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

A. 510(k) Number:

k170317

B. Purpose for Submission:

New device

C. Measurand:

Total beta human chorionic gonadotropin (β-hCG) in human serum and plasma

D. Type of Test:

Quantitative and qualitative chemiluminescent microparticle immunoassay

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Alinity i Total β-hCG Reagent Kit

Alinity i System

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DHA	Class II	21 CFR 862.1155 Human Chorionic Gonadotropin	Clinical Chemistry (75)
JJE	Class I	21 CFR 862.2160 Discrete photometric chemistry analyzer for clinical use	

H. Intended Use:

1. Intended use(s):

See indication for use below.

2. Indication(s) for use:

   The Alinity i Total β-hCG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative and qualitative determination of beta-human chorionic gonadotropin (β-hCG) in human serum and plasma for the early detection of pregnancy on the Alinity i analyzer.

   The Alinity i System is a fully automated analyzer allowing random and continuous access, as well as priority and automated retest processing using chemiluminescent microparticle immunoassay (CMIA) technology. CMIA technology is used to determine the presence of antigens, antibodies, and analytes in samples.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Performance characteristics were determined on the Alinity i System.

I. Device Description:

Alinity i System

The Alinity i System is a family member of the ARCHITECT i Analyzers (e.g., i2000, i2000SR, and i1000SR immunoassay analyzers). The modular design of the Alinity i System may be physically joined with other Alinity modules to form a single workstation or system. The Alinity i System is a fully automated immunoassay analyzer allowing random and continuous access, as well as priority and automated retest processing using chemiluminescent microparticle immunoassay (CMIA) technology. CMIA technology is used to determine the presence of antigens, antibodies, and analytes in samples. It has the following components and functions:

- System Control Module (SCM): contains a user interface computer that provides software interface to the Alinity and provides an interface to a host or middleware computer. The power supply operates the user interface computer and the Reagent and Sample Manager (RSM).

- Reagent and Sample Manager (RSM): Transport system used to load calibrators, controls, specimens, reagents, and onboard solutions (e.g., lifts, positions, and moves racks and catridges to and from different areas).

- Processing Module: Contains the processing center (i.e., where samples and reagents are dispensed and mixed in reaction vessels), supply and pump center (onboard storage area for bulk solutions and reaction vessel solid waste), and the reagent supply center (provides cooled storage for solutions).

Alinity i Total β-hCG Reagent Kit

The Alinity i Total β-hCG Reagent Kit consists of magnetic microbeads coated with anti-hCG monoclonal antibody in TRIS buffer with protein (bovine) stabilizers and anti-hCG monoclonal antibody labeled with acridinium in MES buffer with protein (bovine) stabilizers. The Reagent Kit is composed of two cartridges, and each cartridge contains two vials (microparticle antibody and conjugate antibody) and a spacer (empty cartridge).

The following are required for the Alinity i Total β-hCG Reagent Kit, but are not included in the Reagent Kit: Pre-Trigger Solution (1.32% (w/v) hydrogen peroxide), Trigger Solution (0.35N sodium hydroxide), Concentrated Wash Buffer (Phosphate Buffer Solution), Multi-Assay Manual Diluent Solution (Phosphate Buffer Solution).

The Alinity i Total β-hCG Assay consists of the Alinity i Total β-hCG Reagent Kit and requires the Alinity i Total β-hCG Calibrator Kit, which is sold separately. There are six levels of calibrators (0, 10, 250, 1000, 7500, 15000 mIU/mL) consisting of human serum, sodium azide, and hCG antigen in the Calibrator Kit. The Alinity i Total β-hCG Assay also requires controls, the Alinity i Total β-hCG Control Kit, or other commercially available controls. There are three levels of controls in the Alinity i Total β-hCG Control Kit (25, 750, 5000 mIU/mL), consisting of human serum, sodium azide, and hCG antigen.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ARCHITECT Total β-hCG Assay

