

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k133002

B. Purpose for Submission:

New device

C. Measurand:

Total beta human chorionic gonadotropin (β -hCG) in venous whole blood and plasma

D. Type of Test:

Quantitative enzyme-linked immunoassay

E. Applicant:

Abbott Point of Care, Inc.

F. Proprietary and Established Names:

i-STAT[®] Total Beta-Human Chorionic Gonadotropin (β -hCG) Test

i-STAT[®] Total β -hCG Controls

i-STAT[®] Total β -hCG Calibration Verification Materials

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1155, Human chorionic gonadotropin test system

21 CFR 862.1660, Quality Control Material (assayed and unassayed)

2. Classification:

Class II – Test System

Class I, Reserved – Quality Control material

3. Product code:

DHA – Test system

JJX – Control material

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

The i-STAT[®] Total Beta human Chorionic Gonadotropin (β -hCG) test is an in vitro diagnostic test for the quantitative and qualitative determination of β -hCG in venous whole blood or plasma samples using i-STAT 1 Analyzer Systems. The test is intended to be used as an aid in the early detection of pregnancy and is for prescription use only.

The i-STAT[®] Total β -hCG Controls are used to monitor performance of the i-STAT Total β -hCG test.

The i-STAT[®] Total β -hCG Calibration Verification materials are used to verify the calibration of the i-STAT Total β -hCG test throughout the reportable range.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

i-STAT 1 analyzers (models 300 and 300W)

I. Device Description:

Each i-STAT Total β -hCG assay cartridge includes a sample inlet, sensors to detect the total β -hCG (see test principle below), and the necessary reagents needed to perform the test (shown in the table below). The i-STAT Total β -hCG Controls and Calibration Verification Materials are designed for use with the assay system. The cartridge contains a buffer and preservatives.

Component	Biological Source
Anti – hCG Antibody/ Alkaline Phosphatase Conjugate	Murine IgG : Bovine Intestine
IgG	Murine IgG
IgM	Murine IgM
Sodium Aminophenyl Phosphate	N/A
Heparin	Porcine Intestine

J. Substantial Equivalence Information:

1. Predicate device name(s):

Abbott ARCHITECT[®] Total β -hCG assay
 Cliniqa Beta HCG Control Level 1, 2, 3
 Cliniqa Beta HCG Calibration Verification Control Level 1, 2, 3

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

k983424
 k121237

3. Comparison with predicate:

Characteristics	APOC i-STAT Total β-hCG test (Candidate k133002)	Abbott ARCHITECT Total β-hCG assay (Predicate k983424)
Intended Use	The i-STAT [®] Total Beta human Chorionic Gonadotropin (β -hCG) test is an in vitro diagnostic test for the quantitative and qualitative determination of β -hCG in venous whole blood or plasma samples using i-STAT 1 Analyzer Systems. The test is intended to be used as an aid in the early detection of pregnancy and is for prescription use only.	Same except intended for serum and plasma samples
Assay Methodology	Two site ELISA	Same
Enzyme Detection	Electrochemical	Chemiluminescent Microparticle Immunoassay
Reportable Range	5.0-2000 IU/L undiluted	1.2-15,000 IU/L undiluted
Samples	Sodium and Lithium Heparin whole blood and Sodium and Lithium Heparin plasma	Serum and Heparin or EDTA Plasma

Characteristic	i-STAT Total β-hCG Controls and i-STAT Total β-hCG Calibration Verification Material (Candidate k133002)	Cliniqa Beta HCG Control Level 1, 2, 3 and Cliniqa Beta HCG Calibration Verification Control Level 1, 2, 3 (Predicate k121237)
Intended Use	The i-STAT [®] Total β -hCG Controls are used to monitor performance of the i-STAT Total β -hCG test. The i-STAT [®] Total β -hCG Calibration Verification Materials are used to verify the calibration of the i-STAT Total β -hCG test throughout the reportable range.	Same
Matrix	Human serum with added buffer stabilizers, and purified human hormones	Same
Traceability	WHO 5 th International Reference Standard, 07/364	WHO 4 th International Reference Standard, 75/589
Form	Liquid	Same
Open Vial Stability	30 days	Same
Values	Specific for each lot	Same
Stability	Opened: 30 days at 2-8 °C Shelf Life: 3 years at 2-8 °C	Same

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

- CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods
- CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures
- CLSI EP07-A2: Interference Testing in Clinical Chemistry
- CLSI EP09-A2: Method Comparison and Bias Estimation Using Patient Samples
- CLSI EP12-A2: User Protocol for Evaluation of Qualitative Test Performance
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
- CLSI C28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory
- CLSI I/LA30-A: Immunoassay Interference by Endogenous Antibodies

