DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

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

Re: K142895
Trade/Device Name: Lumipulse ***G*** CA125II Immunoreaction Cartridges
Lumipulse ***G*** CA125II Calibrators
Lumipulse ***G***1200 System
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-associated antigen immunological test system
Regulatory Class: II
Product Code: LTK, JIT, JJE
Dated: May 4, 2015
Received: May 5, 2015

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 regulations (21 CFR Parts 801 and 809), 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" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

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,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology 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)*
k142895

Device Name
Lumipulse G CA125II Immunoreaction Cartridges
Lumipulse G CA125II Calibrators
LUMIPULSE G1200 System

Indications for Use *(Describe)*
Indications for Use (Describe)
Lumipulse G CA125II Immunoreaction Cartridges
For in vitro diagnostic use.

Lumipulse G CA125II is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of CA125 in human serum and plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE G System.

The assay is to be used as an aid in monitoring recurrence or progressive disease in patients with ovarian cancer. Serial testing for patient CA125 assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

Lumipulse G CA125II Calibrators
Lumipulse G CA125II Calibrators are for use in the calibration of the LUMIPULSE G System for the quantitative measurement of CA125 in human serum or plasma (sodium heparin, lithium heparin, or dipotassium EDTA).

LUMIPULSE G1200 System
LUMIPULSE G1200 is intended for in vitro diagnostics use, and is designed to perform automated chemiluminescence immunoassays of specimens using Lumipulse G reagents, conducting various processes such as dispensing, agitation and photometric measurement.

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:

k142895

B. Purpose for Submission:

New device and instrument

C. Measurand:

CA125

D. Type of Test:

Quantitative assay, automated chemiluminescent enzyme immunoassay (CLEIA)

E. Applicant:

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

Contact person: Diana Dickson
(610) 240-3917
dicksond@fdi.com

Summary preparation date**: May 15, 2015**

F. Proprietary and Established Names:

Lumipulse ***G*** CA125II Immunoreaction Cartridges
Lumipulse ***G*** CA125II Calibrators
LUMIPULSE***G***1200 System

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.6010, Tumor-associated antigen immunological test system
   21 CFR § 862.1150, Calibrator
   21 CFR § 862.2160 Discrete photometric chemistry analyzer for clinical use

2. Classification:
   Class II and Class I

3. Product code:
   LTK, Test, Epithelial Ovarian Tumor-Associated Antigen (CA125)

JIT, Calibrator, Secondary
JJE, analyzer, chemistry (photometric, discrete), for clinical use

4. Panel:
   82, Immunology (Assay and instrument)
   75, Chemistry (Calibrators)

H. Intended Use:

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

2. Indication(s) for use:

   Lumipulse ***G*** CA125II Immunoreaction Cartridges

   For in vitro diagnostic use.

   Lumipulse ***G*** CA125II is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of CA125 in human serum and plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE ***G*** System.

   The assay is to be used as an aid in monitoring recurrence or progressive disease in patients with ovarian cancer. Serial testing for patient CA125 assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.

   Lumipulse ***G*** CA125II Calibrators

   Lumipulse ***G*** CA125II Calibrators are for use in the calibration of the LUMIPULSE ***G*** System for the quantitative measurement of CA125 in human serum or plasma (sodium heparin, lithium heparin, or dipotassium EDTA).

   LUMIPULSE ***G***1200 System

   LUMIPULSE ***G***1200 is intended for in vitro diagnostics use, and is designed to perform automated chemiluminescence immunoassays of specimens using Lumipulse ***G*** reagents, conducting various processes such as dispensing, agitation and photometric measurement.

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

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

I. Device Description:

Lumipulse ***G*** CA125II is an assay system, including a set of immunoassay reagents, for the quantitative measurement of CA125 in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G*** System.

Lumipulse ***G*** CA125II Immunoreaction Cartridges REF 234273
Lumipulse ***G*** CA125II Immunoreaction Cartridges 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-CA125 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-CA125 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*** CA125II Calibrators CAL 234266
Each calibrator kit contains one bottle each of Calibrators 1 and 2. The calibrator kit is packaged separately.

