August 26, 2022

Siemens Healthcare Diagnostics, Inc.
Amy Tyler
Regulatory Affairs Professional
500 GBC Drive, P.O. Box 6101
Mail Stop 514
Newark, Delaware 19714

Re: K220262
Trade/Device Name: Dimension EXL LOCI BRAHMS Procalcitonin (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
Dated: January 26, 2022
Received: January 31, 2022

Dear Amy Tyler:

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,

for

Noel Gerald
Branch Chief
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K220262

Device Name
Dimension EXL LOCI BRAHMS Procalcitonin (PCT)

Indications for Use *(Describe)*
The Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay is an in vitro diagnostic test for the quantitative measurement of procalcitonin in human serum and plasma (lithium heparin, sodium heparin, K2EDTA, and K3EDTA) using the Dimension® EXL™ integrated chemistry system with LOCI® Module.

The Dimension EXL LOCI® BRAHMS PCT assay is intended for use in conjunction with other laboratory findings and clinical assessments, as an aid in:

• The risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock.

• 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 percentage change in PCT levels over time.

• 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.

• 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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510(k) Summary of Safety and Effectiveness

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: K220262

1. Date Updated

August 24, 2022

2. Applicant Information

Contact: Amy Tyler
Regulatory Affairs Professional
Address: Siemens Healthcare Diagnostics, Inc.
500 GBC Drive, P.O. Box 6101
Mail Stop 514
Newark, DE 19714, USA
Email: amy.c.tyler@siemens-healthineers.com

3. Regulatory Information

Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT)

Trade Name:	Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT)
Classification Name:	Procalcitonin Assay: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis.
FDA Classification:	Class II
Review Panel:	Microbiology
Product Codes:	PRI, PMT
Regulation Numbers:	21 CFR 866.3215

4. Predicate Device Information

Device Name: B·R·A·H·M·S PCT sensitive KRYPTOR
510(k) Number: DEN150009/K171338
Manufacturer: B·R·A·H·M·S GmbH (Thermo Fisher Scientific)

5. Intended Use / Indications For Use

The Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay is an *in vitro* diagnostic test for the quantitative measurement of procalcitonin in human serum and plasma (lithium heparin, sodium heparin, K2EDTA, and K3EDTA) using the Dimension® EXL™ integrated chemistry system with LOCI® Module.

The Dimension EXL LOCI® BRAHMS PCT assay is intended for use in conjunction with other laboratory findings and clinical assessments, as an aid in:

- The risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock.
- 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 percentage change in PCT levels over time.
- 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.
- Decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

6. Special Conditions for Use Statement

For Prescription Use Only

7. Warnings and Precautions for Test Interpretation

- The Dimension EXL LOCI BRAHMS 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.
- Decisions regarding antibiotic therapy should NOT be based solely on PCT 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, such as age and Sequential Organ Failure Assessment (SOFA) score, are also significant predictors of 28-day cumulative mortality risk.
- PCT levels may not be elevated in patients infected by certain atypical pathogens, such as Chlamydophila pneumoniae and Mycoplasma pneumoniae.
- Certain patient characteristics, such as severity of renal failure or insufficiency, may influence PCT values and should be considered as potentially confounding clinical factors when interpreting PCT values.
- The safety and performance of PCT-guided therapy for individuals younger than 18 years of age, pregnant women, immunocompromised individuals, or those on immunomodulatory agents, was not formally analyzed in the supportive clinical trials.
- Increased PCT levels may not always be related to systemic infection. 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;
- Patients with invasive fungal infections (such as candidiasis and aspergillosis) or acute attacks of plasmodium falciparum malaria; and
- Neonates during the first 2 days of life.

8. Special Instrument Requirement

For use on the Dimension® EXL™ integrated chemistry system with LOCI® Module.

9. Test Principle and Device Description

The Dimension EXL LOCI BRAHMS PCT assay is a homogeneous sandwich chemiluminescent immunoassay based on LOCI technology. The LOCI reagents include two synthetic bead reagents and one biotinylated anti-procalcitonin (anti-PCT) monoclonal antibody. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with two anti-PCT monoclonal antibodies and contains chemiluminescent dye. Sample is incubated with biotinylated antibody and Chemibeads to form bead-PCT-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the procalcitonin (PCT) concentration in the sample.

The Dimension EXL LOCI BRAHMS PCT assay is comprised of the following reagents:

Component	Volume	Ingredients
Biotinylated Antibody Well 1 (W1) and Well 2 (W2) Reagent 1 (R1)	1.0 mL	PCT Biotinylated Antibody-mouse monoclonal (3.5 µg/mL), bovine serum albumin, bovine gamma globulin, goat serum, mouse IgG, rat IgG, sodium azide (<0.1%), buffer, preservatives, and stabilizers
Chemibead Well 3 (W3) and Well 4 (W4) Reagent 2 (R2)	1.0 mL	PCT Chemibead reagent (40 µg/mL), bovine serum albumin, bovine gamma globulin, goat serum, sodium azide (<0.1%), buffer, preservatives, and stabilizers

Component	Volume	Ingredients
Sensibead Well 5 (W5) and Well 6 (W6) Reagent 3 (R3)	0.8 mL	PCT Sensibead reagent (1500 µg/mL), bovine serum albumin, buffer, preservatives, and stabilizers
Assay buffer Well 7 (W7) and Well 8 (W8) Reagent 4 (R4)	3.0 mL (W7) 2.6 mL (W8)	Assay buffer, bovine serum albumin, bovine gamma globulin, goat serum, mouse IgG, sodium azide (<0.1%), preservatives, and stabilizers

10. Purpose of Submission

The purpose of this submission is a premarket notification for a new device:
Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT)

11. Comparison of Candidate Device and Predicate Device

The following table describes the similarities and differences between the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay (Candidate Device) and the B·R·A·H·M·S PCT sensitive KRYPTOR (Predicate Device).