L. Test Principle:

The i-STAT Total β -hCG assay test cartridge uses a two-site enzyme-linked immunosorbant assay (ELISA) method. Antibodies specific for hCG are located on an electrochemical sensor fabricated on a silicon chip. Also deposited in another location on the sensor silicon chip is an antibody/alkaline phosphatase enzyme conjugate specific to a separate portion of

the human chorionic gonadotropin molecule. The whole blood or plasma sample is brought into contact with the sensors allowing the enzyme conjugate to dissolve into the sample. The hCG within the sample becomes labeled with alkaline phosphatase and is captured onto the surface of the electrochemical sensor during an incubation period of approximately seven minutes. The sample, as well as excess enzyme conjugate, is washed off the sensors. Within the wash fluid is a substrate for the alkaline phosphatase enzyme. The enzyme bound to the antibody/antigen/antibody sandwich cleaves the substrate, releasing an electrochemically detectable product. The electrochemical (amperometric) sensor measures this enzyme product, which is proportional to the concentration of hCG within the sample. The default setting on the handheld is a display of the quantitative hCG value as well as a qualitative interpretation of the hCG test result. The handheld can be customized to disable or enable the qualitative hCG interpretation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Two separate precision studies were performed at the point of care (POC). In the first study using spiked lithium heparinized whole blood, all target concentrations were evaluated at the same three POC sites. In the second study for lithium heparinized plasma samples, the 5 IU/L target concentration was evaluated at 3 different POC sites compared to the other evaluated plasma concentrations. Analyses were based on CLSI EP5-A2.

For plasma samples, precision studies were conducted over 5 days on five analyzers, yielding 25 replicates per sample/level across 3 sites for each concentration level (total N=75 per sample concentration level). Results are shown in the Table below:

Reproducibility at 3 POC sites for plasma samples:

Target Concentration	N	Mean (IU/L)	Within-Day		Within-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV
5 IU/L	75	5.5	0.75	13.61	0.88	16.05	1.03	18.7
25 IU/L	75	24.3	1.26	5.16	1.26	5.16	1.26	5.18
1150 IU/L	75	1155.7	49.76	4.31	50.77	4.39	53.08	4.59
1875 IU/L	75	1874.5	104.95	5.60	104.95	5.60	111.11	5.93

For whole blood sample evaluations, at each POC site, 21 replicates were tested for each whole blood sample. The 21 replicates included 3 replicates for each of 7 analyzers at each POC site. Results are shown below:

Reproducibility for whole blood samples:

Target Concentration	POC site #1, N=21			POC site #2, N=21			POC site #3, N=21		
	mean	SD	%CV	mean	SD	%CV	mean	SD	%CV

5 IU/L	5.2	0.81	15.45	5.0	0.39	7.71	5.0	0.42	8.51
25 IU/L	24.8	1.44	5.80	30.5	1.87	6.14	27.9	1.97	7.04
800-1000 IU/L	935.5	60.69	6.49	1008.1	55.65	5.52	842.5	50.55	6.00
1600-2000 IU/L	2039.8	111.61	5.47	1641.0	105.81	6.45	1816.4	132.52	7.30

All blood or plasma sample results with a measured hCG concentration < 5 IU/L will be reported as “<5 IU/L” by the test system.

b. Linearity/assay reportable range:

Linearity study:

A study was performed to demonstrate that the i-STAT Total β -hCG assay is linear across the claimed measuring interval of 5.0 IU/L to 2000.0 IU/L. Lithium heparinized whole blood and plasma samples from 6 donors were spiked with a primary spiking solution prepared from WHO 5th IS (07/364). Nine hCG levels/samples with concentrations well-distributed across the range (from 4.9 IU/L to >2000 IU/L) were prepared by admixing according to recommendations in CLSI EP06-A. Replicate samples (N \geq 10) were tested on multiple i-STAT 1 Analyzers.

