Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191973

B Applicant

Fujirebio Diagnostics, Inc.

C Proprietary and Established Names

Lumipulse G CA19-9-N

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NIG	Class II	21 CFR 866.6010 - Tumor-Associated Antigen Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

CA 19-9

C Type of Test:

Chemiluminescent Enzyme Immunoassay (CLEIA)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indication for Use below.

B Indication(s) 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.

Warning Statement: 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.

C Special Conditions for Use Statement(s):

For Prescription Use Only

D Special Instrument Requirements:

Lumipulse G1200 System (K142895)

IV Device/System Characteristics:

A 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. The 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. The 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.

Materials required but not provided:

1) Lumipulse G CA19-9-N Calibrators: Liquid, CAL 1 and CAL 2
2) Quality Control material
3) Lumipulse G Substrate Solution
4) Lumipulse G Wash Solution
5) Lumipulse G Specimen Diluent 1
6) Sampling tips for LUMIPULSE G System
7) Soda lime for LUMIPULSE G System
8) Lumipulse G Dilution Cartridges

B Principle of Operation:

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 G1200 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 (3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy)-phenyl-1, 2-dioxetane disodium salt) contained in the Substrate Solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generate by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of CA 19-9.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ARCHITECT CA 19-9$_{XR}$ Assay

B Predicate 510(k) Number(s):

K052000

C Comparison with Predicate(s):

Device & Predicate Device(s):	K191973	K052000
Device Trade Name	Lumipulse G CA19-9-N	ARCHITECT CA 19-9$_{XR}$
General Device Characteristic Similarities		
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	The ARCHITECT CA 19-9$_{XR}$ 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 *i* System. The ARCHITECT CA 19-9$_{XR}$ 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

	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 monitoring cancer of the exocrine pancreas.	in conjunction with other clinical methods.
Classification	Class II	Same
Product Code	NIG	Same
Capture Antibody	monoclonal anti-CA19-9 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
General Device Characteristic Differences		
Instrument	LUMIPULSE G System	ARCHITECT *i* System
Methodology	CLEIA	CMIA
Analytical 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	3 levels

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP6-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 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;

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results presented below met the manufacturer's pre-determined acceptance criteria.

1. Precision/Reproducibility:
Precision: Six native human serum samples with various concentrations of CA 19-9 were tested for 20 non-consecutive days with two runs per day in two replicates per run using a single reagent and calibrator lot for a total of 80 (2x2x20) Lumipulse G CA19-9-N test results per sample. The mean Lumipulse G CA19-9-N test result was computed and the within-run, between-run, between-day, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

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

Site-to-site Reproducibility: Six native human serum samples were tested at three sites with two runs per day in three replicates per run using a single reagent and calibrator lot for five non-consecutive days for a total of 30 Lumipulse G CA19-9-N test results per site. Three different LUMIPULSE G1200 Systems were used for testing (one per site) and there were 90

replicates per sample across three sites (2x3x5x3). The mean Lumipulse G CA19-9-N test result was computed and the within-run, between-run, between-day, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

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

Lot-to-Lot Reproducibility: Six native human serum samples were tested at a single site with two runs per day in three replicates per run for five non-consecutive days for a total of 30 Lumipulse G CA19-9-N test results per lot. There were 90 replicates per sample across three lots (2x3x5x3). The mean Lumipulse G CA19-9-N test result was computed and the within-run, between-run, between-day, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

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

2. Linearity:

Two native human serum sample pools (high and low) were prepared. The high sample pool was diluted using the low sample pool in appropriate ratios to obtain 21 concentration levels (0.1 to 530 U/mL) of CA 19-9 that covers the full range of the assay from 0.7 to 500 U/mL. Four replicates were obtained at each concentration level to cover the assay measuring range. Data were analyzed using linear regression based on CLSI EP6-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

Range (U/mL)	Slope (95%CI)	Intercept (95% CI)	R^2
1.11–486.19	1.033 (1.019, 1.047)	–0.008 (–0.080, 0.065)	0.997

Dilution: A total of 15 native human serum sample pools at a known concentration of CA 19-9 were obtained and diluted at three different levels: five sample pools at each of 1:10, 1:100,

and 1:200 dilutions. Each dilution was prepared by manual dilution and automatic on-board dilution. No differences were seen when comparing results from manual and on-board dilution. The recommended manual and automated dilution for Lumipulse G CA19-9-N is 1:10, 1:100 and 1:200 for samples up to 80,000 U/mL.

Hook Effect: The hook effect was evaluated for the Lumipulse G CA19-9-N on the LUMIPULSE G1200 System. No high dose effect was observed for samples containing approximately 200,000 U/mL of CA 19-9.