Attributes	Candidate Device Dimension® EXL™ LOCI® BRAHMS PCT	Predicate Device B·R·A·H·M·S PCT sensitive KRYPTOR® (DEN150009 / K171338)
Intended Use (including indications for use)	The Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay is an *in vitro* diagnostic test for the quantitative measurement of procalcitonin in human serum and plasma (lithium heparin, sodium heparin, K2EDTA, and K3EDTA) using the Dimension® EXL™ integrated chemistry system with LOCI® Module. The Dimension EXL LOCI® BRAHMS PCT assay is intended for use in conjunction with other laboratory findings and clinical assessments, as an aid in: • The risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock.	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,

Attributes	Candidate Device Dimension® EXL™ LOCI® BRAHMS PCT	Predicate Device B·R·A·H·M·S PCT sensitive KRYPTOR® (DEN150009 / K171338)
	• 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 percentage change in PCT levels over time. • 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. • Decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.	• 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
Analyte	Procalcitonin (PCT)	same
Automated	Automated assay	same
Measurement	Quantitative	same
Instrument	Dimension® EXL™ integrated chemistry system with LOCI® Module	KRYPTOR® Test System
Assay format	Sandwich immunoassay	Sandwich immunoassay
Technology	Chemiluminescent technology	Immunofluorescence TRACE® technology TRACE: Time-Resolved Amplified Cryptate Emission

Attributes	Candidate Device Dimension® EXL™ LOCI® BRAHMS PCT	Predicate Device B·R·A·H·M·S PCT sensitive KRYPTOR® (DEN150009 / K171338)
Specimen type	Serum, Plasma (lithium heparin, sodium heparin, K2EDTA, and K3EDTA)	Serum, Plasma (EDTA, lithium heparin and sodium heparin)
Units of measure	Conventional units: ng/mL S.I. units: μg/L	μg/L
Assay Range / Measuring Interval	0.05 to 50.00 ng/mL Measuring range with manual dilution 0.05 to 1000.00 ng/mL	0.02 to 50 μg/L Measuring range with automatic dilution 0.02 to 5000 μg/L
Sample volume	5μL	50μL
Calibration frequency	7 days	15 days
Calibrators	Dimension EXL LOCI BRAHMS Procalcitonin Calibrator (LOCI PCT CAL): 5-level frozen liquid product Level 1: bovine albumin-based product with preservatives. Levels 2-5: serum-based product containing recombinant human procalcitonin and preservatives.	B·R·A·H·M·S PCT sensitive KRYPTOR® Calibrator: Single level: 1 vial of lyophilized recombinant PCT in defibrinated human plasma (range 22.50-27.50μg/L)

12. Standard / Guidance Document References

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) were used as a basis of the study procedures described in this submission:

- Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline–Third Edition (CLSI EP05-A3; Recognition Number 7-251)
- Interference Testing in Clinical Chemistry (CLSI EP07-ED3; Recognition Number 7-275); for general use
- Measurement Procedure Comparison and Bias Estimation Using Patient Samples (CLSI EP09c-ED3; Recognition Number 7-296)
- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline–Second Edition (EP17-A2; Recognition Number 7-233)
- Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (CLSI EP25-A; Recognition Number 7-235)
- Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition (CLSI EP28-A3c; Recognition Number 7-224)
- Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking (CLSI EP34-ED1; Recognition Number 7-290)
- Evaluation of Linearity of Quantitative Measurement Procedures (CLSI EP06-ED2; Recognition Number 7-306)

13. Performance Characteristics for Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT)

13.1 Precision

The precision study was performed in accordance with CLSI EP05-A3. Samples were assayed on the Dimension® EXL™ 200 system in duplicate in two runs per day for 20 days. The following results were obtained:

Precision data for Dimension EXL LOCI BRAHMS PCT lot FB1218

Sample	N[a]		Repeatability		Within-Lab		Repeatability		Within-Lab	
		Mean ng/mL (µg/L)	SD[b] ng/mL (µg/L)	CV[c] (%)	SD ng/mL (µg/L)	CV (%)	Acceptance Criteria %CV	Result	Acceptance Criteria %CV	Result
QC1	80	0.21 (0.21)	0.009 (0.009)	4.3	0.015 (0.015)	7.1	≤ 10.0	PASS	≤ 15.0	PASS
QC2	80	0.98 (0.98)	0.022 (0.022)	2.2	0.034 (0.034)	3.5	≤ 10.0	PASS	≤ 15.0	PASS
QC3	80	0.93 (0.93)	0.023 (0.023)	2.5	0.030 (0.030)	3.2	≤ 10.0	PASS	≤ 15.0	PASS
Plasma	80	0.10 (0.10)	0.004 (0.004)	4.0	0.006 (0.006)	6.0	≤ 15.0	PASS	≤ 20.0	PASS
Serum 1	80	0.10 (0.10)	0.004 (0.004)	4.0	0.005 (0.005)	5.0	≤ 15.0	PASS	≤ 20.0	PASS
Serum 2	80	0.22 (0.22)	0.006 (0.006)	2.7	0.009 (0.009)	4.1	≤ 10.0	PASS	≤ 15.0	PASS
Serum 3	80	0.44 (0.44)	0.009 (0.009)	2.0	0.012 (0.012)	2.7	≤ 10.0	PASS	≤ 15.0	PASS
Serum 4	80	1.68 (1.68)	0.026 (0.026)	1.5	0.050 (0.050)	3.0	≤ 10.0	PASS	≤ 15.0	PASS
Serum 5	80	8.56 (8.56)	0.230 (0.230)	2.7	0.472 (0.472)	5.5	≤ 10.0	PASS	≤ 15.0	PASS

[a] Number of replicates tested

[b] Standard deviation

[c] Coefficient of variation

Precision data for Dimension EXL LOCI BRAHMS PCT lot FC1218

Specimen Type	N[a]		Repeatability		Within-Lab		Repeatability		Within-Lab	
		Mean ng/mL (µg/L)	SD[b] ng/mL (µg/L)	CV[c] (%)	SD (ng/mL)	CV (%)	Acceptance Criteria %CV	Result	Acceptance Criteria %CV	Result
QC1	80	0.21 (0.21)	0.007 (0.007)	3.3	0.013 (0.013)	6.2	≤ 10.0	PASS	≤ 15.0	PASS
QC2	80	0.99 (0.99)	0.042 (0.042)	4.2	0.045 (0.045)	4.5	≤ 10.0	PASS	≤ 15.0	PASS
QC3	80	0.94 (0.94)	0.024 (0.024)	2.6	0.030 (0.030)	3.2	≤ 10.0	PASS	≤ 15.0	PASS
Plasma	80	0.10 (0.10)	0.004 (0.004)	4.0	0.006 (0.006)	6.0	≤ 15.0	PASS	≤ 20.0	PASS
Serum 1	80	0.10 (0.10)	0.003 (0.003)	3.0	0.006 (0.006)	6.0	≤ 15.0	PASS	≤ 20.0	PASS
Serum 2	80	0.22 (0.22)	0.006 (0.006)	2.7	0.008 (0.008)	3.6	≤ 10.0	PASS	≤ 15.0	PASS
Serum 3	80	0.44 (0.44)	0.012 (0.012)	2.7	0.014 (0.014)	3.2	≤ 10.0	PASS	≤ 15.0	PASS
Serum 4	80	1.69 (1.69)	0.036 (0.036)	2.1	0.053 (0.053)	3.1	≤ 10.0	PASS	≤ 15.0	PASS
Serum 5	80	8.63 (8.63)	0.199 (0.199)	2.3	0.499 (0.499)	5.8	≤ 10.0	PASS	≤ 15.0	PASS

[a] Number of replicates tested

[b] Standard deviation

[c] Coefficient of variation

13.2 Reproducibility

The reproducibility study was performed in accordance with CLSI EP05-A3. Samples were assayed with (3) reagent lots on each of three (3) instruments over five (5) days with five (5) replicates per sample per day on each instrument with each reagent lot, yielding 75 results per reagent lot for each sample. Six (6) serum pools were included in this study. The following results were obtained:

