510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K172713

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Lumipulse G B•R•A•H•M•S PCT Immunoreaction Cartridges, Lumipulse G B•R•A•H•M•S PCT Calibrators set

C. Measurand:

Procalcitonin (PCT)

D. Type of Test:

Chemiluminescent Enzyme Immunoassay (CLEIA)

E. Applicant:

Fujirebio Diagnostics, Inc. (FDI)

F. Proprietary and Established Names:

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

G. Regulatory Information:

1. Regulation section:

   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

2. Classification:

   Class II (Special Controls)

3. Product codes:

   PRI, PMT, NTM

4. Panel:

   83 - (Microbiology)

H. Intended Use:

1. Intended use(s):

   See Indications for Use.

2. Indication(s) for 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 is for in vitro diagnostic use in the calibration of Lumipulse G B·R·A·H·M·S PCT on the LUMIPULSE G System.

3. Special conditions for use statement(s):

   For prescription use.

4. Special instrument requirements:

   All data were generated using the LUMIPULSE G1200 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 G1200 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 (IC) consists of 3 × 14 tests.

Each kit contains the following:

- 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

- 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

Each calibrator kit contains one bottle each of Calibrators 1, 2, and Reconstituting Solution. These calibrators are lyophilized and are prepared by adding exactly 0.5 mL of Reconstituting Solution to each lyophilized calibrator. 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

Materials Required - Not Provided:

- Control materials: Controls are not provided
  NOTE: Lumipulse G B•R•A•H•M•S PCT Package insert indicates ‘Use control materials with at least two levels (e.g. low and high)’
  Premarket studies used three Thermo Scientific MAS Omni•CARDIOControls (k122291).
  o Level 1: 0.22 to 0.42 ng/mL
  o Level 2: 1.49 to 2.77 ng/mL
  o Level 3: 6.81 to 12.65 ng/mL
- Purified water
- Micropipettes
- Recommended sample cups; refer to the LUMIPULSE G System Operation Manual.

J. Substantial Equivalence Information:

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:

Similarities		
Item	Device Lumipulse G B•R•A•H•M•S PCT K172713	Predicate B•R•A•H•M•S PCT sensitive KRYPTOR K171338
Device Type	In vitro diagnostic	Same
Classification	Class II	Same
Analyte	Procalcitonin	Same
Regulation	21CFR § 866.3215; Device to detect and measure nonmicrobial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis	Same
Specimen Collection Method	Routine Phlebotomy Techniques	Same
Indications for 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	The B·R·A·H·M·S PCT sensitive KRYPTOR is an immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE) technology to determine the concentration of PCT (procalcitonin) in human serum and EDTA or heparin plasma. The B·R·A·H·M·S PCT sensitive KRYPTOR is intended to be performed on the B·R·A·H·M·S KRYPTOR analyzer family. Used in conjunction with other laboratory findings and clinical assessments. B·R·A·H·M·S PCT sensitive KRYPTOR is intended for use as follows: • to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock, • to determine the change in PCT level

Similarities		
Item	Device Lumipulse G B•R•A•H•M•S PCT K172713	Predicate B•R•A•H•M•S PCT sensitive KRYPTOR K171338
	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.	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.

Differences		
Item	Device Lumipulse G B•R•A•H•M•S PCT K172713	Predicate B•R•A•H•M•S PCT sensitive KRYPTOR K171338
Principle of Operation	Automated Quantitative Chemiluminescent Enzyme Immunoassay (CLEIA)	Time-Resolved Amplified Cryptate Emission (TRACE)
Instrument System	LUMIPULSE G System	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 G1200 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 (3-(2'-Spiroadamantane)-4-Methoxy-4-(3"-Phosphoryloxy) Phenyl- 1, 2-Dioxetane Disodium Salt) 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 (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Prior to the precision study, technicians were required to pass a 3-day (Lot A and B) and 1-day (Lot D) Familiarization Study to demonstrate proficiency on Lumipulse G PCT.

