DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

July 5, 2016

Diana Dickson
Director, Clinical and Regulatory Science
Fujirebio Diagnostics, Inc.
201 Great Valley Parkway
Malvern, PA 19355

Re: K153145
Trade/Device Name: LUMIPULSE G TP-N Immunoreaction Cartridges Set
Regulation Number: 21 CFR 866.3830
Regulation Name: *Treponema pallidum* treponemal test reagents
Regulatory Class: Class II
Product Code: LIP
Dated: May 31, 2016
Received: June 1, 2016

Dear Ms. Dickson:

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

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

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

CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Steven R. Gitterman -S

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K153145

Device Name
Lumipulse *G* TP-N Immunoreaction Cartridges set

Indications for Use *(Describe)*
Lumipulse *G* TP-N Immunoreaction Cartridges Set

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

A. 510(k) Number:

K153145

B. Purpose for Submission:

New device

C. Measurand:

IgG and IgM antibodies to *Treponema pallidum* (T. pallidum)

D. Type of Test:

Qualitative assay, automated chemiluminescent enzyme immunoassay (CLEIA)

E. Applicant:

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

Contact person: Stacey Dolan
(610) 240-3843
dolans@fdi.com

Summary preparation date**: June 28, 2016**

F. Proprietary and Established Names:

Lumipulse ***G*** TP-N Immunoreaction Cartridges Set

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.3830, *Treponema pallidum* treponemal test reagents

2. Classification:
   Class II

3. Product code:
   LIP, Enzyme Linked Immunoabsorption Assay, *Treponema Pallidum*

4. Panel:
   83, Microbiology

H. Intended Use:

1. Intended use(s):
   See indications for use below.

2. Indication(s) for use:

   Lumipulse ***G*** TP-N Immunoreaction Cartridges Set

   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.

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

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) in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G*** System.

Lumipulse ***G*** TP-N Immunoreaction Cartridges Set REF 235041
The Lumipulse ***G*** TP-N Immunoreaction Cartridges Set contains the following:

1. Lumipulse ***G*** TP-N Immunoreaction Cartridges – 3 x 14 tests

   Antibody-Coated Particle Solution
   (Liquid when used, 250 µL/Immunoreaction Cartridge)
   Contains 75 µg/mL recombinant TP antigen (Tp15-17)-coated particles, 75 µg/mL recombinant TP antigen (TpN47)-coated particles, protein stabilizers (bovine) 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 Antigen Solution
   (Liquid, 350 µL/Immunoreaction Cartridge)
   Contains 0.075 µg/mL alkaline phosphatase (ALP: calf) labeled recombinant TP antigen (Tp15-17), 0.075 µg/mL ALP (calf)-labeled recombinant TP antigen

(TpN47) and protein stabilizers (bovine and calf) and chemical stabilizers in 0.1 M sodium chloride/Tris buffer. Preservative: sodium azide.

2. Lumipulse ***G*** TP-N Calibrators – **CAL** Liquid, 1 × 2 Concentrations

CAL N TP calibrator-N (1 × 2.0 mL)
CAL P TP calibrator-P (1 × 2.0 mL)
Contains 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). The material of TP calibrator-P is processed from anti-TP positive but inactivated human serum. Preservative: sodium azide.

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:

Similarities		
	Lumipulse *G* TP-N (k153145)	**ADVIA Centaur Syphilis (SYPH) Assay (Predicate Device) k112343**
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification	Class II	Class II
Regulation Number	21CFR § 866.3830 *Treponema pallidum* treponemal test reagents	21CFR § 866.3830 *Treponema pallidum* treponemal test reagents
Product Usage	Clinical and Hospital laboratories	Clinical and Hospital laboratories
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 diagnostic test or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection.	The ADVIA Centaur Syphilis (SYPH) assay is an *in-vitro* diagnostics 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.
Black box warning (PRECAUTION)	**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.	**WARNING.** The ADVIA Centaur SYPH assay 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.
Assay Type	Direct sandwich immunoassay based on chemiluminescent technology	Direct sandwich immunoassay based on chemiluminescent technology
Specimen Collection Method	Routine Phlebotomy Techniques	Routine Phlebotomy Techniques