Reproducibility data summary for all reagent lots (reagent lots 1, 2, and 3)

Sample ID	N[a]	Mean	Reproducibility									
			Repeatability		Between-Day		Between-Lot		Between-Instrument		Total Reproducibility	
			SD[b]	CV[c]	SD	CV	SD	CV	SD	CV	SD	CV
		ng/mL	ng/mL	%	ng/mL	%	ng/mL	%	ng/mL	%	ng/mL	%
MDP1	225	0.10	0.005	5.0	0.002	2.0	0.004	4.0	0.000	0.0	0.007	7.0
MDP2	225	0.25	0.008	3.2	0.005	2.0	0.005	2.0	0.000	0.0	0.011	4.4
MDP3	225	0.48	0.014	2.9	0.007	1.5	0.010	2.1	0.000	0.0	0.018	3.8
MDP4	225	1.95	0.046	2.4	0.039	2.0	0.045	2.3	0.000	0.0	0.075	3.8
MDP5	225	8.94	0.228	2.6	0.255	2.9	0.123	1.4	0.099	1.1	0.377	4.2
MDP6	225	41.01	2.538	6.2	2.289	5.6	1.073	2.6	1.350	3.3	3.828	9.3

[a] Number of replicates tested

[b] Standard deviation

[c] Coefficient of variation

13.3 Detection Capability

Detection capability was determined in accordance with CLSI EP17-A2.

Limit of Blank (LoB) is the highest value expected in a series of results on a human serum sample that contains no analyte. The assay is designed to have an LoB < Limit of Detection (LoD).

The Limit of Detection (LoD) corresponds to the lowest concentration of procalcitonin that can be detected with a probability of 95%. The assay is designed to have an LoD ≤ 0.04 ng/mL.

Limit of Quantitation (LoQ as functional sensitivity) is the lowest amount of procalcitonin in a material that can be quantitatively determined with stated accuracy. For this assay, the LoQ is defined as the concentration at which the CV is 20% in the precision profile. The assay is designed to have an LoQ ≤ 0.05 ng/mL (using within-lab %CV of 20%).

The results are shown in the following table:

Attribute	Claim
LoB	0.03 ng/mL
LoD	0.04 ng/mL
LoQ	0.05 ng/mL
Lower Limit of Analytical Measuring Range	0.05 ng/mL

13.4 Linearity

Linearity was conducted according to CLSI EP06-ED2. The study was performed using 16 samples spanning the assay range, prepared using high and low human serum pools (11 levels were made using a high pool >50.00 ng/mL and 4 additional levels with concentrations near the lower medical decision levels were made with a second high pool targeted near 4.00 ng/mL).

Regression analysis using first, second, and third order models was conducted to determine the linearity of the assay. Regression statistics (i.e., deviation from linearity for non-linear pools) at all levels tested demonstrated a ≤20% deviation (≤ 0.04 ng/mL for the lowest sample) from the predicted linear fit.

The study demonstrated a linear range of 0.03 to 55.05 ng/mL, which supports a measuring interval of 0.05 to 50.00 ng/mL for the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay.

13.5 Dilution Recovery

Dilution recovery (using manual dilution) was conducted according to CLSI EP34-ED1. Ten native serum specimens with concentrations determined to be greater than 50.00 ng/mL were diluted 1:20 with saline, which is the recommended diluent for this assay. Recoveries for all specimens ranged from 88 to 108% (mean % recovery was 98%). The following results were obtained:

Sample	Dilution	PCT Mean Results ng/mL (µg/L)		% Recovery
		Expected	Observed	
1	1:20	411.3 (411.3)	390.60 (390.60)	95%
2	1:20	300.3 (300.3)	285.40 (285.40)	95%
3	1:20	394.4 (394.4)	413.60 (413.60)	105%
4	1:20	646.2 (646.2)	695.00 (695.00)	108%
5	1:20	203.2 (203.2)	178.80 (178.80)	88%
6	1:20	65.23 (65.23)	61.60 (61.60)	94%
7	1:20	72.43 (72.43)	73.40 (73.40)	101%
8	1:20	216.9 (216.9)	202.20 (202.20)	93%
9	1:20	124.1 (124.1)	118.80 (118.80)	96%
10	1:20	143.1 (143.1)	148.40 (148.40)	104%

Manual dilution of 1:20 increases the upper end of the analytical measuring interval which supports an extended measuring interval from 50.00 ng/mL (50.00 µg/L) to 1000.00 ng/mL (1000.00 µg/L).

13.6 Interference and Cross-Reactivity

Interference testing was conducted using EP07-ED3 for general guidance. Human serum pools at approximately 0.25 ng/mL and 2.00 ng/mL PCT were prepared by pooling native PCT. Each pool was divided into control and test pools. The test pools were spiked with the potentially interfering substances and the control pools were spiked with an equivalent volume of diluent.

Percent interference (% bias) was calculated according to the following equation:

$$\%\ Bias = \frac{(Observed\ Mean - Control\ Mean\ Concentration)}{Control\ Mean\ Concentration} x\ 100$$

Bias >10% is considered interference. Analyte results should not be corrected based on this bias.

The conversion factor from conventional units (ng/mL) to SI units (µg/L) is 1.00. Based on this, all results shown in ng/mL units would have the same values when displayed in µg/L units.

Hemolysis, Icterus, and Lipemia (HIL)

The Dimension EXL LOCI BRAHMS PCT assay is designed to have ≤10% interference from hemoglobin, bilirubin, and lipemia. The following results were obtained:

Substance	Substance Concentration		PCT Analyte Concentration (ng/mL)	% Bias
	Conventional Units	SI Units		
Bilirubin, Conjugated	40 mg/dL	474 µmol/L	0.24	0
Bilirubin, Conjugated	40 mg/dL	474 µmol/L	2.02	0
Bilirubin, Unconjugated	40 mg/dL	684 µmol/L	0.22	0
Bilirubin, Unconjugated	40 mg/dL	684 µmol/L	1.75	1
Hemoglobin	1000 mg/dL	10 g/L	0.20	-5
Hemoglobin	1000 mg/dL	10 g/L	1.61	-7
Lipemia (from Intralipid®)	2000 mg/dL	20 g/L	0.21	0
Lipemia (from Intralipid®)	2000 mg/dL	20 g/L	1.69	3

Non-Interfering Substances

The following substances do not interfere with the Dimension EXL LOCI BRAHMS PCT assay when present in serum, lithium heparin plasma, sodium heparin plasma, K2EDTA plasma, or K3EDTA plasma. Bias due to these substances was ≤10% at PCT analyte concentrations of 0.25 and 2.00 ng/mL.

