December 10, 2017

Fujirebio Diagnostics, Inc.
Stacey Dolan
Manager, Regulatory Affairs
201 Great Valley Parkway
Malvern, Pennsylvania 19355

Re: K172713
Trade/Device Name: Lumipulse G B•R•A•H•M•S PCT Immunoreaction Cartridges, Lumipulse G B•R•A•H•M•S PCT Calibrators set
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 7, 2017
Received: September 8, 2017

Dear Stacey Dolan:

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

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

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

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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

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

Sincerely,

Kristian M. Roth -S For:

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K172713

Device Name
Lumipulse G B•R•A•H•M•S PCT Immunoreaction Cartridges
Lumipulse G B•R•A•H•M•S PCT Calibrators set

Indications for Use *(Describe)*
Lumipulse G B•R•A•H•M•S PCT Immunoreaction Cartridges:

The Lumipulse G B•R•A•H•M•S PCT is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of PCT (procalcitonin) in human serum and plasma (sodium heparin, lithium heparin, sodium citrate or dipotassium EDTA) on the LUMIPULSE G System.

Used in conjunction with other laboratory findings and clinical assessments, Lumipulse G B•R•A•H•M•S PCT is intended for use 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.
• 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.
• 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.
• Aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

Lumipulse G B·R·A·H·M·S PCT Calibrators set

Lumipulse G B·R·A·H·M·S PCT Calibrators set is for in vitro diagnostic use in the calibration of Lumipulse G B·R·A·H·M·S PCT on the LUMIPULSE G System.

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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Section 5 510(k) SUMMARY

Lumipulse® ***G*** PCT

Date: December 6, 2017

A. 510(k) Number:
K172713

B. Purpose of Submission:
New device

C. Measurand:
Procalcitonin

D. Type of Test:
Quantitative assay, automated chemiluminescent enzyme immunoassay (CLEIA)

E. Applicant:

Submitter: Fujirebio Diagnostics, Inc.
201 Great Valley Parkway
Malvern, PA 19355

Contact Person: Stacey Dolan
Manager, Regulatory Affairs
Phone: (610) 240-3843
Fax: (610) 240-3803
Email: dolans@fdi.com

F. Proprietary and Established Names:
Lumipulse® ***G*** B•R•A•H•M•S PCT

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.3215

2. Classification:
   Class II

3. Product codes:
   PRI, NTM, PMT

4. Panel:
   83, Microbiology

H. Intended Use:

1. Intended Use:

Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges

The Lumipulse ***G*** B•R•A•H•M•S PCT is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of PCT (procalcitonin) in human serum and plasma (sodium heparin, lithium heparin, sodium citrate or dipotassium EDTA) on the LUMIPULSE ***G*** System.

Used in conjunction with other laboratory findings and clinical assessments, Lumipulse ***G*** B•R•A•H•M•S PCT is intended for use 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.
- 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.
- 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.
- Aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

Lumipulse ***G*** B•R•A•H•M•S PCT Calibrators Set

Lumipulse ***G*** B•R•A•H•M•S PCT Calibrators set are for in vitro diagnostic use in the calibration of LUMIPULSE ***G*** B•R•A•H•M•S PCT on the LUMIPULSE ***G*** System.

2. Indications for use:
   Same as Intended Use.

3. Special conditions for use statement(s):
   Prescription use only.

4. Special instrument requirements:
   LUMIPULSE ***G***1200 System

I. Device Description:

Lumipulse ***G*** B•R•A•H•M•S PCT is an assay system, including a set of immunoassay reagents, for the quantitative measurement of PCT in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G***1200 System.

Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges: IRC 235058.
The Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges consists of 3 × 14 tests.
Each kit contains the following:

1.) Antibody-Coated Particle Solution
(Liquid when used, 250 µL/Immunoreaction Cartridge) Contains 150 µg/mL anti-PCT monoclonal antibody (mouse) and anti-calcitonin monoclonal antibody (mouse) coated particles, protein stabilizers (bovine and mouse) and chemical stabilizers in 0.15 M sodium chloride/Tris buffer. This solution contains gelatin and turns into gel at 15°C or lower. Preservative: sodium azide.

