510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K153145

B. Purpose for Submission:

New device; to establish substantial equivalence to a predicate device and to obtain market clearance for a new assay designed to detect antibodies to *T. pallidum* in human serum and plasma.

C. Measurand:

Antibodies to *T. pallidum* (IgG and IgM)

D. Type of Test:

A qualitative immunoassay based on chemiluminescent enzyme immunoassay (CLEIA) technology for use on an automated clinical analyzer, the LUMIPULSE *G* System.

E. Applicant:

Fujirebio Diagnostics, Inc.

F. Proprietary and Established Names:

Lumipulse *G* TP-N Immunoreaction Cartridges Set

G. Regulatory Information:

1. Regulation section:

   866.3830
   Treponema pallidum treponemal test reagents

2. Classification:

   Class II (performance standards)

3. Product code:

   LIP, enzyme linked immunoabsorption assay, *Treponema pallidum*

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

   For *in vitro* diagnostic use.
   WARNING: Lumipulse *G* TP-N is not intended for blood and tissue donor screening. United States federal law restricts this device to sale by or on the order of a physician.

   Lumipulse *G* TP-N is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the qualitative determination of antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma (sodium citrate, or dipotassium EDTA) on the LUMIPULSE *G* System. Lumipulse *G* TP-N can be used as an initial diagnostic test or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection.

2. Indication(s) for use:

   The test system, when used in conjunction with nontreponemal based assays, provides serological evidence of infection with *T. pallidum*.

3. Special conditions for use statement(s):

   For Prescription Use

4. Special instrument requirements:

   LUMIPULSE *G*1200 System

I. Device Description:

The Lumipulse *G* TP-N is an assay system, including a set of immunoassay reagents, for the qualitative detection of anti-TP antibodies (IgG and IgM) directed against *Treponema pallidum* (TP) in human serum and plasma (sodium citrate or dipotassium EDTA) on the LUMIPULSE *G* System. The assay is based on a Chemiluminescent Enzyme Immunoassay (CLEIA) technology utilizing a two-step sandwich immunoassay method.

The LUMIPULSE *G*1200 is an automated immunoassay analyzer, capable of measuring chemiluminescence generated by the chemical reaction of antibodies in patient specimens binding to antigens in the test reagents. The critical reagents consist of ferrite microparticles coated with recombinant TP antigens (Tp15-17 and TpN47), a conjugate of the antigens labeled with alkaline phosphatase (ALP) and a substrate solution. The anti-TP antibodies in the specimen bind with the antigens coated on the particles to form immunocomplexes. A

washing step follows which removes any unbound materials. A second reaction is initiated with the addition of the conjugated (ALP-labeled) antigens to form additional complexes. A second wash cycle removes any unbound materials and a substrate solution is added initiating a chemical reaction with emission of a luminescent signal. The luminescence (at 477 nm) is measured by the photometric detector. The amount of antibody in a specimen is automatically calculated from the cutoff value (C), based on the calibration data. The results are reported in cutoff index values (C.O.I.) and interpreted as reactive or nonreactive.

Lumipulse *G* TP-N C.O.I.	**Lumipulse *G* TP-N Result (Judgment)**	**Interpretation**
Specimens with a reported C.O.I. < 1.0	(-)	Nonreactive for treponemal antibodies (Negative)
Specimens with a reported C.O.I. ≥ 1.0	(+)	Reactive for treponemal antibodies (Positive)

The reagents are supplied in cartridges (one cartridge=one test) in sets of 14; each box of reagents sold to a customer contains 3 sets of cartridges (total of 42 tests).

The reagents are provided with two lot-specific calibrators (one negative and one positive) prepared in human plasma.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ADVIA Centaur Syphilis (SYPH) Assay

2. Predicate 510(k) number(s):
   K112343

3. Comparison with predicate:

Characteristics	**Lumipulse *G* TP-N**	**ADVIA Centaur Syphilis (SYPH) Assay (K112343)**
Similarities and Differences		
Intended Use	Lumipulse *G* TP-N is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the qualitative determination of antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma (sodium citrate, or dipotassium EDTA) on the LUMIPULSE *G* System. Lumipulse *G* TP-N can be used as an initial	The ADVIA Centaur Syphilis (SYPH) assay is an *in-vitro* diagnostic immunoassay for the qualitative determination of antibodies to *Treponema pallidum* in human serum or plasma (EDTA, lithium or sodium heparinized, citrate) using the ADVIA Centaur® and ADVIA Centaur® XP systems as an aid in the diagnosis of syphilis.

	diagnostic test or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection. Lumipulse *G* TP-N is not intended for blood and tissue donor screening.	The ADVIA Centaur Syphilis assay is not intended for blood and tissue donor screening.
Methodology	Direct sandwich immunoassay based on chemiluminescent technology.	Direct sandwich immunoassay based on chemiluminescent technology.
Capture Antigens	Recombinant TP antigens: TpN15-TpN17 and TpN47	Recombinant TP antigens: TpN15 andTpN17
Conjugate	Recombinant antigens TpN15-17 and TpN47 conjugated with alkaline phosphatase	Recombinant antigens TpN15 and TpN17 conjugated with acridinium ester
Solid Phase	Ferrite microparticles	Magnetic latex microparticles
Analyte	IgG and IgM antibodies to *Treponema pallidum*	IgG antibodies to *Treponema pallidum*
Assay Cut-off	< 1.0 Nonreactive ≥ 1.0 Reactive	<0.9 Nonreactive ≥ 0.9 to <1.1 Equivocal ≥ 1.1 Reactive
Equivocal Zone	None	Yes
Calibrators	Two calibrators: (a) positive calibrator - anti-TP positive human plasma (b) negative calibrator - delipidized normal human serum	Two calibrators in human plasma
Instrument	LUMIPULSE *G* System	ADVIA Centaur
Assay protocol	2-step	2-step
Specimen Type	Human serum or plasma (potassium EDTA and sodium citrate)	Human serum or plasma (potassium EDTA, lithium or sodium heparin, sodium citrate)
Equivocal Zone	No equivocal zone	Yes: 0.9-1.1
Sample Volume	60 µL	100 µL

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

- ISO 17511:2003 Measurement of Quantities in Biological Samples - Metrological Traceability of Values Assigned to Calibrator and Control Materials
- CLSI EP05-A3 - Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP07-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 EP12-A2 – User Protocol for Evaluation of Qualitative Test Performance – Second Edition
- 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