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
Acetaminophen	20 mg/dL	1324 µmol/L	0.25	-4
Acetaminophen	20 mg/dL	1324 µmol/L	2.02	1
Acetylsalicylic acid	3 mg/dL	166.5 µmol/L	0.24	4
Acetylsalicylic acid	3 mg/dL	166.5 µmol/L	2.04	0
Albumin	6 g/dL	60 g/L	0.21	-5
Albumin	6 g/dL	60 g/L	1.75	-9
Amoxicillin	5.4 mg/dL	147.96 µmol/L	0.22	5
Amoxicillin	5.4 mg/dL	147.96 µmol/L	1.81	2
Azithromycin	1.15 mg/dL	15.4 µmol/L	0.22	0

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
Azithromycin	1.15 mg/dL	15.4 µmol/L	1.78	-1
Caffeine	10.8 mg/dL	556.2 µmol/L	0.24	0
Caffeine	10.8 mg/dL	556.2 µmol/L	2.02	0
Cefotaxime	52.8 mg/dL	1161.6 µmol/L	0.25	0
Cefotaxime	52.8 mg/dL	1161.6 µmol/L	2.02	0
Celecoxib	0.88 mg/dL	23 µmol/L	0.22	0
Celecoxib	0.88 mg/dL	23 µmol/L	1.81	-1
Cetirizine HCl	0.43 mg/dL	11.1 µmol/L	0.22	0
Cetirizine HCl	0.43 mg/dL	11.1 µmol/L	1.81	-3
Cholesterol	400 mg/dL	10.4 mmol/L	0.22	-5
Cholesterol	400 mg/dL	10.4 mmol/L	1.73	-2
Dextran 40	4500 mg/dL	1125 µmol/L	0.26	-4
Dextran 40	4500 mg/dL	1125 µmol/L	2.12	-1
Dextromethorphan	0.00156 mg/dL	0.057 µmol/L	0.24	4
Dextromethorphan	0.00156 mg/dL	0.057 µmol/L	2.04	-5
Dobutamine	0.121 mg/dL	4 µmol/L	0.22	5
Dobutamine	0.121 mg/dL	4 µmol/L	1.81	-3
Dopamine	0.06 mg/dL	3.9 µmol/L	0.25	0
Dopamine	0.06 mg/dL	3.9 µmol/L	2.02	0
Doxycycline	1.8 mg/dL	40.5 µmol/L	0.22	0
Doxycycline	1.8 mg/dL	40.5 µmol/L	1.81	-4
EDTA	0.099 mg/dL	3.4 µmol/L	0.22	5
EDTA	0.099 mg/dL	3.4 µmol/L	1.75	3
Epinephrine	0.18 mg/dL	9.8 µmol/L	0.25	0
Epinephrine	0.18 mg/dL	9.8 µmol/L	2.02	1
Ethanol	400 mg/dL	86.8 mmol/L	0.24	0

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
Ethanol	400 mg/dL	86.8 mmol/L	2.02	-1
Fentanyl	0.03 mg/dL	0.89 µmol/L	0.24	0
Fentanyl	0.03 mg/dL	0.89 µmol/L	2.04	-1
Fluorescein	0.01 mg/dL	0.3 µmol/L	0.22	0
Fluorescein	0.01 mg/dL	0.3 µmol/L	1.75	0
Furosemide	2 mg/dL	60.4 µmol/L	0.24	-8
Furosemide	2 mg/dL	60.4 µmol/L	2.04	-1
HAMA	22.8 mg/mL	22.8 g/L	0.27	-7
HAMA	22.8 mg/mL	22.8 g/L	2.19	-9
Heparin	330 U/dL	3300 U/L	0.25	-4
Heparin	330 U/dL	3300 U/L	2.02	3
Human Immunoglobulin (IgG)	5 g/dL	50 g/L	0.23	-9
Human Immunoglobulin (IgG)	5 g/dL	50 g/L	1.80	-8
Human serum albumin	1 g/dL	10 g/L	0.22	5
Human serum albumin	1 g/dL	10 g/L	1.85	-1
Human serum gamma globulin	2.5 g/dL	25 g/L	0.26	-8
Human serum gamma globulin	2.5 g/dL	25 g/L	2.12	-7
Ibuprofen	21.9 mg/dL	1062.2 µmol/L	0.24	4
Ibuprofen	21.9 mg/dL	1062.2 µmol/L	2.04	-1
Imipenem	118 mg/dL	3941.2 µmol/L	0.22	5
Imipenem	118 mg/dL	3941.2 µmol/L	1.75	3
Levofloxacin	3.6 mg/dL	99.7 µmol/L	0.22	0
Levofloxacin	3.6 mg/dL	99.7 µmol/L	1.75	-1
Loratadine	0.0087 mg/dL	0.27 µmol/L	0.22	5
Loratadine	0.0087 mg/dL	0.27 µmol/L	1.81	-1
Nicotine	0.1 mg/dL	6.2 µmol/L	0.24	-4

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
Nicotine	0.1 mg/dL	6.2 µmol/L	2.04	-5
Noradrenaline	0.2 mg/dL	11.8 µmol/L	0.22	0
Noradrenaline	0.2 mg/dL	11.8 µmol/L	1.75	-2
Oxymetazoline HCl	9 µg/dL	0.3 µmol/L	0.25	0
Oxymetazoline HCl	9 µg/dL	0.3 µmol/L	2.02	2
Phenylephrine	0.003 mg/dL	0.179 µmol/L	0.25	0
Phenylephrine	0.003 mg/dL	0.179 µmol/L	2.02	1
Prednisolone	0.12 mg/dL	3.3 µmol/L	0.22	5
Prednisolone	0.12 mg/dL	3.3 µmol/L	1.81	-1
Rheumatoid Factor	500 IU/mL	500 IU/mL	0.21	-5
Rheumatoid Factor	500 IU/mL	500 IU/mL	1.64	1
Salmeterol	6 µg/dL	0.1 µmol/L	0.24	4
Salmeterol	6 µg/dL	0.1 µmol/L	2.04	-6
Tiotropium	2.16 mg/dL	45.8 µmol/L	0.24	0
Tiotropium	2.16 mg/dL	45.8 µmol/L	2.04	-3
Total Protein	10.6 g/dL	106 g/L	0.22	-9
Total Protein	10.6 g/dL	106 g/L	1.74	-9
Triglycerides	1500 mg/dL	16.9 mmol/L	0.22	-5
Triglycerides	1500 mg/dL	16.9 mmol/L	1.73	-2
Vancomycin	12 mg/dL	82.8 µmol/L	0.25	-4
Vancomycin	12 mg/dL	82.8 µmol/L	2.02	0

Biotin Interference Testing

Biotin testing was performed by spiking a range of concentrations into serum pools with PCT analyte concentrations of 0.25 and 2.00 ng/mL. The results of this testing are shown in the following table.