CAL Liquid, 1 × 2 Concentrations
CAL 1 0 U/mL CA125 calibrator (1 × 1.5 mL)
CAL 2 1000 U/mL CA125 calibrator (1 × 1.5 mL)
Contains 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide.

LUMIPULSE ***G***1200 System

LUMIPULSE *G*1200 is intended for in vitro diagnostics use, and is designed to perform automated chemiluminescence immunoassays of specimens using Lumipulse ***G*** reagents, conducting various processes such as dispensing, agitation, and photometric measurement. The chemiluminescent enzyme immunoassay system is carried out using the ferrite particle coated with antigen or antibody and conjugate with alkaline phosphatase and the chemical luminescent substrate. The luminescence which is produced by the chemiluminescent enzyme immunoassay is measured by photometric detector.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Siemens ADVIA Centaur CA 125II

2. Predicate 510(k) number(s):
   k020828

3. Comparison with predicate:

Similarities		
	Lumipulse *G* CA125II Assay (Proposed Device) k142895	**Siemens ADVIA Centaur CA 125II Assay (Predicate Device) k020828**
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification	Class II	Class II
CFR section	866.6010	866.6010
Product Code	LTK	LTK
Product Usage	Clinical and Hospital laboratories	Clinical and Hospital laboratories
Intended Use	Lumipulse ***G*** CA125II is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of CA125 in human serum and plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE ***G*** System. The assay is to be used as an aid in monitoring recurrence or progressive disease in patients with ovarian cancer. Serial testing for patient CA125 assay values should be used in conjunction with other clinical methods used for monitoring ovarian cancer.	For in vitro diagnostic use in the quantitative, serial determination of CA125 in human serum and to aid in the management of patients with ovarian carcinoma using the ADVIA Centaur® and ADVIA Centaur XP® systems. The test is intended for use as an aid in monitoring patients previously treated for ovarian cancer. Serial testing for CA 125 in the serum of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the ADVIA Centaur CA 125 II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or for use on any other system.
Interpretation of Results	Calibrator Curve	Calibrator Curve
Specimen Collection Method	Routine Phlebotomy Techniques	Routine Phlebotomy Techniques
Antibodies	M11 and OC125 (mouse monoclonal)	M11 and OC125 (mouse monoclonal)
Analyte	Human CA125	Human CA125

Differences		
	Lumipulse *G* CA125II Assay (Proposed Device) k142895	**Siemens ADVIA Centaur CA 125II Assay (Predicate Device) K020828**
Instrument System	LUMIPULSE ***G***1200 System	ADVIA Centaur® and ADVIA Centaur XP®
Principle of Operation	Chemiluminscent Enzyme Immunoassay (CLEIA)	Chemiluminescent Immunoassay (CLIA)
Type of Specimen	Human Serum or Plasma (sodium heparin, lithium heparin, or dipotassium EDTA)	Human Serum
Assay Range	2.5 – 1000 U/mL	2 – 600 U/mL
Calibrators	2 Levels (0 and 1000 U/mL) Ready to Use -Liquid -Supplied as separate kit	2 Levels (Low and High) -Lyophilized -Supplied as separate kit

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

- BS EN 13640:2002 - Stability Testing of In Vitro Diagnostic Reagents
- ISO 17511:2003 Measurement of Quantities in Biological Samples - Metrological Traceability of Values Assigned to Calibrator and Control Materials
- CLSI EP5-A2 - Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition
- CLSI EP7-A2 - Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition
- CLSI C28-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
- FDA Guidance Document for the Submission of Tumor Associated Antigen Premarket Notifications, [510(k)], to FDA
- 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
- FDA Guidance Document - Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 11, 2005)

L. Test Principle:

Lumipulse ***G*** CA125II is an assay system, including a set of immunoassay reagents, for the quantitative measurement of CA125 in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G*** System. CA125 in specimens specifically binds to anti-CA125 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-CA125 monoclonal antibody (mouse) specifically binds to CA125 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 CA125.