L. Test Principle:

Chemiluminescent enzyme immunoassay (CLEIA)

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Three separate studies were conducted to collect data for estimation of precision of the Lumipulse *G* TP-N assay when performed on the LUMIPULSE *G*1200 instrument. Each study used precision panels consisting of the following eight samples:

	Sample Type	**Concentration Level**	**Target C.O.I.**
1	Plasma (sodium citrate)	Moderate Positive	2.1
2	Serum #1	Low Negative	0.2
3	Serum #2	High Negative	0.8
4	Serum #3	Low Positive	1.2
5	Serum #4	High Positive	7.7
6	Serum #5	Moderate Positive	2.0
7	Reactive Control 1	Moderate Positive	2.8
8	Reactive Control 2	High Positive	19.9
9	Nonreactive Control	Negative	0.1

Within-lab Precision

The precision of the Lumipulse *G* TP-N was evaluated in a study at one internal site using the sample panel described above. Each sample was assayed in replicates of two at two separate times of the day for 20 days (n=80 for each sample) using one LUMIPULSE *G*1200 system. The %CV for within-laboratory precision was ≤5.3% for any of the 9 samples. Data from this study are presented below:

Sample	Mean (C.O.I.)	Within-run (Repeatability)		Between-Run		Between-Day		Within-Laboratory* (Total)	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Sodium Citrate Plasma (moderate positive)	2.2	0.042	1.9	0.011	0.5	0.030	1.4	0.053	2.4
Serum 1 (low negative)	0.2	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
Serum 2 (high negative)	0.8	0.043	5.3	0.000	0.0	0.000	0.0	0.043	5.3
Serum 3 (low positive)	1.2	0.037	3.0	0.000	0.0	0.013	1.1	0.039	3.2
Serum 4 (high positive)	7.9	0.117	1.5	0.060	0.8	0.026	0.3	0.134	1.7
Serum 5 (moderate positive)	2.2	0.047	2.2	0.016	0.7	0.005	0.3	0.050	2.3
Reactive Control 1	2.9	0.049	1.7	0.022	0.8	0.013	0.4	0.055	1.9
Reactive Control 2	18.5	0.299	1.6	0.179	1.0	0.071	0.4	0.355	1.9
Nonreactive Control	0.1	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0

*Within-laboratory precision includes within-run, between-run, and between-day components.

Reproducibility

The reproducibility of the Lumipulse *G* TP-N assay was evaluated at three laboratory sites using the sample panel described above. Each sample was assayed in replicates of two at two separate times of the day at each of the sites for 10 days (n=120 for each sample) using one LUMIPULSE *G*1200 System at each site. The %CV for the reproducibility of the assay was ≤ 5.6% for any of the 9 samples. Data from this study are presented below:

Sample	Mean (C.O.I.)	Within-Run (Repeatability)		Between-Run		Between-Day		Between-Site		Reproducibility* (Total)	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Sodium Citrate Plasma (moderate positive)	2.1	0.046	2.1	0.030	1.4	0.037	1.7	0.054	2.5	0.085	4.1
Serum 1 (low negative)	0.2	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
Serum 2 (high negative)	0.8	0.035	4.3	0.016	1.9	0.020	2.4	0.011	1.4	0.045	5.6
Serum 3 (low positive)	1.2	0.033	2.7	0.027	2.3	0.038	3.2	0.012	1.0	0.058	4.9
Serum 4 (high positive)	7.7	0.125	1.6	0.172	2.2	0.106	1.4	0.252	3.3	0.346	4.5
Serum 5 (moderate positive)	2.2	0.044	2.0	0.039	1.8	0.038	1.8	0.048	2.2	0.085	3.9
Reactive Control 1	2.8	0.061	2.2	0.038	1.3	0.038	1.4	0.039	1.4	0.090	3.2

Reactive Control 2	18.3	0.268	1.5	0.143	0.8	0.224	1.2	0.510	2.8	0.634	3.5
Nonreactive Control	0.1	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0

*Reproducibility includes within-run, between-run, between-day, and between-site components.

Lot-to-lot Precision

The lot-to-lot precision of the Lumipulse *G* TP-N assay was evaluated using three lots of Lumipulse *G* TP-N immunoreaction cartridges and calibrators using the sample panel described above. Each sample was assayed in replicates of two at two separate times of the day for each of the lots for 10 days (n=120 for each sample) using one LUMIPULSE *G*1200 System. The %CV for between-lot imprecision was ≤5.7% for any of the 9 samples. Data from this study are presented below:

Sample	Mean (C.O.I.)	Within-Run (Repeatability)		Between-Run		Between-Day		Between-Lot		Within-Laboratory* (Total)	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Sodium Citrate Plasma (moderate positive)	2.2	0.049	2.2	0.018	0.8	0.059	2.7	0.057	2.6	0.097	4.4
Serum 1 (low negative)	0.2	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
Serum 2 (high negative)	0.8	0.026	3.1	0.000	0.0	0.024	2.9	0.041	4.9	0.054	6.8
Serum 3 (low positive)	1.2	0.034	2.8	0.018	1.5	0.029	2.4	0.062	5.0	0.079	6.5
Serum 4 (high positive)	7.9	0.109	1.4	0.120	1.5	0.144	1.8	0.344	4.3	0.407	5.1
Serum 5 (moderate positive)	2.2	0.051	2.3	0.020	0.9	0.044	2.0	0.124	5.7	0.143	6.5
Reactive Control 1	2.9	0.049	1.7	0.047	1.6	0.067	2.3	0.117	4.0	0.151	5.2
Reactive Control 2	19.3	0.252	1.3	0.138	0.7	0.302	1.6	0.824	4.3	0.923	4.8
Nonreactive Control	0.1	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0

* Within-laboratory precision includes within-run, between-run, between-day and between-lot components.

b. Linearity/assay reportable range:

Not applicable; this is a qualitative assay.

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

Calibrator

The Lumipulse *G* TP-N positive calibrator is traceable to an in-house reference standard with a value assigned to correlate with the SERODIA® TP-PA assay.

The positive calibrator is prepared from processed anti-TP positive human plasma. The negative calibrator is prepared in delipidated normal human serum.