Differences		
	Lumipulse *G* TP-N (k153145)	**ADVIA Centaur Syphilis (SYPH) Assay (Predicate Device) k112343**
Instrument System	LUMIPULSE ***G*** System	ADVIA Centaur
Principle of Operation	Automated Chemiluminscent Microparticle Immunoassay (CMIA)	Chemilunescence Enzyme Immunoassay (CLEIA)
Sample Volume	60 µL	100 µL
Capture/Detection Antigen/Antibody	Recombinant antigens TpN15-17 and TpN47 on microparticles and recombinant antigens TpN15-17 and TpN47 alkaline phosphatase conjugates	Recombinant antigens TpN17 and TpN15 as biotin conjugates and recombinant antigens TpN17 and TpN15 as acridinium ester conjugates
Calibrators	2 calibrators - anti-TP positive human plasma is used in the Lumipulse **G** TP-N positive calibrator and delipidized normal human sera are used in the Lumipulse **G** TP-N negative calibrator.	2 calibrators - liquid in human plasma
Cut-off	< 1.0 Non-reactive ≥ 1.0 Reactive	< 0.9 Non-reactive ≥ 0.9 to < 1.1 Equivocal ≥ 1.1 Reactive
Type of Specimen	Human serum or plasma (EDTA or sodium citrate)	Human serum or plasma (EDTA, lithium or sodium heparinized, citrate)
Analyte Detected	IgG and IgM antibodies to *Treponema pallidum*	IgG antibodies to *Treponema pallidum*

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 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 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:

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) in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G*** System.

Anti-TP antibodies in specimens (IgG and IgM) specifically binds to recombinant TP antigens (Tp15-17 and TpN47) on the particles, and antigen-antibody complexes are formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase (ALP: calf)-labeled recombinant TP antigens (Tp15-17 and TpN47) specifically bind to anti-TP antibodies of the immunocomplexes on the particles, and additional immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Substrate Solution is added and mixed with the particles. AMPPD contained in the Substrate Solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of anti-TP antibodies.

*AMPPD: 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane disodium salt

M. Performance Characteristics (if/when applicable):

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

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

   a. *Precision/Reproducibility:*

   The precision of the Lumipulse ***G*** TP-N was evaluated in a study at one internal site conducted according to the Clinical and Laboratory Standards Institute (CLSI) Protocol EP05-A3. One human sodium citrate-based sample (specimen pool) and five human serum-

based samples (specimen pools), two reactive controls and one nonreactive control were 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. 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 3 laboratory sites. One human sodium citrate-based sample (specimen pool) and five human serum-based samples (specimen pools), two reactive controls and one nonreactive control were 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. 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	SD	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.

The lot-to-lot precision of the Lumipulse ***G*** TP-N assay was evaluated using 3 lots of Lumipulse ***G*** TP-N immunoreaction cartridges and calibrators. The above human samples (specimen pools) and three controls were 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. Data from this study are presented below. The %CV for between-lot imprecision was ≤5.7% for any of the 9 samples.

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

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

Calibrators
Calibration of the Lumipulse ***G*** TP-N is traceable to in-house reference calibrators, whose values have been assigned to correlate with SERODIA®–TP·PA.

CAL N TP calibrator-N (1 × 2.0 mL)
CAL P TP calibrator-P (1 × 2.0 mL)

Contains 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). The material of TP calibrator-P is processed from anti-TP positive but inactivated human serum. Preservative: sodium azide.

Stability
Shelf life: The shelf life for Lumipulse ***G*** TP-N is 9 months at 2–10° C.

On board: The Lumipulse ***G*** TP-N cartridges remain stable at the end of shelf life when stored under on-board conditions (12° C). Labeling recommends calibrator storage for 30 days.

Transport: Lumipulse ***G*** TP-N is shipped at 2-10°C.

Sample Stability: Specimens collected in all four matrices (Red top serum tube, SST, K2-EDTA and Sodium Citrate) were stable at 23-27°C for up to 3 days, 2-10 °C for up to 4 days, or -10°C or colder for longer periods.
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.

d. Detection limit:

Samples with a cutoff index (C.O.I.) of < 1.0 are considered nonreactive for syphilis *T. pallidum* antibodies.

Samples with a cutoff index (C.O.I.) ≥ 1.0 are considered reactive for syphilis *T. pallidum* antibodies.

e. Analytical specificity:

Lumipulse ***G*** TP-N 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. Human serum specimens were supplemented with potentially interfering substances. The study showed that the Lumipulse ***G*** TP-N assay is not susceptible to interference from the following substances at the concentrations 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

Lumipulse ***G*** TP-N on the LUMIPULSE ***G***1200 System was evaluated for potential cross-reactivity in other diseases and biological conditions using 282 specimens obtained from patients known to have a variety of microbial and viral infections, biological abnormalities and from drug users. The presence of the potential cross-reactant was confirmed with a FDA cleared assay (where applicable). 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**

All samples reactive with the Lumipulse ***G*** TP-N assay were also reactive with the TP·PA assay, with the exception of 1 Rubella IgG sample and 2 samples from drug users, indicating reactivity to Syphilis (*T. Pallidum* antibodies) rather than cross reactivity.