   Eight panels (five native serum and three recombinant) were tested in duplicate. Thermo Scientific MAS Omni•CARDIO Controls were also tested for validity and precision. The results of the 20-day precision calculations for Lumipulse G B•R•A•H•M•S PCT performed at

Fujirebio Diagnostics, Inc are shown below:

- Lot A Immunoreaction Cartridges (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 CV for the within laboratory precision of the Lumipulse G B•R•A•H•M•S PCT for the eight (8) panels CV ranged from 1.8% to 3.1%. The CV for the within laboratory 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%. The results of the 20-day precision calculations for Lumipulse G B•R•A•H•M•S PCT are shown in Table 1 below:

Table 1: 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 CV for the within laboratory reproducibility for Lumipulse G B•R•A•H•M•S PCT to be ≤ 5.3% in this study. The CV for the within laboratory reproducibility for Lumipulse G B•R•A•H•M•S PCT was determined to be ≤ 3.0% for the panels 1-6. The CV for the within laboratory reproducibility for Lumipulse G B•R•A•H•M•S PCT was determined to be ≤ 5.3% for the three (3) controls. The CV for the within laboratory reproducibility of Lumipulse G B•R•A•H•M•S PCT ranged from 1.8% to 5.3%. The CV for the between-lot reproducibility for Lumipulse G B•R•A•H•M•S PCT was ≤ 6.5%. See Table 2 below.

Table 2: Summary of the Lot-to-Lot Reproducibility for the Combined Data for Lots A, B, 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 reproducibility analyses for the combined site-to-site analysis for Lot A determined the CV for the total reproducibility for Lumipulse G B•R•A•H•M•S PCT to be ≤ 4.9% in this study. The CV for the reproducibility for Lumipulse G B•R•A•H•M•S PCT was determined to be ≤ 4.8% for the six (6) panels. The CV for the reproducibility for Lumipulse G B•R•A•H•M•S PCT was determined to be ≤ 4.9% for the three (3) controls. The CV for the reproducibility of Lumipulse G B•R•A•H•M•S PCT ranged from 2.9% to 4.9%. The CV for the between site reproducibility for Lumipulse G B•R•A•H•M•S PCT was ≤ 4.7%. Results are summarized in Table 3 below.

Table 3: 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:

Dilutions targeted the top of the measurement range of the Lumipulse G B•R•A•H•M•S PCT assay (~120 ng/mL) and went below the LOQ (<0.020 ng/mL). Eleven separate dilutions of the High Serum Pool (HSP) by the Low Serum Pool (LSP) were prepared. Undiluted High and Low serum pools were tested as sample 1 and sample 13 in the dilution series 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. Lumipulse G B•R•A•H•M•S PCT assay was shown to be linear within the actual test results of 0.010 ng/mL to 104.260 ng/mL and supports the claimed Lumipulse G B•R•A•H•M•S PCT measurement range of 0.020 ng/mL – 100.000 ng/mL. Results are summarized in Table 4 below.

Table 4: Linearity

Dilution	Target value (ng/mL)	Mean measured value (ng/mL)	SD (ng/mL)	CV %
1	120	104.260*	2.990	2.9
2	100	86.680	0.529	0.6
3	80	70.449	0.693	1.0
4	60	53.370	0.347	0.7
5	40	35.961	0.100	0.3
6	20	17.555	0.617	3.5
7	10	8.015	0.125	1.6
8	5	4.087	0.085	2.1
9	2	1.613	0.011	0.7
10	0.481	0.424	0.009	2.0
11	0.241	0.228	0.002	0.8
12	0.121	0.111	0.001	1.3
13	0.001	0.010	0.001	6.1

The statistical evaluation of linearity was determined using EP6-A. Linear, quadratic and cubic regressions were fitted. Lumipulse G B•R•A•H•M•S PCT correlated with expected concentrations according to the linear regression formula: $y = 0.008734 + 0.856577x$; $R2 = 0.9979$.

Dilution Verification

A dilution verification study was performed to compare and assess manual dilution and automated (on-board) dilution for Lumipulse G B•R•A•H•M•S PCT. Three specimens (neat, manually diluted 1:10, manually diluted 1:32, automated 1:10) were tested in triplicate. Manual dilutions performed at 1:32 are not recommended for Lumipulse G B·R·A·H·M·S PCT. Automated dilutions for 1:100, 1:200, and 1:1000 on the LUMIPULSE G1200 System can cause erroneous results and should not be used when a specimen exceeds the 100 ng/mL.