M. Performance Characteristics (if/when applicable):

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

1. Analytical performance:

   a. *Precision/Reproducibility:*

   Lumipulse ***G*** CA125II is ≤10% total (within-laboratory) CV (coefficient of variation). Lumipulse ***G*** CA125II demonstrated precision ≤2.6% total %CV in a study run according to the Clinical and Laboratory Standards Institute (CLSI) guideline EP5-A2. Eight human serum-based samples (specimen pools) and two commercially available serum-based controls 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 Conc. (U/mL) n=80	Within-run SD (U/mL)	Within-run %CV	Total SD (U/mL)	Total %CV
Serum 1	21.1	0.36	1.7	0.48	2.3
Serum 2	37.5	0.54	1.4	0.60	1.6
Serum 3	112.2	1.47	1.3	1.80	1.6
Serum 4	254.8	3.74	1.5	3.96	1.6
Serum 5	577.9	10.90	1.9	11.01	1.9
Serum 6	10.9	0.21	1.9	0.26	2.4
Serum 7	454.7	6.51	1.4	8.78	1.9
Serum 8	798.6	13.04	1.6	13.74	1.7
Control 1	20.2	0.47	2.3	0.52	2.6
Control 2	292.5	4.23	1.4	6.60	2.3

Site to site: Lumipulse ***G*** CA125II demonstrated precision ≤6.4% total %CV when tested at 3 external laboratory sites. The human serum-based samples (specimen pools) and two commercially available serum-based controls were assayed in replicates of two at two

separate times of the day at each of the sites for 10 days (n=40 for each sample) using one LUMIPULSE ***G***1200 System. Data from this study are summarized below.

Sample	Mean Conc. (U/mL) n=120	Within-run SD (U/mL)	Within-run %CV	Total SD (U/mL)	Total %CV
Serum 1	21.4	0.40	1.9	1.12	5.2
Serum 2	38.0	0.62	1.6	1.81	4.8
Serum 3	112.5	2.04	1.8	4.44	3.9
Serum 4	254.8	3.27	1.3	9.08	3.6
Serum 5	580.5	9.85	1.7	19.45	3.4
Control 1	21.2	0.62	2.9	1.35	6.4
Control 2	301.8	3.71	1.2	17.22	5.7

Lot-to-lot: Lumipulse ***G*** CA125II demonstrated precision ≤5.2% total %CV when tested using 3 lots of Lumipulse ***G*** CA125II immunoreaction cartridges and calibrators. The human serum-based samples (specimen pools) and two commercially available serum-based controls were assayed in replicates of two at two separate times of the day for each of the lots for 10 days (n=40 for each sample) using one LUMIPULSE ***G***1200 System. Data from this study are summarized below.

Sample	Mean Conc. (U/mL) n=120	Within-run SD (U/mL)	Within-run %CV	Total SD (U/mL)	Total %CV
Serum 1	22.1	0.43	1.9	1.12	5.1
Serum 2	39.1	0.64	1.6	1.88	4.8
Serum 3	118.4	1.53	1.3	6.13	5.2
Serum 4	268.0	3.78	1.4	12.75	4.8
Serum 5	599.3	10.75	1.8	22.45	3.7
Control 1	21.1	0.52	2.5	1.01	4.8
Control 2	305.0	4.06	1.3	14.61	4.8

b. Linearity/assay reportable range:

Lumipulse ***G*** CA125II demonstrated linearity on the LUMIPULSE ***G***1200 system in a study consistent with CLSI guideline EP6-A. One human serum specimen pool and one K2 EDTA plasma specimen pool with high CA125 levels were diluted with one human serum specimen pool and one K2 EDTA plasma specimen pool with low CA125 levels throughout the range of the assay. The linearity was found in the range of 2.5 to 1000 U/mL. Lumipulse ***G*** CA125II correlated with expected concentrations according to the linear regression formulas:

Serum: y= 0.9973(x)+ 1.5017; R-squared: 0.9999
Plasma: y= 1.0147(x)+ 3.9653; R-squared: 0.9996

Lumipulse ***G*** CA125II recovery on the LUMIPULSE ***G***1200 System is 100 ± 15%, ranging from 97% to 115%. A study was performed where known concentrations of OC125 defined antigen were added to human serum and K2 EDTA plasma samples with low endogenous CA125 levels. The concentration of CA125 was determined using the Lumipulse ***G*** CA125II and the resulting percent recovery was calculated.

