October 22, 2019

Fujirebio Diagnostics, Inc.
Kristin Maddaloni
Regulatory Affairs Specialist
201 Great Valley Parkway
Malvern, Pennsylvania 19355

Re: K191973
Trade/Device Name: Lumipulse G CA19-9-N
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-associated antigen immunological test system
Regulatory Class: Class II
Product Code: NIG
Dated: July 22, 2019
Received: July 24, 2019

Dear Kristin Maddaloni:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

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

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Douglas Jeffery, Ph.D.
Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K191973

Device Name
Lumipulse ***G*** CA19-9-N

Indications for Use *(Describe)*
Lumipulse ***G*** CA19-9-N is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative measurement of CA19-9 in human serum or plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE ***G*** System.

The assay is to be used as an aid in the management of patients diagnosed with cancer of the exocrine pancreas who have detectable levels of CA19-9 at some point in their disease process. Serial testing for patient CA19-9 assay values should be used in conjunction with other clinical methods used for monitoring cancer of the exocrine pancreas.

WARNING: The concentration of CA19-9 in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay for CA19-9 used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining serial levels of CA19-9 is changed, the laboratory must perform additional serial testing to confirm baseline values. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored. **Lumipulse *G* CA19-9-N should not be used for cancer screening or diagnosis**.

WARNING: Patients known to be genotypically negative for the Lewis blood group antigen will be unable to produce the CA19-9 antigen even in the presence of malignant tissue. Phenotyping for the presence of the Lewis antigen may be insufficient to detect true Lewis antigen negative individuals. Even patients who are genotypically positive for the Lewis antigen may produce varying levels of CA19-9 based on gene dosage effect.

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

A. GENERAL INFORMATION

Submission Date: July 22, 2019

Submitter Information:

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

Contact Person: Kristin Maddaloni
Regulatory Affairs Specialist
Fujirebio Diagnostics, Inc.
201 Great Valley Pkwy
Malvern, PA 19355
Office: 484-395-2126
maddalonik@fdi.com

B. PURPOSE FOR SUBMISSION

To obtain a substantial equivalence determination for the Lumipulse ***G*** CA19-9-N.

C. MEASURAND

CA 19-9

D. TYPE OF TEST

Quantitative, Chemiluminescent Immunoassay

E. APPLICANT

Fujirebio Diagnostics, Inc.

F. PROPRIETARY AND ESTABLISHED NAMES

Lumipulse® ***G*** CA 19-9-N
Lumipulse® ***G*** CA19-9-N Immunoreaction Cartridges

G. REGULATORY INFORMATION

Trade Name: Lumipulse ***G*** CA19-9-N
Classification: Class II
Regulation: 21 CFR 866.6010

Regulation Name: Tumor-Associated Antigen Immunological Test System
Product Code: NIG – System, Test, Carbohydrate antigen (CA 19-9) for monitoring and management of pancreatic cancer
Panel: 82, Immunology

H. INTENDED USE / INDICATIONS FOR USE

1. Intended Use / Indications for use

   Lumipulse® ***G*** CA19-9-N is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative measurement of CA 19-9 in human serum or plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE ***G*** System.

   The assay is to be used as an aid in the management of patients diagnosed with cancer of the exocrine pancreas who have detectable levels of CA 19-9 at some point in their disease process. Serial testing for patient CA 19-9 assay values should be used in conjunction with other clinical methods used for monitoring cancer of the exocrine pancreas.

2. Warning statements:

   The concentration of CA 19-9 in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay for CA 19-9 used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining serial levels of CA 19-9 is changed, the laboratory must perform additional serial testing to confirm baseline values. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored. Lumipulse ***G*** CA19-9-N should not be used for cancer screening or diagnosis.

   Patients known to be genotypically negative for Lewis blood group antigen are unable to produce the CA 19-9 antigen even in the presence of malignant tissue. Phenotyping for the presence of the Lewis blood group antigen may be insufficient to detect true Lewis antigen negative individuals. Even patients who are genotype positive for the Lewis antigen may produce varying levels of CA 19-9 as the result of gene dosage effect.

3. Special instrument requirements:
   Lumipulse ***G*** System

I. INDICATIONS FOR USE

Indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the pancreas. Serial testing with Lumipulse® ***G*** CA19-9-N for CA 19-9 patient values is used in conjunction with other clinical methods in the management of pancreatic cancer patients.

