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

I Background Information:

A 510(k) Number
K222116

B Applicant
Siemens Healthcare Diagnostics Inc.

C Proprietary and Established Names
Atellica® CI Analyzer, Atellica® IMThyroid Stimulating Hormone 3-Ultra (TSH3-UL), Atellica® CH Albumin BCP (AlbP)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JLW	Class II	21 CFR 862.1690 - Thyroid Stimulating Hormone Test System	CH - Clinical Chemistry
CJW	Class II	21 CFR 862.1035 - Albumin test system	CH - Clinical Chemistry
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:
Addition of previously cleared assays to a new instrument

B Measurand:
Thyroid Stimulating Hormone, Albumin

C Type of Test:
Quantitative, photometry for albumin
Quantitative, chemiluminescence immunoassay for thyroid stimulating hormone

III Intended Use/Indications for Use:

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

B Indication(s) for Use:

The Atellica® CI Analyzer is an automated, integrated system designed to perform in vitro diagnostic tests on clinical specimens. The system is intended for the qualitative and quantitative analysis of various body fluids, using photometric, turbidimetric, chemiluminescent, and integrated ionselective electrode technology for clinical use.

The Atellica® IM Thyroid Stimulating Hormone 3-Ultra (TSH3-UL) assay is for in vitro diagnostic use in the quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin) in human serum and plasma (EDTA and lithium heparin) using the Atellica® CI Analyzer. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

The Atellica® CH Albumin BCP (AlbP) assay is for in vitro diagnostic use in the quantitative measurement of albumin in human serum and plasma (lithium heparin, potassium EDTA) using the Atellica® CI Analyzer. Albumin measurements are used in the diagnosis and treatment of numerous diseases primarily involving the liver or kidneys.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Atellica® CI analyzer

IV Device/System Characteristics:

A Device Description:

Atellica® CI Analyzer

The Atellica® CI Analyzer is an automated, integrated system designed to perform in vitro diagnostic tests on clinical specimens. The system is intended for the qualitative and quantitative analysis of various body fluids, using photometric, turbidimetric, chemiluminescent, and integrated ion selective electrode technology for clinical use.

The Atellica® CI Analyzer with Atellica® Rack Handler supports both clinical chemistry (CH) and Immunoassay (IM) features and contains all the necessary hardware, electronics, and software to automatically process samples and generate results, including sample and reagent dispensing, mixing, and incubating.

Atellica® IM TSH3-UL

The Atellica® IM TSH3-UL assay is performed using the Atellica® IMTSH3-UL ReadyPack® primary reagent pack, Atellica® IM Multi-Diluent 15 ReadyPack ancillary reagent pack, and the Atellica® IM TSH3-UL CAL (calibrator) on the Atellica® CI Analyzer.

The Atellica® IMTSH3-UL ReadyPack® Primary Reagent Pack consists of the following:

- Lite Reagent:
  4.2 mL/reagent pack, Bovine serum albumin (BSA) conjugated to mouse monoclonal anti-TSH (~0.3 µg/mL) labeled with acridinium ester in HEPES buffered saline; mouse IgG; BSA; goat serum; surfactant; preservatives

- Solid Phase:
  16.5 mL/reagent pack, Mouse monoclonal anti-fluorescein antibody covalently linked to paramagnetic particles (~85 µg/mL) in buffer; stabilizers; surfactant; preservatives

- Ancillary Well Reagent:
  4.2 mL/reagent pack, FITC conjugated to mouse monoclonal anti-TSH (~3 µg/mL) in buffer; stabilizers; surfactant; preservatives

The Atellica® IM Multi-Diluent 15 ReadyPack ancillary reagent pack consists of 25.0 mL/pack of Equine serum; sodium azide (0.1%); preservatives

The Atellica® IM TSH3-UL CAL (calibrator) consists of 2.0 mL/vial; buffer; equine serum; sodium azide (< 0.1%); preservatives

Atellica® CH Albumin BCP (AlbP)
The Atellica® CH Albumin BCP (AlbP) assay, also referred to as the Atellica® CH AlbP, is an assay system performed using the Atellica® CH AlbP Reagent Pack and the Atellica® CH AlbP CAL (calibrator) on the Atellica® CI Analyzer.