2.) Enzyme-Labeled Antibody Solution
(Liquid, 350 µL/Immunoreaction Cartridge)
Contains 0.25 µg/mL alkaline phosphatase (ALP: calf)-labeled anti-katacalcin monoclonal antibody (mouse), protein stabilizers (bovine, calf and mouse) and chemical stabilizers in 0.1 M sodium chloride/MES buffer. Preservative: sodium azide.

Lumipulse ***G*** B•R•A•H•M•S PCT Calibrators set CAL SET 234150, Lyophilized, 2 × 2 Concentrations
Each calibrator kit contains one bottle each of Calibrators 1 – 2, and Reconstituting Solution. The calibrator kit is packaged separately.

CAL 1 0 ng/mL PCT calibrator (2 × 0.5 mL/vial)
CAL 2 100 ng/mL PCT calibrator (2 × 0.5 mL/vial)
Contains procalcitonin in 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: ProClin 300.

RS Reconstituting Solution: Liquid, 1 × 10 mL
Preservative: sodium azide.

These calibrators are lyophilized and have to be prepared by adding exactly 0.5 mL of Reconstituting Solution to each lyophilized calibrator.

J. Substantial Equivalence:

1. Predicate device name(s):
   B•R•A•H•M•S PCT sensitive KRYPTOR®

2. Predicate 510(k) number(s):
   k171338

3. Comparison with predicate:

Comparison between the Lumipulse® *G* B•R•A•H•M•S PCT and B•R•A•H•M•S PCT sensitive KRYPTOR®

Similarities and Differences		
	Lumipulse® *G* B•R•A•H•M•S PCT (Proposed Device)	**B•R•A•H•M•S PCT sensitive KRYPTOR® (Predicate Device) K171338**
Device Type	*In vitro* diagnostic	Same
Classification	Class II	Same

Similarities and Differences		
	Lumipulse® *G* B•R•A•H•M•S PCT (Proposed Device)	**B•R•A•H•M•S PCT sensitive KRYPTOR® (Predicate Device) K171338**
Analyte	Procalcitonin	Same
Regulation Number	21CFR § 866.3215; Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis	Same
Product Usage	Clinical and Hospital laboratories	Same
Principle of Operation	Automated Quantitative Chemiluminscent Enzyme Immunoassay (CLEIA)	Time-Resolved Amplified Cryptate Emission (TRACE)
Specimen Collection Method	Routine Phlebotomy Techniques	Same
Intended Use	The Lumipulse ***G*** B•R•A•H•M•S PCT is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of PCT (procalcitonin) in human serum and plasma (sodium heparin, lithium heparin, sodium citrate or dipotassium EDTA) on the LUMIPULSE ***G*** System. Used in conjunction with other laboratory findings and clinical assessments, Lumipulse ***G*** B•R•A•H•M•S PCT is intended for use 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. • 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	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®

Similarities and Differences		
	Lumipulse® *G* B•R•A•H•M•S PCT (Proposed Device)	**B•R•A•H•M•S PCT sensitive KRYPTOR® (Predicate Device) K171338**
	department or other medical wards prior to ICU admission, using a change in PCT level over time. • 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. • Aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.	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

Similarities and Differences		
	Lumipulse® *G* B•R•A•H•M•S PCT (Proposed Device)	**B•R•A•H•M•S PCT sensitive KRYPTOR® (Predicate Device) K171338**
		obstructive pulmonary disease (AECOPD), • to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.
Instrument System	LUMIPULSE ***G*** System	The BRAHMS KRYPTOR analyzer
Assay Type	Two-step sandwich immunoassay based on chemiluminescent technology	Immunofluorescent assay
Type of Specimen	Human serum and plasma (sodium heparin, lithium heparin, sodium citrate or dipotassium EDTA)	Human serum and plasma (EDTA, heparin)
Assay Range	0.020 - 100 ng/mL	0.02-5000ng/mL
Sample Volume	60 µl	50µl

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

- CLSI EP5-A3 - Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP7-A2 - Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition
- CLSI EP28-A3c - Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition
- CLSI EP17-A2 - Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline Second Edition
- CLSI EP6-A - Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP9-A3 – Measurement Procedure Comparison and Bias Estimation Using Patient Samples; approved Guideline – Third Edition
- CLSI EP25-A – Evaluation of Stability of *In Vitro* Diagnostic Reagents: Approved Guideline
- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff
- Test Principle: Guidance for Industry and Food and Drug Administration Staff - eCopy Program for Medical Device Submissions (December 31, 2012)

