510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K192271

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

Access PCT, Access PCT Calibrators

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PTF	Class II	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	83

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Human Procalcitonin (PCT)

C Type of Test:

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of procalcitonin (PCT) levels in human serum and plasma using the Access Immunoassay Systems.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for in vitro quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.

The Access PCT Calibrators are intended to calibrate the Access PCT assay for the quantitative determination of procalcitonin levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For In Vitro Diagnostic Use Only
The Access PCT was validated on the Access 2 System

Warnings and Precautions:
The Access PCT assay 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.

The Access PCT assay is not indicated to be used as an aid in decision making on antibiotic therapy for patients.

Certain patient characteristics, such as severity of renal failure or insufficiency, may influence procalcitonin values and should be considered as potentially confounding clinical factors when interpreting PCT values.

Increased PCT levels may be observed in severe illness such as polytrauma, burns, major surgery, prolonged or cardiogenic shock.

D Special Instrument Requirements:

The Access PCT assay and Access PCT Calibrator set were validated on the Access 2 analyzer only.

IV Device/System Characteristics:

A Device Description:

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of procalcitonin (PCT) levels in human serum and plasma using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progressive to severe sepsis and septic shock.

The Access PCT assay consists of the reagent pack and calibrators.

Materials required but not provided:

- Access PCT Calibrators
  Provided at zero and approximately 0.8, 5, 10, 25, 50 and 100 ng/mL (µg/L).
  Cat. No. C22594
- Quality Control (QC) materials: commercial control material.
- Access Substrate
  Cat. No. 81906
- Access Wash Buffer II
  Cat. No. A16792

Control materials: Controls are not provided

NOTE: Access PCT Package insert indicates 'Include commercially available quality control materials that cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.'

B Principle of Operation:

The Access 2 Immunoassay Systems are microcomputer controlled, random and continuous access instruments used to perform enzyme immunoassays (EIA). The enzyme immunoassays utilize a paramagnetic particle solid phase with chemiluminescent detection to measure analyte concentration. A luminometer measures the amount of light generated by the reaction solution.

V Substantial Equivalence Information:

A Predicate Device Name(s):
VIDAS B·R·A·H·M·S PCT

B Predicate 510(k) Number(s):
K162827

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K192271	Predicate Device K162827
Device Trade Name	Access PCT Assay on Access 2 Immunoassay System	VIDAS B·R·A·H·M·S PCT
General Device Characteristic Similarities	Access PCT Assay on Access 2 Immunoassay System	VIDAS B·R·A·H·M·S PCT
Intended Use/Indications For Use	The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.	VIDAS B·R·A·H·M·S PCT (PCT) is an automated test for use on the instruments of the VIDAS family for the determination of human procalcitonin in human serum or plasma (lithium heparinate) using the ELFA (Enzyme-Linked Fluorescent Assay) technique. Used in conjunction with other laboratory findings and clinical assessments, VIDAS 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 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, using a change in PCT level over time, · to aid in decision making on antibiotic therapy for patients 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) – in an inpatient setting or an emergency department, · to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.
Analyte Measured	Procalcitonin (PCT)	Procalcitonin (PCT)
Sample Type	Human Serum or Plasma (LiHep and EDTA)	Human Serum or Plasma (LiHep)
Method	Automated Assay	Automated Assay
Technology	Immunoassay based on sandwich principle	Immunoassay based on sandwich principle
Assay Duration	Approximately 20 minutes	Approximately 20 minutes
Measuring Range	0.05 - 100 ng/mL	0.05 - 100 ng/mL

General Device Characteristic Differences	Access PCT Assay on Access 2 Immunoassay System	VIDAS B·R·A·H·M·S PCT
Assay Format	Chemiluminescent	ELFA (Enzyme-Linked Fluorescent Assay) technique
Primary Reagent Materials	Dynabeads paramagnetic particles coated with mouse anti-human procalcitonin monoclonal antibody	Solid Phase: Mouse monoclonal anti-procalcitonin immunoglobins coated on interior of the SPR Conjugate: Alkaline phosphatase-labeled mouse monoclonal anti-human procalcitonin