Sample	Target CA125 Levels (U/mL)	Measured Conc. U/mL (n=3)	Expected Conc. (U/mL)	% Recovery
Serum 1	100	102.7	103.2	100
	300	304.6	296.1	103
	500	500.9	502.9	100
	700	710.2	697.2	102
	950	1087.2	945.1	115
Serum 2	100	121.9	119.9	102
	300	318.3	312.8	102
	500	506.8	519.6	98
	700	704.9	713.9	99
	950	981.6	961.8	102
Serum 3	100	104.6	103.7	101
	300	301.3	296.6	102
	500	490.1	503.4	97
	700	679.9	697.7	97
	950	952.4	945.6	101
Plasma 1	100	103.9	101.9	102
	300	293.6	294.8	100
	500	492.8	501.6	98
	700	680.0	695.9	98
	950	944.4	943.8	100
Plasma 2	100	105.5	110.0	96
	300	307.7	302.9	102
	500	507.9	509.7	100
	700	719.5	704.0	102
	950	973.8	951.9	102
Plasma 3	100	106.5	105.2	101
	300	291.2	298.1	98
	500	503.5	504.9	100
	700	684.2	699.2	98
	950	922.3	947.1	97

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For Lumipulse ***G*** CA125II, no high dose hook effect was observed for samples containing up to 200,000 U/mL of OC125 defined antigen on the LUMIPULSE ***G***1200 system. However, values above 20,000 U/mL should be interpreted with caution because reading may be inaccurate above this concentration.

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

Lumipulse ***G*** CA125II Calibrators are for use in the calibration of the LUMIPULSE ***G*** System when used for the quantitative measurement of CA125 in serum or plasma (dipotassium EDTA, lithium heparin, and sodium heparin). 2 Bottles (1.5 mL each) are supplied for the Lumipulse ***G*** CA125II Calibrators. Preservatives: Sodium Azide. The calibrators are at the following concentrations:

Calibrator	Concentration (U/mL)
CAL 1	0
CAL 2	1000

There is currently no known internationally recognized consensus reference method or reference material for standardization. Lumipulse ***G*** CA125II values are expressed as U/mL. This value is related to a Fujirebio Diagnostics maintained reference preparation. Calibration of the Lumipulse ***G*** CA125II is traceable to in-house reference calibrators, whose values have been assigned to correlate to Fujirebio Diagnostics' CA125II RIA.

The real time stability (including open use) has been demonstrated on the LUMIPULSE ***G***1200 system for 10 months. The instrument cartridge and calibrators were found to be stable under simulated transport conditions. Shelf life assignment for the Lumipulse ***G*** CA125II Immunoreaction Cartridges and Calibrators is 10 months at 2–10°C.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) of LUMIPULSE ***G*** CA125II on the LUMIPULSE ***G***1200 system is ≤ 2.0 U/mL.

1) LoB and LoD
The LoB for Lumipulse ***G*** CA125II was 0.1 U/mL.
The LoD for Lumipulse ***G*** CA125II on the LUMIPULSE ***G***1200 system was 0.5 U/mL, determined consistent with the CLSI guideline EP17-A. Seven low level specimens were tested over 3 days using two LUMIPULSE ***G***1200 Systems and two Lumipulse ***G*** CA125II lots giving 120 determinations for each panel.

