum/plasma pairs per sample material were tested in singleton with one reagent lot on one **cobas e** 601 analyzer. Data were evaluated using a regression analysis according to Passing/Bablok.

4.3. 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** 601 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 for PCT concentrations > 0.1 ng/mL and within 0.015 ng/mL for concentrations below 0.1 ng/mL

Table 3: Potentially Interfering Endogenous Substances and Test Concentrations

Potential Interferent	Claim
Intralipid	1500 mg/dL
Biotin	1200 ng/mL
Bilirubin	25 mg/dL
Hemoglobin	900 mg/dL
Rheumatic Factor	1500 IU/mL

4.4. Exogenous Interferences – Drugs

The effect on quantitation of analyte in the presence of drugs was determined by comparing values obtained from samples spiked with 34 pharmaceutical compounds into two human serum

samples and tested on the **cobas e** 601 analyzer. The substances were found not to affect test performance at the tested concentration. Recovery was within ± 10 % of the reference value.

Table 4: Potentially Interfering Drugs and Test Concentrations

Potential Interferent	Drug Level Tested (mg/L)
Acetylcysteine	150
Ampicillin	75
Ascorbic acid	52.5
Cyclosporine	1.8
Cefoxitin	750
Heparin	3300 U/L
Levodopa	7.5
Methyldopa	22.5
Metronidazole	123
Phenylbutazone	321
Doxycycline	18
Acetylsalicylic acid	30
Rifampicin	48
Acetaminophen	156
Ibuprofen	219
Theophylline	60
Imipenem	1180
Cefotaxime	900
Vancomycin	3500
Dopamine	130
Noradrenaline	2
Dobutamine	11.2
Furosemide	20
Cromolyn	24
Alcohol	4000
Azithromycin	11.5
Cetirizine HCl	3.6
Dextromethorphan	1.4
Levofloxacin	17.5
Loratadine	0.3
Nicotine	1
Oxymetazoline HCl	0.09
Phenylephrine	0.18
Tiotropium	0.0216

4.5. Analytical Specificity/Cross-reactivity

The specificity of the Elecsys® BRAHMS PCT was determined using native human serum samples spiked with potential cross-reactant compounds.

The samples were tested on a **cobas e** 601 Immunoassay Analyzer. Recovery within ± 15 % of initial value at PCT concentrations of ~0.5 ng/mL and ~2 ng/mL were verified for the following cross-reactant concentrations:

- 30 ng/mL human katacalcin
- 10 ng/mL human calcitonin
- 10000 ng/mL human alpha-CGRP
- 10000 ng/mL human beta-CGRP
- 30000 ng/mL Calcitonin Salmon
- 30000 ng/mL Calcitonin Eel

4.6. Reagent On-Board Stability

A fresh Elecsys BRAHMS PCT test kit was placed on the **cobas e** 601 analyzer and calibrated. Reference values for the samples tested were determined (day 0). After 8, 15, 22 and 29 days (1, 2, 3 and 4 weeks) the same samples were measured with the same reagent kit kept under on-board condition. Re-calibration was performed at every measuring time point.

Samples tested include eight (8) human serum (HS) sample pools. Each sample was tested in two-fold determination. Samples were targeted with values near medical decision levels of 0.1 ng/mL, 0.25 ng/mL, 0.5 ng/mL and 2.0 ng/mL as one sample range, along with sample ranges at low, medium and high PCT concentration ranges relative to the measuring range. Mean recovery values for each sample range were calculated. Elecsys BRAHMS PCT reagent kits can be kept on board of the instruments for up to 4 weeks (28 days). A new calibration of the kit kept

on board is recommended every 7 days.