General Device Characteristic Differences	Access PCT Assay on Access 2 Immunoassay System	VIDAS B·R·A·H·M·S PCT
		immunoglobins
Sample Volume	35 µL	200 µL
LoB	0.005 ng/mL	0.01 ng/mL
LoD	0.01 ng/mL	0.03 ng/mL
LoQ	0.02 ng/mL	0.05 ng/mL
Hook Effect	No hook effect up to procalcitonin concentrations of 5,000 ng/mL	No hook effect up to procalcitonin concentrations of 2,600 ng/mL
Expected Results (Upper Reference Limit)	95th percentile of 0.065 ng/mL with a 95% Confidence Interval (CI) of 0.054 – 0.085 ng/mL	99th percentile 0.09 ng/ml 95th percentile < 0.05 ng/mL

VI Standards/Guidance Documents Referenced:

CLSI EP28-A3c *Defining, Establishing, and Verifying Reference Interval in the Clinical Laboratory*, Third Edition

CLSI EP05-A3 *Evaluation of Precision of Quantitative Measurement Procedures*, Third Edition

CLSI EP06-A *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*, First Editions

CLSI EP07:2018 *Interference Testing in Clinical Chemistry*, Third Edition

CLSI EP17-A2 *Evaluation of Detection for Clinical Laboratory Measurement Procedures*, Second Edition

CLSI EP25-A *Evaluation of Stability on In Vitro Diagnostic Reagents*, First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A single site validation study was performed to determine the imprecision of the Access PCT assay using a protocol based on CLSI EP05- A3 (Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition).

The 10 member panel sample set, including 7 contrived serum levels and Bio-Rad Specialty

Lyphochek control levels 1, 2, and 3 were tested on three (3) reagent lots and three (3) calibrator lots. The samples were run at one external site on one Access 2 Immunoassay System and were run in replicates of 2 for a total of 20 days, with two (2) runs per day (separated by a minimum of two hours), for a total of 40 valid runs. Eighty (80) replicates were used for imprecision analysis according to CLSI EP05-A3. Two (2) calibration curves on three (3) calibrator lots and three (3) reagent pack lots were utilized during the 20 day precision study.

Total imprecision, within run imprecision (repeatability), between run, and between day variation was evaluated in terms of percent coefficient of variation, %CV. The acceptance criteria for total imprecision is a standard deviation (SD) ≤ 0.012 for values < 0.150 ng/mL and a CV ≤ 8.0% for values ≥ 0.150 ng/mL. Acceptance criteria for within run imprecision is SD ≤ 0.009 ng/mL for values < 0.150 ng/mL & CV ≤ 6% for values ≥ 0.150 ng/mL. Results of the study are in the Table below.

Access PCT Total Imprecision, Access 2

Sample ID	N	Mean (ng/mL)	Total SD	Between Day CV (SD)	Between Run CV (SD)	Repeatability CV (SD)	Total Imprecision
PANEL1	80	0.274	0.012	3.2% (0.009)	1.0% (0.003)	2.8% (0.008)	4.4%
PANEL2	80	0.428	0.024	3.8% (0.016)	3.3% (0.014)	2.6% (0.011)	5.7%
PANEL3	80	1.408	0.070	3.4% (0.048)	2.4% (0.034)	2.8% (0.039)	5.0%
PANEL4	80	7.586	0.320	3.2% (0.239)	1.6% (0.121)	2.3% (0.175)	4.2%
PANEL5	80	76.312	2.885	1.9% (1.452)	2.3% (1.773)	2.3% (1.753)	3.8%
PANEL6	80	0.090	0.006	5.8% (0.005)	2.7% (0.002)	3.2% (0.003)	7.2%
PANEL7	80	0.177	0.010	4.3% (0.008)	1.7% (0.003)	3.2% (0.006)	5.6%
QC1	80	0.676	0.024	2.2% (0.015)	2.1% (0.014)	1.9% (0.013)	3.6%
QC2	80	2.152	0.069	0 (0)*	2.6% (0.056)	1.9% (0.040)	3.2%
QC3	80	20.652	0.667	1.1% (0.228)	2.6% (0.531)	1.6% (0.333)	3.2%

*Values with 0 (0) indicate an Integer 0 was reported where the statistical model failed to result a valid variance estimate and assigned a nominal 0. We preserve its original form to differentiate nominal from numerical results.