- Guidance for Industry and Food and Drug Administration Staff - Refuse to Accept Policy for 510(k)s (August 4, 2015)

L. Test Principle:

Lumipulse ***G*** B•R•A•H•M•S PCT is an assay system, including a set of immunoassay reagents, for the quantitative measurement of PCT in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G***1200 System.
PCT in specimens specifically binds to anti-PCT monoclonal antibody (mouse) and anti-calcitonin monoclonal antibody (mouse) on the particles, and antigen-antibody immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase (ALP: calf)-labeled anti-katacalcin monoclonal antibody (mouse) specifically binds to PCT of the immunocomplexes on the particles, and additional immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Substrate Solution is added and mixed with the particles. AMPPD contained in the Substrate Solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of PCT.

M. Performance Characteristics

Data were generated using the LUMIPULSE ***G***1200 System.

1. Analytical performance:

   a. *Precision/Reproducibility:*

      20 Day

      The results of the 20-day precision calculations for Lumipulse ***G*** B•R•A•H•M•S PCT performed at FDI are shown below:
      - Lot A ICs/Lot A Calibrators for Control Levels 1-3 and Panels 1-6
      - Lot D ICs/Lot D Calibrators for Panels 7 and 8

      The analyses determined the total precision for the Lumipulse ***G*** B•R•A•H•M•S PCT assay to be ≤ 4.7%. The total precision of the Lumipulse ***G*** B•R•A•H•M•S PCT for the eight (8) panels ranged from 1.8% to 3.1%. The total precision of the Lumipulse ***G*** B•R•A•H•M•S PCT for the three (3) controls ranged from 3.3% to 4.7%. The precision of all controls and panels for the 20-day Precision Study met the acceptance criteria of a CV ≤ 10%.

Summary for FDI 20-day Precision (n=80 for each sample) for Lot A (Controls and Panels 1-6) and Lot D (Panels 7 and 8)

		Within-Run (Repeatability)		Between Run		Between-Day		Within-Laboratory (Total)	
Sample	**Mean (ng/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	0.662	0.010	1.6%	0.026	3.9%	0.014	2.1%	0.031	4.7%
Control Level 2	3.911	0.045	1.2%	0.129	3.3%	0.026	0.7%	0.139	3.6%
Control Level 3	14.978	0.163	1.1%	0.393	2.6%	0.245	1.6%	0.490	3.3%
Panel 1	0.300	0.005	1.6%	0.004	1.5%	0.003	1.0%	0.007	2.4%
Panel 2	2.219	0.032	1.5%	0.016	0.7%	0.027	1.2%	0.045	2.0%
Panel 3	12.323	0.129	1.0%	0.144	1.2%	0.098	0.8%	0.217	1.8%
Panel 4	36.217	0.379	1.0%	0.308	0.8%	0.445	1.2%	0.661	1.8%
Panel 5	54.132	0.596	1.1%	0.529	1.0%	0.642	1.2%	1.024	1.9%
Panel 6	80.361	1.265	1.6%	0.879	1.1%	0.632	0.8%	1.666	2.1%
Panel 7	0.112	0.002	2.0%	0.002	2.2%	0.001	1.1%	0.004	3.1%
Panel 8	0.534	0.010	1.9%	0.008	1.5%	0.003	0.6%	0.013	2.5%

Lot-To-Lot Reproducibility for Combined Data

The precision analyses for the combined lot-to-lot analysis for Lots A, B and C determined the total precision for Lumipulse ***G*** PCT to be ≤ 5.3% in this study. The total precision for Lumipulse ***G*** B•R•A•H•M•S PCT to be ≤ 3.0% for the six (6) panels. The total precision for Lumipulse ***G*** PCT to be ≤ 5.3% for the three (3) controls. The total precision of Lumipulse ***G*** B•R•A•H•M•S PCT ranged from 1.8% to 5.3%. The between-lot precision for Lumipulse ***G*** B•R•A•H•M•S PCT was ≤ 6.5%.