Manual dilutions and automated dilutions performed at 1:10 are recommended for Lumipulse G B•R•A•H•M•S PCT.

Spike and Recovery

Three individual apparently healthy serum samples were spiked and compared to the diluent with the identical concentration. Percent recovery was calculated as follows for individual spiked samples and was found to be within 100 ± 10% for all samples tested. See study results in Table 5 below.

- % Recovery = (Mean Measured Natural Test Sample Matrix Concentration (ng/mL) - Endogenous Sample Concentration/Mean Measured Specimen Diluent 1 Concentration (ng/mL)) x 100%

Table 5: Spike and Recovery.

	Sample ID	Sample Mean (ng/ml)	Diluent (ng/ml)	Recovery (%)
Serum Sample 1	Endogenous	0.011	0	
	2	0.097	0.091	95
	3	0.223	0.223	95
	4	0.445	0.455	95
	5	1.67	1.719	97
	6	8.885	9.073	98
	7	30.317	31.553	96
	8	44.417	45.649	97
	9	63.408	63.252	100
	10	86.949	82.587	105
Serum Sample 2	Endogenous	0.016	0.000	
	2	0.099	0.091	91
	3	0.22	0.223	91
	4	0.433	0.455	92
	5	1.684	1.719	97
	6	8.83	9.073	97
	7	28.963	31.553	92
	8	45.224	45.649	99
	9	62.08	63.252	98
	10	86.22	82.587	104
Serum Sample 3	Endogenous	0.008	0.000	
	2	0.096	0.091	97
	3	0.225	0.223	97
	4	0.44	0.455	95
	5	1.661	1.719	96
	6	8.75	9.073	96
	7	30.363	31.553	96
	8	45.014	45.649	99
	9	61.666	63.252	97
	10	84.661	82.587	103

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

Traceability:

Lumipulse G B·R·A·H·M·S PCT values are expressed as ng/mL, and are related to a Fujirebio Inc. maintained reference preparation. The calibrators for the Lumipulse G B·R·A·H·M·S PCT product are manufactured gravimetrically and are traceable to B·R·A·H·M·S PCT sensitive Kryptor.

Master calibration data is 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 recorded master calibration data and the 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.

Recalibration is required after a pre-determined calibration interval, when 30 days have elapsed since the previous calibration; quality control results fall out of range or when a new Lumipulse G B·R·A·H·M·S PCT Immunoreaction Cartridge lot is loaded.

Reagent Stability:

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. The shelf-life stability protocols and acceptance criteria were reviewed and found to be acceptable.

On-Board Immunoreaction Cartridge Stability Study

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

On Board Sample Stability Study

A study was performed to establish stability claims for the stability of samples on-board the LUMIPULSE G1200 instrument using Lumipulse G B·R·A·H·M·S PCT. Samples have an on-board stability up to 3 hours.

Reagent 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 are 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.

Sample Stability Study

The purpose of this study was to establish the stability of serum and plasma samples for Lumipulse G B·R·A·H·M·S PCT. The following information regarding sample stability are provided in Table 6 and will be included in the final labeling.

Table 6: Sample Stability

Tube	Condition 1 (25°C ±2°C)	Condition 2 (2°C-10°C)	Condition 3 (25°C ±2°C *)
SST	7 Hours	2 Days	3 Hours
Red Top	4 Hours	1 Day	7 Hours
K_2EDTA, Lithium Heparin, Sodium Heparin, and Sodium Citrate	1 Day	2 Days	8 Hours

*Samples were tested after the draw (after introduction of PCT spike) while kept on-the-clot/separator/cells.

Sample Freeze Thaw Stability Study

A study to establish the maximum number of freeze thaw cycles acceptable for samples being measured by Lumipulse G B·R·A·H·M·S PCT assay was performed. Specimens can be frozen and thawed up to and including 3 freeze thaw cycles for the Lumipulse G B·R·A·H·M·S PCT for the following tube types: SST Serum, Red Top Serum, K_2EDTA Plasma, Sodium Heparin Plasma, Lithium Heparin Plasma, and Sodium Citrate Plasma.

d. Detection limit:

The LoB, LoD and LoQ were determined using methods consistent with the guidelines in the CLSI protocol EP17-A2.