The Atellica® CH AlbP Reagent Pack consists of two wells of reagent 1: 18.3 mL Bromocresol Purple (1.1 mmol/L), acetate buffer, surfactant, microbial inhibitor. Materials required, but not provided, consist of the Atellica® CH AlbP CAL (calibrator).

Principle of Operation:
Atellica® IM TSH3-UL assay
The Atellica® IM TSH3-UL assay employs anti-FITC (fluorescein isothiocyanate) monoclonal antibody covalently bound to paramagnetic particles, a FITC-labeled anti-TSH capture mouse monoclonal antibody, and a tracer consisting of a proprietary acridinium ester and an anti-TSH mouse monoclonal antibody conjugated to bovine serum albumin (BSA) for chemiluminescent detection. A direct relationship exists between the amount of TSH present in the patient sample, with a sample volume of 75 µL, and the amount of relative light units (RLUs) detected by the system.

Atellica® CH AlbP assay
The Atellica® CH AlbP assay employs photometric determination to measure albumin. Albumin binds to bromocresol purple (BCP) dye in mildly acidic pH to form an albumin-BCP complex. An increase in absorbance at 596/694 nm is proportional to the concentration of albumin in the sample, when a sample volume of 4 µL is tested.

B Instrument Description Information:

1. Instrument Name:
   Atellica® CI Analyzer

2. Specimen Identification:
   The specimen is held in a tube with a barcode label. The system identifies the specimen by scanning the barcode. This is the primary use case for sample identification. The system also

supports manual entry of sample IDs to support the needs of the customer and the use of a Laboratory Information System (LIS).

3. Specimen Sampling and Handling:
   For CH assays, the sample volume on the Atellica® CI Analyzer is 4–50µL. For IM assays, the sample volume on the Atellica® CI Analyzer is 10–100 µL.

   Specimen sampling and handling procedures are analyte specific and documented in the respective reagent method sheets.

4. Calibration:
   Calibration methods and procedures are analyte specific and documented in the respective reagent method sheets.

5. Quality Control:
   Labeling recommends that at least two levels (ex: low and high) of an appropriate quality control material be tested. Quality control procedures are analyte specific and documented in the respective reagent method sheets.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Trinidad IM Thyroid Stimulating Hormone (TSH) Assay, Trinidad IM TSH Calibrators, Trinidad Immunoassay (IM) System

Trinidad CH system, Trinidad CH Albumin BCP reagent (Alb_P), Trinidad CH Albumin BCP Calibrator

B Predicate 510(k) Number(s):

K151792, K151767

C Comparison with Predicate(s):

Comparison of TSH Assay:

Device & Predicate Device(s):	K151792	K222116
Device Trade Name	Trinidad IM Thyroid Stimulating Hormone (TSH) Assay, Trinidad IM TSH Calibrators, Trinidad Immunoassay (IM) System	Atellica® IM Thyroid Stimulating Hormone 3-Ultra (TSH3-UL)
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin)	Same

Operating principle	Electrolyte, Photometric and Turbidimetric	Same
General Device Characteristic Similarities	K151792	K222116
Sample Type	Serum, EDTA plasma, lithium heparin plasma	Same
Detection Antibody	Monoclonal murine anti-TSH antibody BSA conjugate labeled with acridinium ester (AE)	Same
Capture Antibody	Anti-fluorescein labeled (FITC) monoclonal murine anti-TSH antibody covalently bound to paramagnetic particles (PMP)	Same
Assay range	0.008–150.000 µIU/mL	Same
General Device Characteristic Differences		
Detection Limit	LoB(µIU/mL) 0.001 LoD(µIU/mL) 0.008	LoB(µIU/mL) 0.004 LoD(µIU/mL) 0.005

Comparison of Albumin Assay:

Device & Predicate Device(s):	K151767	K222116
Device Trade Name	Trinidad CH Albumin BCP reagent (Alb_P), Trinidad CH Albumin BCP Calibrator	Atellica® CH Albumin BCP (AlbP)
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative measurement of albumin	Same
Operating principle	bromocresol purple (BCP) dye-binding method	Same
Assay range	0.5–8.0 g/dL	Same
Sample type	Serum, plasma (lithium heparin, potassium EDTA)	Same
General Device Characteristic Differences		
Detection Limit	LoD (g/dL) 0.2 LoQ (g/dL) 0.4	LoD (g/dL) 0.5 LoQ (g/dL) 0.5