J. DEVICE DESCRIPTION

Reagents
The Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges (cat. # 235126) consists of 3 × 14 tests. Each kit contains the following:

1) Antibody-Coated Particle Solution
(Liquid when used, 250 µL/Immunoreaction Cartridge)
Contains 150 µg/mL anti-CA19-9 monoclonal antibody (mouse)-coated particles, protein stabilizers (bovine and mouse) and chemical stabilizers in 0.15 M sodium chloride/Tris buffer. This solution contains gelatin and turns into gel at 15 °C or lower. Preservative: sodium azide.

2) Enzyme-Labeled Antibody Solution
(Liquid, 350 µL/Immunoreaction Cartridge)
Contains 0.5 µg/mL alkaline phosphatase (ALP: calf)-labeled anti-CA19-9 monoclonal antibody (mouse), protein stabilizers (bovine, calf, and mouse) and chemical stabilizers in 0.05 M sodium chloride/Bis-Tris buffer. Preservative: sodium azide.

K. SUBSTANTIAL EQUIVALENCE INFORMATION

1. Predicate device name(s):
ARCHITECT® CA 19-9™$_{XR}$ Assay

2. Predicate 510(k) number(s):
K052000

3. Comparison with predicate:

	Lumipulse® *G* CA19-9-N	**ARCHITECT® CA 19-9™ $_{XR}$ (K052000) (Predicate)**
Assay Intended Use	Lumipulse® ***G*** CA19-9-N is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative measurement of CA 19-9 in human serum or plasma (sodium heparin, lithium heparin, or dipotassium EDTA) on the LUMIPULSE ***G*** System. The assay is to be used as an aid in the management of patients diagnosed with cancer of the exocrine pancreas who have detectable levels of CA 19-9 at some point in their disease process. Serial testing for patient CA19-9 assay values should be used in conjunction with other clinical methods used for	The ARCHITECT® CA 19-9™ assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of 1116-NS-19-9 reactive determinants in human serum and plasma on the ARCHITECT iSystem. The ARCHITECT® CA 19-9™ assay is to be used as an aid in the management of pancreatic cancer patients with a detectable level of Ca 19-9 at some point in their disease process and in conjunction with other clinical methods.

	Lumipulse® *G* CA19-9-N	**ARCHITECT® CA 19-9™ *XR* (K052000) (Predicate)**
	monitoring cancer of the exocrine pancreas.	
SIMILARITIES		
Classification	Class II	Same
Product Code	NIG	Same
Regulation	21 CFR 866.6010	Same
Antibody Type and Source	monoclonal antibody (mouse)	Same
Sample Type	human serum and plasma	Same
Reagent Storage	Store at 2-10°C	Store at 2-8°C
Sample Size	100 µL	< 100 µL
Calibration Frequency	Every 30 days	Same
DIFFERENCES		
Instrument	Lumipulse ***G*** System	ARCHITECT *i* System
Methodology	CLEIA	CMIA
Measuring Range	0.7-500 U/mL	2-1200 U/mL
Capture	Monoclonal anti-CA19-9 antibody (mouse)-coated particles	Monoclonal anti-CA 19-9 antibody coated paramagnetic microparticles
Conjugate Antibody	ALP (calf)-labeled anti-CA19-9 monoclonal mouse antibody	Acridinium labeled monoclonal anti-CA 19-9 F(ab')2 conjugate
Calibrators	2 level set (1 vial/level): • Cal 1: 0 U/mL • Cal 2: 500 U/mL	6 level set: • Calibrator A: anti-microbial agent, protein stabilizers in TRIS buffer • Calibrator B-F: Recombinant human 1116-NS-19-9 in TRIS buffer
Calibration Range	0-500 U/mL	0-1200 U/mL
Controls	2 levels every 24 hours	3 levels every 24 hours

L. STANDARDS/GUIDANCE DOCUMENTS REFERENCED

- CLSI EP05-A3 - Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP06-A - Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP07 – Interference Testing in Clinical Chemistry; Approved Guideline – Third Edition
- CLSI EP09-A3 – Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition
- CLSI EP14-A2 - Evaluation of Matrix Effects; Approved Guideline – Second Edition
- CLSI EP17-A2 - Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25-A – Evaluation of Stability of *In Vitro* Diagnostic Reagents: Approved Guideline
- CLSI EP28-A3c - Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition

- CLSI EP34 - Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking; Approved Guideline – First Edition

M. TEST PRINICIPLE

Lumipulse® ***G*** CA19-9-N is an assay system, including a set of immunoassay reagents, for the quantitative measurement of CA 19-9 in human serum and plasma (sodium heparin, lithium heparin, or dipotassium EDTA) based on CLEIA technology by a two-step immunoassay method on the LUMIPULSE ***G***1200 System. CA 19-9 in specimens specifically binds to anti-CA19-9 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-CA19-9 monoclonal antibody (mouse) specifically binds to CA 19-9 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 generate by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of CA 19-9.

N. PERFORMANCE CHARACTERISTICS

1. Analytical Performance

a. Reproducibility/Precision

<u>20-Day Precision</u>
The single site precision study was conducted using the Lumipulse ***G*** CA19-9-N at an external laboratory according to CLSI *EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures*. Six native human serum-based panels targeting the measuring range were assayed in replicates of two at two separate times of the day for 20 non-consecutive days (n=80 for each sample) using one LUMIPULSE ***G***1200 System and one Lumipulse ***G*** CA19-9-N lot. Lumipulse ***G*** CA19-9-N demonstrated precision ≤5.3% (total %CV). Within-Laboratory (Total) precision combines Within-run, Between-run, and Between-day precision, and the results are presented below.

		Within-Run (Repeatability)		Between Run Within Day		Between-Day		Within-Laboratory (Total)	
Sample	**Mean (U/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 1	2.9	0.1	2.7%	0.0	1.6%	0.1	4.3%	0.2	5.3%
Panel 2	38.9	0.6	1.6%	0.4	1.0%	0.8	2.2%	1.1	2.9%
Panel 3	173.9	2.1	1.2%	1.3	0.8%	2.6	1.5%	3.6	2.1%
Panel 4	318.9	3.9	1.2%	3.3	1.0%	3.6	1.1%	6.3	2.0%
Panel 5	452.8	4.7	1.0%	3.3	0.7%	4.7	1.0%	7.5	1.6%
Panel 6	20.0	0.3	1.6%	0.3	1.3%	0.8	3.8%	0.9	4.3%

Site-to-site Precision

The site-to-site precision studies were conducted using the Lumipulse ***G*** CA19-9-N at the internal laboratory and two additional sites according to CLSI EP05-A3. A panel of six serum samples targeting the measuring range were assayed in triplicate per run with two runs per day across five nonconsecutive days for a total of ten runs per site (n=30 replicates per site). Three different LUMIPULSE ***G***1200 Systems were used for testing (one per site). The controls were tested in singlicate per run. This data was combined for site-to-site analysis. One Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges lot and one Lumipulse ***G*** CA19-9-N Calibrator lot were used for testing. Lumipulse ***G*** CA19-9-N demonstrated precision ≤ 11.3% (total %CV). Within-Laboratory (Total) precision combines within-run, between-run and between-day precision, and data are presented below.

		Between Site		Between Day		Between Run		Within-Run (Repeatability)		Reproducibility (Total)	
Sample	**Mean (U/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 1	2.4	0.0	0.0%	0.1	2.3%	0.3	10.7%	0.1	2.6%	0.3	11.3%
Panel 2	33.8	0.4	1.0%	1.0	2.9%	1.7	5.2%	0.5	1.5%	2.1	6.2%
Panel 3	152.2	2.6	1.7%	4.0	2.7%	5.6	3.7%	1.5	1.0%	7.5	4.9%
Panel 4	280.5	5.1	1.8%	11.2	4.0%	7.9	2.8%	2.8	1.0%	14.9	5.3%
Panel 5	396.2	12.3	3.1%	13.1	3.3%	16.4	4.1%	3.9	1.0%	24.7	6.2%
Panel 6	17.3	0.2	0.9%	0.0	0.0%	1.3	7.6%	0.3	1.6%	1.3	7.8%

Lot-to-Lot Precision

The lot-to-lot study was conducted using three lots of Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges and Calibrators at the internal laboratory according to CLSI EP05-A3. A panel of 6 native serum samples targeting the measuring range were assayed in triplicate per run with 2 runs per day across 5 nonconsecutive days for a total of 10 precision runs per lot (n=30 replicates per lot). There were 90 replicates per Panel across all three lots. Lumipulse ***G*** CA19-9-N demonstrated within total laboratory precision ≤ 7.3% (total %CV). The between-lot precision for Lumipulse ***G*** CA19-9-N was ≤ 6.1%.