The precision of controls and panels for the lot-to-lot reproducibility met the targeted acceptance criteria of a CV ≤ 10%.

Summary of the Lot-to-Lot Reproducibility for the Combined Data for Lots A, B and C (n=120 for each sample)

		Between Lots		Between Day		Between Run		Within Runs (Repeatability)		Within-Laboratory (Total)	
Sample	**Mean (ng/L)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	0.634	0.030	4.7%	0.013	2.0%	0.030	4.7%	0.009	1.4%	0.033	5.3%
Control Level 2	3.816	0.137	3.6%	0.016	0.4%	0.127	3.3%	0.055	1.4%	0.139	3.7%
Control Level 3	14.875	0.313	2.1%	0.141	0.9%	0.434	2.9%	0.164	1.1%	0.487	3.3%
Panel 1	0.290	0.012	4.3%	0.004	1.3%	0.006	2.0%	0.005	1.8%	0.009	3.0%
Panel 2	2.163	0.075	3.4%	0.021	1.0%	0.038	1.8%	0.026	1.2%	0.048	2.2%
Panel 3	12.332	0.320	2.6%	0.221	1.8%	0.133	1.1%	0.122	1.0%	0.280	2.3%
Panel 4	38.147	2.280	6.0%	0.363	1.0%	0.467	1.2%	0.367	1.0%	0.701	1.8%
Panel 5	57.114	3.392	5.9%	0.856	1.5%	0.625	1.1%	0.674	1.2%	1.248	2.2%
Panel 6	86.233	5.585	6.5%	1.018	1.2%	1.138	1.3%	1.489	1.7%	2.141	2.5%

Site to Site Reproducibility for Combined Data

The precision analyses for the combined site-to-site analysis for Lots A determined the total precision for Lumipulse ***G*** B•R•A•H•M•S PCT to be ≤ 4.9% in this study. The total precision for Lumipulse ***G*** B•R•A•H•M•S PCT to be ≤ 4.8% for the six (6) panels. The total precision for Lumipulse ***G*** PCT to be ≤ 4.9% for the three (3) controls. The total precision of Lumipulse ***G*** B•R•A•H•M•S PCT ranged from 2.9% to 4.9%. The between-site precision for Lumipulse ***G*** B•R•A•H•M•S PCT was ≤ 4.7%.

The precision of the controls and panels for the site-to-site reproducibility met the targeted acceptance criteria of a CV ≤10%.

Summary of the Site-to-Site Reproducibility for the Combined Data for Lot A (n=120 for each panel)

		Between Sites		Between Days		Between Runs		Within Runs (Repeatability)		Reproducibility (Total)	
Sample	**Mean (ng/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	0.647	0.019	2.9%	0.023	3.5%	0.020	3.0%	0.012	1.8%	0.032	4.9%
Control Level 2	3.872	0.077	2.0%	0.109	2.8%	0.096	2.5%	0.054	1.4%	0.149	3.8%
Control Level 3	15.062	0.085	0.6%	0.337	2.2%	0.312	2.1%	0.166	1.1%	0.481	3.2%
Panel 1	0.291	0.008	2.8%	0.008	2.7%	0.010	3.6%	0.005	1.9%	0.014	4.8%
Panel 2	2.170	0.033	1.5%	0.049	2.3%	0.061	2.8%	0.032	1.5%	0.075	3.5%
Panel 3	12.297	0.375	3.0%	0.222	1.8%	0.417	3.4%	0.170	1.4%	0.485	3.9%
Panel 4	37.074	1.303	3.5%	0.586	1.6%	1.182	3.2%	0.361	1.0%	1.354	3.6%
Panel 5	55.428	2.043	3.7%	1.144	2.1%	1.385	2.5%	0.613	1.1%	1.846	3.3%
Panel 6	82.850	3.868	4.7%	1.006	1.2%	1.719	2.1%	1.285	1.6%	2.365	2.9%

b. Linearity/assay reportable range:

Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System demonstrated linearity in a study consistent with the guidelines in the CLSI Protocol EP6-A.9) High and low sample pools were created using patient serum samples that contained naturally expressed PCT. The linearity was found in the range of 0.010 ng/mL to 104.260 ng/mL. Lumipulse G B•R•A•H•M•S PCT correlated with expected concentrations according to the linear regression formula:

- y= 0.008734 + 0.856577; R-squared: 0.9979

High dose effect is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For Lumipulse ***G*** B•R•A•H•M•S PCT on the LUMIPULSE ***G***1200 System, no high dose effect was observed for samples containing approximately 12,000 ng/mL of PCT.