Comparison of the Analyzers:

Device & Predicate Device(s):	K151767	K222116
Device Trade Name	Trinidad CH system	Atellica® CI analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	Automated, clinical chemistry analyzer intended for in vitro diagnostic tests on clinical specimens	Same
Operating principle	Electrolyte, Photometric and Turbidimetric	Same
General Device Characteristic Differences	K151767	K222116
Software	Atellica Solution	Atellica® CI Software
Assay Capacity On-Board	Up to 70 assays	Up to 20 assays

Device & Predicate Device(s):	K151792	K222116
Device Trade Name	Trinidad Immunoassay (IM) System	Atellica® CI analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	Automated, immunoassay analyzer intended for in vitro diagnostic tests on clinical specimens	Same
Operating principle	Chemiluminescence using magnetic- particle solid phase and chemiluminescent label	Same
General Device Characteristic Differences		
Software	Atellica Solution	Atellica® CI Software
Assay Capacity On-Board	Up to 42 assays	Up to 20 assays

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures, Third Edition
- CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures, Second Edition
- CLSI EP07, Interference Testing in Clinical Chemistry, Third Edition
- CLSI EP09c, Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Third Edition
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Second Edition
- CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, Third Edition
- CLSI EP34, Establishing, and Verifying an Extended Measuring Interval through Specimen Dilution and Spiking, First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Repeatability and intermediate precision were evaluated following the recommendations in the CLSI guideline EP05-A3.

Thyroid Stimulating Hormone:

Six serum samples, three EDTA plasma samples, three lithium heparin plasma samples, and three control samples were each assayed over 20 days, in duplicate, two runs per day, for a total of 80 results per sample tested on one instrument. The results of the 20-day precision study are shown in the table below (n = 80 for each panel):

Sample	N	Mean µIU/mL	Repeatability		Within-Laboratory Precision	
			SD µIU/mL	%CV	SD µIU/mL	%CV
Serum A	80	0.017	0.0009	5.3	0.0015	8.8
Serum B	80	0.156	0.0018	1.2	0.0047	3.0
Serum C	80	1.129	0.0152	1.3	0.0262	2.3
Serum D	80	9.848	0.1213	1.2	0.1996	2.0
Serum E	80	58.362	0.6498	1.1	1.4346	2.5
Serum F	80	120.833	1.6610	1.4	3.5474	2.9
EDTA Plasma A	80	1.408	0.0170	1.2	0.0311	2.2
EDTA Plasma B	80	39.662	0.6028	1.5	0.9500	2.4
EDTA Plasma C	80	97.894	1.2965	1.3	2.8148	2.9
Heparin Plasma A	80	1.706	0.0230	1.3	0.0321	1.9

Sample	N	Mean µIU/mL	Repeatability		Within-Laboratory Precision	
			SD µIU/mL	%CV	SD µIU/mL	%CV
Heparin Plasma B	80	40.719	0.4539	1.1	0.8526	2.1
Heparin Plasma C	80	97.533	1.4809	1.5	3.1898	3.3
Control 1	80	0.387	0.0057	1.5	0.0091	2.4
Control 2	80	4.745	0.0812	1.7	0.1136	2.4
Control 3	80	32.012	0.4122	1.3	0.7244	2.3

Albumin:

Three serum samples and one Serum QC sample were each assayed over 20 days, in duplicate, two runs per day, for a total of 80 results per sample tested on one instrument. The results of the 20-day precision study are shown in the table below (n = 80 for each panel):

Sample	N	Mean g/dL	Repeatability		Within-Laboratory Precision	
			SD g/dL	%CV	SD g/dL	%CV
Serum 1	80	2.7	0.03	1.1	0.06	2.2
Serum QC 1	80	3.1	0.04	1.3	0.08	2.6
Serum 2	80	3.6	0.03	0.8	0.09	2.5
Serum 3	80	7.1	0.04	0.6	0.12	1.7

A reproducibility study was conducted using three serum samples, where the samples were run in five replicates, on three instruments, using three reagent lots, for five days. The results of the reproducibility (five days) study are shown in the table below (n = 225 for each panel):

Sample	N	Mean g/dL	Repeatability		Reproducibility	
			SD g/dL	%CV	SD g/dL	%CV
Serum 1	225	2.7	0.03	1.2	0.05	1.9
Serum 2	225	3.7	0.03	0.9	0.05	1.4
Serum 3	225	7.1	0.04	0.6	0.11	1.5