The study demonstrated that Access PCT assay meet design input requirements for total imprecision on the Access 2 with an SD ≤ 0.012 ng/mL for values < 0.150 ng/mL and a CV ≤ 8.0% for values ≥ 0.150 ng/mL. The Access PCT assay also met the within run imprecision (repeatability) design input requirements with an SD ≤ 0.009 ng/mL for values < 0.150 ng/mL and CV ≤ 6.0% for values ≥ 0.150 ng/mL.

The acceptance criteria established and demonstrated by the sponsor provides evidence that Access PCT is substantially equivalent to the predicate device.

2. Linearity:

Two studies were performed to demonstrate the linearity of the Access PCT assay based on CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. The linearity study data was used to evaluate the percent recovery for spiked samples by evaluating known concentrations of procalcitonin in serum samples.

In both studies three Access 2 Immunoassay Systems were used, three reagent pack lots and one calibrator lot. Three quality controls were run in replicates of two on each day of testing to verify the system was in control.

In the study analyzing the full range of the assay, one high sample and one low sample were mixed to make nine sample concentrations evenly distributed across the analytical measuring range. Four replicates of the seven mixed samples, eight replicates of the low sample and four replicates of the high sample were tested. In addition to the high and low PCT concentration samples, seven mixtures were tested in this study. The low sample was run in replicates of eight, and all other samples were run in replicates of four.

In the study analyzing the low end of the assay range, one high sample and one low sample were mixed to make ten sample concentrations evenly distributed between 0.007 ng/mL and approximately 3 ng/mL. The low sample was run in replicates of eight, and all other samples were run in replicates of four.

The Access PCT assay demonstrated acceptable linearity throughout the analytical measuring range of 0.05 ng/mL to approximately 100 ng/mL. The Access PCT assay was designed to be linear, with a maximum deviation from linearity of ≤ 10% for values > 0.150 ng/mL and ≤ 0.012 ng/mL for values ≤ 0.150 ng/mL.

The data from the full assay range study was analyzed based on CLSI EP06-A using a weighted linear regression. The PCT linearity study was designed using 9 dilutions and was evaluated against the linearity specification of ± 10%. Analysis using all 9 dilutions resulted in some of the highest concentrations having non-linearity > 10%. Per CLSI EP06-A: 2003 section 5.3.3, the high concentration point was removed, and linearity was re-assessed. The remaining samples used to evaluate linearity still cover the full measuring interval of the assay. All linearity results using the reduced 8 dilution point range met the linearity specification.

The obtained results are summarized in the table below:

Linearity Analysis – Full Range of Assay

Dilution (%)	Expected Concentration (ng/mL)	Predicted Observed Linear Concentration (ng/mL)	Predicted Observed Non-Linear (Cubic) Concentration (ng/mL)	Predicted Difference (ng/mL)	Predicted Deviation from Linearity (%)	Criteria
0	0.006	0.006	0.006	0.000	N/A	≤ ± 0.012 ng/mL
14.3	14.976	15.954	15.602	-0.352	-2	≤ ± 10%
28.6	29.945	31.901	32.405	0.504	2	≤ ± 10%
42.9	44.915	47.849	49.540	1.691	4	≤ ± 10%
57.1	59.884	63.796	66.132	2.335	4	≤ ± 10%
71.4	74.854	79.744	81.304	1.560	2	≤ ± 10%
85.7	89.823	95.691	94.180	-1.511	-2	≤ ± 10%
100	104.793	111.639	103.886	-7.754	-7	≤ ± 10%

Linearity Analysis – Low Range of Assay

Dilution (%)	Expected Concentration (ng/mL)	Predicted Observed Linear Concentration (ng/mL)	Predicted Observed Non-Linear (Cubic) Concentration (ng/mL)	Predicted Difference (ng/mL)	Predicted Deviation from Linearity (%)	Criteria
0	0.007	0.007	0.007	0.000	0	≤ ± 0.012 ng/mL
6.25	0.184	0.184	0.180	-0.004	-2	≤ ± 10%
12.5	0.361	0.360	0.353	-0.007	-2	≤ ± 10%
25	0.714	0.712	0.703	-0.009	-1	≤ ± 10%
37.5	1.068	1.064	1.056	-0.008	-1	≤ ± 10%
50	1.421	1.417	1.413	-0.004	0	≤ ± 10%
62.5	1.775	1.769	1.774	0.005	0	≤ ± 10%
75	2.128	2.121	2.138	0.017	1	≤ ± 10%
87.5	2.482	2.474	2.507	0.033	1	≤ ± 10%
100	2.835	2.826	2.879	0.053	2	≤ ± 10%