The LoB for Lumipulse G B•R•A•H•M•S PCT was 0.0095 ng/mL. The LoD for Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System was 0.0114 ng/mL. Seven low level specimens were tested over three days using two LUMIULSE G1200 Systems and two Lumipulse G B•R•A•H•M•S PCT lots for a total of 120 determinations per panel.

The LoQ for Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System was 0.0114 ng/mL. The % Total Error (TE), % bias and %CV were calculated:

- 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. High Dose Hook Effect

For Lumipulse G B•R•A•H•M•S PCT on the LUMIPULSE G1200 System, no high dose effect was observed for samples containing approximately 12,000 ng/mL of PCT.

f. Analytical specificity:

Interference Testing:

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. See Tables 7 and 8 below.

Table 7: Endogenous Interferents

Endogenous Interferent	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

Table 8: Exogenous Interferent

Exogenous Interferent	Concentration (mg/dL)
Acetaminophen	20.01
Acetylsalicylic Acid	65.22
1% Ethanol	789
Azithromycin	2
Caffeine	6
Celecoxib	24
Cetirizine HCl	0.55
Dextromethorphan	0.1
Dobutamine	1.13
Dopamine	13
Doxycycline	5
Epinephrine	0.18
Furosemide	2
Heparin	8000
Ibuprofen	50.03
Imipenem	118
Levofloxacin	2.93
Loratadine	0.05
Nicotine	0.1
Noradrenaline (norepinephrine)	0.2
Oxymetazoline HCl	0.09
Phenylephrine	6
Prednisolone	0.3
Salmeterol	0.006
Tiotropium	0.0022
Vancomycin	300

Cross Reactivity*:*

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 (serum pool 1, 2, 3, 4 and 5, respectively) 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. The % cross-reactivity for each individual sample was calculated using the following equation. See results in Table 9 below.

- % Cross Reactivity = (Mean Concentration$_{Test}$ (ng/mL) – Mean Concentration$_{Control}$ (ng/mL) / Concentration $_{Cross\ Reactant}$ (ng/mL)) X 100

Table 9: Cross Reactivity

Interferent	Sample ID	Mean Test Concentration (ng/mL) (n=3)	Mean Control Concentration (ng/mL) (n=3)	% Cross Reactivity
Human Calcitonin 10 ng/mL	Serum Pool 1	0.113	0.115	-0.020%
	Serum Pool 2	0.263	0.265	-0.020%
	Serum Pool 3	0.537	0.532	0.050%
	Serum Pool 4	2.111	2.014	0.970%
	Serum Pool 5	77.004	77.275	-2.710%
Human Katacalcin 10 ng/mL	Serum Pool 1	0.113	0.116	-0.030%
	Serum Pool 2	0.268	0.266	0.020%
	Serum Pool 3	0.537	0.541	-0.040%
	Serum Pool 4	2.118	2.134	-0.160%
	Serum Pool 5	76.476	76.417	0.590%
α-CGRP 10,000 ng/mL	Serum Pool 1	0.113	0.113	0.000%
	Serum Pool 2	0.261	0.263	0.000%
	Serum Pool 3	0.525	0.530	0.000%
	Serum Pool 4	2.126	2.131	0.000%
	Serum Pool 5	78.339	77.526	0.008%
β-CGRP 10,000 ng/mL	Serum Pool 1	0.117	0.115	0.000%
	Serum Pool 2	0.269	0.265	0.000%
	Serum Pool 3	0.540	0.534	0.000%
	Serum Pool 4	2.173	2.175	0.000%
	Serum Pool 5	77.705	77.443	0.003%
Salmon Calcitonin 13.2 µg/mL	Serum Pool 1	0.116	0.111	0.000%
	Serum Pool 2	0.265	0.272	0.000%
	Serum Pool 3	0.537	0.537	0.000%
	Serum Pool 4	2.185	2.157	0.000%
	Serum Pool 5	77.137	77.801	-0.005%
Eel Calcitonin 7.5 µg/mL	Serum Pool 1	0.115	0.114	0.000%
	Serum Pool 2	0.264	0.263	0.000%
	Serum Pool 3	0.542	0.525	0.000%
	Serum Pool 4	2.172	2.141	0.000%
	Serum Pool 5	77.631	78.072	-0.006%

f. Assay cut-off: See clinical cut-off

2. Comparison studies:

a. Method comparison with predicate device:

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-A3C.