4.7. Calibration Stability

The Elecsys BRAHMS PCT assay was calibrated with a fresh reagent kit on Day 0 using one **cobas e** 601 analyzer. After 3, 6, and 9 weeks a new reagent kit of the same lot was used with recovery of samples being determined using the calibration curve established on Day 0 for that reagent kit lot. Forteen (14) human serum samples were tested in duplicate. Recovery compared to the reference value was calculated as absolute deviation in ng/mL or relative deviation in %. Samples were targeted with values near medical decision levels of 0.1 ng/mL, 0.25 ng/mL, 0.5 ng/mL and 2.0 ng/mL along with samples spread across the measuring range. Mean recovery values for each sample range were calculated. The resulting data support the package-insert claim of 8 weeks lot calibration stability when using the same reagent kit lot.

4.8. LoQ according to CLSI EP17-A2

The Limit of Quantitation (LoQ) of the Elecsys BRAHMS PCT assay was determined according to CLSI EP17-A2. The LoQ represents the lowest amount of analyte that can be quantitatively determined with stated accuracy, precision, and experimental conditions. The LoQ was calculated based on intermediate precision according to CLSI EP17-A2. The LoQ was determined as the lowest concentration of analyte that can be quantified with an intermediate precision of no more than 20%.

A five-day LoQ experiment was carried out with one reagent lot on one **cobas e** 601 analyzer. Samples tested included seven native human serum (HS) samples and were measured in five-fold determination for each run. A total of 150 measuring points were collected.

The mean values and the intermediate precision (coefficient of variation and standard deviation) for each LoQ sample were calculated. To determine the LoQ, samples were sorted according to the concentration of their measured mean value. The LoQ is defined as the mean value of the

sample that is first to fulfill the specification for intermediate precision, and for which there is no lower-concentration sample that exceeds the specification. The LoQ data are represented in the table below.

Table 5. LoQ Data – cobas e 601 analyzer

Sample Type	Day					Mean (ng/mL)	SD (ng/mL)	CV (%)
	1	2	3	4	5			
HS 1	0.032 0.030 0.022 0.033 0.029	0.029 0.021 0.023 0.020 0.024	0.026 0.031 0.022 0.032 0.025	0.021 0.028 0.021 0.023 0.022	0.021 0.028 0.020 0.024 0.018	0.025	0.004	18.0
HS 2	0.042 0.046 0.050 0.038 0.048	0.041 0.044 0.039 0.047 0.045	0.043 0.037 0.043 0.037 0.044	0.041 0.041 0.043 0.040 0.043	0.045 0.041 0.044 0.045 0.045	0.043	0.003	7.7
HS 3	0.056 0.050 0.051 0.047 0.053	0.057 0.046 0.048 0.043 0.054	0.052 0.048 0.048 0.045 0.050	0.052 0.040 0.044 0.045 0.046	0.057 0.046 0.052 0.049 0.050	0.049	0.004	9.0
HS 4	0.066 0.068 0.067 0.069 0.068	0.063 0.058 0.068 0.065 0.064	0.067 0.070 0.064 0.071 0.065	0.059 0.064 0.073 0.073 0.062	0.062 0.064 0.062 0.067 0.061	0.066	0.004	5.8
HS 5	0.069 0.068 0.072 0.072 0.072	0.062 0.067 0.063 0.065 0.065	0.068 0.058 0.073 0.063 0.069	0.067 0.058 0.066 0.064 0.064	0.068 0.056 0.068 0.062 0.067	0.066	0.004	6.8
HS 6	0.088 0.091 0.092 0.095 0.090	0.090 0.092 0.091 0.085 0.095	0.088 0.089 0.090 0.094 0.086	0.083 0.093 0.084 0.091 0.083	0.089 0.089 0.084 0.097 0.085	0.089	0.004	4.4
								LoQ: 0.025 ng/mL

HS: human serum

The LoQ was determined to be 0.025 ng/mL. The LoQ claim for the Elecsys BRAHMS PCT assay is 0.06 ng/mL.

Based on LoQ testing the following total error values were calculated.