In addition, the linearity data was analyzed to evaluate percent recovery for each intermediate mixture sample used for the linearity evaluation. The expected value for each sample was computed based on the observed concentration of the low sample, high spiked sample, and the proportion of each of the high and low samples in the mixture. Percent recovery was then calculated as the observed value for each sample as a proportion of the expected value. The observed range of percent recovery values was 94% - 112%

Total Error, % Bias and %TE were determined for the low range and full range of the assay. Calculations were based on expected values in the linearity study.

Total Error, % Bias and %TE for full range of Access PCT assay on Access 2

Level	Average	True Value	CV	%Bias	%TE
1	0.006172	0.006	18.21%	2.87%	39.58%
2	15.30795	14.976	4.24%	2.22%	10.71%
3	33.2836	29.945	3.42%	11.15%	18.60%
4	49.97116	44.915	2.05%	11.26%	15.72%
5	67.47711	59.884	2.50%	4.03%	9.54%
6	83.27752	74.854	3.51%	11.25%	18.90%
7	95.10243	89.823	3.33%	5.88%	12.79%
8	107.2041	104.793	3.48%	2.30%	9.27%

Total Error, % Bias and %TE for low range of Access PCT assay on Access 2

Level	Average	True Value	%CV	%Bias	%TE
1	0.00678169	0.007	2928.30%	-3.12%	5563.59%
2	0.164568	0.184	3.49%	-10.56%	16.69%
3	0.3248502	0.361	3.74%	-10.01%	16.62%
4	0.63953029	0.714	3.21%	-10.43%	16.07%
5	0.963938	1.068	3.31%	-9.74%	15.61%

Level	Average	True Value	%CV	%Bias	%TE
6	1.292071	1.421	2.85%	-9.07%	14.16%
7	1.596889	1.775	4.60%	-10.03%	18.15%
8	1.926938	2.2128	5.12%	-12.92%	21.66%
9	2.26644	2.482	4.60%	-8.68%	16.93%
10	2.77105	2.835	3.56%	-2.26%	9.08%

3. Analytical Specificity/Interference:

Potential cross-reactive substances were added to serum patient samples at three concentrations of procalcitonin (approximately 0.25 ng/mL, 0.5 ng/mL, and 2.0 ng/mL). Stock solutions of potential cross- reactants were prepared volumetrically using calibrated pipettes and the appropriate solvent. This stock solution was added directly to the serum in no more than 5% (v/v) final concentration. Control samples were prepared in the same manner using the solvent, without the cross-reactant added. Control and test samples were tested on the Access 2 instrument within 24 hours of preparation, using three reagent lots. Testing of human calcitonin, human katacalcin, human alpha CGRP and human beta CGRP, with Access PCT found that there is no significant cross-reactivity, as defined by a change in concentration between the diluent control and the test samples that is less than the expected within assay variability between samples.

Potential interfering substances were spiked into patient samples. Results from these spiked patient samples were evaluated against that of the unspiked sample. In accordance with CLSI EP07, third edition, interference testing was completed on patient serum samples containing four levels of procalcitonin at three clinically relevant concentrations of 0.25 ng/mL, 0.5 ng/mL and 2.0 ng/mL and an additional procalcitonin concentration of approximately 80 ng/mL. Potential interferents were tested at one concentration above therapeutic concentration range as directed by CLSI EP07, third edition. See Table 2 below for the list and concentrations of each interferent.