Substance	Substance Concentration		PCT Analyte Concentration (ng/mL)	% Bias
	Conventional Units	SI Units		
Biotin (mega dose)	3510 ng/mL	14.356 µmol/L	0.23	-26
Biotin (mega dose)	3510 ng/mL	14.356 µmol/L	1.88	-29
Biotin	1500 ng/mL	6.135 µmol/L	0.23	-4
Biotin	1500 ng/mL	6.135 µmol/L	1.88	-19
Biotin	1200 ng/mL	4.908 µmol/L	0.23	0
Biotin	1200 ng/mL	4.908 µmol/L	1.78	-2
Biotin	600 ng/mL	2.454 µmol/L	0.23	4
Biotin	600 ng/mL	2.454 µmol/L	1.88	1
Biotin	300 ng/mL	1.227 µmol/L	0.23	0
Biotin	300 ng/mL	1.227 µmol/L	1.88	-2
Biotin	150 ng/mL	0.614 µmol/L	0.23	0
Biotin	150 ng/mL	0.614 µmol/L	1.88	-3
Biotin	99.6 ng/mL	0.407 µmol/L	0.23	0
Biotin	99.6 ng/mL	0.407 µmol/L	1.88	-2
Biotin	80.4 ng/mL	0.329 µmol/L	0.23	0
Biotin	80.4 ng/mL	0.329 µmol/L	1.88	-1
Biotin	39.6 ng/mL	0.162 µmol/L	0.23	4
Biotin	39.6 ng/mL	0.162 µmol/L	1.88	-3
Biotin	30.0 ng/mL	0.123 µmol/L	0.23	4
Biotin	30.0 ng/mL	0.123 µmol/L	1.88	-1
Biotin	20.4 ng/mL	0.083 µmol/L	0.23	0
Biotin	20.4 ng/mL	0.083 µmol/L	1.88	-1
Biotin	9.6 ng/mL	0.039 µmol/L	0.23	4
Biotin	9.6 ng/mL	0.039 µmol/L	1.88	0

HAMA Interference Testing

HAMA testing was performed at a range of concentrations to determine the level at which HAMA would cause >10% interference. Both HAMA 1 and HAMA 2 were tested in serum pools with PCT analyte concentrations of 0.25 and 2.00 ng/mL. The results of this testing are shown in the following table.

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
HAMA 1	65.0 mg/mL	65.0 g/L	0.21	-10
HAMA 1	65.0 mg/mL	65.0 g/L	1.64	-12
HAMA 2	65.0 mg/mL	65.0 g/L	0.21	-14
HAMA 2	65.0 mg/mL	65.0 g/L	1.64	-13
HAMA 1	32.5 mg/mL	32.5 g/L	0.27	-11
HAMA 1	32.5 mg/mL	32.5 g/L	2.19	-12
HAMA 2	32.5 mg/mL	32.5 g/L	0.27	-7
HAMA 2	32.5 mg/mL	32.5 g/L	2.19	-11
HAMA 1	22.8 mg/mL	22.8 g/L	0.27	-7
HAMA 1	22.8 mg/mL	22.8 g/L	2.19	-9
HAMA 2	22.8 mg/mL	22.8 g/L	0.27	-7
HAMA 2	22.8 mg/mL	22.8 g/L	2.19	-7
HAMA 1	16.3 mg/mL	16.3 g/L	0.27	-4
HAMA 1	16.3 mg/mL	16.3 g/L	2.19	-9
HAMA 2	16.3 mg/mL	16.3 g/L	0.27	-4
HAMA 2	16.3 mg/mL	16.3 g/L	2.19	-5
HAMA 1	0.001 mg/mL	0.001 g/L	0.21	0
HAMA 1	0.001 mg/mL	0.001 g/L	1.64	4
HAMA 2	0.001 mg/mL	0.001 g/L	0.21	-5
HAMA 2	0.001 mg/mL	0.001 g/L	1.64	2

Interfering Substances

The following substances were observed to have >10% interference in serum pools with PCT analyte concentrations of 0.25 and 2.00 ng/mL. The Instructions For Use contains limitations statements for these substances at the concentrations listed in the following table.

Substance	Substance Concentration		PCT Analyte Concentration ng/mL	% Bias
	Conventional Units	SI Units		
Biotin	3510 ng/mL	14.356 µmol/L	0.23	-26
Biotin	3510 ng/mL	14.356 µmol/L	1.88	-29
HAMA 1	32.5 mg/mL	32.5 g/L	0.27	-11
HAMA 1	32.5 mg/mL	32.5 g/L	2.19	-12
HAMA 2	32.5 mg/mL	32.5 g/L	0.27	-7
HAMA 2	32.5 mg/mL	32.5 g/L	2.19	-11
Total Protein	15.0 g/dL	150 g/L	0.22	-18
Total Protein	15.0 g/dL	150 g/L	1.74	-18

Note: HAMA interference listed in the IFU does not differentiate between HAMA 1 and HAMA 2.

Cross-Reactivity

Potential cross-reactivity was evaluated using EP07-ED3 for general guidance. Human serum pools at approximately 0.25 ng/mL and 2.00 ng/mL PCT were prepared by pooling native PCT. Each pool was divided into control and test pools. The test pools were spiked with the potentially cross-reacting substances and the control pools were spiked with an equivalent volume of diluent. Cross-reactivity was calculated using the following equation:

$$\%\ Cross-reactivity = 100\frac{|Test - Control|}{[Compound]}$$

The results of this testing are shown in the following table.

Cross-Reactant	Cross-Reactant test concentration		PCT Analyte Concentration ng/mL	% Cross-Reactivity
	Conventional units	SI Units		
Calcitonin (Human)	8 ng/mL	8 µg/L	0.23	0.00%
Calcitonin (Human)	8 ng/mL	8 µg/L	1.79	-0.50%
Calcitonin (Eel)	30 ng/mL	30 µg/L	0.23	-0.03%
Calcitonin (Eel)	30 ng/mL	30 µg/L	1.79	-0.13%

Cross-Reactant	Cross-Reactant test concentration		PCT Analyte Concentration ng/mL	% Cross-Reactivity
	Conventional units	SI Units		
Calcitonin (Salmon)	30 ng/mL	30 µg/L	0.24	-0.03%
Calcitonin (Salmon)	30 ng/mL	30 µg/L	1.78	0.07%
Katacalcin (Human)	30 ng/mL	30 µg/L	0.23	-0.03%
Katacalcin (Human)	30 ng/mL	30 µg/L	1.79	-0.20%
α-CGRP	30 ng/mL	30 µg/L	0.23	0.00%
α-CGRP	30 ng/mL	30 µg/L	1.79	0.00%
β-CGRP	30 ng/mL	30 µg/L	0.23	0.00%
β-CGRP	30 ng/mL	30 µg/L	1.79	0.00%

13.7 Hook Effect

A study was performed to evaluate whether a hook effect occurs with the assay for PCT concentrations up to 2000.00 ng/mL. For patient specimens with PCT concentrations between 50.00 ng/mL and 2000.00 ng/mL the assay will report results as “Above Assay Range” (> 50.00 ng/mL).