2) LoQ
The LoQ for Lumipulse ***G*** CA125II on the LUMIPULSE ***G***1200 system was 0.5 U/mL, determined consistent with the guidelines in the CLSI guideline EP17-A. Since the percent total error in all cases is less than 30%, LoQ equals LoD.

e. Analytical specificity:

The Lumipulse ***G*** CA125II on the LUMIPULSE ***G***1200 system demonstrated an average interference of ≤ 10% (for each compound) in a study consistent with the guidelines in the CLSI guideline EP7-A2. Human serum and K2 EDTA plasma specimen pools were supplemented with potentially interfering compounds. The following compounds were tested and found not to interfere with the test.

Endogenous Interferences	Test Concentration
Free Bilirubin (unconjugated)	60 mg/dL
Conjugated Bilirubin	60 mg/dL
Triglycerides (Intralipid 20% Emulsion)	3000 mg/dL
Hemoglobin	500 mg/dL
Human Serum Albumin	12 g/dL
Immunoglobulin G (IgG)	5 g/dL
Biotin	19.7 mg/dL
Human Anti-Mouse Antibodies (HAMA)	1,000 ng/mL
Rheumatoid Factor (RF)	1,000 IU/mL

Therapeutic drug Interferences	Test Concentration
Carboplatin	600 µg/mL
Cisplatin	180 µg/mL
Clotrimazole	0.3 µg/mL
Cyclophosphamide	800 µg/mL
Dexamethansone	20 µg/mL
Doxorubicin	120 µg/mL
Erlotinib	150 ug/mL
Etoposide	10 ug/mL
5-Fluorouracil	900 ug/mL
Gemcitabine	100 ug/mL
Leucovorin	750 µg/mL
Magestrol Acetate	10 ug/mL
Melphalan	15 µg/mL
Methotrexate	450 µg/mL
Paclitaxel	3.5 ng/mL
Tamoxifen	60 ug/mL

f. Assay cut-off:

See Clinical Cutoff in M (4) below

2. Comparison studies:

a. Method Comparison

Lumipulse ***G*** CA125II method comparison study was performed on the LUMIPULSE ***G***1200 system using specimens consistent with CLSI guideline EP9-A3 using the weighted Deming regression method to compare Lumipulse ***G*** CA125II to ADVIA Centaur CA 125II. The ADVIA Centaur CA 125II has a different measuring range than the Lumipulse ***G*** CA125II therefore the results limited to the measurement range of both devices (102 samples). The samples tested ranged from 15.5–822.2 U/mL. The data are summarized in the following table.

Lumipulse *G* CA125II vs. ADVIA Centaur CA 125II

n	Correlation Coefficient (r)	Intercept (95% CI)	Slope (95% CI)	Average Bias (U/mL)
102	0.9745	-0.87	1.13	25.6
		-6.32 – 4.58	1.06 – 1.12	

The data summarized in the following table include results from a study with specimens above the measurement range of both devices requiring dilution (120 samples). The samples tested ranged from 15.5–1128.8 U/mL.

Lumipulse *G* CA125II vs. ADVIA Centaur CA 125II

n	Correlation Coefficient (r)	Intercept (95% CI)	Slope (95% CI)	Average Bias (U/mL)
120	0.9829	1.55	1.08	18.2
		-2.89 – 5.99	1.03 – 1.13	

b. *Matrix Comparison*

The Lumipulse ***G*** CA125II matrix comparison study was performed on the LUMIPULSE ***G***1200 system to evaluate the difference across tube types (SST, K2EDTA, Lithium Heparin, and Sodium Heparin) versus the means of the control samples (Red top serum) analyzed per CLSI guideline EP9-A3. The slope for each tube type when compared to the control had 95% confidence intervals that lay entirely within the range 0.9 to 1.1 and the correlation coefficients were ≥ 0.9.