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

   k983424

3. Comparison with predicate:

   Alinity i Total β-hCG Reagent Kit

Similarities		
Item	Candidate Device Alinity i Total β-hCG Reagent Kit	Predicate ARCHTECT Total β-hCG Assay K983424
Intended Use	The Alinity i Total β-hCG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative and qualitative determination of beta-	Same

Similarities		
Item	Candidate Device Alinity i Total β-hCG Reagent Kit	Predicate ARCHTECT Total β-hCG Assay K983424
	human chorionic gonadotropin (β-hCG) in human serum and plasma for the early detection of pregnancy on the Alinity i analyzer.	
Specific Analyte Detected	Total β-hCG	Same
Formulation	Microparticles – Anti-β-hCG (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers. Minimum concentration: 0.06% solids. Preservatives: antimicrobial agents. Conjugate – Anti-β-hCG (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizers. Minimum concentration: 2.9 µg/mL. Preservative: antimicrobial agent.	Same
Assay Protocol	2 step	Same
Calibration Curve Type	6-point, 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted)	
Specimen Type	Serum and plasma	Same
Traceability	4th WHO reference standard 75/589	4th WHO reference standard 75/589

Differences		
Item	Candidate Device Alinity i Total β-hCG Reagent Kit	Predicate ARCHTECT Total β-hCG Assay K983424
Measuring Range	2.4 – 15,000 mIU/mL	1.2 – 15,000 mIU/mL
Tube Types	Serum: Serum, Serum	Serum: Serum, Serum

Differences		
Item	Candidate Device Alinity i Total β-hCG Reagent Kit	Predicate ARCHTECT Total β-hCG Assay K983424
	Separator Plasma: Dipotassium EDTA, Tripotassium EDTA, Lithium heparin, Lithium heparin plasma separator, Sodium heparin	Separator Plasma: Potassium EDTA, Lithium heparin, Sodium heparin

Alinity i System

Similarities		
Item	Candidate Device Alinity i System	Predicate ARCHTECT i System K983424
Intended Use	The Alinity i System is a fully automated, random/continuous access, immunoassay analyzer, which utilizes chemiluminescent microparticle immunoassay (CMIA) detection technology for both large and small molecular weight analytes.	Same
Detection Technology	Chemiluminescent Microparticle Immunoassay (CMIA)	Same
Sample Handling	Robotic sample handler (RSH) transport system that has random and continuous access to samples. Autoretest Capability Priority and batch sample loading	Same
Reagent Handling	The on-board storage area cooler and the septum cap provide evaporation control. Continuous Reagent Access.	Same
User Interface	Continuous access to Trigger and Pre-Trigger and reconstituted Wash Buffer	

Similarities		
Item	Candidate Device Alinity i System	Predicate ARCHTECT i System K983424
	solutions are stored on-board.	

Differences		
Item	Candidate Device Alinity i System	Predicate ARCHTECT i System K983424
Dedicated Pretreatment Lane	Includes dedicated pretreatment lane	N/A
Dedicated Wash Station	Dedicated wash cups for sample pipettor and reagent pipettors	Sample pipettor and reagent pipettors do not have dedicated wash cups

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

CLSI C24-A3 Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions: Approved Guideline-Third Edition

CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods-Approved Guideline-Second Edition

CLSI EP6-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP7-A2 Interference Testing in Clinical Chemistry-Approved Guideline-Second Edition, 2nd Edition

CLSI EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples-Approved Guideline-Third 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, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition

IEC 61010-1:2010, Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General Requirements.