Controls

Commercially available Quality Controls reactive for IgG and IgM antibodies to *Treponema pallidum* were analyzed with each run during the clinical study to establish the validity of all runs. The summary of the QC data (mean C.O.I., SD, and %CV) is shown below:

	N	**Mean C.O.I.**	**SD**	**%CV**
QC1 (nonreactive)	176	0.1	0.00	0.00
QC 2 (reactive)	176	2.86	0.154	5.40

Sample Stability Studies

The stability of TP antibodies in serum (no additive), serum collected in serum separator tubes (SST), dipotassium EDTA (K_2EDTA) plasma, and sodium citrate (Na citrate) plasma was evaluated using paired samples from 30 blood donors. Each donor sample set consisted of 4 tubes (serum (no additive), serum (SST), K_2EDTA plasma, and Na citrate plasma). The samples were spiked with a highly TP-reactive sample to the following target concentrations:

- 3 matched sample sets spiked targeting C.O.I. of 5.0
- 12 matched sample sets spiked targeting C.O.I. of 0.8
- 12 matched sample sets spiked targeting C.O.I. of 1.3
- 3 matched sample sets were left unspiked

Baseline measurements were established on the day of the draw (Day 0) for use as the control.

The stability of TP antibodies in serum (no additive), serum (SST), K_2EDTA plasma and Na citrate plasma samples was evaluated at the following storage conditions for the indicated time periods:

- Refrigerated stability (at 2-10°C) ≤ 4 days
  - Time points tested: Day 0, Day 1, Day 3, Day 4 and Day 5
- Room temperature stability (at 25° +/- 2°C) ≤ 3 days
  - Time points tested: Day 0, Day 1, Day 2 and Day 3
- Frozen stability (at ≤ -20° +/- 10°C) ≤ 14 days.
  - Time points tested: Day 0, Day 14 and Day 15

Each sample was tested in triplicate at each time point. The evaluation of results was performed separately for each analyte concentration level, storage condition, and time point.

The acceptance criteria were defined as:

- The qualitative status of nonreactive samples should remain unchanged at each time point and each condition, relative to Day 0.
- The qualitative status of reactive samples should remain unchanged at each time point and each condition, relative to Day 0.

Additionally, the mean C.O.I. value for each positive sample and the mean percent difference for the mean C.O.I. value for each sample at each time point relative to Day 0 were calculated and presented in the submission.

The results supported sample stability as shown:

Sample Type	**2-10°C**	**25°C (+/- 2°C)**	**-20°C (+/- 10°C)**
Serum (no additive)	4 days	3 days	14 days
Serum (SST)	4 days	3 days	14 days
K_2EDTA plasma	4 days	3 days	14 days
Na citrate plasma	4 days	3 days	14 days

An additional study was conducted to evaluate freeze thaw stability of the TP antibodies in serum (no additive), serum (SST), K_2EDTA plasma, and sodium citrate plasma samples. The study utilized matched sample sets from 60 blood donors. Each donor sample set consisted of 4 tubes (serum (no additive), serum (SST), K_2EDTA plasma and sodium citrate plasma). The samples were spiked with a highly TP-reactive sample to the following target concentrations:

- 4 matched sample sets spiked targeting C.O.I. of 5.0
- 21 matched sample sets spiked targeting C.O.I. of 0.8
- 21 matched sample sets spiked targeting C.O.I. of 1.3
- 10 matched sample sets spiked targeting C.O.I. of 2.0
- 4 matched sample sets were left unspiked

The samples were aliquoted and baseline measurements were established on the day of the draw (Day 0). The samples were placed in the freezer at ≤ -20°C. Each freeze/thaw cycle consisted of ≥ 30 minutes at ≥ -20°C; each sample was visually inspected to confirm that the sample was frozen. Samples were tested in triplicate after 1, 5, 7, and 10 freeze/thaw cycles.

The results were evaluated for their qualitative status (negative or positive). In addition, the mean C.O.I. value for each sample was calculated at freeze/thaw cycles 1, 5, 7, and 10 and the mean percent difference in C.O.I. value was calculated for each sample, at each cycle, relative to the mean C.O.I. value of the unfrozen sample. The data showed that all nonreactive samples, for serum (no additive), serum (SST), and Na citrate plasma, remained nonreactive after all freeze/thaw cycles. Similarly, all samples spiked to a C.O.I. of ≥ 1.0 were reactive after all freeze/thaw cycles for serum (no additive), serum (SST), and Na citrate plasma. The results for the K_2EDTA plasma were not acceptable as a change in reactivity was observed at various freeze/thaw cycles.

The results of the study support a claim of freeze/thaw stability up to 10 times for the following samples: serum (no additive), serum (SST), and Na citrate plasma. The Lumipulse *G* TP-N labeling bears a statement that K_2EDTA plasma samples should not be frozen and thawed.

On-board Stability

The stability of TP antibodies in serum and sodium citrate plasma samples left on the instrument before testing was evaluated using a panel of 7 samples (C.O.I. values 0.2, 0.8, 1.2, 2.1, 2.2, and 7.7). The samples were pipetted into sample cups and placed on the sample rack unit. The baseline measurements were established (Time 0) and the samples were retested after 3 hours and after 5 hours. Each sample was tested in triplicate. The results were evaluated for the qualitative status of each sample (reactive/nonreactive) and the mean percent difference of the mean C.O.I. value for each sample at each time point relative to Time 0 was calculated. The results showed no change in the reactivity status of any of the samples up to 5 hours and the mean percent difference of reactive specimens, relative to Time 0, ranged from 0% to 8%. The data support the Lumipulse *G* TP-N on-board sample stability of up to 5 hours.

On-clot Stability

An additional study was conducted to establish stability of TP antibodies in on-the-clot serum samples when held at 40°C prior to testing with the Lumipulse *G* TP-N assay. The tested sample sets are described above. The baseline measurements were established on the day of draw. The sample tubes, on clot, were placed at 40°C for continuous storage. The samples were evaluated on day 5 and were tested in triplicate with the Lumipulse *G* TP-N assay.