Sample	N	Mean g/dL	Between-Day		Between-Instrument		Between-Lot	
			SD g/dL	%CV	SD g/dL	%CV	SD g/dL	%CV
Serum 1	225	2.7	0.03	1.3	0.02	0.7	0.01	0.2
Serum 2	225	3.7	0.03	0.9	0.01	0.4	0.01	0.3
Serum 3	225	7.1	0.06	0.9	0.00	0.0	0.07	1.1

2. Linearity:

Thyroid Stimulating Hormone:
A high TSH serum pool was created using native samples with known high TSH values. The high TSH serum pool was serially diluted with a low sample TSH pool (i.e. TSH-free serum sample) to create 14 TSH serum samples distributed across the analytical measuring interval. All samples were run in quintuplet on one Atellica® CH Analyzer, with 3 reagent lots. The results of the linearity study support the claimed measuring interval of 0.008 µIU/mL to 150.000 µIU/mL.

Dilution Recovery:
Studies were conducted in accordance with the CLSI guideline EP34. The dilution study results support the sponsor's labeling claims that samples with TSH concentrations above the 150 µIU/mL may be diluted automatically by the analyzer (i.e. 1:2 and 1:5) with a sample volume of 100 µL and 80 µL, respectively for serum and plasma samples.

Albumin:
A high serum pool was created by spiking native samples with albumin (bovine serum albumin powder from Sigma Aldrich). The low albumin serum pool was created by diluting serum samples with CH diluent. The high serum pool was diluted with the low serum pool to create nine albumin serum samples distributed across the analytical measuring interval. All samples were run in quintuplet on one Atellica® CI Analyzer, with one reagent lot. The results of the linearity study support the claimed measuring interval of 0.5 g/dL to 8.0 g/dL.

3. Analytical Specificity/Interference:
Interference testing was conducted in accordance with CLSI guideline EP07-ed3.

Thyroid Stimulating Hormone:
Two human serum specimen pools with native analyte, concentrations of approximately 0.8 and 9.0 µIU/mL, were supplemented with potentially interfering compounds at levels listed in the table below. Significant interference was defined as more than ±10% bias as compared to the control results. The results of the interference study are summarized in the table below:

Substances	Maximum concentration tested that demonstrated no significant interference
Hemoglobin	500 mg/dL
Conjugated bilirubin	40 mg/dL
Unconjugated bilirubin	40 mg/dL
Lipemia (Intralipid)	1000 mg/dL
Biotin	0.35 mg/dL
Acetaminophen	15.60 mg/dL
N-Acetylcysteine	15.00 mg/dL
Acetylsalicylic acid	3.00 mg/dL
Ampicillin	7.50 mg/dL
Ascorbic Acid	5.25 mg/dL

Substances	Maximum concentration tested that demonstrated no significant interference
Carbimazole	3.00 mg/dL
Cefoxitin	495.00 mg/dL
Cyclosporine	0.18 mg/dL
Doxycycline	1.80 mg/dL
Heparin	7500 units/dL
Ibuprofen	21.90 mg/dL
Levodopa	0.75 mg/dL
Levothyroxine	0.0429 mg/dL
Liothyronine	0.0075 mg/dL
Methimazole	8.00 mg/dL
Methyldopa	2.25 mg/dL
Metronidazole	12.30 mg/dL
Octreotide	0.03 mg/dL
Phenylbutazone	32.10 mg/dL
Propranolol	24.00 mg/dL
Propylthiouracil	30.00 mg/dL
Rifampicin	4.80 mg/dL
Theophylline	6.00 mg/dL
Total Protein	15.0 g/dL
Cholesterol	400 mg/dL
Rheumatoid Factor	1500 IU/mL

The following information pertains to limitations of the assay:

i. Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.

ii. Do not use samples that contain fluorescein. Fluorescein levels > 0.24 µg/mL may decrease results in this assay. Evidence suggests that patients undergoing retinal fluorescein angiography can retain amounts of fluorescein in the body for up to 48–72 hours post-treatment.