L. Test Principle:

The Alinity i Total β-hCG Reagent Kit is a two-step immunoassay for the quantitative and qualitative determination of β-hCG in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology. A specific mouse anti-hCG monoclonal antibody is coated on the magnetic beads; another monoclonal antibody is labeled with an acridinium-labeled conjugate. After addition of sample, calibrator, or controls to the microbead-antibody conjugate, the mixture is incubated in the reaction vessel (RV) allowing β-hCG present in samples, calibrator, or controls to bind to the monoclonal antibody on the bead. A magnet attracts the paramagnetic microparticles (which are bound to β-hCG) to a wall of the RV. The wash zone assembly washes the reaction mixture to remove unbound materials. After a washing step, the chemiluminescent, acridinium-labled conjugate is added to the RV, reacting with hCG already bound to the magnetic beads to form sandwich complexes. The wash zone assembly washes the reaction mixture once more to remove unbound materials. Subsequently, the Pre-Trigger Solution (hydrogen peroxide) is added to prepare the mixture for the chemiluminescent reaction. Then the Trigger Solution (sodium hydroxide) is added to initiate a chemiluminescent reaction. The resulting chemiluminescent reaction is measured as Relative Light Units, which is proportional to the concentration of total β-hCG present in samples. For qualitative interpretation of the Alinity i Total β-hCG test results, specimens with β-hCG levels less than or equal to 5.00 mIU/mL will be reported in the INTERPRETATION field on the test results screen or printout as "NEGATIVE." Specimens with β-hCG greater than or equal to 25.00 mIU/mL will be reported as "POSITIVE." Specimens with β-hCG levels greater than 5.00 mIU/mL and less than 25.00 mIU/mL will be reported with concentrations only. No interpretation will be reported for these results.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Quantitative:

   Precision studies were conducted using five levels of pooled human serum specimens, prepared by spiking normal human male serum with β-hCG, and three levels of hCG controls, each tested on two lots of Alinity i Total β-hCG Reagent Kit and two Alinity i Systems. Precision samples were tested in a minimum of 2 runs per day, 2 replicates per run, over 20 non-consecutive days.

   Results from the two reagent lots were similar on the two systems. Results from one representative lot and analyzer 1 are provided in the table below.

Sample	N	Mean	Within-Run		Between-Run		Between-day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Panel B	120	5.38	0.32	5.9	0.19	3.5	0.19	3.6	0.42	7.8
Panel C	122	167.4	3.63	2.2	2.4	1.5	1.7	1.0	4.7	2.8
Panel D	119	9212	181.9	2.0	144	1.6	92	1.0	249.7	2.7
Panel E	120	12768	353.1	2.8	194.8	1.5	0	0	403.2	3.2
High Control	119	4869	72.4	1.5	68.5	1.4	85.9	1.8	131.6	2.7
Low Control	118	26.6	0.85	3.2	0.98	3.7	0.57	2.2	1.42	5.3
Medium Control	119	768.4	12.5	1.6	9.7	1.3	7.9	1.0	17.7	2.3

Precision results from all reagent lots and all systems are shown below:

Sample	N	Mean	Within-Run		Within-Lab	
			SD	%CV	SD	%CV
Panel B	400	5.33	0.269	5.0	0.41	7.6
Panel C	400	165.2	3.68	2.2	4.58	2.9
Panel D	399	9421.1	194.7	2.1	265.2	2.8
Panel E	400	13069	314.7	2.4	412.8	3.2
High Control	399	4971.9	73.1	1.5	110.2	2.2
Low Control	398	25.4	0.84	3.3	1.29	5.1
Medium Control	399	765.8	1.4	3.3	14.8	1.9

Qualitative:

Precision studies were conducted using two lots of Alinity i Total β-hCG Reagent Kit and two Alinity i Systems. Nine levels of human serum samples were prepared, tarketing the 5 mIU/mL and 25 mIU/mL cutoffs, by spiking normal human serum with positive pregnant female donor pool. Samples were tested for a minimum of 20 replicates, 2 runs per day for one day, where each run was independently calibrated. Qualitative results are provided in the table below.