B•R•A•H•M•S PCT sensitive KRYPTOR testing was performed following the appropriate QC procedures and manufacturer's instruction specified in the B•R•A•H•M•S PCT sensitive KRYPTOR package insert.

Sample testing with Lumipulse G B•R•A•H•M•S PCT was performed on three LUMIPULSE G1200 Systems utilizing two lots of ICs, one lot of calibrators, and four calibrator curves. There were 102 samples from female subjects (45.7%) and 121 samples from male subjects (54.3%) in the method comparison sample set. The PCT range of samples tested and age demographics are found in Tables 10 and 11 below.

Table 10: Total Samples per Specified Lumipulse G B•R•A•H•M•S PCT Ranges

Lumipulse G B•R•A•H•M•S PCT Ranges	Number of Samples
0.000-0.250 ng/mL	53
0.251-0.500 ng/mL	35
0.501-2.000 ng/mL	47
2.001-10.000 ng/mL	32
10.001-20.000 ng/mL	11
20.001-50.000 ng/mL	27
50.001-100.000 ng/mL	10
100.001-250.000 ng/mL	7
250.001-1000.000 ng/mL	1
TOTAL	223

Table 11: Summary of Age Demographics for Evaluable Subjects

Age Group (years)	Evaluable Subjects
22-29	2
30-39	9
40-49	14
50-59	21
60-69	63
70-79	52
80-89	44
90-99	18
Total	223
Mean Age	69.3
Median Age	70.0
Standard Deviation (SD) (years)	14.9
Minimum Age	26
Maximum Age	98

Two separate analysis of the study data were performed, one with analysis restricted to samples with B•R•A•H•M•S PCT sensitive KRYPTOR assays no more than 50.0 ng/mL and one with an extended analysis including all samples tested. Weighted Deming and Passing-Bablok regressions were performed with slope, correlation coefficient, intercept and mean difference along with 95% CIs determined and found to be acceptable. Bland-Altman Plots with mean % difference, percent limits of agreement and 95% CIs for Lumipulse G PCT and the predicate with B•R•A•H•M•S PCT sensitive KRYPTOR were also calculated and found to be acceptable.

Analysis of Samples within the Predicate Measurement Range:

207 were samples tested with Lumipulse G B•R•A•H•M•S PCT had results ranging from 0.054-58.156 ng/mL with B•R•A•H•M•S PCT sensitive KRYPTOR results for these same samples ranged from 0.024-48.430 ng/mL. Weighted Deming Regression results are found in Table 12. The clinical bias and confidence intervals (CIs) at the clinical decision points are listed in Table 13.

Table 12: Weighted Deming Regression for Lumipulse G B•R•A•H•M•S PCT when compared to B•R•A•H•M•S PCT sensitive KRYPTOR (measurement range 0.020-50.000 ng/mL)

n	**Correlation Coefficient (r)**	**Intercept (95% CI)**	**Slope (95% CI)**	**Mean Difference (ng/mL)**	
207	0.9535	-0.0044 (-0.0223, 0.0135)	1.0199 (0.9633, 1.0765)	0.185	

Table 13: Clinical bias and CIs at the clinical decision points

Clinical Decision Point (ng/mL)	**Bias (ng/mL)**	**Lower CI**	**Upper CI**
0.100	-0.0031	-0.0180	0.0117
0.250	-0.0009	-0.0148	0.0130
0.500	0.0027	-0.0185	0.0239
2.000	0.0246	-0.0749	0.1242

From the total 207 individual lithium heparin plasma samples tested, the percent agreement between the Lumipulse G B•R•A•H•M•S PCT and B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 0.500 ng/mL was determined. See Table 14 for 2 x 2 summary table.