Analyses demonstrated linearity across the claimed measuring interval of 5.0 IU/L to 2000.0 IU/L. The linear regression analysis results are:

Whole blood: $y=1.04x+0.69$, $r=0.9901$

Plasma: $y=0.92x-0.35$, $r=0.9929$

Recovery study

A dilution recovery study was performed using lithium heparinized whole blood and plasma samples from six donors. Each donor sample was then mixed with a primary spiking solution prepared from WHO 5th IS (07/364) to prepare 9 levels of samples, which were then tested on at least ten assay cartridges. Percent recovery or absolute bias was calculated at each level as shown below:

Level	Whole Blood			Plasma		
	Mean (expected)	Mean (observed)	% recovery or absolute bias	Mean (expected)	Mean (observed)	% recovery or absolute bias
1	1936.4	1974.6	102.0 %	1972.6	1811.5	91.8 %
2	972.7	989.3	101.7 %	986.5	895.5	90.8 %
3	644.8	677.4	105.1 %	657.5	622.1	94.6 %
4	484.2	509.5	105.2 %	493.3	475.0	96.3 %
5	242.2	261.4	107.9 %	246.9	234.1	94.8 %
6	121.3	128.2	105.7 %	123.5	109.2	88.4 %
7	60.6	62.9	103.8 %	61.8	54.5	88.2 %
8	24.3	26.6	109.5 %	24.8	22.6	91.0 %
9	5.1	5.8	0.7 IU/L	5.3	4.5	0.8 IU/L

For whole blood samples with hCG concentrations >5 IU/L, the individual % recovery ranged from 91.1% to 118.5%, and for plasma samples from 81.8% to 103.3% when compared to WHO hCG 5th IS. For whole blood samples with hCG at a concentration of ~5 IU/L, the individual bias ranged from 0.3 to 1.1 IU/L, and for plasma samples from -0.2 to -1.2 IU/L, when compared to WHO hCG 5th IS.

The sponsor has a limitation in their labeling that states “End-users may obtain individual results with >15% negative bias for plasma samples when hCG concentrations are > 5 IU/L”.

Hook effect evaluation:

The assay was evaluated for high dose hook effect in lithium heparinized plasma and whole blood samples. Samples were spiked to high levels of hCG using commercially available hCG. Each sample was diluted into the measuring interval of the i-STAT Total β -hCG assay and results were multiplied by the dilution factor in order to assign the actual concentration of the sample being tested. Seven samples with hCG levels ranging from 100,000 to >600,000 IU/L were evaluated.

The Sponsor defines a sample unaffected by hook as a sample that produced a signal greater than the signal produced by a sample at 2000 IU/L (such that the i-STAT Analyzer would indicate a result of “> 2000.0 IU/L”). Plasma samples with hCG concentrations up to 450,000 IU/L showed no hook effect. Whole blood samples with hCG concentrations up to 650,000 IU/L showed no hook effect.

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

Traceability:

The measurands in the Controls and Calibration Verification Materials are traceable to the WHO 5th International Standard (NIBSC Code 07/364). The traceability process is based on EN ISO17511.

Stability and Value Assignment:

Stability and value assignment of Controls and Calibration Verification Materials was previously reviewed under k121237. Control materials have target concentrations of 25, 1000, and 1500 IU/L. Calibration Verification Materials have target concentrations of 3, 1000, and 2000 IU/L.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were determined in accordance with CLSI document EP17-A2. The LoB study was performed by measuring 195 replicates of one blank lithium heparin plasma pool and 144 replicates of one blank lithium heparin whole blood sample pool over five days with 2 reagent lots. The LoD study was performed by measuring 192 replicates of 4 low concentration lithium heparin plasma samples and 182 replicates of 6 low concentration lithium heparin whole blood samples over 5 days with 2

reagent lots. The LoQ study was performed by measuring 155 replicates of 4 low concentration lithium heparin plasma samples and 92 replicates of 6 low concentration lithium heparin whole blood samples over 6 days with 2 reagent lots. The results demonstrated $LoB < LoD \leq LoQ < 5.0$ IU/L. Recovery at the claimed lower assay limit of 5 IU/L is shown above in section M.1.b. and summarized below:

Sample Type	Bias
Lithium Heparinized Plasma	-0.2 to -1.2 IU/L
Lithium Heparinized Whole Blood	0.3 to 1.1 IU/L

e. *Analytical specificity:*

Interference:

Following CLSI guideline EP07-A2, potential exogenous and endogenous interferents were spiked into both lithium heparinized whole blood and lithium heparinized plasma with various hCG concentrations including hCG concentrations near decision limits. Measured hCG concentrations in the presence of interferent were compared to measured hCG concentrations in control samples without interferent, and recoveries were determined. The following compounds were tested at the concentrations shown below. No interference was observed. All recoveries in the presence of the compounds shown below were within +/- 10% (the criterion defined by the Sponsor).

