510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K191085

B Applicant

Genalyte, Inc.

C Proprietary and Established Names

Maverick RNP Assay and Maverick Diagnostic System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LKO	Class II	21 CFR 866.5100 - Antinuclear Antibody Immunological Test System	IM - Immunology
JJE	Class I	21 CFR 862.2160 - Discrete photometric chemistry analyzer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New instrument and new assay

B Measurand:

IgG autoantibodies specific for ribonucleoprotein (RNP)

C Type of Test:

Semi-quantitative immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

The Maverick RNP Assay is an immunoassay for the semi-quantitative determination of anti-RNP IgG antibodies in human serum on the Maverick Diagnostic System. The presence of anti-RNP antibodies, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of Mixed Connective Tissue Disease (MCTD).

The Maverick Diagnostic System (MDS) is an automated immunoassay analyzer intended for in vitro diagnostic use to determine analytes in a clinical laboratory. The system's assay applications utilize silicon photonics technology.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

The Maverick RNP Assay can only be used with the Maverick Diagnostic System (MDS).

IV Device/System Characteristics:

A Device Description:
The Maverick RNP assay consists of:

- A silicon chip spotted with antinuclear antigens and quality control proteins housed in a carrier in foil pouch with desiccant. Each chip contains two assays.
- A sealed and prefilled stripwell in foil pouch. Each stripwell contains:
  - Assay Buffer (wells A1, B1, C1, D1 & A2, B2, C2, D2) clear liquid containing PBS, Tween®-20, proprietary proteins, and preservative
  - RNP Assay Detection Reagent (wells E1 & E2) clear liquid containing goat anti-human IgG, PBS, Tween®-20 proprietary proteins, and preservative

The MDS consists of the Maverick instrument, computer, software, and peripherals including a bar code reader and a monitor. The MDS instrument is provided with necessary electronics, optics, fluidics, software and mechanical hardware to perform assays in a semi-automated fashion. The MDS instrument has two independently controlled bays, each of which can accept separate chip and reagent consumables that contain two tests. Two samples can be run simultaneously in each bay, or four samples total per instrument. Each bay contains mechanisms to independently accept the reagent stripwell and chip (in carrier) assay components (consumable

interface); control their positioning (Y-Z Stage); provide laser input for scanning the chip and detect light frequencies output by the chip (photodiode in optics scanner). On the side of the instrument there is a fluidics component for each bay that consists of two electronically-driven syringe pumps fluid lines and manifold.

The computer component of the MDS manages the user interface, the software which controls the instrument, and provides a gateway between instrument and the cloud. The system uses cloud-based retrieval of protocols for each kit; after the test is completed, the raw data is uploaded to the cloud where algorithms evaluate the controls and process the data into assay results. Test results are returned to the laboratory's information system.

B Principle of Operation:

The assay relies on silicon photonics that uses ring resonance to measure binding of macromolecules to sensors on a miniature silicon chip. The Maverick Diagnostic System detects changes in resonance wavelength as macromolecules such as autoantibodies bind to their respective antigens that are bound to the chip.

The silicon chips have two fluidic channels to run two independent assays. Each channel consists of 16 silicon clusters each with 4 rings. The chip is assembled into a chip carrier that is inserted into Maverick Diagnostic System to run the assay. The RNP assay chip consists of the analyte RNP and internal controls described below. Purified native Ribonucleic acid protein (RNP), Human Serum Albumin (HSA), goat anti-human IgG, and Human IgG are spotted on one cluster each per channel. The remaining 11 ring clusters are not spotted with a reagent.

The Maverick RNP assay is an immunoassay. Patient sample is added to wells of a stripwell which already contains required buffers. The stripwell and the chip carrier are loaded into the Maverick instrument. When diluted sample is flowed over the chip, anti-RNP IgG antibodies, if present in the sample, will bind to the captured RNP. Any non-specifically bound antibodies from the sample will be removed in a wash step followed by flowing a detection reagent containing anti-human IgG for specific detection of the autoantibodies bound to the immobilized antigen. This immunoassay does not require a conjugated secondary antibody for detection. As more mass binds during the assay run, the shift in resonant wavelength is determined and converted into reportable units (AU/mL) using Genalyte's analysis algorithm.

C Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?	☒	☐
Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?	☐	☒
Software		
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.	☒	☐

1. Instrument Name:
   Maverick Diagnostic System (MDS)

2. Specimen Identification:
   The user scans the sample into the MDS software at the beginning of the test.

3. Specimen Sampling and Handling:
   Sample handling instructions are provided in the device labeling.

4. Calibration:
   A lot specific calibration curve is generated by Genalyte for each kit lot. The coefficients of the curve are entered into assay configuration on MDS Cloud. The barcode for each kit contains lot information which uses lot-specific curve coefficients in the Cloud. The raw result is converted to arbitrary units (AU/mL) using curve coefficients. The AU/mL value is proportional to the autoantibody levels present in the patient specimen. The results will be interpreted as positive or negative based on the assay's clinical cutoff.

5. Quality Control:
   External controls are not provided with the assay kit. The sponsor recommends that users run positive and negative controls on a regular basis.

   Internal controls are incorporated into the assay test chip; a negative control to assess non-specific binding; a positive control that verifies a serum sample has been added; and a system control that assesses the system function. The internal controls must be met to report a test result.

V Substantial Equivalence Information:

A Predicate Device Name(s):
QUANTA FLASH SM, QUANTA FLASH RNP, QUANTA FLASH SM CALIBRATORS, QUANTA FLASH RNP CALIBRATORS, QUANTA FLASH SM CONTROLS

B Predicate 510(k) Number(s):
K123593

C Comparison with Predicate(s):

Device & Predicate Device(s):	K191085	K123593
Device Trade Name	Maverick RNP Assay	QUANTA Flash RNP
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Maverick RNP Assay is an immunoassay for the semi-quantitative determination of anti-RNP IgG antibodies in human serum on the Maverick Diagnostic	The QUANTA Flash RNP is a chemiluminescent immunoassay for the semi-quantitative determination of IgG anti-ribonucleoprotein (RNP) antibodies in

	System. The presence of anti-RNP IgG antibodies, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of Mixed Connective Tissue Disease (MCTD). The Maverick Diagnostic System (MDS) is an automated immunoassay analyzer intended for in vitro diagnostic use to determine analytes in a clinical laboratory. The system's assay applications utilize silicon photonics technology.	human serum. The presence of anti-RNP antibodies, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of Systemic Lupus Erythematosus (SLE) and Mixed Connective Tissue Disease (MCTD).
Assay Type	Semi-quantitative	Same
Traceability	In -house standards	Same
Sample Type	Serum	Same
Analyte-Detected	Human antibodies specific to RNP	Same
Kit Storage	2 – 8 ℃	Same
General Device Characteristic Differences		
Instrumentation	Maverick Diagnostic System	BIO-FLASH chemiluminescent analyzer
Detection/Operating Principle	Photonic ring immunoassay	Chemiluminescent immunoassay
Solid phase	Silicone rings fabricated on a chip	Paramagnetic microparticles (beads)
Antigen	Native RNP/Sm antigen, purified from Bovine thymus	Native RNP/antigen, purified from calf thymus
Conjugate, Detection Antibody	No conjugate, anti-human IgG	Isoluminol conjugated anti-human IgG
Calibration	Lot specific Master Curve	Lot specific Master Curve and two

		calibrators (sold separately)
Cut-off	31.0 AU/mL	20 CU
Assay Range	21.0 to 240.0 AU/mL	3.5 to 643.8 CU

VI Standards/Guidance Documents Referenced:

EP05-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Edition
EP06-A, Evaluation of Linearity of Quantitative Measurement, Approved Guideline, Second Edition
EP07, Interference Testing in Clinical Chemistry, Approved Guideline, Third Edition
EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition
EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Addition
EP37-A, Supplemental Tables for Interference Testing in Clinical Chemistry

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results met the Manufacturer's pre-determined acceptance criteria.

1. Precision/Reproducibility:

Precision was evaluated by testing six samples with levels covering the assay measuring range. Samples were tested in duplicates per run, two runs per day, per bay of the instrument, for 21 days. There are two bays in an instrument, but each bay and its result are independent of the other. In some cases, the test did not provide a result if the run is invalid or did not meet internal quality controls; those tests were not re-run.