Interfering Substances Tested

Substance	Interferent Concentration Tested
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	100 mg/dL
Azithromycin	1.20 mg/dL
Bilirubin (Conjugated)	40 mg/dL
Bilirubin (Unconjugated)	40 mg/dL
Caffeine	6.0 mg/dL
Cefotaxime/Cefotaxin	90 mg/dL
Celecoxib	24 mg/dL
Cetirizine HCL	0.36 mg/dL
Dextromethorphan	0.14 mg/dL
Dobutamine	1.12 mg/dL
Dopamine	13 mg/dL
Doxycycline	5.0 mg/dL

Epinephrine (adrenaline)	0.18 mg/dL
Ethanol	400 mg/dL
Fentanyl	1.0 mg/dL
Furosemide	5.98 mg/dL
Hemoglobin	400 mg/dL
Heparin	8000 IU/L
Human Serum Albumin	12 g/dL
Ibuprofen	50 mg/dL
Imipenem	18 mg/dL
Levoflaxacin	1.75 mg/dL
Loratadine	0.03 mg/dL
Naproxen	50 mg/dL
Nicotine	0.1 mg/dL

The acceptance criterion is defined as a change in concentration between the diluent control and the test sample within the variability expected between sample, which is ± 10%. No potential interference was found to exceed the acceptance criterion.

NOTE: Biotin interference was not evaluated since the Access PCT assay does not use biotin: streptavidin chemistry.

Human Anti-mouse Antibody (HAMA)/ Rheumatoid Factor (RF) -
Testing of characterized HAMA/RF samples was performed to evaluate blocker effectiveness in the Access PCT assay. Native samples tested were serum and EDTA patient samples. Testing performed used three lots of reagent and three Access 2 instruments. Testing was completed on a "Control" reagent pack with the conjugate diluent and the reagent buffer containing blockers and a "Test" conjugate diluent and reagent buffer that did not contain blockers. The same lot of stock conjugate was used in the control and test for each of the reagent packs. One lot of conjugate diluent without blockers and one lot of reagent without blockers was used. All other reagent components (paramagnetic particles and NaOH) were matched for the control and test packs. One hundred eighteen (118) HAMA/RF samples were characterized by vendors as a specific type of interferent sample. All samples were tested in replicates of five on each of the three reagent pack lots (control and test).

"True interference" was defined as the percent difference between the control and the test pack which is greater than two times the within laboratory (total) imprecision requirement of the assay. Two times the total imprecision of the assay equals ± 16% for samples ≥ 0.15 ng/mL and ± 0.024 ng/mL for samples below 0.15 ng/mL.

Effectiveness of blocking against heterophile antibodies

Reagent pack lot ID	Platform	Type of INTERFERENT	N	Results		Percentage of samples
Pack lot 1	Access 2 (511354)	HAMA/Rheumatoid factor	29	No Interference	13	45%
				Blocked	16	55%
Pack lot 2	Access 2 (511435)	HAMA/Rheumatoid factor	56	No Interference	30	54%
				Blocked	26	46%
Pack lot 3	Access 2 (509756)	HAMA/Rheumatoid factor	33	No Interference	20	61%
				Blocked	13	39%

The Access PCT reagent pack has been formulated to minimize the effects of HAMA/RF interference. Immunoenzymatic assay technology may demonstrate interferences from heterophile antibodies, including HAMA. While this assay has been formulated to minimize the effects of these antibodies, the following cautionary note has been included in the "Limitations of the Procedure" section of the product insert.

> "For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce human anti-animal antibodies, e.g., HAMA, that interfere with immunoassays. Additionally, other antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies."
>
> "Other potential interferences in the patient sample could be present and may cause erroneous results in immunoassays. Some examples that have been documented in literature include rheumatoid factor, endogenous alkaline phosphatase, fibrin, and proteins capable of binding to alkaline phosphatase. Carefully evaluate results if the sample is suspected of having these types of interferences."

4. Carryover

Verification studies were performed to determine potential assay carryover for the Access PCT assay on the Access 2 instrument. This testing used samples at 0.25 ng/mL and the medical decision points of 0.5 ng/mL and 2.0 ng/mL as the "low samples". Serum samples spiked with the highest calibrator served as the "high samples". Testing alternated five replicates of low samples, at each level, with two replicates of the high sample. Testing was performed over two days using one instrument and five reagent packs for each low sample level tested. Three commercial quality controls were run in duplicate on each day to verify the system was in control.

Results are in the table below.