13.8 Sample Carryover

Sample carryover was performed using eleven separate runs. Each run consisted of testing a pattern of high (1068.88 ng/mL PCT) and low (≤0.10 ng/mL PCT) analyte samples for a total of 21 tests per run. The high sample was prepared by spiking recombinant procalcitonin into a normal human serum sample and the low sample was a normal human serum sample containing ≤0.10 ng/mL PCT (no spiking or dilution occurred). The following test order was used for each run, with L corresponding to the low sample and H corresponding to the high sample: L1, L2, L3, H1, H2, L4, H3, H4, L5, L6, L7, L8, H5, H6, L9, H7, H8, L10, H9, H10, L11.

No sample carryover from high samples into low samples was observed when a pattern of high and low samples was tested (sample carryover was calculated to be 0.00 ng/mL).

13.9 Method Comparison

The method comparison study was designed in accordance with CLSI EP09c-ED3 to compare the performance of the Dimension EXL LOCI BRAHMS Procalcitonin (PCT) assay to that of the predicate device (B·R·A·H·M·S PCT sensitive KRYPTOR).

A total of 595 native human serum samples within the concentration range of 0.05-1000.00 ng/mL were tested with the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay and the predicate device (B·R·A·H·M·S PCT sensitive KRYPTOR). Samples recovering >50.00 ng/mL were diluted manually with saline using a 1:20 dilution and tested.

Data analysis for method comparison was completed for both the measuring interval (n=555) and the extended measuring interval (n=595) for each Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay lot. Weighted Deming and Passing and Bablok regression statistics were calculated. Data was further analyzed for concordance (percent agreement) between the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay and the predicate B·R·A·H·M·S PCT sensitive KRYPTOR at each Clinical cutoff / Medical Decision Level (MDL).

Method comparison statistics for weighted Deming regression and Passing and Bablok regression for the measuring interval (0.05-50.00 ng/mL (0.05-50.00 µg/L))

Parameter	Lot FB1218		Lot FC1218	
	Weighted Deming Regression	Passing and Bablok Regression	Weighted Deming Regression	Passing and Bablok Regression
N	555	555	555	555
Slope	1.07	1.07	1.04	1.04
95% Confidence Interval	1.05 to 1.10	1.05 to 1.09	1.02 to 1.07	1.02 to 1.06
Intercept (ng/mL)	-0.01	-0.01	0.00	-0.01
95% Confidence Interval	-0.02 to 0.00	-0.02 to -0.01	-0.01 to 0.00	-0.01 to 0.00
Correlation coefficient (r)	0.958	0.958	0.963	0.963
Sample range (ng/mL)	0.02 to 49.03	0.02 to 49.03	0.02 to 49.03	0.02 to 49.03

Concordance data for Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) lot FB1218 (measuring interval, 0.05-50.00 ng/mL (0.05-50.00 µg/L)).

PCT Results at 0.10 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.10 ng/mL	≤0.10 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.10 ng/mL	489	6	495
			≤0.10 ng/mL	11	49	60
			Total	500	55	555
Positive % Agreement	=	97.8%	95% Confidence Interval:	96.5%	-	99.1%
Negative % Agreement	=	89.1%	95% Confidence Interval:	80.9%	-	97.3%
Overall % Agreement	=	96.9%	95% Confidence Interval:	95.5%	-	98.4%

PCT Results at 0.25 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.25 ng/mL	≤0.25 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.25 ng/mL	401	11	412
			≤0.25ng/mL	10	133	143
			Total	411	144	555
Positive % Agreement	=	97.6%	95% Confidence Interval:	96.1%	-	99.1%
Negative % Agreement	=	92.4%	95% Confidence Interval:	88.0%	-	96.7%
Overall % Agreement	=	96.2%	95% Confidence Interval:	94.6%	-	97.8%

PCT Results at 0.50 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.50 ng/mL	≤0.50 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.50 ng/mL	294	11	305
			≤0.50 ng/mL	12	238	250
			Total	306	249	555
Positive % Agreement	=	96.1%	95% Confidence Interval:	93.9%	-	98.3%
Negative % Agreement	=	95.6%	95% Confidence Interval:	93.0%	-	98.1%
Overall % Agreement	=	95.9%	95% Confidence Interval:	94.2%	-	97.5%

PCT Results at 2.00 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>2.00 ng/mL	≤2.00 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>2.00 ng/mL	188	9	197
			≤2.00 ng/mL	5	353	358
			Total	193	362	555
Positive % Agreement	=	97.4%	95% Confidence Interval:	95.2%	-	99.7%
Negative % Agreement	=	97.5%	95% Confidence Interval:	95.9%	-	99.1%
Overall % Agreement	=	97.5%	95% Confidence Interval:	96.2%	-	98.8%

Cross-Tabulation of concordance data for all samples (n=555) for Dimension® EXL™ LOCI® BRAHMS Procalcitonin versus Predicate for lot FB1218 (measuring interval)

Dimension EXL LOCI BRAHMS PCT (ng/mL)	B·R·A·H·M·S PCT sensitive KRYPTOR (ng/mL)					
	≤0.10	>0.10 - ≤0.25	>0.25 - ≤0.50	>0.50 - ≤2.00	>2.00	Total
≤0.10	49	11	0	0	0	60
>0.10 - ≤0.25	6	67	10	0	0	83
>0.25 - ≤0.50	0	10	85	12	0	107
>0.50 - ≤2.00	0	1	10	92	5	108
>2.00	0	0	0	9	188	197
Total	55	89	105	113	193	555

Concordance data for Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) lot FC1218 (measuring interval, 0.05-50.00 ng/mL (0.05-50.00 µg/L))

PCT Results at 0.10 ng/mL Cut-Off

					B·R·A·H·M·S PCT sensitive KRYPTOR		
					>0.10 ng/mL	≤0.10 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT				>0.10 ng/mL	486	6	492
				≤0.10 ng/mL	14	49	63
				Total	500	55	555
Positive % Agreement	=	97.2%	;	95% Confidence Interval:	95.8%	-	98.6%
Negative % Agreement	=	89.1%	;	95% Confidence Interval:	80.9%	-	97.3%
Overall % Agreement	=	96.4%	;	95% Confidence Interval:	94.8%	-	97.9%

PCT Results at 0.25 ng/mL Cut-Off

					B·R·A·H·M·S PCT sensitive KRYPTOR		
					>0.25 ng/mL	≤0.25 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT				>0.25 ng/mL	402	11	413
				≤0.25ng/mL	9	133	142
				Total	411	144	555
Positive % Agreement	=	97.8%	;	95% Confidence Interval:	96.4%	-	99.2%
Negative % Agreement	=	92.4%	;	95% Confidence Interval:	88.0%	-	96.7%
Overall % Agreement	=	96.4%	;	95% Confidence Interval:	94.8%	-	97.9%