3. Clinical studies:

a. Clinical sensitivity:

See 3(c) below

b. Clinical specificity:

See 3(c) below

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

Monitoring of Disease status in Patients Diagnosed with Ovarian Cancer

The effectiveness of Lumipulse ***G*** CA125II on the LUMIPULSE ***G***1200 system as an aid in monitoring of disease status in ovarian cancer patients was determined by assessing changes in CA125 levels in serial serum samples from 59 patients compared to changes in disease status. A study involving a total of 289 pairs of observations was undertaken with an average number of 5.9 observations per patient. A positive change in CA125 was defined as an increase in the value that was at least 20% greater than the previous value of the test. This level of change takes into account the variability of the assay. Sixty-seven percent (67%) or 35/52 of the patient samples with a positive change correlated with the disease progression while seventy-six percent (76%) or 180/237 of the patient serial samples with no significant change in CA125 value correlated with no progression. The total concordance was seventy-four percent (74% or 215/289).

Lumipulse ***G*** CA125II Performance Measurements (%):

Performance Measurement		SE	Lower 95% CI	Upper 95% CI
Sensitivity	67.3	18.70	29.9	100.0
Specificity	76.0	7.45	61.0	90.9
Total Concordance	74.4	6.74	60.9	87.9
PPV	38.0	10.57	16.9	59.2
NPV	91.4	8.96	73.4	100.0

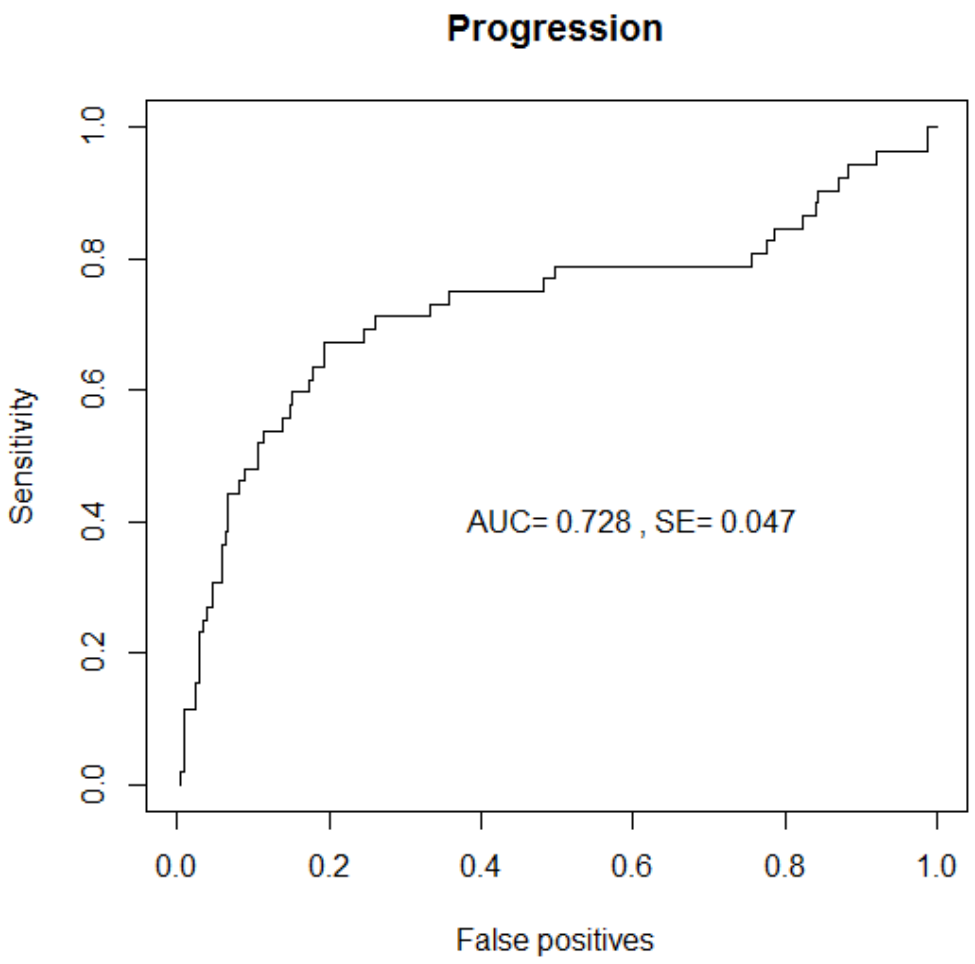
SE = Standard Error
CI = Confidence Interval

The following table presents the data in a 2 x 2 format.