Total Carryover Results for Access PCT

Sample Concentration (ng/mL)	High Calibrator		High Sample	
	Difference (ng/mL)	% Shift Spec ≤ 10%	Difference (ng/mL)	% Shift Spec ≤ 10%
~ 0.25	Pack 2		Pack 4	
	0.007	4%	0.014	8%
	Pack 3		Pack 5	
	0.011	6%	-0.008	-4%
~ 0.50	Pack 2		Pack 4	
	-0.012	-4%	-0.0002	-0.1%
	Pack 3		Pack 5	
	-0.020	-6%	-0.004	-1%
~ 2.0	Pack 2		Pack 4	
	-0.015	-1%	-0.109	-7%
	Pack 3		Pack 5	
	-0.024	-2%	-0.090	-6%

In all cases, the shift between initial testing of target concentrations and testing of target concentrations after high concentrations was < 10%, which is in within the inter sample variability of the assay and is therefore acceptable.

5. Assay Reportable Range:
The assay reportable range is the same as the predicate, 0.05 ng/mL – 100 ng/mL.

6. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Sample Stability
The in vitro stability of procalcitonin antigen in serum gel, serum no-gel, lithium heparin plasma and EDTA plasma patient samples using Access PCT assay was characterized at one internal site to determine sample handling and storage conditions. All four sample types, serum gel, serum no gel, LiHep plasma and EDTA plasma, were obtained from individual donors with normal procalcitonin levels. Samples were prepared by spiking all four sample types obtained with recombinant PCT antigen to procalcitonin concentrations throughout the Access PCT measuring range. Samples were obtained from both internal and external sites.

The study was run on at least one reagent pack lot and two calibrator lots on two Access 2 immunoassay systems. Three quality controls were run in replicates of two on each day of each run to verify that the instrument was in control.

Parameters evaluated in the study include:

- Short-term stability at room temperature 20°C to 25°C
- Short-term stability at cooler temperature 2°C to 10°C
- Short-term stability at freezer temperature -30°C to -15°C
- Sample Freeze/Thaw cycles stored at temperature -30°C to -15°C

Short-term stability at room temperature 20°C to 25°C was evaluated at 4 and 16 hours. One aliquot from each subject was tested immediately to determine baseline values (time 0). The remaining aliquots were stored at room temperature with one aliquot tested at each of the subsequent time points.

Results are in Tables below.

Access PCT Sample Stability Room Temperature and Cooler

	Room Temperature (20°C to 25°C)		Cooler (2°C to 10°C)	
	4 hours	**16 hours**	**24 hours**	**48 hours**
Sample Type	**Mean % Concentration Difference**		**Mean % Concentration Difference**	
Serum Gel	-3%	-9%	-6%	-8%
Serum No Gel	-2%	-7%	-1%	-4%
Plasma LiHep	-2%	-4%	-2%	-4%
Plasma EDTA	-1%	-4%	-2%	-4%

Access PCT Sample Stability Freezer

	Freezer (-30°C to -15°C)			
	30 Days	**45 Days**	**60 Days**	**75 Days**
Sample Type	**Mean % Concentration Difference (Samples with concentration ≥ 0.150 ng/mL)**			
Serum Gel	-8%	-4%	-7%	-6%
Serum No Gel	-7%	-2%	-7%	-6%
Plasma LiHep	-9%	-10%	-9%	-9%
Plasma EDTA	-6%	-4%	-8%	-6%

The sample handling study using serum and plasma samples with the Access PCT assay met the criterion at each storage condition. Patient samples can be stored for 16 hours at room temperature, 48 hours at 2 to 10°C, 75 days at -30°C to -15°C and frozen (freeze/thaw) up to three times.

Calibrators

The Access PCT Calibrators are a seven-level calibrator set intended to calibrate the Access PCT assay for the quantitative determination of procalcitonin levels in human serum and plasma using the Access Immunoassay Systems. The calibrators are provided at seven levels – zero and approximately 0.8, 5, 10, 25, 50, and 100 ng/mL. The calibrators contain a lyophilized HEPES buffer with protein (bovine serum albumin).