PCT Results at 0.50 ng/mL Cut-Off

					B·R·A·H·M·S PCT sensitive KRYPTOR		
					>0.50 ng/mL	≤0.50 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT				>0.50 ng/mL	295	9	304
				≤0.50 ng/mL	11	240	251
				Total	306	249	555
Positive % Agreement	=	96.4%	;	95% Confidence Interval:	94.3%	-	98.5%
Negative % Agreement	=	96.4%	;	95% Confidence Interval:	94.1%	-	98.7%
Overall % Agreement	=	96.4%	;	95% Confidence Interval:	94.8%	-	97.9%

PCT Results at 2.00 ng/mL Cut-Off

					B·R·A·H·M·S PCT sensitive KRYPTOR		
					>2.00 ng/mL	≤2.00 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT				>2.00 ng/mL	189	10	199
				≤2.00 ng/mL	4	352	356
				Total	193	362	555
Positive % Agreement	=	97.9%	;	95% Confidence Interval:	95.9%	-	99.9%
Negative % Agreement	=	97.2%	;	95% Confidence Interval:	95.5%	-	98.9%
Overall % Agreement	=	97.5%	;	95% Confidence Interval:	96.2%	-	98.8%

Cross-Tabulation of concordance data for all samples (n=555) for Dimension® EXL™ LOCI® BRAHMS Procalcitonin versus Predicate for lot FC1218 (measuring interval)

Dimension EXL LOCI BRAHMS PCT (ng/mL)	B·R·A·H·M·S PCT sensitive KRYPTOR (ng/mL)					
	≤0.10	>0.10 - ≤0.25	>0.25 - ≤0.50	>0.50 - ≤2.00	>2.00	Total
≤0.10	49	14	0	0	0	63
>0.10 - ≤0.25	6	64	9	0	0	79
>0.25 - ≤0.50	0	10	88	11	0	109
>0.50 - ≤2.00	0	1	8	92	4	105
>2.00	0	0	0	10	189	199
Total	55	89	105	113	193	555

Method comparison statistics for weighted Deming regression and Passing and Bablok regression for the extended measuring interval (0.05-1000.00 ng/mL (0.05-1000.00 µg/L))

Parameter	Lot FB1218		Lot FC1218	
	Weighted Deming Regression*	Passing and Bablok Regression*	Weighted Deming Regression	Passing and Bablok Regression
N	595	595	595	595
Slope	1.08	1.07	1.05	1.05
95% Confidence Interval	1.05 to 1.10	1.05 to 1.09	1.02 to 1.07	1.04 to 1.07
Intercept (ng/mL)	-0.01	-0.01	0.00	-0.01
95% Confidence Interval	-0.02 to 0.00	-0.02 to -0.01	-0.01 to 0.00	-0.02 to 0.00
Correlation coefficient (r)	0.988	0.988	0.991	0.991
Sample range (ng/mL)	0.02 to 691.00	0.02 to 691.00	0.02 to 691.00	0.02 to 691.00

*Data shown in IFU

Concordance data for Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) lot FB1218 (extended measuring interval, 0.05-1000.00 ng/mL (0.05-1000.00 µg/L))

PCT Results at 0.10 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.10 ng/mL	≤0.10 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.10 ng/mL	529	6	535
			≤0.10 ng/mL	11	49	60
			Total	540	55	595
Positive % Agreement	=	98.0%	95% Confidence Interval:	96.8%	-	99.2%
Negative % Agreement	=	89.1%	95% Confidence Interval:	80.9%	-	97.3%
Overall % Agreement	=	97.1%	95% Confidence Interval:	95.8%	-	98.5%

PCT Results at 0.25 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.25 ng/mL	≤0.25 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.25 ng/mL	441	11	452
			≤0.25ng/mL	10	133	143
			Total	451	144	595
Positive % Agreement	=	97.8%	95% Confidence Interval:	96.4%	-	99.1%
Negative % Agreement	=	92.4%	95% Confidence Interval:	88.0%	-	96.7%
Overall % Agreement	=	96.5%	95% Confidence Interval:	95.0%	-	98.0%

PCT Results at 0.50 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.50 ng/mL	≤0.50 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.50 ng/mL	334	11	345
			≤0.50 ng/mL	12	238	250
			Total	346	249	595
Positive % Agreement	=	96.5%	95% Confidence Interval:	94.6%	-	98.5%
Negative % Agreement	=	95.6%	95% Confidence Interval:	93.0%	-	98.1%
Overall % Agreement	=	96.1%	95% Confidence Interval:	94.6%	-	97.7%

PCT Results at 2.00 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>2.00 ng/mL	≤2.00 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>2.00 ng/mL	228	9	237
			≤2.00 ng/mL	5	353	358
			Total	233	362	595
Positive % Agreement	=	97.9%	95% Confidence Interval:	96.0%	-	99.7%
Negative % Agreement	=	97.5%	95% Confidence Interval:	95.9%	-	99.1%
Overall % Agreement	=	97.6%	95% Confidence Interval:	96.4%	-	98.9%

Cross-Tabulation of concordance data for all samples (n=595) for Dimension® EXL™ LOCI® BRAHMS Procalcitonin versus Predicate for lot FB1218 (extended measuring interval)

Dimension EXL LOCI BRAHMS PCT (ng/mL)	B·R·A·H·M·S PCT sensitive KRYPTOR (ng/mL)					
	≤0.10	>0.10 - ≤0.25	>0.25 - ≤0.50	>0.50 - ≤2.00	>2.00	Total
≤0.10	49	11	0	0	0	60
>0.10 - ≤0.25	6	67	10	0	0	83
>0.25 - ≤0.50	0	10	85	12	0	107
>0.50 - ≤2.00	0	1	10	92	5	108
>2.00	0	0	0	9	228	237
Total	55	89	105	113	233	595

Concordance data for Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) lot FC1218 (extended measuring interval, 0.05-1000.00 ng/mL (0.05-1000.00 µg/L))

PCT Results at 0.10 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.10 ng/mL	≤0.10 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.10 ng/mL	526	6	532
			≤0.10 ng/mL	14	49	63
			Total	540	55	595
Positive % Agreement	=	97.4%	95% Confidence Interval:	96.1%	-	98.7%
Negative % Agreement	=	89.1%	95% Confidence Interval:	80.9%	-	97.3%
Overall % Agreement	=	96.6%	95% Confidence Interval:	95.2%	-	98.1%

PCT Results at 0.25 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.25 ng/mL	≤0.25 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.25 ng/mL	442	11	453
			≤0.25ng/mL	9	133	142
			Total	451	144	595
Positive % Agreement	=	98.0%	95% Confidence Interval:	96.7%	-	99.3%
Negative % Agreement	=	92.4%	95% Confidence Interval:	88.0%	-	96.7%
Overall % Agreement	=	96.6%	95% Confidence Interval:	95.2%	-	98.1%