Target Concentration (mIU/mL)	Negative ≤ 5 mIU/mL	Indeterminate >5 mIU/mL to <25 mIU/mL	Positive ≥ 25 mIU/mL
0.00	176/176	0/176	0/176
2.32*	401/401	0/401	0/401

3.00	176/176	0/176	0/176
4.00	176/176	0/176	0/176
5.33*	100/400	300/400	0/400
6.00	0/176	176/176	0/176
8.00	0/176	176/176	0/176
21.00	0/175	175/175	0/175
23.00	0/176	139/176	37/176
25.35*	0/398	173/398	225/398
27.00	0/176	0/176	176/176
29.00	0/176	0/176	176/176

* Concentrations obtained from the 20 day precision study

b. Linearity/assay reportable range:

Linearity

Linearity was established by preparing ten sample dilutions, with concentrations from 2.47 - 16424 mIU/mL, created by mixing different proportions of a normal human serum sample, spiked with WHO 4th International Standard β-hCG stock, and a normal human female serum sample without detectable hCG. Four replicates were measured for each sample and the mean of these replicates was compared to the expected values. Linearity results are presented below in terms of expected versus observed.

Sample/Pool Number`	**Expected (mIU/mL)**	**Observed (mIU/mL)**	**% Recovery**
1	16424.1	16424.1	100
2	14049.1	14894.9	106
3	8017.2	8776.0	109.5
4	4013.6	4151.1	103.4
5	999.4	1013.3	101.4
6	505.6	516.7	102.2
7	63.0	64.3	102.0
8	6.77	6.33	90.6
9	3.67	3.47	94.6
10	2.47	2.54	102.9
11	1.52	<2.4	N/A
12	0.02	<2.4	N/A

The expected values were plotted against the recovered β-hCG values. Linear regression, excluding sample/pool number 12, gave the following equation:

y=1.04x-0.25, r=0.9997

The results support the claimed measuring range of this device, 2.4 - 15000 mIU/mL.

Auto Dilution

Verification studies were performed to determine the sample dilution recovery of the Alinity i Total β-hCG Reagent Kit. Sample dilution recovery was tested on 25 spiked human serum samples. Each sample was diluted using the 1:15 automated dilution protocol on both the Alinity i System and the ARCHITECT i analyzer.

This study was run on one Alinity i System and on one ARCHITECT i analyzer, using one reagent lot, one calibrator lot, and one control lot. All samples were run in triplicates. The results are summarized in the tables below.

	Alinity i System	**ARCHITECT i**	
Sample Number	**Mean (mIU/mL)**	**Mean (mIU/mL)**	**% Difference**
1	218717.82	200232.24	9.2
2	203131.63	195012.55	4.2
3	196328.61	188041.63	4.4
4	185329.57	178650.32	3.7
5	180890.33	174660.14	3.6
6	180425.16	173980.78	3.7
7	169725.49	164263.72	3.3
8	166891.83	160249.78	4.1
9	158035.52	156032.68	1.3
10	151884.93	153239.89	-0.9
11	147574.08	146307.41	0.9
12	138507.52	141448.37	-2.1
13	133549.87	130406.53	2.4
14	125924.33	124416.08	1.2
15	123483.88	122046.47	1.2
16	115394.76	115451.28	0
17	110761.35	114382.42	-3.2
18	72943.87	75095.82	-2.9
19	43233.67	44944.67	-3.8
20	34700.44	35941.67	-3.5
21	28308.59	30144.74	-6.1
22	19034.47	19688.63	-3.3
23	13970.72	14317.74	-2.4
24	9150.23	9540.40	-4.6
25	7268.13	7567.19	-4.0

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

Traceability:

The calibrators for the Alinity i Total β-hCG Reagent Kit are traceable to the World

Health Organization (WHO) 4th Internation Standard (IS) for hCG (75/589). The Alinity i Total β-hCG controls were cleared under k983424 with the name ARCHITECT Total β-hCG Controls.

d. Detection limit:

Limit of blank:

The limit of blank was determined by running replicates of at least 10 on 3 days to obtain a minimum of 60 replicates of 3 β-hCG negative human male serum samples with three lots of Alinity i Total β-hCG Reagent Kit on two Alinity i Systems. The limit of blank was determined non-parametricically. The highest value of the three lots was the limit of blank, which was determined to be 0.20 mIU/mL.