The results were analyzed by calculating the percent difference of the mean of the measurements after the storage, for each sample type (matrix), as compared to the mean of the measurements on day 0 (baseline). The criteria for acceptable stability were:

- The status of nonreactive (negative) samples should remain unchanged.
- The status of reactive (positive) samples should remain unchanged

The results showed that although the reactive status for all samples remained unchanged after 5 and 6 days of storage at 40°C, the observed percent difference in the means of the measurements, for the samples tested, ranged from -14% to 0% on day 5 and from -15% to -7% on day 6. The following statement and precaution were added to the package insert:

Serum samples kept on the clot and stored under ambient temperatures (not to exceed 40°C) must be tested within 5 days of collection. ***However, it is recommended that separated serum be removed from the clot as soon as possible.*** *In analytical studies, a loss of reactivity ranging from 7-14% was observed when on-the-clot serum samples were held at 40°C for 5 days; although no change in positivity was observed for the low positive samples in the study, a false negative result in clinical samples with low antibody*

levels is possible.

Hook Effect

The sponsor conducted a study to demonstrate that the assay is not susceptible to the Hook effect where high levels of antibodies may interfere with the formation of the immune complexes, giving false nonreactive results. Highly reactive serum sample and plasma sample (C.O.I. ~ 400) were serially diluted with a nonreactive human serum or plasma, respectively. All samples (dilutions) were tested in triplicate. The mean signal values and the mean C.O.I. values were calculated for each dilution. The results showed that there was no increase in signal at any dilution when comparing to the signal from the dilution immediately preceding. The study demonstrated that the assay is not subject to Hook effect in samples with TP antibody levels up to C.O.I. values of 350.

Carryover

The LUMIPULSE *G*1200 System uses disposable tips for sampling specimens preventing carryover (analyte contamination) between samples. Additionally, the cartridge design allows for each sample to be analyzed in its own reaction well further preventing a possibility of contamination from a previous sample.

Reactivity with IgG and IgM Treponemal Antibodies

The ability of the Lumipulse *G* TP-N assay to detect both IgG and IgM type treponemal antibodies was evaluated by testing six syphilis positive human sera known to contain measurable levels of both types of treponemal antibodies. A sample containing only IgG type antibodies was included in the study as an IgG control.

All test samples were analyzed with the *T. pallidum* IgM ELISA kit according to the package insert and all samples had quantifiable IgM values, while the IgG control sample did not have quantifiable IgM. The samples were then tested in triplicate on the LUMIPULSE *G*1200, using the Lumipulse *G* TP-N assay to determine the reactivity of each sample (C.O.I. = total IgG and IgM values). Next, all samples were treated with BUF059 IgG/RF Stripper solution as directed in the package insert, to remove all IgG. Following the stripping procedure all samples were tested with the *T. pallidum* IgG ELISA kit to determine the sample IgG values and to ensure that samples were stripped of IgG. The test samples and the IgG control sample were then analyzed in triplicate with the Lumipulse *G* TP-N assay to determine the reactivity (C.O.I. = IgM value). The test samples remained reactive in the Lumipulse *G* TP-N assay after IgG depletion with C.O.I. values >1.0, while the IgG control sample became nonreactive after IgG depletion, demonstrating that the Lumipulse *G* TP-N assay detects both types of TP antibodies.

d. Detection limit:

Not applicable.

e. Analytical specificity:

Interference

Lumipulse *G* TP-N assay was evaluated for potential interference from endogenous substances and from therapeutic drugs in a study consistent with the guidelines in the CLSI Protocol EP7-A2.[11] Five human serum pools were prepared at the following targeted TP concentrations:

Panel	Sample Information	Composition	Target C.O.I
1	Negative Serum	Native Human Serum	0.1.
2	Low Positive Serum	Native Human Serum	1.3-1.6
3	Moderate Positive Serum	Native Human Serum	2.0-5.0
4	Moderate Positive Plasma	Native Human Sodium Citrate Plasma	2.0-5.0
5	High Positive Serum	Native Human Serum	7.0-22.0

Stock solutions of the selected interferents were prepared at high concentrations in appropriate diluents to minimize the volume used for spiking. Each sample was split into two equal aliquots for each interferent, where one aliquot was spiked with the interferent stock solution, while the other aliquot was spiked with an equal volume of the stock diluent. All samples were tested in triplicate with the Lumipulse *G* TP-N assay.

The results were evaluated by calculating the percent difference in C.O.I. between the spiked and unspiked (control) samples. The acceptance criteria were set such that all positive (reactive) samples must demonstrate ≤10% change in C.O.I. and the reactivity status of nonreactive (negative) samples should remain negative.

All substances tested demonstrated < 10% change in the mean C.O.I. for positive (reactive) samples. The reactivity status of negative (nonreactive) samples remained unchanged. The study showed that the Lumipulse *G* TP-N assay is not susceptible to interference from the endogenous substances at the concentrations tested, as shown below:

Endogenous Interferences	Test Concentration
Free Bilirubin (unconjugated)	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Triglycerides (Intralipid 20% Emulsion)	3000 mg/dL
Hemoglobin	500 mg/dL
Human Serum Albumin	12 g/dL
Gamma Globulin	30 mg/mL

Biotin	500 ng/mL
Human Anti-Mouse Antibodies (HAMA)	1000 ng/mL
Rheumatoid Factor (RF)	1000 IU/mL
Cholesterol	400 mg/mL
Ascorbic Acid	3 mg/mL

Therapeutic Drug Interferences	**Test Concentration**
Abacavir Sulfate	3.85 µg/mL
Acetylsalicylic Acid	3.62 mmol/L
Carbamazepine	50.8 µmol/L
Diphenhydramine	19.6 µmol/L
Metformin	310 µmol/L
Metoprolol Tartrate	18.7 µmol/L
Penicillin G Benzathine	500 IU/mL
Rosuvastatin Calcium	30 ng/mL
Warfarin	32.5 µmol/L

Cross-reactivity

Lumipulse *G* TP-N on the LUMIPULSE *G*1200 System was evaluated for potential cross-reactivity in other diseases and biological conditions by testing 282 specimens obtained from patients known to have a variety of microbial and viral infections, biological abnormalities, and from subjects known to be drug users. The presence of the potential cross-reactant was confirmed with a FDA cleared assay (where applicable). The samples were also tested with a predicate EIA. The results are shown below:

Clinical Category	Number Tested	Number of Reactive Specimens	
		Lumipulse *G* TP-N	FDA Cleared EIA
Lyme Disease	10	0	0
Anti-Nuclear Antibody (ANA)	10	0	0
Rheumatoid Factor (RF)	10	1	0
Human Anti-Mouse Antibody (HAMA)	10	0	0
Hepatitis A Infection (HAV) total	20	2	3
Hepatitis A Infection (HAV) IgM	10	0	0
Hepatitis B Infection (HBV)	10	0	0
Hepatitis C Infection (HCV)	10	2	3
Human Immunodeficiency Virus (HIV)	11	6	8
Cytomegalovirus (CMV) IgG	10	0	0
Cytomegalovirus (CMV) IgM	10	0	0
Epstein-Barr Virus (EBV) IgG	10	1	1
Herpes Simplex Virus (HSV) IgG	10	1	1
Rubella IgG	10	1	0
Rubella IgM	10	0	0
Toxoplasma IgG	10	0	0
Toxoplasma IgM	10	1	1
Varicella Zoster Virus (VZV) IgG	10	0	0
Lupus (SLE)	10	2	2
Drug users	20	14	17
Myeloma patients	13	0	1
Flu Vaccine recipients	26	0	0
Hyper IgG	10	2	2
Hyper IgM	10	0	1
Leptospirosis	2	0	0
Total Samples Tested	**282**	**33**	**40**

The samples were obtained from commercial vendors and their TP status was unknown. Among the samples tested, 33 samples were reactive in Lumipulse *G* TP-N assay. Of those, 30 samples were also reactive in the TP-PA assay.

A comparison of results of the Lumipulse *G* TP-N assay, a predicate EIA and the TP-PA assay for the study above is shown below:

Lumipulse *G* TP-N	EIA	Total Subjects	TP-PA (Reference Standard)	
			+	-
+	+	31	29	2
+	-	2	1	1
-	+	9	1	8
-	-	240	0	NA*
Total		282	31	11

* Not applicable; samples were not tested with TP-PA if both the Lumipulse *G* TP-N and the predicate EIA tested nonreactive.

f. Assay cut-off:

The luminescence of the primary calibrator for the Lumipulse *G* TP-N assay was originally set to obtain concordance with the Serodia TP-PA assay results. The cutoff was initially determined by ROC analysis of results obtained from testing 417 specimens with values assigned using Serodia TP-PA assay (312 nonreactive, 99 reactive and 6 intermediate). First, the Index Value was calculated based on the ratio of the luminescence of the assay sample to the luminescence of the positive calibrator, when run on the Lumipulse *G* TP-N assay. The cutoff point was selected as that Index Value that provided for a 100% sensitivity and specificity among the specimens tested. The Lumipulse *G* TP-N results are expressed as a cutoff index (C.O.I.) value. The C.O.I. for a specimen is calculated using the following formula:

C.O.I. = S / C
S = luminescence of specimen (assay sample)
C = (luminescence of TP-N Positive Calibrator) x 0.12*

*The luminescence at the cut-off point was determined to be 12% of the Lumipulse *G* TP-N Positive Calibrator.

The analytically selected cutoff was further validated in a clinical study in the intended use population.

2. Comparison studies:

a. Method comparison with predicate device:

The results of the Lumipulse *G* TP-N assay were compared to a composite comparator based on an algorithm of results obtained from three commercially available syphilis assays: (a) treponemal chemiluminescent enzyme immunoassay (EIA), a nontreponemal Rapid Plasma Reagin assay [RPR], and a second treponemal assay (*Treponema pallidum* Particle Agglutination [TP-PA]). Additional details of how the final comparator result was determined are provided below in the “Clinical Studies” section.

b. Matrix comparison:

The suitability of various blood collection tube types for use with the Lumipulse *G* TP-N assay was evaluated in an analytical study. Venous blood samples were obtained from 60 donors in matched sets in the following vacutainer tube types:

- Serum (no additive)-used as the control
- Serum separator
- K_2EDTA
- Lithium heparin
- Sodium heparin
- Sodium citrate

Each matched set of samples (serum and plasma) was tested with the Lumipulse *G* TP-N assay within 8 hours of collection. Four sets of 12 samples were spiked with a highly reactive TP stock solution to the following target C.O.I. values: 0.8, 1.3, 2.0, and 5.0. One set of 12 samples was left unspiked. Each sample was tested in duplicate. A mean C.O.I was calculated for each sample. The tube type was acceptable if the slope of the correlation between the given tube and the control (serum) is within the 0.9 - 1.1 range.

The sponsor performed a weighted Deming regression analysis to evaluate the difference in results across tube types (SST serum, K_2EDTA plasma, lithium heparin plasma, sodium heparin plasma, and sodium citrate plasma) versus the results of the control samples (serum).

Weighted Deming Regression Analysis

Tube Type	N	Concentration Range		Slope			Intercept			Pearson Correlation Coefficient
		Min	Max	Estimate	Lower 95%CI	Upper 95%CI	Estimate	Lower 95% CI	Upper 95% CI	
SST	60	0.1	6.2	1.0126	0.9957	1.0296	-0.0015	-0.0032	0.0003	0.9972
K2EDTA	60	0.1	5.6	0.9521	0.9238	0.9804	0.0045	0.0016	0.0073	0.992
Lithium Heparin	60	0.1	6.9	1.3174	1.288	1.3468	-0.0318	-0.0347	-0.0288	0.9941
Sodium Heparin	60	0.1	7.1	1.2996	1.2716	1.3276	-0.0302	-0.0329	-0.0275	0.9959
Sodium Citrate	60	0.1	5.6	0.9224	0.8929	0.9519	0.0072	0.004	0.0103	0.9874

The results for each matrix type were also examined for bias at the cutoff, using Deming Regression analysis.

Estimation of Systematic Difference at the Cutoff Point (1.0)

Tube Type	Bias at Cutoff (n=1)		
	Estimate	**Lower 95% CI**	**Upper 95% CI**
SST	0.011139	-0.00409	0.026363
K_2EDTA	-0.04339	-0.06891	-0.01787
Lithium Heparin	0.285646	0.25919	0.312103
Sodium Heparin	0.26941	0.24404	0.294779
Sodium Citrate	-0.07044	-0.09687	-0.04401

Based on the results it was determined that the 95 % CI for the slope for lithium heparin and sodium heparin plasma exceeds the range between the acceptance range of 0.9 and 1.1. Similarly, the data showed that lithium heparin and sodium heparin plasma tube types present a significantly higher bias when compared to the serum tube type control than the SST, K_2EDTA plasma, and sodium citrate plasma tube types, based on a sample size of 60 individual donors. It was determined that lithium heparin and sodium heparin plasma are not suitable for analysis with the Lumipulse *G* TP-N assay.