Samples for the studies were native high positive samples diluted with immunoglobulin depleted serum. Samples were prepared before the sample was diluted and added to the chip. The results for each bay are summarized below:

Bay 1:

			Repeatability		Between Run		Within Day		Between Day		Within Laboratory	
Sample	**N**	**Mean (AU/mL)**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**
PRC-01	83	23.63	4.43	18.8%	0.00	0.0%	4.43	18.8%	1.74	7.4%	4.76	20.2%
PRC-02	84	33.36	2.13	6.4%	1.07	3.2%	2.38	7.1%	1.04	3.1%	2.60	7.8%
PRC-03	83	55.99	2.86	5.1%	3.11	5.6%	4.22	7.5%	0.00	0.0%	4.22	7.5%
PRC-04	83	120.59	6.57	5.4%	1.77	1.5%	6.80	5.6%	6.05	5.0%	9.10	7.5%
PRC-05	84	170.27	5.14	3.0%	4.49	2.6%	6.83	4.0%	0.69	0.4%	6.86	4.0%
PRC-06	84	205.45	7.04	3.4%	5.69	2.8%	9.05	4.4%	2.79	1.4%	9.47	4.6%

Bay 2:

			Repeatability		Between Run		Within Day		Between Day		Within Laboratory	
Sample ID	**N**	**Mean**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**
PRC-01	84	23.10	2.36	10.2%	1.23	5.3%	2.66	11.5%	1.60	6.9%	3.10	13.4%
PRC-02	84	33.85	2.24	6.6%	1.06	3.1%	2.48	7.3%	1.20	3.5%	2.76	8.1%
PRC-03	83	56.24	2.74	4.9%	1.75	3.1%	3.25	5.8%	1.50	2.7%	3.58	6.4%
PRC-04	83	117.94	4.77	4.0%	3.10	2.6%	5.69	4.8%	5.09	4.3%	7.63	6.5%
PRC-05	83	167.07	4.46	2.7%	5.21	3.1%	6.86	4.1%	1.64	1.0%	7.05	4.2%
PRC-06	84	199.80	7.15	3.6%	0.00	0.0%	7.15	3.6%	5.40	2.7%	8.97	4.5%

Kit lot-to-lot imprecision was evaluated by testing four samples with levels covering the assay measuring range. Samples were tested in replicates of two per run, four runs per day, per bay of the instrument, for five days using three different kit lots. Samples for the studies were native high positive samples diluted with immunoglobulin depleted serum. Samples were prepared before the sample was diluted and added to the chip. The results are summarized below:

			Repeatability		Between Day		Within Kit Lot		Between Kit Lot		Reproducibility	
Sample	**N**	**Mean**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**
RPK-01	238	33.02	2.46	7.5%	1.10	3.3%	2.70	8.2%	2.43	7.3%	3.63	11.0%
RPK-02	239	61.55	4.57	7.4%	3.49	5.7%	5.75	9.3%	2.20	3.6%	6.16	10.0%
RPK-03	235	103.58	6.76	6.5%	4.51	4.4%	8.13	7.8%	6.98	6.7%	10.71	10.3%
RPK-04	237	139.95	8.86	6.3%	4.23	3.0%	9.81	7.0%	5.84	4.2%	11.42	8.2%

Instrument-to-Instrument imprecision was evaluated by testing six samples with levels covering the assay measuring range. Samples were tested in replicates of two per run, four runs per day, per bay of the instrument, for 5 days (maximum n = 40 per bay). Each instrument has two bays and the samples were tested on three different instruments (maximum n = 240 per sample). Samples for the studies were native high positive samples diluted with immunoglobulin depleted serum. Samples were prepared before the sample was diluted and added to the chip. The results are summarized below:

			Repeatability		Between Day		Within Instrument		Between Instruments		Reproducibility	
Sample	**N**	**Mean (AU/mL)**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**
RPI-01	239	31.66	2.42	7.6%	2.15	6.8%	3.24	10.2%	1.21	3.8%	3.46	10.9%
RPI-02	240	61.17	4.50	7.4%	2.52	4.1%	5.15	8.4%	2.35	3.8%	5.66	9.3%
RPI-03	239	106.21	5.74	5.4%	2.97	2.8%	6.46	6.1%	4.68	4.4%	7.98	7.5%
RPI-04	240	149.37	6.90	4.6%	5.63	3.8%	8.90	6.0%	5.88	3.9%	10.67	7.1%
RPI-05	240	24.16	2.63	10.9%	0.74	3.1%	2.73	11.3%	1.32	5.5%	3.03	12.6%
RPI-06	240	213.88	15.79	7.4%	6.18	2.9%	16.95	7.9%	6.75	3.2%	18.25	8.5%

2. Linearity:

The Maverick RNP assay's linearity was tested by diluting six native positive serum samples with analyte-free sera to generate a dilutions series with analyte concentrations across the measuring range in equidistant dilutions. Each dilution was tested four to six times. The

observed values were graphed against the calculated values and a linear regression was performed. The linear range was determined to be 21.00 – 240 AU/mL for the assay. The results are summarized in the table below:

Sample	Test Range (AU/mL)	Slope (95% CI)	Y-intercept (95% CI)	R^2
1	25.04 – 232.99	1.00 (0.96 – x 1.03)	2.03 (-1.79 – 5.86)	0.99
2	49.95 – 150.86	1.01 (0.94 –1.09)	19.66 (13.60 – 25.72)	0.95
3	29.39 – 182.53	0.95 (0.90 – 0.99)	12.30 (7.55 – 17.03)	0.98
4	22.72 – 72.20	0.95 (0.88 – 1.02)	5.60 (2.55 – 8.65)	0.98
5	27.85 – 95.29	0.97 (0.92 – 1.02)	4.55 (1.85 – 7.24)	0.99
6	24.06 – 60.10	0.97 (0.88 – 1.06)	4.31 (0.63 – 7.99)	0.98

Hook Effect: Two high concentrations specimens were serially diluted to assess the presence of any artifactual decrease in assay signal associated with anti-RNP antibody excess (hook effect). No hook effect was demonstrated in sample levels up to 683.68 AU/mL.

3. Analytical Specificity/Interference:

The Maverick RNP Assay was evaluated for any potential interference form biological and external interferents. Three native samples corresponding to the negative range, near the assay cut-off, and moderate positive range were tested with spiked interferents and without interferents (controls). The recovery was calculated by comparing to control samples spiked with the same volume of diluents. No significant interference was detected for the following substances up to the concentrations listed in the table below:

Interferant	Interferent Conc.
Albumin	35.0 gm/L
Biotin	240.0 mg/dL
Cholesterol	75.0mg/dL
Conjugated bilirubin	25.0 mg/dL
Cyclophosphamide	13.73 mg/dL
Diltiazem	0.045 mg/dL
Hemoglobin	125.0 mg/dL
Hydroxychloroquine	33.0 µg/mL
Immunoglobulin A	25.0 mg/dL
Immunoglobulin G	200.0 mg/dL
Immunoglobulin M	100.0 mg/dL
Mycophenolate Mofetil	42.0 µg/mL
Naproxen	36.0 mg/dL

Interferant	Interferent Conc.
Prednisone	0.00125 mg/dL
Rheumatoid Factor	209.0 IU/mL
Triglycerides	250.0 mg/dL

The assay package insert instructs users not to use hemolyzed, lipemic or icteric samples.

4. Assay Reportable Range:
   The assay's reportable range is 21.0 – 240.0 AU/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   Traceability:
   There are currently no recognized international standards for the measurement of antibodies specific for RNP.

   Stability:
   Kit stability (unopened): Real time and accelerated stability testing of three lots of kits, supports a claim of six months for unopened kits stored at 2–8°C.

   Kit stability (opened): The assay kit is a single-use individually packaged. The assay's package insert instructs users to allow for at least 30 minutes for the kit to come to room temperature before use but keep the kit on the bench no longer than 2 hours before use.

   Sample stability: The study supported sample stability for one week at 2–8°C.