		Between Lot		Between Day		Between Run		Within-Run		Within Laboratory (Total)	
Sample	**Mean (U/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 1	2.3	0.1	6.1%	0.1	2.2%	0.0	1.9%	0.1	2.7%	0.2	7.3%
Panel 2	34.6	0.3	0.7%	0.5	1.5%	0.5	1.5%	1.2	3.4%	1.4	4.1%
Panel 3	158.1	4.7	3.0%	0.0	0.0%	2.8	1.8%	1.7	1.1%	5.7	3.6%
Panel 4	290.6	10.1	3.5%	4.0	1.4%	6.1	2.1%	2.7	0.9%	12.8	4.4%
Panel 5	412.6	12.0	2.9%	6.9	1.7%	7.2	1.7%	4.4	1.1%	16.2	3.9%
Panel 6	17.1	0.4	2.4%	0.3	1.7%	0.2	1.0%	0.2	1.3%	0.6	3.4%

b. Linearity

Linearity:
Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System demonstrated linearity in a study consistent with the guidelines in the CLSI Protocol *EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures.* High and low sample pools were created using patient serum samples that contained naturally expressed CA 19-9. The linearity was found in the range 0.7 to 531.3 U/mL. Lumipulse ***G*** CA19-9-N correlated with expected concentrations per the linear regression formula:

$y= -6.08*10^{-2}+1.10x-5.58*10^{-4}x^2+7.85*10^{-7}\ x^3$; $R^2=0.9983$

Dilution:
The recommended manual dilution for Lumipulse ***G*** CA19-9-N is 1:10, 1:100, and 1:200.

The recommended automated dilution for Lumipulse ***G*** CA19-9-N is 1:10, 1:100 and 1:200 for samples up to 80,000 U/mL. Automated dilutions for samples exceeding 80,000 U/mL is not recommended.

Spike Recovery:
Three normal human serum specimens with known endogenous CA 19-9 levels were split into 6 aliquots and spiked with various concentrations of CA 19-9 (50 U/mL, 150 U/mL, 250 U/mL, 375 U/mL and 450 U/mL). Aliquots were assayed in triplicate. The percent recovery was calculated. The percent recoveries ranged from 95% to 109%. The obtained percent recovery was between 100 ± 10% of the expected value for each spiked level. Therefore, the assay meets the acceptance criterion.

The assay measuring range is from 0.7 U/mL to 500 U/mL.

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

Expected Values:
Lumipulse ***G*** CA19-9-N Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G*** System for the quantitative determination of CA 19-9 in human serum and plasma. Two bottles (1.5 mL each) are supplied for the Lumipulse ***G*** CA19-9-N Calibrator kit. Preservative: Sodium azide. The calibrators are at the following concentrations:

Calibrator	Concentration (U/mL)
CAL 1	0
CAL 2	500

Traceability:
Calibration of the Lumipulse ***G*** CA19-9-N is traceable to in-house reference calibrators, whose values have been assigned to correlate to Fujirebio Diagnostics' CA19-9 RIA.

Shelf life:
The shelf life for Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges and the Lumipulse ***G*** CA19-9 Calibrators is 12 months at 2–10°C.

On board the LUMIPULSE ***G***1200:
The Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges are sealed unit dose stored at 2–10°C. To reduce risk for any misuse, the package insert states "The Lumipulse ***G*** CA19-9 Immunoreaction Cartridges can be stored (refrigerated unit) on-board the LUMIPULSE ***G*** System for a maximum of 30 days".

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

Transport Conditions:
Lumipulse ***G*** CA19-9-N Immunoreaction Cartridges and the Lumipulse ***G*** CA19-9 Calibrators are stable up to 12 months and are shipped at 2-10°C.

d. Detection Limit

The Limit of Blank (LoB), Limit of Detection (LoD), and Functional Sensitivity for the Lumipulse ***G*** CA19-9-N were determined in accordance with the CLSI Guideline *EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*. Two blank and seven low level serum specimens were tested in replicates of ten over 3 days on 2 LUMIPULSE ***G***1200 Systems with 2 runs per day and 2 Lumipulse ***G*** CA19-9-N lots were tested giving 60 determinations for each specimen per lot.