3. Analytical Specificity/Interference:
Native human serum samples at CA 19-9 concentrations of approximately 32.3 U/mL, 197.9 U/mL, and 344.7 U/mL were supplemented with a total of 10 potential endogenous and 12 therapeutic drug interferents as listed below.

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

The Lumipulse G CA19-9-N on the LUMIPULSE G1200 System demonstrated an average interference of <10% from the test results in three replicates for each potential interferent.

4. Assay Reportable Range:
The analytical measuring interval (AMI) of the Lumipulse G CA19-9-N is 0.7 U/mL to 500.0 U/mL. When the test samples are diluted (1:200), the claimed reportable range of the Lumipulse G CA19-9-N is 0.7 U/mL to 80,000.0 U/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   a. 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 radioimmunoassay.

   b. Real Time Regent Stability: Six human serum samples at different level of CA 19-9 were prepared for testing the real time stability of Lumipulse G CA19-9-N Immunoreaction Cartridges (IC) and the Lumipulse G CA19-9 Calibrators. Three lot combinations of Lumipulse G CA19-9-N ICs and Lumipulse G CA19-9-N Calibrators were utilized. The reagents were evaluated across four time points: Study Initiation, 6 months, 12 months, and 13 months. Each sample was tested in three runs and three replicates per run for a total of nine replicates at Study Initiation and in two runs and three replicates per run for a total of six replicates at 6 months, 12 months, and 13 months. The Lumipulse G CA19-9-N ICs and Calibrators are stable for 12 months at 2–10°C.

   c. On board Reagent Stability: Six human serum samples at different level of CA 19-9 were prepared for testing the on-board stability of Lumipulse G CA19-9-N Immunoreaction Cartridges (IC) and the Lumipulse G CA19-9 Calibrators on the LUMIPULSE G1200. A single lot of Lumipulse G CA19-9-N ICs and Lumipulse G CA19-9-N Calibrators were utilized. The reagents were evaluated in three replicates across four time points as follows: Study Initiation, 30 days, 12 months ± 5 days, and 13 months ± 5 days. The Lumipulse G CA19-9-N ICs and Calibrators on the LUMIPULSE G 1200 are stable up to 30 days on board. The study is ongoing.

   d. Transport Conditions: The recommended transport condition for Lumipulse G CA19-9-N Immunoreaction Cartridges (IC) and the Lumipulse G CA19-9 Calibrators is at 2–10°C.

   e. Sample Stability: Sample stability was tested using eight human serum samples collected across five tube types (SST serum, Red Top serum, K2 EDTA plasma, Lithium heparin plasma, and sodium heparin plasma). Two conditions for sample stability were evaluated: 2–10°C and −20±10°C. Five aliquots were stored at 2–10°C and tested at Day 1, Day 4, Day 7, Day 14, and Day 15. Three aliquots were stored at −20°C±10°C and tested at Day 7, Day 14, and Day 15. The samples were run on the LUMIPULSE G1200. The results demonstrated that:

      - Samples collected across five tube types (SST serum, Red Top serum, K2 EDTA plasma, Lithium heparin plasma, and sodium heparin plasma) may be stored at 2–10°C for up to 4 days.

      - Samples collected across five tube types (SST serum, Red Top serum, K2 EDTA plasma, Lithium heparin plasma, and sodium heparin plasma) may be stored at −20°C ±10°C for up to 14 days.

   f. Expected Values: The calibrators are at two concentrations, 0 U/mL(CAL1) and 500 U/mL (CAL2).

6. Detection Limit:

Limit of Blank (LoB):

Two blank samples were prepared by diluting normal healthy serum with human serum expressing ultra-low CA 19-9. Each sample was tested in ten replicates in each run with two runs per day for three days using two regent lots and two instruments. There was a total of 60 replicates per sample. The LoB was estimated as the 95th percentile of the distribution of test results using a non-parametric method. The highest estimate among the two lots was used as the claimed LoB. The LoB was determined to be 0.1 U/mL.

Limit of Detection (LoD):

Seven serum samples containing low levels of CA 19-9 were tested in ten replicates in two runs per day for three days using two regent lots and two instruments. Each lot was run on one LUMIPULSE G1200 instrument. For each lot combination, there was a total of 60 replicates per sample per reagent lot combination. The study design generated a total of 60 test determinations with each reagent lot and instrument combination. The study was conducted independently with two reagent lots and the highest estimate among the two lots was used as the claimed LoD. The LoD was determined to be 0.19 U/mL.

Limit of Quantification (LoQ):

Seven serum samples containing low levels of CA 19-9 were tested in ten replicates in two runs per day for three days using two regent lots and two instruments. Each lot was run on one LUMIPULSE G1200 instrument. For each lot combination, there was a total of 60 replicates per sample per reagent lot combination. The study design generated a total of 60 test determinations with each reagent lot and instrument combination. The LoQ was calculated to be 0.57 U/mL by identifying the measurand level at which a measurement procedure demonstrated total within-lab imprecision of 15 %CV. The claimed LoQ is 0.57 U/mL

7. Assay Cut-Off:

See Clinical Cut-off below.