In the cases of patients with renal insufficiency, including many diabetics, retention could be much longer. Such samples can produce falsely depressed values when tested with this assay and should not be tested. Testing of samples spiked with a theoretical maximum level of fluorescein (250 µg/mL) used in these patients have resulted in TSH levels < 0.06 µIU/mL instead of the true value of 27.99 µIU/mL.

iii. As with any immuno-recognition measurement of a peptide, extremely rare genetic variants of TSH may exhibit varying degrees of detection in this assay.

Cross-Reactivity Testing:

Cross-reactivity studies were performed to evaluate the susceptibility of the Atellica® IM TSH3-UL assay to cross-reactivity with the following endogenous structural analogs to human TSH: human follicle stimulating hormone (FSH), human luteinizing hormone (LH),

and human chorionic gonadotropin (hCG). Five replicates of four samples with the following concentrations were tested: 0.3 µIU/mL, 3.6 µIU/mL, 51 µIU/mL, and 114 µIU/mL TSH. Significant cross reactivity was defined as >5% bias in expected results compared to the control. The following cross-reactants demonstrated no reactivity at the concentrations tested:

Cross-reactant	Cross-reactant concentration tested (µIU/mL)
Human Chorionic Gonadotropin	200,000
Follicle Stimulating Hormone	1,500
Luteinizing Hormone	600

High Dose Hook Effect:

The high-dose hook effect of the Atellica® IM TSH3-UL assay on the Atellica® CI Analyzer was assessed by testing 15 serial dilutions of human TSH, ≥95% pure, reconstituted in horse serum. Each sample was tested in replicates of three. No high dose hook effect was observed for samples containing approximately 3,000 µIU/mL of TSH.

The sponsor includes the following statement in the Atellica® IM TSH3-UL assay package insert: "High TSH concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with TSH concentrations as high as 3000 µIU/mL (mIU/L) will report > 150.000 µIU/mL (mIU/L)."

Albumin:

Two pools of serum samples (~3.5 g/dL and ~5.0 g/dL) were spiked with interfering substances and tested in quintuplet with 3 reagent lots on one Atellica® CI Analyzer. Interference was determined by testing controls (no interfering substance added) and matched test sample (with interfering substance added). Significant interference was defined as more than ±10% bias as compared to the control results. The results of the interference study are summarized in the table below:

Substances	Maximum concentration tested that demonstrated no significant interference
Hemoglobin	1000 mg/dL
Conjugated bilirubin	30 mg/dL
Unconjugated bilirubin	30 mg/dL
Lipemia (Triglycerides)	2000mg/dL
Lipemia (Intralipid)	500 mg/dL
Biotin	0.351 mg/dL
Acetaminophen	15.60 mg/dL
N-Acetylcysteine	15.00 mg/dL

Substances	Maximum concentration tested that demonstrated no significant interference
Acetylsalicylic acid	3.00 mg/dL
Ampicillin	7.50 mg/dL
Ascorbic Acid	5.25 mg/dL
Cefoxitin	75.00 mg/dL
Cholesterol	400 mg/dL
Cyclosporine	0.18 mg/dL
Heparin	3300 IU/L
Ibuprofen	21.90 mg/dL
Immunoglobin G	5 g/dL
Levodopa	0.75 mg/dL
Rifampicin	4.80 mg/dL
Rheumatoid Factor	1500 IU/mL
Theophylline	6 mg/dL

4. Assay Reportable Range:
   TSH: 0.008 µIU/mL to 150.000 µIU/mL.
   Albumin: 0.5 g/dL to 8.0 g/dL.

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

   Traceability:
   Atellica® IM TSH3-UL
   The Atellica® IM TSH3-UL assay and calibrators are traceable to the World Health Organization (WHO) 3rd International Standard for human TSH (IRP 81/565). Assigned values for calibrators are traceable to this standardization.

   Atellica® CH AlbP
   The Atellica® CH AlbP assay and calibrators are traceable to ERM DA470k Reference Material.

   Stability:
   Atellica® IM TSH3-UL
   Protocols and acceptance criteria for on-board/open vial stability studies for the Atellica® IM TSH3-UL ReadyPack primary reagent pack® Lite reagent, Atellica® IMMulti-Diluent 15, and Atellica® IMTSH-UL calibrator were reviewed and found to be acceptable to support an on-board stability of 90 days, 7 days, and 28 days at 2-8ºC, respectively. The calibrator pack and lot calibration have a stability of 63 days.