6. Detection Limit:

   Limit of Blank (LoB) was determined by assaying each of four immunoglobulin depleted analyte-free serum samples in replicates of six, on each instrument bay (two bays) with two reagent lots for four days. A maximum of 48 results per sample per kit lot (192 results per lot) were generated. LoB for each lot was calculated separately as the 95th percentile using the non-parametric method, as the dataset showed non-normal distribution. The LoB of both two lots was below the measuring range and was claimed to be < 7.5 AU/mL.

   Limit of Detection (LoD) was determined by assaying four very low-level native samples tested in replicates of six in both bays over four days on two reagent lots to achieve a maximum of 48 results per sample per lot (i.e., up to 192 replicates per lot). LoD value was calculated as the
   LoB + 1.645 x SD of the replicates for the low-level samples. The LoD of both lots of the assay were below the measuring range and was claimed to be < 7.5 AU/mL.

   Limit of Quantitation (LoQ) was determined by assaying four low-level native samples tested in replicates of six in both bays over three days on two reagent lots to achieve a maximum of 36 results per sample per lot (up to 144 replicates per lot). The LoQ was calculated by determining the lowest analyte concentration that resulted in a total within laboratory CV <20%. The highest value among two lots was chosen as LOQ. The LoQ claim is 21.00 AU/mL.

7. Assay Cut-Off:

   A ROC analysis established the assay cut-off by optimizing the sensitivity and specificity of 171 samples from normal and autoimmune diseases and 27 anti-RNP positive samples with unknown diagnosis. These samples were not included in the method comparison or clinical sensitivity and specificity determination. The cut-off of the anti-RNP IgG assay is 31.00 AU/mL.

8. Accuracy (Instrument):
   Not applicable.

9. Carry-Over:
   The chip and chip carrier which has sippers are single use. Therefore, after running a test each chip will be disposed. A new chip will be used for the next assay. The flow during an assay run is one way through sippers and to the waste. There is no possibility for sample carry-over between runs.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A subset of samples from the clinical sensitivity and specificity study (below) and some additional samples (total n = 273) were tested with the Maverick RNP Assay and the predicate. The results that were within the assays' ranges (n = 110) were compared and shown below:

		Predicate		
		Pos	**Neg**	**Total**
Maverick RNP Assay	**Pos**	68	5	73
	Neg	3	34	37
	Total	71	39	110

Positive Percent Agreement: 95.8% (95% CI 88.3% – 98.6%)
Negative Percent Agreement: 87.2% (95% CI 73.3% – 94.4%)

2. Matrix Comparison:
   Not applicable; serum is the only indicated sample matrix.

C Clinical Studies:

1. Clinical Sensitivity:

   A total of 371 clinically characterized serum samples, including 33 MCTD, 60 SLE, and 278 other autoimmune and infectious disease samples (see below) that could be expected in the differential diagnosis of mixed connective tissue disease (MCTD) were tested on the Maverick RNP Assay. The results of the study are shown below:

		MCTD Diagnosis		
		Positive	Negative	Total
Maverick RNP Assay	Positive	28	2	30
	Negative	5	276	281
	Total	33	278	381

Clinical Sensitivity (95% CI): 84.8% (69.1 – 93.3%)
Clinical specificity (95% CI): 99.3% (97.4 – 99.8%)

2. Clinical Specificity:

Disease	*n*	*# Positive*
SLE	60	17 (28.3%)
APS	22	0
Autoimmune Hepatitis	7	0
Primary Biliary Cholangitis	15	0
Crohn's Disease	15	0
Ulcerative Colitis	15	0
Dermatomyositis	11	0
Polymyositis	16	0
Grave's Disease	10	0
Hashimoto's	17	0
Osteoporosis	11	0
RA	52	0
Scleroderma	27	1 (3.7%)
Sjogren's Syndrome	30	1 (3.3%)
Hepatitis B	11	0
Hepatitis C	10	0
HIV	5	0
Syphilis	4	0
Non-SLE Specificity	*278*	*2 (0.7%)*

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

A panel of 120 presumptively healthy normal volunteers (60 females and 60 males with ages ranging from 20 to 61 years) was tested. All samples were below the cut-off of 31.00 AU/mL (i.e., negative). The expected value for normal samples is negative.

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

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.