S0: Lyophilized HEPES buffer with protein (bovine), ≤ 0.1 % sodium azide, and 0.1% ProClin300

S1-S6: Recombinant human Procalcitonin at levels of approximately 0.8, 5, 10, 25, 50 and 100 ng/mL(µg/L), respectively, in lyophilized HEPES buffer with protein (bovine), ≤ 0.1 % sodium azide, and 0.1% ProClin 300

The Access PCT Calibrator kit contains one vial of each calibrator level and one Calibration Card. The S0-S6 calibrator vials contain lyophilized material. The calibrator vials are intended for storage at 2 - 10°C or colder. Once reconstituted, the 2.0 mL vial calibrators are stable at 20-25°C for 4 hours, or 90 days at -30 to -15°C and can be frozen and thawed up to 3 times.

Calibration cards are provided with each calibrator kit. Calibration cards contain bar codes that are encrypted with the individual calibrator concentrations for each calibrator level.

7. Limit of Blank (LoB), Detection (LoD) and Quantitation (LoQ):
Studies were performed to determine the LoB, LoD and LoQ in the Access PCT assay using a protocol based on CLSI EP17-A2 (Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition).

LoB

Three Access PCT S0 calibrator lots and one lot of Access Wash Buffer II were used for the LoB determination. One hundred (120) total replicates for each reagent pack lot were tested across two instruments (60 per instrument). LoB was calculated for each reagent pack lot. Of the total replicates, per reagent pack lot, ninety (90) were comprised of S0 calibrators (30 replicates of each of three lots) and thirty (30) were comprised of Access Wash Buffer II that were measured for the LoB determination. LoB was evaluated on one calibrator lot. Two Access 2 instruments and three reagent lots were used in the study design. Three days of testing were performed evaluating five replicates of each of the zero analyte sample. Three quality controls were run in replicates of two on each day to verify the systems were in control. The LoB was determined using the 95% non-parametric percentile of the 120 replicates for each of three evaluations. The results of this study demonstrate that the Access PCT assay met the acceptance criterion of ≤ 0.005 ng/mL.

LoD

The study was run on one Access 2 Immunoassay Systems, using three reagent lots and one calibrator lot. For estimation of LoD, ten serum samples, ten lithium heparin plasma, and ten EDTA plasma samples containing low levels of procalcitonin analyte were measured. One run per day, approximately nine replicates per run were performed on each day of testing, resulting in a maximum of forty-five replicates for each instrument/pack lot combination. Three quality controls were run in replicates of two on each day to verify the systems were in control. The LoD was determined by fitting the precision profile model between within-lab standard deviation (SD) and concentration. The SD, which was based on the precision model, was multiplied by the 95th percentile of the standard normal distribution and added to the LoB to calculate the LoD per CLSI EP17-A2. The results of this study demonstrate that the Access PCT met the acceptance criterion of ≤ 0.01ng/mL.

LoQ

As indicated in CLSI EP17-A2, in situations where bias cannot be determined,

within-laboratory precision is used as the sole acceptance goal. Bias is defined as the difference between the expectation of the test results and an accepted reference value, which is not available for the PCT analyte. Therefore, the LoQ approach outlined in CLSI EP17-A2 based upon a precision profile experiment in the low-end region of the measuring interval was used for the Access PCT assay. This method used three Access 2 Immunoassay Systems in the study design with three reagent lots and one calibrator lot. For estimation of LoQ, approximately ten native serum samples, ten native EDTA (plasma) samples, and ten native lithium heparin (plasma) containing low levels of procalcitonin analyte were prepared. Samples were tested over five days, one run per day, 9 replicates per run, for each pack lot. This resulted in a maximum of 45 replicates for each sample on each pack lot tested. Three quality controls were run in replicates of two on each day to verify the systems were in control. A variance components model was used to estimate the within- run and within-laboratory (total) %CV for each sample on each instrument and reagent lot combination. A log-log quadratic precision profile model was fitted to within- laboratory (total) %CV versus observed sample mean. The fitted precision profile was used to calculate the 20% CV LoQ. The acceptance criteria are 20% CV at ≤ 0.02 ng/mL. The results of this study demonstrate that the Access PCT assay met the acceptance criterion of a LoQ ≤ 0.02 ng/mL.

B Clinical Studies:

1. Method Comparison with Predicate Device:
   Method concordance (agreement) results to VIDAS B·R·A·H·M·S PCT were used to establish positive and negative agreement at clinical decision points (0.5 ng/mL and 2.0 ng/mL).

   Method comparison samples were residual serum samples from standard of care PCT testing obtained from vendors' specific SOPs with IRB/EC waiver of informed consent.