Limit of detection and Limit of quantitation:

Ten low-level hCG samples (2 samples at each of 5 unique target concentration levels of approximately 0.6, 1.2, 2.4, 3.6, 4.2 mIU/mL) were prepared from β-hCG negative human male serum samples spiked with β-hCG. These samples were tested with three lots of Alinity i Total β-hCG Reagent Kit on two Alinity i Systems with a minimum of 10 replicates per run over 3 days (minimum N=60). The LoD, 0.67 mIU/mL, was determined parametrically using the highest calculated LoD from the three reagent lots. The assay LoQ claimed by the sponsor is 2.42 mIU/mL based on a total error goal of ≤ 25%.

e. Analytical specificity:

Cross-Reactivity:

A cross-reactivity study was performed for Thyroid Stimulating Hormone (TSH), Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), and Human Chorionic Gonadotropin (hCG) alpha subunit, added to human female serum containing hCG (> 25 mIU/mL) and to hCG negative human female serum. Results from these cross-reactant spiked samples were evaluated against that of the unspiked serum sample alone, defined as the control. No cross-reactivity (defined by the sponsor as < ±10% bias between the test pool and control pool for samples with > 25 mIU/mL hCG, and < 5 mIU/mL bias for samples with hCG negative human female serum) was observed at the concentrations that were tested for TSH, LH, FSH, and hCG α subunit as shown below.

Substance	**Concentration**
TSH	100 µIU/mL
LH	500 mIU/mL
FSH	500 mIU/mL
hCG α subunit	500 mIU/mL

Isoform Recognition:

Known concentrations of commercially available WHO reference standards (isoforms) were diluted in hCG negative human female serum for isoform recognition studies. The results (as shown in the table below) demonstrated that the Alinity i Total β-hCG Reagent Kit measures four hCG isoforms: intact hCG, β subunit of hCG, nicked hCG and nicked β-hCG, while free α subunit and β-core fragment yield no detectable response.

Isoform	WHO Code	Concentration (pmol/mL)	Recovery
hCG	99/688	0.01128	103.5%
hCG-β, subunit	99/650	0.11	86.3%
hCG, nicked dimer	99/642	0.01326	95%
hCG-β, nicked β subunit	99/692	0.2244	85.8%
hCG-β, subunit, purified	75/551	0.11256	93.7%
hCG-β, beta core fragment	99/708	0.225	N/A*
hCG-α, subunit, purified	99/720	0.01428	N/A*

* the beta core fragment and alpha subunit are not detectable by the assay as the Test Mean is less than the LoQ of the assay

Interference Study:

Two normal human female serum pools containing 7 mIU/mL and 50 mIU/mL hCG were spiked with various endogenous substances and therapeutic drugs. Results from these spiked serum samples were compared to results of the unspiked serum sample alone, defined as the control. There was no significant interference (defined by the sponsor as < ±10% between the test pool and the control pool) up to the concentrations summarized below.

Test Substance	Concentration
Ampicillin	53 mg/L
Ascorbic Acid	6 mg/mL
Atropine	20 mg/dL
Bilirubin	20 mg/mL
Bilirubin Conjugated	20 mg/mL
Calcium Dobesilate	200 mg/dL