   Atellica® CH AlbP
   Protocols and acceptance criteria for on-board/open vial stability studies for the Atellica® CH AlbP reagent pack were reviewed and found to be acceptable to support an on-board stability of up to 61 days at 2-8ºC. The calibrator pack has a stability of 24 days, and the lot calibration has a stability of 30 days.

6. Detection Limit:
Detection limit studies were conducted in accordance with CLSI guideline EP17-A2.

Thyroid Stimulating Hormone:
Limit of Blank:
Five samples with no detectable TSH levels were tested. The samples were tested in four replicates, run twice a day on two Atellica® CI Analyzers using three reagent lots over five testing days (n = 400 measurements per reagent lot). The limit of blank was estimated by the 95th percentile of 400 values for each lot. The limit of blank was determined to be 0.004 µIU/mL.

Limit of Detection:
Five low- level samples were tested in four replicates, run twice a day on two Atellica® CI Analyzers using three reagent lots over five testing days (n = 400 measurements per reagent lot). The limit of detection was determined to be 0.008 µIU/mL.

Limit of Quantitation:
Seven human serum pools with low levels of TSH were tested. The samples were tested in duplicate, run twice a day on two Atellica® CI Analyzers using three reagent lots over 20 testing days (n = 80 measurements per reagent lot). Calibration was performed on day 1 of the study. The limit of quantitation was defined as the value at which the within laboratory CV is ≤ 20% and determined to be 0.008 µIU/mL.

LoB	LoD	LoQ
0.004 µIU/mL	0.008 µIU/mL	0.008 µIU/mL

Albumin:
Limit of Blank:
Five samples with no detectable albumin levels were tested. The samples were tested in six replicates on one Atellica® CI Analyzer, using three reagent lots over three testing days (n = 90 measurements per reagent lot). The limit of blank was estimated by the 95th percentile of 90 values for each lot. The limit of blank was determined to be 0.1 g/dL for serum.

Limit of Detection:
Four low-level albumin samples were tested. The samples were tested in six replicates on one Atellica® CI Analyzer, using three reagent lots over three testing days (n = 90 measurements per reagent lot). The Limit of Detection was determined parametrically using the pooled standard deviation (SDL) for all samples from a given reagent lot, using the following equation: $\boldsymbol{LoD = LoB + cpSDL}$, where "cp" represents the capability potential. The limit of detection was determined to be between 0.43-0.53 g/dL for serum, and support a limit of detection of 0.5 g/dL.

Limit of Quantitation:
Five serum pools with target Albumin concentrations between 0.4-0.5 g/dL were tested, four low level serum pools were created by diluting the base serum pools with CH diluent and one QC sample was diluted with CH diluent to serve as a control. The samples were tested in five replicates on one Atellica® CI Analyzer, using three reagent lots over five testing

days (n = 125 measurements per reagent lot). Calibration was performed on day one of the study. The sponsor defined the LoQ as the concentration with ≤ 10% within-laboratory precision.

LoB	LoD	LoQ
0.1 g/dL	0.5 g/dL	0.5 g/dL

7. Assay Cut-Off:
   Not applicable.

8. Accuracy (Instrument):
   See section VII.B.1. below.

9. Carry-Over:
   Information regarding the potential impact of carry-over on the candidate device was reviewed and determined to be acceptable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Studies were conducted in accordance with CLSI guideline EP09c-ed3.

   Thyroid Stimulating Hormone:
   A method comparison study compared the performance of the candidate test system (Atellica® IM TSH3-UL on the Atellica® CI Analyzer) to the performance of the predicate, the Atellica® IM Thyroid Stimulating Hormone (TSH) assay run on the Atellica® IM Analyzer (K151792). A total of 112 matched, native serum samples ranging from 0.013-144.030 µIU/mL were tested in duplicate using one reagent over seven days, using one analyzer. Weighted Deming regression analysis was performed with the first replicate result. The data is summarized in the table below:

n	Weighted Deming Regression	Correlation Coefficient	Sample Range Tested (µIU/mL)
112	y = 0.96x – 0.001	0.996	0.013-144.030