Based on the data, the following samples may be used for analysis with the Lumipulse *G* TP-N assay:

- Serum (no additive)
- SST serum
- K_2EDTA plasma
- Sodium citrate plasma

The following table summarizes the data analysis for the acceptable tube types.

Matrix Comparison	**Sample Range (C.O.I.)**	**Correlation Coefficient**	**Intercept (95% CI)**	**Slope (95% CI)**	**Bias (95% CI)**
SST versus Red Top	0.1 – 6.2	0.997	-0.002	1.013	.0111
			(-0.003 – 0.000)	(0.996 – 1.03)	(-0.004 – 0.026)
K_2EDTA versus Red Top	0.1 – 5.6	0.992	0.004	0.952	-0.043
			(0.002 – 0.007)	(0.924 – 0.980)	(-0.069 – -0.0179)
Sodium Citrate versus Red Top	0.1 – 5.6	0.987	0.007	0.922	-0.070
			(0.004 – 0.010)	(0.893 – 0.952)	(-0.097 – -0.044)

3. Clinical Studies:

In a multi-center clinical study, samples from a total of 2791 subjects were submitted for testing. Among those, there were 1316 specimens prospectively collected from the intended use population and 1475 specimens that were pre-selected from a retrospective collection. After exclusion of 26 specimens from the prospective collection (due to hemolyzed/lipemic samples, lack of test results, protocol exclusions, and exclusions based on subject data review) and three samples from pre-selected retrospective

collection (due to lack of test results), there were a total of 1290 (46%) evaluable prospective samples and a total of 1472 (54%) evaluable retrospective samples. The study samples were tested at four clinical sites.

The prospective collection consisted of specimens collected sequentially from all patients prescribed a laboratory test for syphilis between defined periods of time. The specimens were collected from seven sites representing different geographical regions of the US including both low prevalence sites and high prevalence sites.

The retrospective samples included specimens from 379 pregnant women, 520 HIV positive subjects (298 remnant samples from reference laboratories and 222 collected at a research facility), 130 known to be *T. pallidum* (TP)-reactive by previous laboratory testing, 68 samples collected at a research facility from patients clinically diagnosed with syphilis, as well as 375 samples consisting of remnants of specimens sent to a laboratory for routine syphilis testing.

Additionally, 289 samples from subjects with well-characterized medically diagnosed syphilis and 474 samples from apparently healthy subjects, including 75 pediatric and 399 adult/not pregnant subjects were tested with the Lumipulse *G* TP-N assay.

Comparison of Results

The clinical performance of the Lumipulse *G* TP-N was evaluated by comparing the assay results with the comparator result based on an algorithm of results from three FDA cleared tests: a treponemal test (EIA), a nontreponemal Rapid Plasma Reagin (RPR) test, and a second treponemal test, *Treponema pallidum* particle agglutination (TP-PA) assay. Because the clinical diagnosis of syphilis must be supported by two reactive laboratory tests, consisting of a treponemal assay and a nontreponemal assay, or at least two treponemal assays, employing an algorithm of three syphilis tests to determine the comparator result presents the most comprehensive picture of the syphilis serological status.

The clinical performance of the Lumipulse *G* TP-N assay was determined by calculating percent agreement between the Lumipulse *G* TP-N result and the Final Comparator Result. The Final Comparator Result was determined using a two out of three rule (EIA, RPR, and TP-PA). In cases where the EIA result was “equivocal” (as per the device labeling), and the TP-PA result was “inconclusive”, the Final Comparator Result could not be determined; those results would be excluded from the final analysis (there were no indeterminate final comparator results in this study). The table below shows how the final comparator result was determined.

EIA (Treponemal Test)	RPR (Nontreponemal Test)	TP-PA (2nd Treponemal Test)	Final Comparator Result
Negative	Negative	Positive	**Negative**
		Negative	**Negative**
		Inconclusive	**Negative**
Negative	Positive	Positive	**Positive**
		Negative	**Negative**
		Inconclusive	**Negative**
Positive	Positive	Positive	**Positive**
		Negative	**Positive**
		Inconclusive	**Positive**
Positive	Negative	Positive	**Positive**
		Negative	**Negative**
		Inconclusive	**Positive**
Equivocal	Negative	Positive	**Positive**
		Negative	**Negative**
		Inconclusive	**Indeterminate**
Equivocal	Positive	Positive	**Positive**
		Negative	**Negative**
		Inconclusive	**Indeterminate**

Performance of the Lumipulse *G* TP-N assay with Prospective Samples

The age range for the 1290 evaluable subjects was 18 to 92 with a median age of 42. The population contained more male subjects compared to female subjects (66% vs. 34%, respectively). Subjects were from different locations across the US. Each of those specimens was analyzed with the Lumipulse *G* TP-N assay and with the three reference assays.

A summary of the serological test profile for the study samples in the prospective population is shown below.

EIA	RPR	TP·PA	Final Comparator Result	Lumipulse *G* TP-N	Number of Subjects
Negative	Negative	Negative	Negative	Negative	1031
Positive	Negative	Positive	Positive	Positive	119
Positive	Positive	Positive	Positive	Positive	90
Positive	Negative	Positive	Positive	Negative	14
Positive	Negative	Negative	Negative	Negative	14
Negative	Positive	Negative	Negative	Negative	5
Positive	Negative	Negative	Negative	Positive	4
Positive	Negative	Inconclusive	Positive	Negative	3
Positive	Positive	Negative	Positive	Positive	3
Equivocal	Negative	Negative	Negative	Negative	2

EIA	RPR	TP·PA	Final Comparator Result	Lumipulse *G* TP-N	Number of Subjects
Negative	Negative	Positive	Negative	Negative	2
Negative	Positive	Positive	Positive	Positive	2
Negative	Negative	Positive	Negative	Positive	1
				Total	**1290**

The positive percent agreement (PPA) and the negative percent agreement (NPA) of the Lumipulse *G* TP-N assay results when compared to the Final Comparator Result, along with the 95% confidence interval (CI), in the prospective samples from the intended use population is shown below.