   On the Access 2, among the 238 samples, 2 samples were reported as over the Access PCT measuring range (>100 ng/mL) and 18 samples were reported below IVD VIDAS B·R·A·H·M·S PCT measurable range (<0.05 ng/mL). The 20 samples that were outside either assay's measuring range were excluded from analyses. Five samples were excluded based on visual sample quality observation after thawing. Additionally, 3 samples were not tested on the VIDAS instrument. Therefore, a total of 207 samples with paired Access PCT and VIDAS B·R·A·H·M·S PCT measurements were included for analyses. Distribution of PCT levels for the 207 samples, as measured by the VIDAS B·R·A·H·M·S PCT assay, were:

Distribution of sample values in method comparison study

PCT Value (ng/mL)	Number of Samples
≤0.5	83
>0.5 - ≤2.0	41
>2.0 - ≤10	51
>10 - ≤20	9
>20 - ≤50	16
>50 - ≤100	7

After daily maintenance, the IUO Access PCT assay was calibrated on all instruments and reagent lots as required for study testing. After a passing calibration curve was obtained, the site performed daily QC using Bio-Rad Specialty Lyphochek QC material. If QC met acceptance criteria, the site performed method comparison and method concordance.

The percent agreement and corresponding 95% confidence intervals (CI) for each clinical decision point (0.5 and 2.0 ng/mL) are presented in the two tables below. The number of samples that agree or disagree according to the clinical decision points are indicated.

Method concordance at 0.5 ng/mL

	VIDAS B·R·A·H·M·S PCT		
Access PCT Assay	**≤ 0.5 ng/mL**	**> 0.5 ng/mL**	**Total**
≤ 0.5 ng/mL	78	0	78
> 0.5 ng/mL	5	124	129
Total	83	124	207
Negative percent agreement 94.0% CI [86.5% - 98.0%] Positive percent agreement 100.0% CI [97.1% - 100%] Overall percent agreement 97.8% CI [94.5%- 99.2%]			

Method Concordance at 2.0 ng/mL

	VIDAS B·R·A·H·M·S PCT		
Access PCT Assay	**≤ 2.0 ng/mL**	**> 2.0 ng/mL**	**Total**
≤ 2 ng/mL	122	2	124
>2 ng/mL	2	81	83
Total	124	83	207
Negative percent agreement 98.4% CI [94.3% - 99.8%] Positive percent agreement 97.6% CI [91.6% - 99.7%] Overall percent agreement 98.3% CI [95.1% - 99.5%]			

Concordance for Clinical Decision Points

	VIDAS B·R·A·H·M·S PCT			
Access PCT	≤ 0.5 ng/mL	>0.5 - ≤ 2.0 ng/mL	> 2.0 ng/mL	Total
≤ 0.5 ng/mL	78	0	0	78
> 0.5 - ≤ 2.0 ng/mL	5	39	2	46
> 2.0 ng/mL	0	2	81	83
Total	83	41	83	207

2. Regression Analysis:
Results were evaluated using Weighted Deming analysis following CLSI EP09c guideline

N	Range of Observations (ng/mL)	Intercept (ng/mL) [95% CI]	Slope [95% CI]	Correlation Coefficient (r)
207	0.06 -86.71	0.02 [0.00 – 0.04]	0.96 [0.94 – 0.99]	0.99

3. Matrix Comparison:
A comparison of forty-three (43) matched sets of serum gel, serum no gel, plasma lithium heparin, and plasma EDTA samples with procalcitonin concentrations ranging from approximately 0.19 to 86 ng/mL were compared using Passing-Bablok linear regression analysis, the results of the study are below.

Matrices compared	Regression Slope	95% CI Lower Bound	95% CI Upper Bound
serum (gel) vs. serum (no gel)	0.99	0.98	1.00
lithium heparin plasma vs. serum (no gel)	0.96	0.95	0.97
lithium heparin plasma vs. serum (gel)	0.97	0.96	0.99
EDTA plasma vs. serum (no gel)	1.03	1.01	1.04
EDTA plasma vs. serum (gel)	1.04	1.03	1.05
EDTA plasma vs. lithium heparin plasma	1.06	1.05	1.08

VIII Proposed Labeling:

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

IX Conclusion:

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