The LoB for Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System was determined to be 0.10 U/mL.

The LoD for Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System was determined to be 0.19 U/mL.

The LoQ was expressed through Functional Sensitivity; the lowest amount measured and detected by Lumipulse ***G*** CA19-9-N assay. The Functional Sensitivity was calculated to be 0.57 U/mL.

e. Analytical Specificity/Cross Reactivity

No data provided.

f. Interfering Substances

The endogenous and exogenous interference studies followed the guidance of CLSI Guideline *EP07, Interference Testing in Clinical Chemistry*. Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System demonstrated an average interference of ≤10% for each compound shown in the table below. Human serum specimen pools with CA 19-9 concentrations of approximately 32.3 U/mL, 197.9 U/mL, and 344.7 U/mL were supplemented with potentially interfering compounds. The following compounds were

tested using Lumipulse ***G*** CA19-9-N and found not to interfere with the assay.

Endogenous Interferences	**Test Concentration**
Free Bilirubin (unconjugated)	60 mg/dL
Conjugated Bilirubin	60 mg/dL
Triglycerides (Intralipid 20% Emulsion)	3,000 mg/dL
Hemoglobin	500 mg/dL
Hemoglobin	1000 mg/dL
Total Protein (Human Serum Albumin)	15 g/dL
Immunoglobulin G (IgG)	5 g/dL
Biotin	19.7 mg/dL
HAMA IgG	1000 ng/dL
RF IgM	1000 IU/mL
Therapeutic Drug Interferences	**Test Concentration**
5-Fluorouracil	39.0 mg/dL
Cisplatin	5.70 mg/dL
Cyclophosphamide	37.5 mg/dL
Cytarabine	3.0 mg/dL
Doxorubicin HCl	4.0 mg/dL
Gemcitabine	38.2 mg/dL
Leucovorin	11.4 mg/dL
Methotrexate	90.9 mg/dL
Paclitaxel	6.7 mg/dL
Pegylated Liposomal Doxorubicin (Doxil®)	5.2 mg/dL
Streptozotocin	3.96 mg/dL
Tamoxifen	6.0 mg/dL

g. High Dose Hook Effect

The Hook Effect was evaluated for the Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System. No high dose effect was observed for samples containing approximately 200,000 U/mL of CA 19-9.

h. Assay Cut-off

See Clinical Cut-off Section 3 below.

i. Specimen Stability

The following storage conditions were tested in the specimen stability studies and the results are as follows.

- Specimens may be stored at refrigerated (2-10°C) for up to 4 days.
- Specimens may be stored frozen (-20°C ±10°C) for up to 14 days.
- Specimens on-board the LUMIPULSE ***G*** System should be tested within 3 hours.
- Avoid freezing or thawing samples. Do not perform freeze/thaw cycle 2 or more times.
- Do not use heat inactivated specimens.

j. Matrix Comparison

The Anticoagulant Matrix Comparison Study followed the guidance of the CLSI Guideline *EP14-A2, Evaluation of Matrix Effects*. Lumipulse ***G*** CA19-9-N on the LUMIPULSE ***G***1200 System was evaluated for matrix differences by performing a study using fifty (50) matched sets of serum (red top and serum separator tubes (SST)) and plasma (K_2EDTA, sodium heparin and lithium heparin) samples. The results demonstrated equivalency between matrices and are presented in the following table.