- Negative percent agreement (NPA): 95.5% (84/88), 95% CI: 88.9%, 98.2%
- Positive percent agreement (PPA): 96.6% (115/119), 95% CI: 91.7%, 98.7%

Table 14: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR at 0.500 ng/mL cut-off

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)		
	≤0.500	>0.500	Total
≤0.500	84	4	88
>0.500	4	115	119
Total	88	119	207

From the total 207 individual lithium heparin plasma samples tested, the percent agreement between the Lumipulse G B•R•A•H•M•S PCT and B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 2.000 ng/mL was determined. See Table 15, 16 and 18 for 2 x 2, 3 x 3 summary and regression analyses, respectively. Additionally, Table 17 presents a cross-tabulation of all samples within each medical decision point range.

• NPA: 99.2% (132/133), 95% CI: 95.9%, 99.9%
• PPA: 95.9% (71/74), 95% CI: 88.7%, 98.6%

Table 15: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR at 2.000 ng/mL cut-off

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)		
	≤2.000	>2.000	Total
≤2.000	132	1	133
>2.000	3	71	74
Total	135	72	207

Table 16: 3x3 Table: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)			
	≤0.500	0.501<PCT≤2.000	>2.000	Total
0.500	84	4	0	88
0.501<PCT≤2.000	4	40	1	45
>2.000	0	3	71	74
Total	88	47	72	207

Table 17: Cross Tabulation of all Samples (n=207) within each Medical Decision Point Range

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/m)L	Lumipulse G PCT (ng/mL)				
	0.0237-0.100	0.101-0.250	0.251-0.500	0.501-2.000	2.001-58.200
0.0237-0.100	4	5	0	0	0
0.101-0.250	6	32	5	2	0
0.251-0.500	0	6	26	2	0
0.501-2.000	0	0	4	40	1
2.001-58.200	0	0	0	3	71

Table 18: Regression Analyses (N=207)

	Parameter	Estimate	Lower CI	Upper CI
Weighted Deming	Intercept	-0.0044	-0.0223	0.0135
	Slope	1.0199	0.9633	1.0765
Passing- Bablok	Intercept	-0.007	-0.025	0.004
	Slope	1.000	0.981	1.038

Analysis of Samples with the Lumipulse G B•R•A•H•M•S PCT extended measurement range:

223 samples tested with Lumipulse G B•R•A•H•M•S PCT had results ranging from 0.054-348.940 ng/mL and B•R•A•H•M•S PCT sensitive KRYPTOR results for these same samples ranged from 0.024-345.900 ng/mL. Weighted Deming Regression results are found in Table 19. The clinical bias and CIs at the clinical decision points were determined. No evidence of bias was found at the medical decision points. (See results in Table 20.)

Table 19: Weighted Deming Regression for Lumipulse G B•R•A•H•M•S PCT when compared to B•R•A•H•M•S PCT sensitive KRYPTOR (measurement range >0.020 ng/mL)

n	Correlation Coefficient (r)	Intercept (95% CI)	Slope (95% CI)	Mean Difference (ng/mL)	Percent difference mean
223	0.9846	-0.0025 (-0.0195, 0.0145)	1.0103 (0.9601, 1.0605)	-0.232	6.8%

Table 20: Bias at Clinical Decision Points

Clinical Decision Point (ng/mL)	Bias	Lower CI	Upper CI
0.100	-0.0022	-0.0167	0.0122
0.250	-0.0014	-0.0151	0.0124
0.500	0.0001	-0.0198	0.0199
2.000	0.0087	-0.0800	0.0975

Data was analyzed for concordance at the 0.500 ng/mL cut-off. (See Table 21 for 2 x 2 summary.) The percent agreement between the Lumipulse G B•R•A•H•M•S PCT and B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 0.500 ng/mL for the 223-individual lithium heparin plasma samples tested was determined:

- NPA: 95.5% (84/88), 95% CI: 88.9%, 98.2%
- PPA: 97.0% (131/135), 95% CI: 92.6%, 98.8%

Table 21: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 0.500 ng/mL

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)		
	≤0.500	>0.500	Total
≤0.500	84	4	88
>0.500	4	131	135
Total	88	135	223