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

Calibration of the Lumipulse ***G*** B·R·A·H·M·S PCT is traceable to in-house reference calibrators, whose values have been assigned to correlate to Thermo Fisher Scientific Inc.'s B·R·A·H·M·S PCT sensitive Kryptor.

Cal Set Contains Cal 1 and Cal 2 (2 x 0.5 mL/vial) and Reconstituting Solution (1 x 10 mL). Preservative: ProClin 300. The calibrators are at the following concentrations:

Calibrator Level	PCT Concentration (ng/mL)
CAL 1	0
CAL 2	100

Master calibration data are recorded in a two-dimensional bar code on the Lumipulse G B•R•A•H•M•S PCT Immunoreaction Cartridge case. The calibration curve is created based on the recorded master calibration data and measured calibration data. The PCT concentration of a specimen is automatically calculated from the calibration curve. The result of the calculation is reported in ng/mL.

Shelf life

The shelf life for Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges and the Lumipulse ***G*** B•R•A•H•M•S PCT Calibrators is 6 months at 2–10°C.

On board the LUMIPULSE ***G***1200

The Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges are sealed unit dose stored at 2-10°C. To reduce risk for any misuse, the package insert states *The* Lumipulse ***G*** B•R•A•H•M•S PCT *Cartridges can be stored on-board the LUMIPULSE* ***G*** *System for a maximum of 30 days.*

The package insert recommends calibrator curve storage on the LUMIPULSE ***G***1200 for a maximum of 30 days.

Transport Conditions

Lumipulse ***G*** B•R•A•H•M•S PCT Immunoreaction Cartridges and the Lumipulse ***G*** B•R•A•H•M•S PCT Calibrators are shipped at 2-10°C.

Materials will be shipped to the end user using an insulated container and a predetermined configuration of gel (cold and/or frozen) packs to maintain the product for up to 72 hours when stored at ambient temperature.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) of Lumipulse ***G*** B•R•A•H•M•S PCT on the LUMIPULSE ***G***1200 System is ≤0.0114 ng/mL.

1) LoB and LoD

   The LoB for Lumipulse ***G*** B•R•A•H•M•S PCT was 0.0095 ng/mL. The LoD for Lumipulse ***G*** PCT on the LUMIPULSE ***G***1200 System was 0.0114 ng/mL, determined consistent with the guidelines in the CLSI Protocol EP17-A2, Seven low level specimens were tested over 3 days using two LUMIULSE ***G***1200 Systems and two Lumipulse G PCT lots giving 120 determinations per panel.

2) LoQ

The LoQ for Lumipulse ***G*** B•R•A•H•M•S PCT on the LUMIPULSE ***G***1200 System was 0.0114 ng/mL, determined consistent with the guidelines in the CLSI Protocol EP17-A2.

A modeling analysis was conducted to evaluate the LOQ and for each lower cut-off (i.e., 0.10 ng/mL and 0.25 ng/mL). The Max % Total Error, % bias and %CV were calculated, see below.

TE ≤ 11.4% at 0.25 ng/mL (with a % bias ≤ -5.7% and a precision CV ≤ 2.8%)

TE ≤ 14.1% at 0.10 ng/mL (with a % bias ≤ -9.2% and a precision CV ≤ 2.5%)

e. Analytical specificity:

Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System demonstrated an average interference of ≤10% (for each compound) in a study consistent with the guidelines in the CLSI Protocol EP7-A2 Human serum specimen pools with procalcitonin concentrations of approximately 0.25 and 2.0 ng/mL were supplemented with potentially interfering compounds. The following compounds were tested using Lumipulse G B•R•A•H•M•S PCT and found not to interfere with the assay.