PCT Results at 0.50 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>0.50 ng/mL	≤0.50 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>0.50 ng/mL	335	9	344
			≤0.50 ng/mL	11	240	251
			Total	346	249	595
Positive % Agreement	=	96.8%	95% Confidence Interval:	95.0%	-	98.7%
Negative % Agreement	=	96.4%	95% Confidence Interval:	94.1%	-	98.7%
Overall % Agreement	=	96.6%	95% Confidence Interval:	95.2%	-	98.1%

PCT Results at 2.00 ng/mL Cut-Off

				B·R·A·H·M·S PCT sensitive KRYPTOR		
				>2.00 ng/mL	≤2.00 ng/mL	Total
Dimension EXL LOCI BRAHMS PCT			>2.00 ng/mL	229	10	239
			≤2.00 ng/mL	4	352	356
			Total	233	362	595
Positive % Agreement	=	98.3%	95% Confidence Interval:	96.6%	-	100.0%
Negative % Agreement	=	97.2%	95% Confidence Interval:	95.5%	-	98.9%
Overall % Agreement	=	97.6%	95% Confidence Interval:	96.4%	-	98.9%

Cross-Tabulation of concordance data for all samples (n=595) for Dimension® EXL™ LOCI® BRAHMS Procalcitonin versus Predicate for lot FC1218 (extended measuring interval)

Dimension EXL LOCI BRAHMS PCT (ng/mL)	B·R·A·H·M·S PCT sensitive KRYPTOR (ng/mL)					
	≤0.10	>0.10 - ≤0.25	>0.25 - ≤0.50	>0.50 - ≤2.00	>2.00	Total
≤0.10	49	14	0	0	0	63
>0.10 - ≤0.25	6	64	9	0	0	79
>0.25 - ≤0.50	0	10	88	11	0	109
>0.50 - ≤2.00	0	1	8	92	4	105
>2.00	0	0	0	10	229	239
Total	55	89	105	113	233	595

13.10 Matrix Comparison

The matrix comparison study was conducted in accordance with CLSI EP09C-ED3 to evaluate the comparison between serum and plasma samples. A total of 76 matched sets (Serum, Lithium Heparin plasma, Sodium Heparin plasma, K2EDTA plasma, and K3EDTA plasma) spanning the assay range were evaluated, except for RST (rapid serum tubes) where 75 matched sets were evaluated. SST (serum separator tube) and RST were both included in this study. The SST was used as the control tube for comparison with all other tubes. Matched samples were spiked with equal amounts of recombinant procalcitonin (PCT) in order to span the assay range. No significant difference was observed based on Passing-Bablok regression analysis. Results are shown in the following table.

Specimen Type (x)	Comparison Specimen Type (y)	N	Sample range (ng/mL)	Regression Equation	Correlation Coefficient (r)
Serum (SST)	Serum (RST)	75	0.05-46.59	y = 1.00x + 0.00 ng/mL	0.998
Serum (SST)	Lithium Heparin	76	0.05-46.59	y = 0.99x + 0.00 ng/mL	0.997
Serum (SST)	Sodium Heparin	76	0.05-46.59	y = 0.98x + 0.01 ng/mL	0.998
Serum (SST)	K2EDTA	76	0.05-46.59	y = 0.99x + 0.00 ng/mL	0.996
Serum (SST)	K3EDTA	76	0.05-46.59	y = 1.00x + 0.01 ng/mL	0.996

14. Clinical Study

Not applicable

14.1 Reference Interval

The reference Interval for the B·R·A·H·M·S PCT sensitive KRYPTOR assay was verified for serum and plasma specimens from 33 apparently healthy individuals with the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay according to CLSI EP28-A3c. The reference interval claim in the Instructions For Use is <0.10 ng/mL [<0.10 µg/L].

15. Traceability and Value Assignment

An International Reference for PCT is not available. Values assigned to the Dimension EXL LOCI PCT CAL are traceable to a reference preparation of PCT. The standardization is maintained through patient-sourced internal standards verified using the B·R·A·H·M·S PCT sensitive KRYPTOR assay. Assigned values for calibrators are traceable to this standardization.

16. Clinical Cut-Off

Not applicable

17. Stability

Stability studies for Dimension® EXL™ LOCI® BRAHMS PCT reagents were conducted according to CLSI EP25-A.

17.1 Reagent Stability – Shelf Life

Real time shelf life stability studies are being conducted with three (3) Dimension® EXL™ LOCI® BRAHMS PCT reagent lots. Reagents are stored under normal storage conditions (refrigerated at 2-8°C) for the duration of the study. The studies are ongoing. At this time, two (2) lots have demonstrated 12 months of stability when stored at 2-8°C.

17.2 Reagent Stability – Calibration Interval

The calibration interval was evaluated with three (3) reagent lots. The results from these studies support a claim of 7 days for the calibration interval.

17.3 Reagent Stability – Unopened Onboard Stability

Unopened onboard stability was evaluated with two (2) reagent lots. The results from these studies support a claim of 30 days for the unopened product when stored onboard the instrument.

17.4 Reagent Stability – Opened Onboard Stability

Opened onboard stability was evaluated with three (3) reagent lots. The results from these studies support a claim of 3 days for the opened onboard (open-well) product.

17.5 Sample Stability

Sample stability was evaluated at multiple storage conditions to support storage and handling recommendations in the Instructions For Use. Specimens from the following tube types were prepared and tested at each medical decision level as well as near the upper limit of the assay range: serum (Serum Separator Tube (SST) and Rapid Serum Tube (RST)) and plasma (lithium heparin (Li Hep), sodium heparin (Na Hep), K2EDTA, and K3EDTA). All samples were prepared by spiking freshly drawn serum or plasma specimens with native PCT at the desired concentration levels.

The results from the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay sample stability studies support that serum (SST and RST) and plasma (Li Hep, Na Hep, K2EDTA, and K3EDTA) samples can be subjected to the following conditions and still generate accurate results when tested using the Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT) assay:

- Storage at room temperature (25°C) for up to 8 hours
- Storage at refrigerated temperature (2-8°C) for up to 24 hours
- Storage at frozen temperature (-70°C) for up to 90 days
- Storage at frozen temperature (-20°C) for up to 90 days
- Freeze-thawed up to 6 cycles
- On the instrument (sample wheel) for up to 1 hour before processing

18. Proposed Labeling

The labeling is sufficient and it meets the requirements of 21 CFR Parts 801 and 809, as applicable and the special controls for this device under 21 CFR 866.3215.

19. Conclusion

The results from the performance studies support that the Candidate Device**,** Dimension® EXL™ LOCI® BRAHMS Procalcitonin (PCT), is substantially equivalent to the Predicate Device, B·R·A·H·M·S PCT sensitive KRYPTOR (DEN150009 / K171338).