Change in Disease State per Sequential Pair			
Change in CA125 Concentration	**No progression**	**Progression**	**Total**
≤ 20%	180	17	197
> 20%	57	35	92
Total	237	52	289

A ROC curve for the diagnosis of progression from the ratio of successive CA125II readings is shown below.

The area under the AUC curve is 0.728 with SE 0.047; this is highly statistically significantly better than the no-association AUC of 0.5.



4. Clinical cut-off**:**

   There is no conventional cut-off for this assay; however, CA125 is significantly elevated if it is at least 20% higher than the previous assay.

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

The distribution of CA125 levels determined on the LUMIPULSE ***G***1200 system in healthy premenopausal women and healthy postmenopausal women is shown in the table below:

	All Healthy Subjects	**Premenopausal Healthy Subjects**	**Postmenopausal Healthy Subjects**
N	240	120	120
Mean	12.2	13.6	10.7
(SD)	(9.3)	(12.0)	(5.0)
Median	10.4	11.7	9.6
Range (min, max)	2.9, 123.9	3.7, 123.9	2.9, 30.2
Reference Interval (2.5^{th} percentile, 97.5^{th} percentile)	4.4, 30.2	4.4, 33.8	3.7, 24.2
Proportion below 97.5^{th} Percentile	97.5%	95.8%	100.0%

All Lumipulse ***G*** CA125II concentrations are presented as U/mL.

In this study 99.2% of the healthy female subjects had a CA125 assay value at or below 35.0 U/mL.

The distribution of CA125 levels determined on the LUMIPULSE ***G***1200 system in benign conditions is shown in the table below:

	Benign Gynecological Disease	**Other Benign Disease**	**Congestive Heart Failure**	**Hypertension**	**Pregnant**
N	260	40	40	40	40
Mean	42.0	30.5	26.3	31.2	23.8
(SD)	(291.1)	(80.0)	(25.3)	(49.8)	(13.1)
Median	14.9	11.4	18.9	16.9	17.0
Range (min, max)	4.3, 4677.0	4.5, 493.2	5.3, 145.9	5.2, 238.4	9.2, 54.7
Reference Interval (2.5^{th} percentile, 97.5^{th} percentile)	5.0, 143.1	4.5, 485.0	5.3, 144.0	5.2, 238.2	9.2, 54.6
Proportion below 97.5^{th} Percentile	86.5%	92.5%	75.0%	80.0%	72.5%

All Lumipulse ***G*** CA125II concentrations are presented as U/mL.

The distribution of CA125 levels determined in malignancy conditions is shown in the table below:

	Ovarian Cancer	Bladder Cancer	Breast Cancer	Endo-metrial Cancer	GI Cancer	Lung Cancer
N	105	40	40	40	40	40
Mean (SD)	360.8 (768.3)	19.7 (14.4)	96.0 (417.5)	50.2 (131.3)	45.5 (152.3)	124.5 (242.5)
Median	84.7	13.4	16.4	19.4	13.7	42.5
Range (min, max)	5.7, 3923.5	4.1, 69.0	5.8, 2660.0	5.9, 835.5	7.3, 976.8	8.4, 957.9
Reference Interval (2.5^{th} percentile, 97.5^{th} percentile)	7.1, 3495.5	4.1, 68.4	5.8, 2597.9	5.9, 818.6	7.3, 955.1	8.4, 957.4
Proportion below 97.5^{th} Percentile	35.2%	77.5%	67.5%	72.5%	77.5%	40.0%

All Lumipulse ***G*** CA125II concentrations are presented as U/mL.

It is recommended that each laboratory establish its own reference value for the population of interest for Lumipulse ***G*** CA125II on the LUMIPULSE ***G***1200.

N. Proposed Labeling:

The labeling satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion

The results of these analytical (nonclinical) and clinical studies demonstrate that the Lumipulse ***G*** CA125II assay is substantially equivalent to the performance of the Siemens ADVIA Centaur CA 125II assay.