Endogenous Interferences	**Test Concentration**
Free Bilirubin (unconjugated)	50 mg/dL
Conjugated Bilirubin	50 mg/dL
Hemoglobin	400 mg/dL
Total Protein (Human Serum Albumin)	12 g/dL
Triglycerides (Intralipid 20% Emulsion)	2500 mg/dL
Immunoglobulin G (IgG)	5 g/dL
Biotin	19.7 mg/dL
Human Anti-Mouse Antibodies (HAMA)	1,000 ng/mL
Rheumatoid Factor (RF)	1,000 IU/mL

Therapeutic Drug Interferences	**Test Concentration (mg/dL)**
Acetaminophen	20.01
Acetylsalicylic Acid	65.22
1% Ethanol	789.00
Azithromycin	2.00
Caffeine	6.00
Celecoxib	24.00
Cetirizine HCl	0.55
Dextromethorphan	0.10
Dobutamine	1.13
Dopamine	13.00
Doxycycline	5.00
Epinephrine	0.18
Furosemide	2.00
Heparin	8000.00
Ibuprofen	50.03
Imipenem	118.00
Levofloxacin	2.93

Loratadine	0.05
Nicotine	0.10
Noradrenaline (norepinephrine)	0.20
Oxymetazoline HCl	0.09
Phenylephrine	6.00
Prednisolone	0.30
Salmeterol	0.006
Tiotropium	0.0022
Vancomycin	300.00

Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System was evaluated for cross-reactivity of the assay with other substances that are similar in structure to PCT in a study consistent with the guidelines in the CLSI Protocol EP7-A2. Human serum specimens with PCT concentrations of approximately 0.1, 0.25, 0.5, 2.0 and 80 ng/mL were supplemented with potentially cross-reacting compounds. The compounds were tested at the concentrations listed below and found to have the following percent cross-reactivity:

Cross-reactant	Test Concentration	Mean % Cross Reactivity
Human Calcitonin	10 ng/mL	-0.346%
Human Katacalcin	10 ng/mL	0.076%
α-CGRP	10,000 ng/mL	0.002%
β-CGRP	10,000 ng/mL	0.001%
Salmon Calcitonin	13.2 µg/mL	-0.001%
Eel Calcitonin	7.5 µg/mL	-0.001%

f. Assay cut-off:
See Clinical Cutoff in 4 below.

2. Comparison studies:

a. Method Comparison

The Lumipulse G B•R•A•H•M•S PCT method comparison was performed on the LUMIPULSE G1200 System in a study consistent with the guidelines in CLSI Protocol EP09-A3.

The weighted Deming regression method was used to compare Lumipulse G B•R•A•H•M•S PCT to B•R•A•H•M•S PCT sensitive KRYPTOR. The lithium heparin specimens tested ranged from 0.054-58.156 ng/mL for Lumipulse G B•R•A•H•M•S PCT. The data are summarized in the following table.

Lumipulse *G* B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR				
n	**Correlation Coefficient (r)**	**Intercept (95% CI)**	**Slope (95% CI)**	**Mean Difference (ng/mL)**
207	0.9535	-0.0044 (-0.0223 to	1.0199 (0.9633 to	0.185

	0.0135)	1.0765)

b. Matrix Comparison

The Lumipulse ***G*** B•R•A•H•M•S PCT matrix comparison study was performed to evaluate the difference across tube types (SST, K2EDTA, Lithium Heparin, Sodium Heparin, and Sodium Citrate) versus the means of the control samples (Red top serum) analyzed per CLSI guideline EP9-A3. The slope for each tube type when compared to the control had 95% confidence intervals that lay entirely within the range 0.9 to 1.1 and the correlation coefficients were ≥ 0.9.

3. Clinical studies:

a. Clinical sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

See Expected Values below.

5. Expected values/Reference range**:**

In a population of 213 self-reported healthy individuals, the 95th percentile, upper reference range limit was calculated at 0.045 ng/mL.

It is recommended that each laboratory establish its own range, which may be unique to the population it serves depending upon geographical, patient, and environmental factors.

N. Proposed Labeling

The labeling satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion

The results of these analytical (nonclinical) and clinical studies demonstrate that the Lumipulse ***G*** B•R•A•H•M•S PCT assay is substantially equivalent to the performance of the B•R•A•H•M•S PCT sensitive KRYPTOR.