Lumipulse *G* TP-N	Final Comparator Result		PPA (%)	95% CI	NPA (%)	95% CI
	Reactive	Nonreactive				
Reactive	215	4	92.7	88.6, 95.4	99.6	99.0, 99.9
Nonreactive	17	1054				

The prospective study population consisted of subjects sent for routine syphilis testing, those with previous history of syphilis, pregnant women and persons positive for HIV. The percent agreement of the Lumipulse *G* TP-N assay results when compared to the Final Comparator Result, along with the 95% confidence interval (CI), in each category of the prospective samples, is shown below.

Category	PPA (%)	95% CI	NPA (%)	95% CI
Routine Syphilis	90.4 (94/104)	83.2, 94.7	99.7 (933/936)	99.1, 99.9
Previously Diagnosed with Syphilis*	96.9 (94/97)	91.3, 98.9	100 (12/12)	75.8, 100
Pregnant (Unknown Trimester)	NA	NA	100 (41/41)	91.4, 100
HIV Positive*	93.7 (74/79)	86.0, 97.3	98.6 (72/73)	92.6, 99.8

NA=Not applicable, no positive results obtained/determined

*52 subjects had a previous history of syphilis and were HIV positive. These subjects are counted in each category separately.

Performance of the Lumipulse *G* TP-N assay with Retrospective (pre-selected) Samples

The age range for the 1472 evaluable subjects was 14 to 89 with a median age of 33. The retrospective study population had more female than male subjects (57% vs. 43%, respectively). Subjects were from different locations across the US. Each of those specimens was analyzed with the Lumipulse *G* TP-N assay and with the three reference assays.

A summary of the serological test profile for the retrospective samples is shown below.

EIA	**RPR**	**TP·PA**	**Final Comparator Result**	**Lumipulse *G* TP-N**	**Number of Subjects**
Negative	Negative	Positive	Negative	Negative	6
Negative	Negative	Negative	Negative	Negative	844
Negative	Negative	Negative	Negative	Positive	10
Negative	Negative	Inconclusive	Negative	Negative	2
Negative	Positive	Negative	Negative	Positive	20
Positive	Positive	Positive	Positive	Positive	277
Positive	Positive	Positive	Positive	Negative	4
Positive	Positive	Negative	Positive	Negative	2
Positive	Positive	Inconclusive	Positive	Negative	1
Positive	Negative	Positive	Positive	Positive	234
Positive	Negative	Positive	Positive	Negative	20
Positive	Negative	Negative	Negative	Negative	28
Positive	Negative	Negative	Negative	Positive	8
Positive	Negative	Inconclusive	Positive	Positive	2
Positive	Negative	Inconclusive	Positive	Negative	4
Equivocal	Negative	Negative	Negative	Negative	10
				Total	**1472**

The positive percent agreement (PPA) and the negative percent agreement (NPA) Lumipulse *G* TP-N assay results when compared to the Final Comparator Result , along with the 95% confidence interval (CI), in the retrospective samples is shown below.

Lumipulse *G* TP-N	**Final Comparator Result**		**PPA (%)**	**95% CI**	**NPA (%)**	**95% CI**
	Reactive	**Nonreactive**				
Reactive	513	18	94.3	92.0, 96.0	98.1	97.0, 98.8
Nonreactive	31	910				

The percent agreement of the Lumipulse *G* TP-N assay results when compared to the Final Comparator Result, along with the 95% confidence interval (CI), in each category of the retrospective samples, is shown below.

Category	PPA (%)	95% CI	NPA (%)	95% CI
Pregnant	96.8 (92/95)	91.1, 98.9	96.8 (275/284)	94.1, 98.3
HIV	90.3 (214/237)	85.9, 93.4	97.5 (276/283)	95.0, 98.8
Reactive by Previous Laboratory Testing	99.2 (121/122)	94.6, 99.8	100.0 (8/8)	67.6, 100.0
Routine Syphilis Testing	91.2 (31/34)	77.0, 97.0	99.7 (340/341)	98.4, 99.9
Medically Diagnosed Syphilis (Unknown Stage)	98.2 (55/56)	90.6, 99.7	91.7 (11/12)	64.6, 98.5

Performance in Pregnant Women

A total of 420 pregnant women were tested in this study. The percent agreement between the Lumipulse *G* TP-N assay and the Final Comparator Result with samples from pregnant women in the prospective and retrospective populations is shown in the table below.

Category	PPA (%)	95% CI	NPA (%)	95% CI
Prospective				
Unknown Trimester	NA (0/0)	NA	100 (41/41)	91.4, 100
Retrospective				
First Trimester	100 (21/21)	84.5, 100	100 (93/93)	96.0, 100
Second Trimester	96.8(30/31)	83.8, 99.4	94.7 (90/95)	88.3, 97.7
Third Trimester	95.4 (41/43)	84.5, 98.7	95.8 (92/96)	89.8, 98.4

Performance in Persons with HIV

A total of 672 subjects with HIV were tested in this study. The percent agreement between the Lumipulse *G* TP-N and the Final Comparator Result with samples from HIV positive subjects in the prospective and retrospective populations is shown in the table below.

Category	PPA (%)	95% CI	NPA (%)	95% CI
Prospective				
HIV Positive	93.7 (74/79)	86.0, 97.3	98.6 (72/73)	92.6, 99.8
Retrospective				
HIV Positive	90.3 (214/237)	85.9, 93.4	97.5 (276/283)	95.0, 98.8

Performance in Medically Diagnosed Individuals

The performance of the Lumipulse *G* TP-N assay was evaluated with samples from subjects who were medically diagnosed with primary, secondary, or latent syphilis. The diagnosis of syphilis and the stage of the disease were made by a licensed physician based on the patient's clinical symptoms, medical history and laboratory test results at the time of the diagnosis. The 289 subjects evaluated ranged in age from 18 to 78 with a median age of 44. Subjects were from Argentina (52%) and Florida (48%). The reactivity of the Lumipulse *G* TP-N assay with samples from subjects medically diagnosed with syphilis is presented by the disease stage and the treatment status.