Data was analyzed for concordance at the 2.000 ng/mL cut-off. The percent agreement between the Lumipulse G B•R•A•H•M•S PCT and B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 2.000 ng/mL for the 223-individual lithium heparin plasma samples tested was determined. See Table 22, 23 and 25 for 2 x 2, 3 x 3 summary tables and regression analyses, respectively. Additionally, Table 24 presents a cross-tabulation of all samples within each medical decision point range

- NPA: 99.2% (132/133), 95% CI: 95.9%, 99.9%
- PPA: 96.7% (87/90), 95% CI: 90.7%, 98.9%

Table 22: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR at cut-off 2.000 ng/mL

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)		
	≤2.000	>2.000	Total
≤2.000	132	1	133
>2.000	3	87	90
Total	135	88	223

Table 23: 3x3 Table: Lumipulse G B•R•A•H•M•S PCT vs. B•R•A•H•M•S PCT sensitive KRYPTOR

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G B•R•A•H•M•S PCT(ng/mL)			
	≤2.000	0.501<PCT≤2.000	>2.000	Total
≤2.000	84	4	0	88
0.501<PCT≤2.000	4	40	1	45
>2.000	0	3	87	90
Total	88	47	88	223

Table 24: Cross Tabulation of all Samples (n=223) within each Medical Decision Point Range

B•R•A•H•M•S PCT sensitive KRYPTOR (ng/mL)	Lumipulse G PCT (ng/mL)				
	0.0237-0.100	0.101-0.250	0.251-0.500	0.501-2.000	2.001-58.200
0.0237-0.100	4	5	0	0	0
0.101-0.250	6	32	5	2	0
0.251-0.500	0	6	26	2	0
0.501-2.000	0	0	4	40	1
2.001-58.200	0	0	0	3	87

Table 25: Regression Analyses (N=223)

	Parameter	Estimate	Lower CI	Upper CI
Weighted Deming	Intercept	-0.0025	-0.0195	0.0145
	Slope	1.0103	0.9601	1.0605
Passing-Bablok	Intercept	-0.005	-0.017	0.006
	Slope	0.995	0.977	1.013

b. Matrix comparison (Specimen Tube Type Study):

The Lumipulse G B•R•A•H•M•S PCT matrix comparison study was performed to evaluate the difference across tube types (SST, K_2EDTA, Lithium Heparin, Sodium Heparin, and Sodium Citrate) versus the means of the control samples (Red top serum) analyzed per CLSI guideline EP9-A3. Donor blood was drawn into 78 matched sets of collection tubes. 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. Results are summarized in Table 26 below.

Table 26: Weighted Deming Regression Analysis Summary of Different Tube Type versus Red Top Tubes

Tube Type	n	Concentration Range (ng/mL)		Slope			Intercept			Pearson Correlation Coefficient
		Min	Max	Estimate	Lower 95%CI	Upper 95%CI	Estimate	Lower95% CI	Upper95 % CI	
SST	77	0.014	83.435	1.0023	0.9800	1.0246	-0.0081	- 0.0191	0.0029	0.9968
K_2EDTA	77	0.015	77.148	1.0208	1.0002	1.0414	-0.0077	- 0.0190	0.0036	0.9973
Li Heparin	77	0.014	83.076	1.0010	0.9560	1.0459	0.0018	- 0.0121	0.0086	0.9961
Na Heparin	77	0.015	79.150	1.0264	1.0070	1.0458	-0.0049	-0.0200	0.0101	0.9983
Citrate	77	0.013	87.614	1.0399	1.0171	1.0626	-0.0095	- 0.0218	0.0028	0.9963

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-offs:

   28-day mortality:

   ΔPCT ≤ 80%
   - A decrease in the PCT levels below or equal to 80% defines a positive ΔPCT test result representing a higher risk for 28-day all-cause mortality of patients diagnosed with severe sepsis or septic shock.

   ΔPCT > 80%
   - A decrease in the PCT levels of more than 80% defines a negative ΔPCT test result representing a lower risk for 28-day all-cause mortality of patients diagnosed with severe sepsis or septic shock.

   Progression Risk:

   - **PCT > 2 ng/mL:** A PCT level above 2.0 ng/mL on the first day of ICU admission is associated with a high risk for progression to severe sepsis and/or septic shock.
   - **PCT < 0.5 ng/mL:** A PCT level below 0.5 ng/mL on the first day of ICU admission is associated with a low risk for progression to severe sepsis and/or septic shock.