   Albumin:
   A method comparison study compared the performance of the candidate test system (Atellica® CH AlbP assay on the Atellica® CI Analyzer) to the performance of the predicate, the Atellica® CH Albumin BCP (AlbP) assay on the Atellica® CH Analyzer (K151767). A total of 106 matched, native serum samples ranging from ~0.6-7.5 g/dL were tested using one reagent lot and one analyzer over five days. Of the 106 native samples, one sample was diluted to meet the lower end of the measuring interval and two native samples were spiked to meet the upper end of the measuring interval. Weighted Deming regression analysis was performed using results from the first replicate. The data is summarized in the table below:

n	Weighted Deming Regression	Correlation Coefficient	Sample Range Tested (g/dL)
106	y = 0.98x + 0.0	0.999	0.6-7.5

2. Matrix Comparison:
Studies were conducted in accordance with CLSI guideline EP09c-ed3.

Thyroid Stimulating Hormone:
A matrix comparison study was conducted utilizing 65 matched lithium heparin plasma, EDTA plasma and serum samples. One native sample was excluded from the final analysis because the results were below the assay range of detection. Seven sets of samples were spiked with TSH to cover the upper range of the assay. The TSH values ranged from 0.023 to 134.942 µIU/mL. All samples were assayed in duplicate with one reagent lot on one Atellica® CI Analyzer over three days. The results were analyzed using weighted Deming regression. The first replicate of each data set was used for the analysis. Results are summarized in the table below:

Test Specimen	Reference Specimen	n	Weighted Deming Regression	Correlation Coefficient	Sample Interval (µIU/mL)
Lithium Heparin Plasma	Serum	64	1.00x + 0.001 µIU/mL	1.00	0.023-134.942
Potassium EDTA Plasma	Serum	64	1.00x - 0.001 µIU/mL	1.00	0.023-134.942

The results support the sponsor's claims for lithium heparin and potassium EDTA plasma samples.

Albumin:
A matrix comparison study was conducted utilizing 55 matched Potassium EDTA plasma and serum samples and 76 matched serum and lithium heparin samples. Two sets of samples were spiked with Albumin to cover the upper range of the assay and three sample sets were diluted with CH diluent to cover the lower range of the assay. The Albumin values ranged from 0.5-7.9 g/dL. All samples were assayed in duplicate with one reagent lot on one Atellica® CI Analyzer. The results were analyzed using weighted Deming regression. The first replicate of each data set was used for the analysis. Results are summarized in the table below:

Test Sample	Comparison sample type	n	Weighted Deming Regression	Correlation Coefficient	Sample range (g/dL)
Lithium Heparin Plasma	Serum	76	1.01x + 0.0 g/dL	0.995	0.5-7.9
Potassium EDTA Plasma	Serum	55	0.99x + 0.0 g/dL	0.997	0.5-7.9

The results support the sponsor's claims for lithium heparin and potassium EDTA plasma samples.

C Clinical Studies:

1. Clinical Sensitivity:
   Not Applicable.

2. Clinical Specificity:
   Not Applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):
   Not Applicable.

D Clinical Cut-Off:
Not Applicable.

E Expected Values/Reference Range:
Reference intervals for the pediatric population (infants, children, and adolescents) were established in accordance with the CLSI guideline EP28-A3c.

Thyroid Stimulating Hormone:
The reference interval was previously established on the Advia Centaur System, including the pediatric reference intervals. Verification studies were performed using the candidate device, where testing was conducted according to CLSI Guideline EP28-A3c. The study results support the original reference range established with the predicate device. The expected values for serum samples are as follows:

Age Range	Reference Range
Infants (01 – 23 months)	0.87 – 6.15 µIU/mL
Children (02 – 12 years)	0.67 – 4.16 µIU/mL
Adolescents (13-20 years)	0.48 – 4.17 µIU/mL
Adults (≥ 21 years)	0.55 – 4.78 µIU/mL

Albumin:
The reference interval for the Atellica® CH Albumin BCP (AlbP) assay was previously established using literature in K51767, i.e. Willey DA, Savory J, Lasky F. An Evaluation of a Revised Albumin Method for the aca® discrete clinical analyzer, Du Pont Company, Wilmington, DE, August 1982.) To verify the reference interval, a transferability and verification study was conducted according to CLSI Guideline EP28-A3c. The study results support the cited reference interval of 3.4-5.0 g/dL for adults for serum and plasma samples.

F Other Supportive Instrument Performance Characteristics Data:
Not applicable.

VIII Proposed Labeling:

The labeling does support the finding of substantial equivalence for this device.

IX Conclusion:

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