Table 6: Total Error

Expected value (ng/ml)	Elecsys BRAHMS PCT		
	%CV	%Bias	%TE
2.00	0.19	0.12	0.43
0.50	0.77	0.54	1.81
0.30	1.30	0.94	3.08
0.25	1.56	1.15	3.72
0.15	2.64	2.00	6.34
0.10	3.99	3.10	9.69
0.05	8.12	6.56	19.97

4.9. Clinical Performance Evaluation - Method Comparison to Predicate

A method comparison of the Elecsys BRAHMS PCT assay and the predicate was performed using 496 native serum human clinical samples. A concordance analysis was performed with the predicate device. Only samples in which the result from the candidate and the predicate device were within the measuring range were included in the concordance analysis. The clinical concordance analysis of the Elecsys BRAHMS PCT clinical performance study shows more than 96% total agreement between the Elecsys BRAHMS PCT and the 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.

Further clinical performance study data can be found referenced in K173927 and K160729.

Table 7: PCT Agreement between Elecsys BRAHMS PCT and Predicate at 0.1 ng/mL

Elecsys BRAHMS PCT on cobas e 601	Predicate		Total
	> 0.1 ng/mL	≤ 0.1 ng/mL	
> 0.1 ng/mL	354	1	355
≤ 0.1 ng/mL	7	134	141

Total	361	135	496

Table 8: PCT Agreement between Elecsys BRAHMS PCT and Predicate at 0.25 ng/mL

Elecsys BRAHMS PCT on cobas e 601	Predicate		Total
	> 0.25 ng/mL	≤ 0.25 ng/mL	
> 0.25 ng/mL	278	1	279
≤ 0.25 ng/mL	6	211	217
Total	284	212	496

Table 9: PCT Agreement between Elecsys BRAHMS PCT and Predicate at 0.5 ng/mL

Elecsys BRAHMS PCT on cobas e 601	Predicate		Total
	> 0.5 ng/mL	≤ 0.5 ng/mL	
> 0.5 ng/mL	220	0	220
≤ 0.5 ng/mL	4	272	276
Total	224	272	496

Table 10: PCT Agreement between Elecsys BRAHMS PCT and Predicate at 2.0 ng/mL

Elecsys BRAHMS PCT on cobas e 601	Predicate		Total
	> 2.0 ng/mL	≤ 2.0 ng/mL	
> 2.0 ng/mL	141	2	143
≤ 2.0 ng/mL	3	350	353
Total	144	352	496

Table 11: Comparison Elecsys BRAHMS PCT vs Predicate

N = 496 (135 ≤ 0.1 ng/mL, 212 ≤ 0.25 ng/mL; 272 ≤ 0.5 ng/mL; 352 ≤ 2.0 ng/mL)

Cutoff (> vs. ≤)	Positive Agreement (95% CI)	Negative Agreement (95% CI)	Total Agreement	Cohen's Kappa
0.10 ng/mL	98.1%	99.3%	98.4%	0.960
	(96.1 – 99.1)	(95.9 – 99.9)		
0.25 ng/mL	97.9%	99.5%	98.6%	0.971
	(95.5 – 99.0)	(97.4 – 99.9)		
0.50 ng/mL	98.2%	100.0%	99.2%	0.984
	(95.5 – 99.3)	(98.6 -100.0)		
2.00 ng/mL	97.9%	99.4%	99.0%	0.975
	(94.1 - 99.3)	(98.0 – 99.8)		

Table 12: Weighted Deming and Passing Bablok Regression Analysis

Parameter	Passing Bablok Regression	Weighted Deming (λ=1) Regression Analysis
n	**474**	**474**
Slope	**0.990**	**0.969**
95% CI	**[0.984; 0.994]**	**[0.963; 0.975]**
Intercept	**-0.003**	**0.004**
95% CI	**[-0.004; -0.001]**	**[0.002; 0.005]**
Pearson Correlation Coefficient (R)	**1.000**	**1.000**
Sample Range	**[0.02; 85.69]**	**[0.02; 85.69]**