Caffeine	20 mg/dL
Cyclosporine	5 mg/L
Cefoxitin	660 mg/L
Doxcycline	30 mg/L
EDTA	80 mg/dL
Gentisic Acid	20 mg/dL
Hemoglobin	500 mg/mL
Ibuprofen	50 mg/dL
Levodopa	20 mg/L
Methyldopa	15 mg/L
Metronidazole	120 mg/L
Phenylbutazone	400 mg/L
Rheumatoid Factor	194 IU/L
Rifampicin	64 mg/L
Sodium Heparin	3000 U/L
Theophylline	40 mg/L
Triglycerides	3000 mg/mL
Total Protein	12 g/dL
Acetaminophen	20 mg/mL
Acetylsalicylic Acid	66 mg/mL
Acetylcysteine	167 mg/mL
Salicylic Acid	70 mg/mL

The sponsor added the following limitation to their labeling:

Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as Alinity i Total β-hCG that employ mouse monoclonal antibodies. Additional information may be required for diagnosis (Primus FJ et al., 1988 and Schroff RW et al., 1985).

Hook effect:

Hook effect was not tested for the Alinity i Total β-hCG Reagent Kit. The device is a 2-step assay with a wash step prior to the addition of the detection antibody.

f. Assay cut-off:

Hormone levels greater than or equal to 25 mIU/mL are reported as positive. Hormone levels less than or equal to 5 mIU/mL are reported as negative. Indeterminate results are reported as concentrations between 5-25 mIU/mL.

2. Comparison studies:

a. Method comparison with predicate device:

Quantitative:

A total of 250 serum samples covering the claimed measuring range were assayed in singlicate using the Alinity i Total β-hCG Reagent Kit on the Alinity i System and in duplicate using the ARCHITECT Total hCG assay for ARCHITECT system (predicate device; k983424) over a minimum of three days. There were 34 samples excluded from the analyisis because the results were outside the measuring interval of 2.40 to 15,000 mIU/mL; therefore, 210 samples were analyzed. Five samples were considered outliers, but were included in the analysis. One replicate from each sample tested on the Alinity i System and the mean results from each sample on the predicate were used in the analysis shown below. Sample values on the Alinity i System ranged from 2.9 – 14692 mIU/mL. The results are summarized in the table below.

Parameter	Deming Regression
n	210
Slope	1.00
95% CI	1.00 to 1.02
Intercept	0.12
95% CI	-0.22 to 0.45
Correlation Coefficient (R^2)	1.00

Qualitative:

A total of 381 serum samples covering the claimed measuring range were tested using the Alinity i Total β-hCG Reagent Kit on the Alinity i System and on the ARCHITECT Total hCG assay for ARCHITECT i analyzer (predicate device; k983424). The qualitative results are summarized in the table below.

		Predicate test		
Alinity i Total hCG Results		Positive ≥ 25 mIU/mL	Indeterminate > 5 mIU/mL – < 25 mIU/mL	Negative ≤ 5 mIU/mL
	Positive	201/202	0/44	0/135
	Indeterminate	1/202*	44/44	3/135*
	Negative	0/202	0/44	132/135

*Discordant samples -Qualitative

Alinity i Total hCG Result (mIU/mL)	Predicate Result (mIU/mL)
24.42	26.41
5.25	4.58
5.06	4.62
5.16	4.80

b. Matrix comparison:

A matrix comparison study was performed to evaluate tube types suitable for use with the Alinity i Total β-hCG Reagent Kit and Alinity i System. Forty five matched samples spanning the measurement range (4.4 mIU/mL – 12,049 mIU/mL) of the Alinity i Total β-hCG Reagent Kit were analyzed on one system using one reagent lot and one calibrator lot. Results of each sample type listed below were analyzed against the control (serum plastic SRP), as shown below:

Tube Type	N	Passing-Bablok Slope (95% CI)	Passing-Bablok Intercept (95% CI)
Dipotassium EDTA	45	0.98 (0.97-0.99)	0.62 (0.22-1.02)
Lithium heparin	45	1.01 (1.00-1.02)	0.84 (0.41-1.27)
Sodium heparin	45	1.01 (1.00-1.03)	0.77 (0.46-1.08)
Lithium heparin plasma seperator	45	1.01 (1.00-1.02)	0.76 (0.44-1.08)
Serum separator	45	1.02 (1.01-1.03)	0.18 (-0.18-0.53)
Tripotassium EDTA	45	0.94 (0.93-0.95)	0.66 (0.35-0.96)