Medically Diagnosed Subjects			**Lumipulse G TP-N**	
Syphilis Stage	**Treatment Status**	**N**	**Number of Reactive (%)**	**Number of Nonreactive (%)**
Primary	Treated	2	2 (100%)	0 (0%)
	Untreated	27	27 (100%)	0 (0%)
Secondary	Treated	25	25 (100%)	0 (0%)
	Untreated	30	30 (100%)	0 (0%)
Latent	Treated	5	5 (100%)	0 (0%)
	Untreated	200	183 (91.5%)	17* (8.5%)

*13/17 nonreactive samples tested nonreactive by TP-PA and 15/17 tested nonreactive by RPR.

Performance in Apparently Healthy Individuals

The performance of the Lumipulse *G* TP-N assay was evaluated with samples from apparently healthy individuals. The 474 samples tested included 75 pediatric subjects and 399 adult/not pregnant subjects ranging in age from 2 months to 68 years of age (63% male and 37% female). The reactivity of the Lumipulse *G* TP-N assay in apparently healthy population is shown below.

Category	**Lumipulse *G* TP-N Result**		
	Number of Reactive (%)	**Number of Nonreactive (%)**	**Total**
Adults	1* (0.3)	398 (99.7)	399
Pediatrics	0 (0.0)	75 (100.0)	75
Total	1 (0.2)	473 (99.7)	474

*The one reactive sample also tested reactive by TP-PA and RPR.

a. Clinical Sensitivity:

The clinical sensitivity of the assay is expressed as percent agreement of the Lumipulse *G* TP-N assay results with the Final Comparator Result, as explained above.

b. Clinical specificity:

The clinical specificity of the assay is expressed as percent agreement of the Lumipulse *G* TP-N assay results with the Final Comparator Result, as explained above.

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

Of the total number of 3552 samples tested in the clinical study, 12 invalid results were generated on the initial testing and had to be retested, each producing a final valid result. The calculated rate of invalids in this study was 0.34% with a 95% confidence interval of 0.19% to 0.59%.

4. Clinical cut-off**:**

Not applicable.

5. Expected Values

In this clinical study, there were a total of 1290 specimens prospectively collected from the intended use population were tested with the Lumipulse *G* TP-N assay. The distribution of the Lumipulse *G* TP-N results in the prospective population in this study, stratified by age and gender, is shown in the table below.

Age Range	**Gender**	**Lumipulse *G* TP-N Result**		Total
		Number of Reactive (%)	**Number of Nonreactive (%)**	
18 to 21	Female	0 (0%)	22 (100%)	22
	Male	3 (10%)	26 (90%)	29
22 to 29	Female	0 (0%)	90 (100%)	90
	Male	27 (18%)	119 (82%)	146
30 to 39	Female	3 (3%)	115 (97%)	118
	Male	40 (21%)	149 (79%)	189
40 to 49	Female	7 (11%)	56 (89%)	63
	Male	28 (18%)	127 (82%)	155
50 to 59	Female	32 (26%)	89 (74%)	121
	Male	53 (22%)	188 (78%)	241
60 to 64	Female	5 (20%)	20 (80%)	25
	Male	16 (28%)	42 (72%)	58
≥ 65	Female	0 (0%)	6 (100%)	6
	Male	5 (19%)	22 (81%)	27
Total		**219 (17%)**	**1071 (83%)**	**1290**

N. Instrument Name:

LUMIPULSE *G*1200

O. System Descriptions:

LUMIPULSE *G*1200 is intended for *in vitro* diagnostic use and is designed to perform automated chemiluminescence immunoassays of specimens using LUMIPULSE G reagents,

conducting various processes such as sample aspiration and dispensing, agitation, timed incubation and photometric measurement.

There are two primary software components that make up the Lumipulse G TP-N Immunoassay:

1. The Lumipulse *G* TP-N Assay Definition File (ADF), and
2. The LUMIPULSE *G* System software.

The ADF is a file that contains assay specific-parameters and interpretive criteria including the sequence of steps by which a given assay is executed.

The LUMIPULSE *G* System software interprets information from the Lumipulse *G* TP-N ADF to direct how the LUMIPULSE *G* instrument interacts with the assay.

The LUMIPULSE *G*1200 instrument platform was originally cleared under K142895.

1. Modes of Operation:

   This is a fully automated immunoassay analyzer.

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X_____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X_____

2. Software:

   The current version of the LUMIPULSE *G*1200 system software is v3.21.

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X_____ or No _____

   The LUMIPULSE *G* System software is the computer program that interprets system and assay information, calculates results, and provides the interface for controlling the system hardware. The software interface is the portion of the computer program which a user operates to make selections and enter information. The interface allows users to initiate commands or make choices by selecting icons, buttons, items from lists, etc. The LUMIPULSE *G* System software interface is designed to provide consistent and easy access to system information, software functions, and troubleshooting.

3. Specimen Identification:

   Patient samples are barcoded and barcodes are read by the instrument. The assay to be performed can be identified by manual entry of the patient ID number and associated information or information can be imported from a host computer.

4. Specimen Sampling and Handling:

   Specimen processing is automated. Sample containers are set in Sample Racks. Barcode IDs attached to sample container are read, along with the type of Sample rack and Rack ID. The operator follows the system prompts and inputs the appropriate sample, rack, and assay information. The LUMIPULSE *G* System automatically performs various processes including dispensing, agitation, washing, photometric measurement, and result calculation.

   Two methods of designating the assay to be performed are:

   1. Rack ID assay, in which the entire rack of samples is tested by one assay (sample position in the rack is manually entered), and
   2. Patient ID assay, in which each sample is individually designated for its own assay.

   The Rack ID assay is conducted according to the Rack ID and rack position where samples are registered during the sample registration process. Samples are manually set in the positions in the rack where they are registered.

   The Patient ID assay is conducted according to the Patient ID barcode on the sample containers. Sample containers can be set in any position of any rack.

5. Calibration:

   Calibration is required after assay installation and entails generation of an active calibration curve. Assays do not need to be calibrated every time they are run; however, certain variables make recalibration necessary. Calibration must be performed when a new reagent lot is used, when 60 days elapsed since the previous calibration, when the controls are out of range, and when documentation accompanying a new version of an existing assay states that calibration is required.

6. Quality Control:

   Quality control is addressed by running external controls with at least two levels, e.g., negative or nonreactive, and positive or reactive. Quality control material is not provided with the assay.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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