Tube Type	n	Concentration Range (U/mL)		Slope			Intercept			Pearson Correlation Coefficient
		Min	Max	Estimate	Lower 95%CI	Upper 95%CI	Estimate	Lower 95% CI	Upper 95% CI	
SST	50	3.7	441.2	1.0094	0.9634	1.0553	0.7764	-3.0258	4.5785	0.9943
K_2EDTA	50	4.2	456.0	1.0039	0.9860	1.0218	-0.1197	-0.4746	0.2352	0.9977
Lithium Heparin	50	4.8	430.3	0.9885	0.9605	1.0165	0.6344	0.0075	1.2614	0.9938
Sodium Heparin	50	3.9	470.2	0.9981	0.9746	1.0215	0.7679	-0.0781	1.6138	0.9981

k. Method Comparison

The Lumipulse ***G*** CA19-9-N Method Comparison Study followed the guidance of CLSI Document *EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples* and was performed on the LUMIPULSE ***G***1200 System. The weighted Deming regression method was used to compare the performance of the Lumipulse ***G*** CA19-9-N to the ARCHITECT CA 19-9XR run on the ARCHITECT *i* System on a total of 84 matched human serum samples. The samples tested ranged from 3.0 to 454.8 U/mL for Lumipulse ***G*** CA19-9 and 2.07 to 1056.05 U/mL for ARCHITECT CA 19-9XR assay. The data are summarized in the following table.

	Lumipulse G CA19-9-N vs. ARCHITECT CA19-9XR				
Regression Analysis	n	Correlation Coefficient (r)	Intercept (95% CI)	Slope (95% CI)	Average Bias (U/mL)
Weighted Deming	84	0.6628	1.8650	1.3179	164.15%
			-0.9314 to 4.6615	1.0108 to 1.6250	

The data summarized in the following table include results from a study with specimens above the measurement range of both devices requiring dilution (103 samples). The samples tested ranged from 3.0 to 1187.0 U/mL for Lumipulse ***G*** CA19-9-N and 2.07 to 1121.01 U/mL for ARCHITECT CA19-9XR.

Lumipulse G CA19-9-N vs. ARCHITECT CA19-9XR				
n	Correlation Coefficient (r)	Intercept (95% CI)	Slope (95% CI)	Average Bias (U/mL)
103	0.7380	1.8585	1.3198	143.45%
		-0.73934 to 4.4563	1.0780 to 1.15617	

2. Clinical Studies

a. Clinical Sensitivity

Not Applicable.

b. Clinical Specificity

Not Applicable.

c. Other Clinical Supportive data:

Monitoring of Disease State in Patients Diagnosed with Pancreatic Cancer

The effectiveness of Lumipulse ***G*** CA19-9-N as an as an aid in the management of patients diagnosed with cancer of the exocrine pancreas who have detectable levels of CA 19-9 at some point in their disease process was determined on the LUMIPULSE ***G***1200 System by assessing changes in CA 19-9 levels in serial serum samples from 83 patients compared to changes in disease status. A study involving a total of 374 pairs of observations was undertaken with an average number of 5.6 observations per patient. A positive change in CA 19-9 was defined as an increase in the value that was at least 15% greater than the previous value of the test. This level of change takes into account the variability of the assay. Sixty-five percent (65%) or 45/70 of the patient samples with a positive change correlated with the disease progression while sixty-one percent 61% or 184/304 of the patient serial samples with no significant change in CA 19-9 value correlated with no progression. The total concordance was sixty-one percent (61% or 229/374).

Lumipulse *G* CA19-9-N Performance Measurements (%)

Performance Measurement	Value	Standard Error	Lower 95% CI*	Upper 95% CI
Sensitivity	64.29	4.42	55.49	73.08
Specificity	60.53	2.48	55.60	65.45
Total Concordance	61.23	2.22	56.81	65.65
PPV	27.27	2.63	22.04	32.50
NPV	88.04	1.87	84.32	91.76

*CI = Confidence Interval

The following table presents the data in a 2 × 2 format:

Change in Disease Status per Sequential Pair

Change in CA 19-9 Concentration	No Progression	Progression	Total
< 15%	184	25	209
≥ 15%	120	45	165
Total	304	70	374

3. Clinical Cut-Off

See Expected Values below.

4. Expected Values/Reference Range

A total of 240 serum specimens obtained from an apparently healthy adult population (22-93 years old) were tested using the Lumipulse ***G*** CA19-9-N per CLSI EP28-A3c. The observed ranges are listed below.