   LRTI Antibiotic Decision Making:

   - **PCT < 0.10 ng/mL:** Antibiotic therapy strongly discouraged.

- **PCT 0.10-0.25 ng/mL:** Antibiotic therapy discouraged.
- **PCT 0.26-0.50 ng/mL:** Antibiotic therapy encouraged.
- **PCT >0.50 ng/mL:** Antibiotic therapy strongly encouraged.
- **PCT ≤ 0.25 ng/mL:** Antibiotic therapy may be discontinued
- **ΔPCT > 80%:** Antibiotic therapy may be discontinued

Sepsis Antibiotic Discontinuation:

- **ΔPCT > 80%:** Antibiotic therapy may be discontinued
- **PCT ≤ 0.50 ng/mL:** Antibiotic therapy may be discontinued

The LUMIPULSE PCT Change Calculator, for use with calculations for assessing Cumulative 28-day Risk of All-Cause Mortality, Initiation and Discontinuation, is a web-based software that will be published on the sponsor's controlled website and made available to end users via the Internet by entering the following URL (www.fujirebio-pct-calculator.com). The calculator software is validated for use on Microsoft Internet Explorer, Google Chrome, Mozilla Firefox, Apple Safari.

5. Expected values/Reference range:

Results from a total of 213 samples were used to determine the distribution of Lumipulse G B•R•A•H•M•S PCT results in apparently healthy individuals. Subject demographics for age are presented in Table 27 and subject demographics for race are presented in Table 28 for the apparently healthy subjects. Descriptive statistics for the Lumipulse G B•R•A•H•M•S PCT results are presented in Table 29 for the apparently healthy subjects.

Table 27: Summary of Age Demographics for Healthy Subjects

Age Group (years)	Apparently Healthy (All)	Apparently Healthy (Females)	Apparently Healthy (Males)
22-29	73	38	35
30-39	57	25	32
40-49	57	26	31
.50-59	21	9	12
60-69	5	3	2
≥ 70	0	0	0
Unknown	0	0	0
Total	213	101	112
Mean Age (years)	7	36	37
Median Age (years)	35	33	36
Standard Deviation (SD) (years)	11	11	11
Minimum Age (years)	22	22	22
Maximum Age (years)	68	62	68

Table 28: Summary of Race and Ethnicity Demographics for Healthy Subjects

	Apparently Healthy (All)	Apparently Healthy (Females)	Apparently Healthy (Males)
White	87	45	42
Black/African American	40	18	22
Hispanic	61	31	30
Asian/Pacific Islander	0	0	0
Other	0	0	0
Unknown	25	7	18
Total	213	101	112

To determine the upper limit of normal for the Lumipulse G B•R•A•H•M•S PCT assay, calculations of the 95% reference interval were performed for the overall set of apparently healthy females, apparently healthy males, and combined apparently healthy females and males in the study according to CLSI EP28-A3. These results are presented in Table 29 below.

Table 29: Lumipulse G B•R•A•H•M•S PCT Summary of 95% Reference Interval for Apparently Healthy Females, Apparently Healthy Males and Combined Apparently Healthy Females and Males

	Cohort		
	Apparently Healthy (All)	Apparently Healthy (Females)	Apparently Healthy (Males)
N	213	101	112
95% Reference Interval (ng/mL)	0.003 - 0.045	0.003 - 0.029	0.004 - 0.045
Lower 95% Reference Limit (90% Confidence Interval [CI]) (ng/mL)	0.003 (0.002 - 0.004)	0.003 (0.002 - 0.004)	0.004 (0.002 - 0.005)
Upper 95% Reference Limit (90% CI) (ng/mL)	0.045 (0.030 - 0.068)	0.029 (0.017 - 0.065)	0.045 (0.037 - 0.103)

Overall, 98.1% (209/213) of the apparently healthy subjects had a Lumipulse G B•R•A•H•M•S PCT value equal to or below 0.045 ng/mL. 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 is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable and the special controls for this device type under 21 CFR 866.3215.

O. Conclusion:

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