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

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

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Serum samples from 128 apparently healthy, non-pregnant premenopausal (ages 18 - 41), 140 perimenopausal women (ages 42- 55), and 137 postmenopausal women (ages >55) were tested using the Alinity i Total β-hCG Reagent Kit. The 2.5 and 97.5 percentiles of the concentration values were considered the expected value range of the Alinity i Total β-hCG assay. Results are listed below:

Reference Population age (years)	N subjects	Median (mIU/mL)	90% CL of Normal Range (mIU/mL)	90% CL of Lower Range (mIU/mL)	90% CL of Upper Range (mIU/mL)
18-41	128	< 2.4	< 2.4	< 2.4	< 2.4 to 0.75
42-55	140	< 2.4	< 2.4 to 4.87	< 2.4	3.88 to 9.15
> 55	137	< 2.4	< 2.4 to 7.60	<2.4 to < 2.4	6.07 to 11.02

* the normal range are 2.5 and 97.5 percentiles

N. Instrument Name:

Alinity i System

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ____X____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X_____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X_____ or No _____

3. Specimen Identification:

   Specimens that are labeled with a barcode will be scanned in automatically when placed into the Reagent and Sample Manager (RSM) area or manually using the bar code scanner on the System Control Module (SCM) shelf.

4. Specimen Sampling and Handling:

   The Alinity i Total β-hCG Reagent Kit is for use with serum and plasma samples. If the samples contain fibrin, red blood cells, or other particulate matter, then recentrifuge. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material any lipid layer before testing.

5. Calibration:

The Alinity i Total β-hCG Reagent Kit on Alinity i System utilizes a RFID card that is preprogrammed with a reagent lot specific master curve and is supplied with each kit. The full calibration curve consists of six levels of concentration points and is specific to the Alinity i processing module. A full calibration is created by using one of the three calibration (data reduction) methods:

- Point to point method
  - Uses the average relative light units value obtained at each calibrator compared to the calibrator concentration to generate a calibration curve
- Linear regression method
  - Uses the linear relationship between the relative light unit value and the concentration of the analyte in the sample to generate a calibration curve
- Four-parameter calibration (4PLC) method
  - Uses the difference between predicated and observed calibrator concentrations or signals to generate a calibration curve

A two-point adjust calibration assay has master calibration data encoded within a two-dimensional bar code on the reagent cartridge label. After the operator loads a reagent cartridge on a processing module, the system performs a scan and stores master calibration data in the system software. The stored data is specific for the Alinity i Total β-hCG Reagent Kit, but the data must be adjusted to fit a specific processing module. Therefore, the operator must run two calibrators. The Alinity i System provides four methods of calibration adjustment (ratio technique method, linear transformation method, parameter method, and curve shape methods).

6. Quality Control:

Quality control can be performed using Alinity i Total hCG controls. Controls should be tested once every 24 hours each day of use. Control intervals should be adjusted to match each individual laboratory's requirements. Values should fall within established ranges and if not, laboratories should follow its established quality control procedures.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Within Assay Sample Carryover:

A high sample containing ≥ 1,000,000 mIU/mL hCG, a protected low sample containing 0-3.75mIU/mL hCG , and an unprotected low sample containing 0-3.75 mIU/mL hCG were tested on the Alinity i System. For each carryover run, the following steps were performed:

A. Wash Buffer
B. Protected Low Sample: Not exposed to potential sample carryover

C. High Sample
D. Unprotected Low Sample
E. Repeat A-D for 15 iterations across 5 runs

The median difference between the protected sample and the unprotected sample was 0.22 mIU/mL.

Q. Proposed Labeling:

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

R. Conclusion:

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