	Apparently Healthy Males and Females (Combined)	Apparently Healthy Males	Apparently Healthy Females
N	240	120	120
Mean (SD)	11.0 (11.7)	10.5 (11.4)	11.5 (12.1)
Median	6.7	6.2	7.6
Range (min, max)	<0.7, 63.9	<0.7, 63.9	<0.7, 57.5
Reference Interval (2.5th Percentile, 97.5th Percentile)	<0.7, 50.0	<0.7, 40.1	<0.7, 50.6
N (%) with CA19-9 ≤25.0	88.8%	88.3%	89.2%
N (%) with CA19-9 ≤50.0	97.5%	98.3%	96.7%
N (%) with CA19-9 ≤75.0	100.0%	100.0%	100.0%

All Lumipulse ***G*** CA19-9-N concentrations are presented in U/mL.

In addition to the normal cohort, 75 serum samples from patients with benign pancreatic conditions and 120 from patients with malignant pancreatic disease were tested.

The following tables summarizes the sample distribution, diseases/conditions and distribution of CA 19-9 results. All Lumipulse ***G*** CA19-9-N concentrations are presented in U/mL.

	Pancreatitis	Benign Lung Disease	Benign Renal Disease	Cirrhosis	Diabetes	Gallbladder Disease	Hepatitis	Rectal Polyps
N	75	39	40	38	40	41	42	40
Mean (SD)	58.2 (227.0)	31.9 (70.7)	21.9 (31.1)	33.3 (36.1)	15.4 (15.1)	45.3 (110.5)	32.4 (37.1)	20.0 (26.2)
Median	18.5	13.8	12.6	20.6	9.9	12.0	21.6	8.8
Range (min, max)	<0.7, 1966.0	<0.7, 441.6	<0.7, 180.6	<0.7, 183.9	<0.7, 69.5	<0.7, 630.0	<0.7, 159.3	<0.7, 84.5
Reference Interval (2.5th Percentile, 97.5th Percentile)	<0.7, 181.4	<0.7, 105.7	<0.7, 68.3	4.7, 120.9	<0.7, 56.0	<0.7, 334.2	<0.7, 151.6	<0.7, 83.7
N (%) with CA 19-9 ≤25.0	62.7%	71.8%	70.0%	57.9%	80.0%	68.3%	61.9%	80.0%
N (%) with CA 19-9 ≤50.0	84.0%	87.2%	90.0%	84.2%	95.0%	82.9%	78.6%	85.0%
N (%) with CA 19-9 ≤75.0	89.3%	89.7%	97.5%	89.5%	100.0%	90.2%	90.5%	87.5%

	Exocrine Pancreatic*	Biliary	Breast	CRC*	Gall-bladder	Liver	Lung	Ovarian	Stomach
N	120	40	40	38	40	40	40	39	37
Mean (SD)	2873.1 (8721.0)	2640.0 (9765.6)	19.7 (31.2)	254.7 (964.6)	147.5 (349.3)	732.2 (2431.9)	21.0 (31.9)	453.6 (2418.2)	287.1 (1555.6)
Median	182.7	73.3	6.9	8.5	20.4	24.4	10.8	12.8	6.3
Range (min, max)	<0.7, >50000.0	7.1, >50000.0	<0.7, 142.8	<0.7, 5050.0	<0.7, 1385.0	<0.7, 11660.0	<0.7, 181.4	<0.7, 15130.0	<0.7, 9480.0
Reference Interval (2.5th Percentile, 97.5th Percentile)	<0.7, 32606.0	7.7, 37861.3	<0.7, 129.4	<0.7, 3434.9	<0.7, 1216.3	<0.7, 8335.2	<0.7, 87.8	3.0, 1559.2	<0.7, 1362.7
N (%) with CA19-9 ≤25.0	21.7%	25.0%	77.5%	68.4%	60.0%	52.5%	80.0%	61.5%	83.8%
N (%) with CA19-9 ≤50.0	28.3%	42.5%	90.0%	81.6%	75.0%	62.5%	90.0%	76.9%	86.5%
N (%) with CA19-9 ≤75.0	34.2%	50.0%	95.0%	84.2%	82.5%	70.0%	95.0%	82.1%	86.5%

*Treatment-Naïve Exocrine Pancreatic; CRC – Colorectal;

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

O. INSTRUMENT NAME

Lumipulse ***G***1200 System (K142895)

P. PROPOSED LABELING

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

Q. CONCLUSION

The results of these analytical (nonclinical) and clinical studies demonstrate that the Lumipulse ***G*** CA19-9-N is substantially equivalent to the performance of the ARCHITECT® CA 19-9™ *XR* (K052000).