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

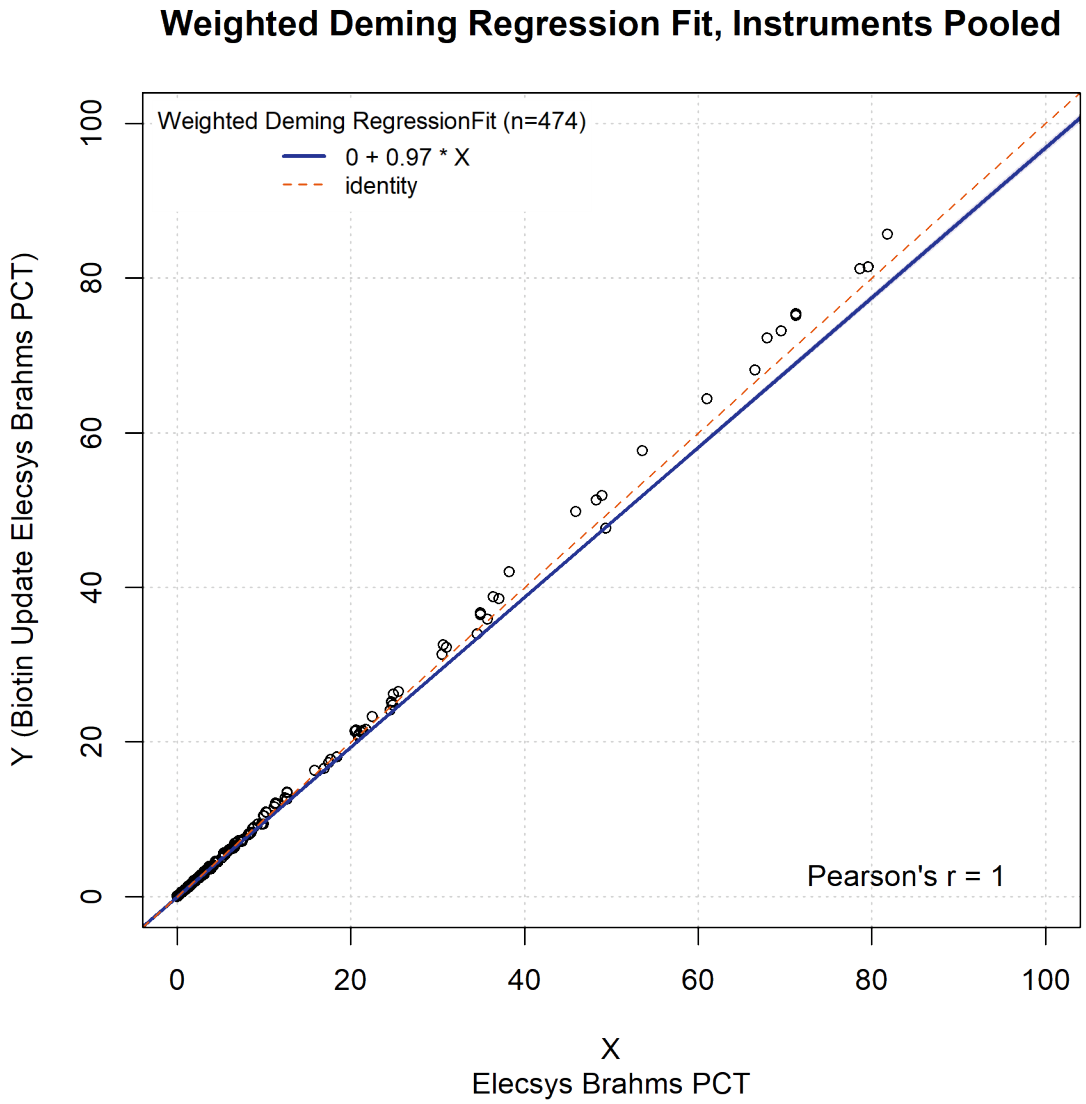
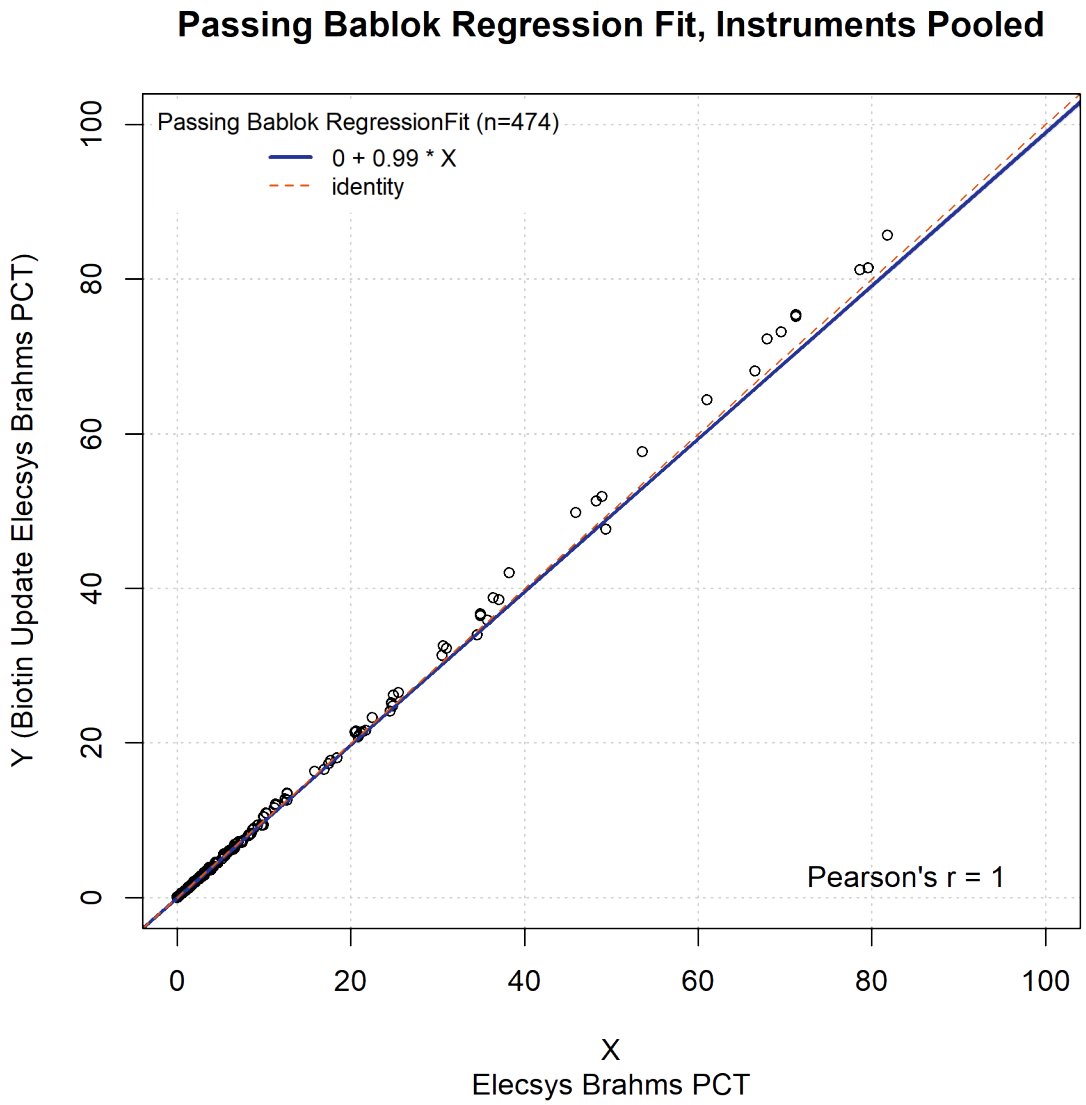


Figure 2: Passing Bablok Regression plots of Elecsys BRAHMS PCT versus Predicate



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.