Substance	Test Concentration
Acetaminophen	1660 uM
Acetyl Salicylic Acid	3620 uM
Allopurinol	294 uM
Ampicillin	152 uM
Ascorbic Acid	342 uM
Atenolol	37.6 uM
Atropine	20 mg/dL
Caffeine	308 uM
Captopril	23 uM
Chloramphenicol	155 uM
Diclofenac	169 uM
Digoxin	6.53 uM
Dopamine	5.87 uM
Enalaprilat	0.86 uM
Erythromycin	81.6 uM
Furosemide	181 uM
Gentisic Acid	117 uM
Ibuprofen	2425 uM
Isosorbide dinitrate	636 uM
Methyldopa	71 uM
Nicotine	6.2 uM

Nifedipine	1156 uM
Phenytoin	198 uM
Propranolol	7.71 uM
Salicylic acid	4340 uM
Sodium Heparin	90 U/mL
Theophylline	222 uM
Verapamil	4.4 uM
Warfarin	65.2 uM
Albumin	60 g/L
Bilirubin	342 uM
Cholesterol	13 mM
Hemoglobin	2 g/L
Triglyceride	37 mM
Uric Acid	1.4 mM

Specificity:

Assay specificity was determined by testing hCG spiked lithium heparinized whole blood and heparinized plasma samples in the presence of LH (450 IU/L), FSH (300 IU/L) , and TSH (100 mIU/L), and comparing test results to hCG samples in the absence of these additional hormones. Recoveries were all within +/- 10% (criteria defined by the Sponsor).

Hematocrit (HCT):

The effect of different hematocrit levels was evaluated using hCG levels in whole blood samples (20-30 IU/L and 1200-1500 IU/L) with hematocrit levels falling in one of four bins: Zero (plasma), Low (25% – 35%), Nominal (36% – 43%), and High (44% - 51%). The labeling indicates that imprecision (CV) and bias exceeding 10% have been observed in samples with HCT > 50%PCV (packed cell volume).

f. Assay cut-off:

See detection limit above (M.1.d.).

2. Comparison studies:

a. Method comparison with predicate device:

The method comparison study was done in accordance with the CLSI guideline EP09-A2. The measurements were obtained at four external POC sites, where whole blood samples were collected and immediately tested in duplicate with the candidate device. The collection tubes were then transferred to the hospital laboratory. The plasma portion was separated from the red cells and the plasma portion of each sample was tested in duplicate with both the candidate and the predicate devices. Testing was performed by 6-8 operators at each POC site. Each sample was tested with a minimum of two lots of i-STAT Total β -hCG cartridges and six i-STAT 1 Analyzers were used at each POC site.

The analyses of the first measurements of the whole blood (candidate device), plasma (candidate device) vs plasma (predicate) from all sites are shown below:

	i-STAT (Whole Blood) vs. ARCHITECT (Fresh Plasma)	i-STAT (Fresh Plasma) vs. ARCHITECT (Fresh Plasma)
N	134	134
Slope	0.95 (0.92 to 0.97)	1.02 (1.00 to 1.04)
Intercept	2.39 (1.14 to 3.64)	-0.22 (-1.17 to 0.73)
R	0.99 (0.98 to 0.99)	0.99 (0.98 to 1.00)

b. *Matrix comparison:*

The matrix comparison study was done in accordance with the CLSI guideline EP09-A2. Forty samples spanning the measurement range of the i-STAT Total β -hCG test were prepared from 40 donor samples by spiking with a stock solution containing commercially available hCG antigen. Results of each sample type listed below were analyzed against the control (Li-heparin plasma), as shown below.

Parameter	Na-Heparin Whole Blood	Li-Heparin Whole Blood	Na-Heparin Plasma
N	40	40	40
Deming Slope (95% CI)	0.94 (0.91 – 0.98)	0.98 (0.95 – 1.01)	0.98 (0.95 – 1.00)
Deming Intercept (95% CI)	0.5 (0.3 – 0.6)	0.5 (0.2 – 0.7)	-0.5 (-1.9 – 0.8)

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:

The reference range study was performed according to CLSI Guideline C28-A3c. Human plasma and whole blood samples from apparently healthy non-pregnant women were tested to determine the reference range for the i-STAT Total β -hCG test. The results are listed below:

Reference Population age (years)	N Subjects	N Whole blood results	N Plasma results	Median (IU/L)	Range (IU/L)	95th Percentile (IU/L), [95% CI]
≥ 18 and < 40	123	122	120	0	0 – 3.9	0.7 [0.3, 1.6]
≥ 40	125	125	124	0	0 – 9.6	4.5 [4.0, 5.4]
≥ 40, pre-menopausal	68	68	68	0	0 – 2.5	--
≥ 40, post-menopausal	57	57	56	1.5	0 – 9.6	--

N. Proposed Labeling:

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

O. Conclusion:

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