Results comparing the Lumipulse ***G*** TP-N, a FDA cleared EIA and TP·PA assay for the study above are 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 on the TP·PA if both the Lumipulse ***G*** TP-N and the FDA Cleared EIA tested non-reactive

f. Assay cut-off:

Lumipulse ***G*** TP-N was developed in 1997. 312 negative specimens, 99 positive specimens, and 6 intermediate specimens previously assigned using TP-PA were measured with Lumipulse ***G*** TP-N in order to establish its cut-off index. There is clear separation of negative and positive results when using a cut-off value of 1.0.

2. Comparison studies:

a. Method Comparison

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 and/or protocol deviations) 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 a defined period of time. The specimens were collected from 7 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 (250 without syphilis, 129 with syphilis), 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 subjects and 399 adult/not pregnant subjects were tested with the Lumipulse ***G*** TP-N assay.

The overall success rate during clinical testing was 99.7% (3540/3552). All 12 specimens were retested and valid results were obtained after a single retest.

1. 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 Food and Drug Administration (FDA) cleared tests: a treponemal test (EIA), a non-treponemal Rapid Plasma Reagin (RPR) test, and a second treponemal test, *Treponema pallidum* particle agglutination (TP·PA). A determination of positive, negative or indeterminate result was made for each test according to the directions in the labeling.

The final comparator result was determined using a 2 out of 3 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 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 described below.

Reference Comparator Algorithm			
EIA (Treponemal Test)	**RPR (Non-treponemal Test)**	**TP·PA (Second 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.

Percent agreement between the Lumipulse ***G*** TP-N and the Final Comparator Result

The Positive Percent Agreement (PPA) was 92.7% (Confidence Interval (CI) 88.6%, 95.4%) and the Negative Percent Agreement (NPA) was 99.6% (CI 99.0%, 99.9%).

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 summary of the serological test profile for the prospective study 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	Indeterminate	Positive	Negative	3
Positive	Positive	Negative	Positive	Positive	3
Equivocal	Negative	Negative	Negative	Negative	2
Negative	Negative	Positive	Negative	Negative	2
Negative	Positive	Positive	Positive	Positive	2
Negative	Negative	Positive	Negative	Positive	1
				Total	1290

The study population consisted of subjects sent for routine syphilis testing, those with previous history of syphilis, pregnant women (3%), and persons positive for HIV. The percent agreement of the Lumipulse ***G*** TP-N assay results when compared to the Final Comparator Result 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.

Due to variance in geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented.

Performance of the Lumipulse G TP-N assay with Retrospective Samples

The age range for the 1472 evaluable subjects was 14 to 89 with a median age of 33. The retrospective population had more female than male subjects (57% vs. 43%, respectively). Subjects were from different locations across the US. The pregnant subjects were evenly split across each trimester.

Percent agreement between the Lumipulse ***G*** TP-N and the Final Comparator Result

The Positive Percent Agreement (PPA) was 94.3% (CI 92.0%, 96.0%) and the Negative Percent Agreement (NPA) was 98.1% (CI 97.0%, 98.8%).

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				

A summary of the serological test profile for the retrospective samples is summarized in the following table.

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	Indeterminate	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	Indeterminate	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	Indeterminate	Positive	Positive	2
Positive	Negative	Indeterminate	Positive	Negative	4
Equivocal	Negative	Negative	Negative	Negative	10
				Total	1472

The percent agreement of the Lumipulse ***G*** TP-N assay results when compared to the Final Comparator Result 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)	95.5, 99.9	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

The percent agreement between the Lumipulse ***G*** TP-N 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

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

The performance of the Lumipulse ***G*** TP-N assay was also evaluated with samples from medically diagnosed syphilis subjects, based on clinical information and laboratory test results.

The age range for the 289 subjects evaluated was 18 to 78 with a median age of 44. The population was predominantly male (67%). 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 syphilis stage and 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).

Category	Lumipulse *G* TP-N Result		Total
	Number of Reactive (%)	**Number of Nonreactive (%)**	
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

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.

b. *Matrix Comparison*
Lumipulse ***G*** TP-N on the LUMIPULSE ***G***1200 was evaluated for matrix differences by performing a study using sixty (60) matched sets of serum (red top and serum separator tubes (SST)) and plasma (K2EDTA and sodium citrate) samples. The results demonstrated equivalency between the matrices and are presented in the following table:

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

3. Clinical studies:

   a. Clinical sensitivity:

   Not applicable (See item 2a above)

   b. Clinical specificity:

   Not applicable (See item 2a above)

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

4. Clinical cut-off**:**

   Not applicable

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

The distribution of 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

6. Conclusion

The results of these analytical (nonclinical) and clinical studies demonstrate that the performance of the Lumipulse ***G*** TP-N assay is substantially equivalent to the performance of the ADVIA Centaur Syphilis (SYPH) assay.

N. Proposed Labeling:

The labeling satisfies the requirements of 21 CFR Part 809.10.