B Comparison Studies:

1. Method Comparison:

A total of 130 human serum samples were obtained for the method comparison study. The test samples were collected in red-top or serum separator tubes (SST). Only the samples with the test results within the measuring range for both the Lumipulse G CA19-9-N and the ARCHITECT CA 19-9$_{XR}$ were included in the regression analysis (n=84). 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 19-9$_{XR}$ assay. The linear regression analysis obtained from Passing-Bablok and Weighted Deming regression analysis comparing the Lumipulse G CA19-9 and ARCHITECT CA 19-9$_{XR}$ test results is shown below:

Regression Analysis	n	Correlation Coefficient (R)	Intercept (95% CI)	Slope (95% CI)	Average Bias (%)
Passing-Bablok	84	0.6628	15.742 (4.770, 26.588)	0.903 (0.706, 1.160)	164.15
Weighted Deming	84	0.6628	1.865 (−0.931, 4.662)	1.318 (1.011, 1.625)	164.15

2. Matrix Comparison:
The Anticoagulant Matrix Comparison Study was conducted using 50 donor-matched sets of serum (red top and serum separator tubes (SST)) and plasma (K2EDTA, sodium heparin and lithium heparin) samples. The linear regression analysis obtained from Weighted Deming regression analysis comparing the Lumipulse G CA19-9-N test results of the control matrix sample (Red Top Serum) to the Lumipulse G CA19-9-N test results of each matrix sample (SST, K2EDTA, Lithium Heparin, and Sodium Heparin) is shown below:

Tube Type	n	Concentration Range (U/mL)	Correlation Coefficient (R)	Intercept (95% CI)	Slope (95% CI)
SST	50	3.7–441.2	0.994	0.776 (−3.026, 4.579)	1.009 (0.963, 1.055)
K2 EDTA	50	4.2–456.0	0.998	−0.120 (−0.475, 0.235)	1.004 (0.986, 1.022)
Lithium Heparin	50	4.8–430.3	0.994	0.634 (0.008, 1.261)	0.989 (0.961, 1.017)
Sodium Heparin	50	3.9–470.2	0.998	0.768 (−0.078, 1.614)	0.998 (0.975, 1.022)

C Clinical Studies:

1. Clinical Sensitivity:
The clinical performance of the Lumipulse G CA19-9-N assay was determined on the LUMIPULSE G1200 System by assessing changes in CA 19-9 levels in serial serum samples from patients with exocrine pancreatic cancer and comparing the results to changes in the disease status. The patients were females and males with a historically/pathologically confirmed diagnosis of exocrine pancreatic cancers at any stage (Stage IA to IV). A minimum of three to a maximum of 12 serial blood draws were collected from each patient. The subject inclusion and exclusion criteria are as follows:

Inclusion criteria:

- Female or Male
- 22 years of age or older
- Diagnosed with exocrine pancreatic cancer
- Appropriate informed consent or remnant sample documentation

Exclusion criteria:

- Less than 22 years old
- No diagnosis of exocrine pancreatic cancer
- Invalid informed consent or remnant sample documentation

The clinical data collected for each subject included the following: subject ID, age, gender, race/ethnicity, date of cancer diagnosis, histology, grade, and stage. For each subject sample draw, the following information will be collected, if available: chemotherapeutic treatment information (onset date, end date, regimen), imaging information (type, findings), physical exam date and findings, sample draw date, procedure information (type, date and findings), clinical disease status (see below for description), date or recurrence, and date of death (if subject expired).

Of the 83 patients, the age ranged from 47 to 87 years with a median of 65 years. Seventy-four subjects (89.2%) were Caucasian/White and the remaining subjects included six (7.2%) African American, two (2.4%) Asian/Pacific Islander, and one (1.2%) Other. A total of 374 pairs of observations were obtained from 83 patients with an average number of 5.6 observations per patient with a minimum of two follow up visits after the initial visit. Each patient's clinical disease status was evaluated by the clinical evidence which was identified by reviewing the compilation of procedures and clinical notes which may have included but were not limited to: imaging of various modalities, physical exam, physician transcription notes, and/or other laboratory data. The clinical disease status was categorized to NED (no evidence of disease), SD (stable disease), PD (progressive disease), or RD (Responding disease) based on the change in the clinical evidence at the follow up visit compared to the previous visit.

The CA 19-9 ratio distribution by clinical status is summarized below when the Lumipulse G CA19-9-N test result at a follow up visit was compared to the level at the previous visit.

Clinical Disease Status	**n**	**Minimum**	**1st Quartile**	**Median**	**3rd Quartile**	**Maximum**
NED	37	0.35	0.81	0.92	1.42	4.15
SD	250	0.04	0.77	1.06	1.49	100.79
PD	70	0.10	0.98	1.43	2.41	22.85
RD	17	0.22	0.56	0.73	0.89	2.24
Total	374					

Based on the quantitative measures of CA 19-9 using the Lumipulse G CA19-9-N assay, a positive change in CA 19-9 was defined as an increase in the CA 19-9 level that was at least 15% greater at the follow up visit compared to the level at the previous value visit. Sixty-five percent (65%) or 45/70 of the patient samples with a positive change correlated with the disease progression in the disease status category (NED, SD, PD, and RD) while 61% (184/304) of the patient serial samples with no significant change in CA 19-9 value correlated with no progression. The total concordance was 61% (229/374).

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

The estimates of sensitivity, specificity, PPV, and NPV along with 95% confidence intervals were calculated for the Lumipulse G CA19-9-N assay using the cut-off of a ≥15% change in CA 19-9 concentration as shown below.

Performance Measurement	Performance Measure % (95% CI)
Sensitivity	64.29 (55.49, 73.08)
Specificity	60.53 (55.60, 65.45)
Total Concordance	61.23 (56.81, 65.65)
PPV	27.27 (22.04, 32.50)
NPV	88.04 (84.32, 91.76)

2. Clinical Specificity:
   See Section C.1 above.

3. Other Clinical Supportive Data:
   The clinical performance of the Lumipulse G CA19-9-N assay on the LUMIPULSE G1200 System at different % change in CA 19-9 was evaluated against that of the predicate ARCHITECT CA 19-9$_{XR}$ (K052000) on the ACTHITECT i2000SR System using the test results obtained from the same patient cohort (See Section C.1 above). The CA 19-9 ratio distribution by clinical status was summarized below when the ARCHITECT CA 19-9$_{XR}$ test result at the follow up visit was compared to the level at the previous visit.

Clinical Disease Status	n	Minimum	1st Quartile	Median	3rd Quartile	Maximum
NED	33	0.45	0.82	1.05	1.73	2.65
SD	202	0.04	0.68	1.00	1.58	376.15
PD	51	0.21	0.97	1.58	3.44	43.99
RD	15	0.19	0.44	0.68	0.84	2.05
Total	301					

The estimates of sensitivity, specificity, PPV, and NPV along with 95% confidence intervals were calculated for the predicate assay, ARCHITECT CA 19-9$_{XR,}$ (K052000) using the cut-off of a $\geq$ 14% change in CA 19-9 concentration as shown below.

Change in CA 19-9 Concentration	No Progression	Progression	Total
< 14%	156	18	174
≥ 14%	94	33	127
Total	250	51	301

Performance Measurement	ARCHITECT CA 19-9$_{XR}$ Performance Measure % (95% CI)
Sensitivity	64.71 (53.07, 76.34)
Specificity	62.40 (57.29, 67.51)
Total Concordance	62.79 (58.24, 67.34)
PPV	25.98 (19.89, 32.08)
NPV	89.66 (85.79, 93.52)

The table below compared the clinical sensitivity and specificity for disease progression between the Lumipulse G CA19-9-N assay and the ARCHITECT CA 19-9$_{XR}$ assay for a series of % change in the CA 19-9 level within each assay's measuring range using the ROC curve analysis.

	Lumipulse G CA19-9-N (N=374 paired observations)		ARCHITECT CA 19-9$_{XR}$ (N=301 paired observations)	
% Change in CA 19-9	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
10	67.1	55.6	66.7	60.8
20	62.9	62.8	64.7	64.4
30	55.7	68.8	62.8	68.4
40	52.9	73.0	54.9	70.4
50	44.3	76.6	54.9	72.8

D Clinical Cut-Off:

See Expected Values below.

E Expected Values/Reference Range:

A total of 240 serum specimens obtained from an apparently healthy adult population (22 to 93 years old) were tested using the Lumipulse G CA19-9-N assay and the observed ranges are listed below. All Lumipulse G CA19-9-N concentrations are presented in U/mL.

	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 (2.5^{th} Percentile, 97.5^{th} Percentile)	<0.7, 50.0	<0.7, 40.1	<0.7, 50.6
N (%) with CA19-9 $\leq$ 25.0	88.8%	88.3%	89.2%
N (%) with CA19-9 $\leq$ 50.0	97.5%	98.3%	96.7%
N (%) with CA19-9 $\leq$ 75.0	100.0%	100.0%	100.0%

In addition to the normal cohort, 75 serum samples from patients with benign pancreatic conditions and 120 from patients with exocrine pancreatic cancers were tested. The following tables summarizes the sample distribution, diseases/conditions, and distribution of the Lumipulse G CA19-9-N assay results 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.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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