TOTAL BETA-HUMAN CHORIONIC GONADOTROPIN (β-hCG)

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 the 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.

SUMMARY AND EXPLANATION OF THE TEST

Human chorionic gonadotropin (hCG) is a glycoprotein hormone that is secreted by the syncytiotrophoblastic cells of the placenta. It is a complex molecule, consisting of two antigenically different glycoprotein subunits, alpha (α) and beta (β). The α subunit is found in other pituitary glycoprotein hormones (luteinizing hormone [LH], follicle stimulating hormone [FSH] and thyroid stimulating hormone [TSH]), as well as hCG. The β subunit is specific to hCG, yet exhibits considerable homology with LH. Both the intact hCG molecule and the free subunit are found in early pregnancy. Both β forms (intact and free) are detected by this test.

Physiologically, hCG appears to maintain the corpus luteum, thereby allowing synthesis of progesterone and estrogens that support the endometrium. Generally, as pregnancies progress, the placenta assumes the production of these hormones. hCG levels increase to a peak concentration, then decrease and plateau. Generally, hCG circulates as the intact molecule. The subunits are cleaved rapidly and cleared by the kidneys.[1]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The i-STAT Total β-hCG test uses a two-site enzyme-linked immunosorbant assay (ELISA) method. Antibodies specific for β-hCG are located on an electrochemical sensor fabricated on a silicon chip. Also deposited in another location on the sensor silicon chip is an anti-βhCG antibody/alkaline phosphatase enzyme conjugate specific to a separate portion of the β subunit of the hCG molecule. The system is capable of detecting whole molecule (intact) hcg as well as the free β subunit, but not the β core fragment (β subunit missing the carboxyl terminal end). 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 β-hCG within the sample. Also positioned on the silicon chip is a (conductivity) sensor to assess the hematocrit value of the sample. This value is required in the calculation of the β-hCG concentration in whole blood samples.

For additional information on the system, refer to the i-STAT 1 System Manual.

Abbott

REAGENTS

Each i-STAT Total β-hCG cartridge contains all the necessary reagents for the test. A list of reactive ingredients is provided below:

Reactive Ingredient	Biological Source	Minimum Quantity
Antibody/Alkaline Phosphatase Conjugate	Murine IgG : Bovine Intestine	0.003 µg
IgG	Murine IgG	8 µg
IgM	Murine IgM	3 µg
Sodium Aminophenyl Phosphate	N/A	1.8 mg
Heparin	Porcine Intestine	0.45 IU

Warnings and Precautions

For *in vitro* diagnostic purposes.

Although the sample is contained within the cartridge, cartridges should be disposed of as biohazardous waste according to local, state, and national regulatory guidelines.

For additional warnings and precautions pertaining to the i-STAT System, refer to the i-STAT 1 System Manual.

Cartridge Storage Instructions

When refrigerated at 2-8 °C (35-46 °F), cartridges are stable until the expiration date. Cartridges may be stored at room temperature at 18-30 °C (64-86 °F) for the timeframe indicated on the cartridge box. Individual cartridges may be used after standing five minutes at room temperature. An entire box of cartridges should stand at room temperature for one hour prior to use. All cartridges should be used immediately after opening the portion pack (individual cartridge package). If the portion pack has been punctured, the cartridge should not be used.

INSTRUMENTS

For a detailed description of the instrument and system procedures, refer to the i-STAT 1 System Manual.

Customizing the Handheld to Display a Qualitative β-hCG Result

The default setting on the handheld displays a quantitative β-hCG value as well as a qualitative interpretation of the β-hCG test result. The handheld can be customized to disable or enable the qualitative β-hCG interpretation.

Quantitative β-hCG Result	Qualitative β-hCG Interpretation*	Handheld Display
β-hCG ≤ 5.0 IU/L	Negative	hCG QUAL (-)
5.0 < β-hCG < 25.0 IU/L	Indeterminate	hCG QUAL ( )
β-hCG ≥ 25.0 IU/L	Positive	hCG QUAL (+)

If enabled, qualitative interpretations will always be displayed with quantitative values.

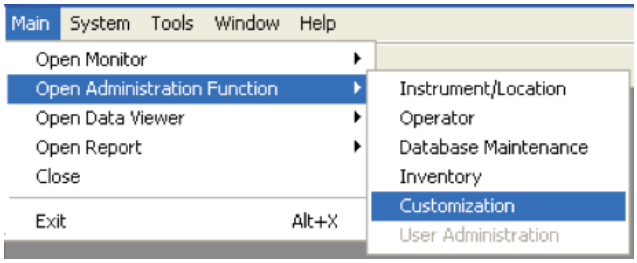
***Note:** The Qualitative β-hCG Interpretation displayed on the i-STAT 1 analyzer screen is based on the quantitative β-hCG result **prior** to rounding. Thus, due to rounding, a Quantitative β-hCG result of 5.0 IU/L may be displayed with a Qualitative β-hCG result of either Negative (-) or Indeterminate ( ). Similarly, a Quantitative β-hCG result of 25.0 IU/L may be displayed with a Qualitative β-hCG result of either Indeterminate ( ) or Positive (+).

A. Customizing the Handheld to Disable or Enable the Qualitative β-hCG Result Using the Handheld Keypad:

1. Press  to turn on the handheld
2. Press  to change screen to Administration Menu
3. Press  (Customization)
4. Press  (Change)
5. Press  (no password is required)
6. Press  (Results)
7. Press  (Units and Ranges)
8. Press  to scroll to the page that displays hCG Qual
9. Press  (hCG)
10. Press  (Disabled) OR  (Enabled)
11. Press  to turn handheld off and save the settings.

B. Customizing the Handheld to Disable or Enable the Qualitative β-hCG Result Using the Central Data Station (CDS Version 5)

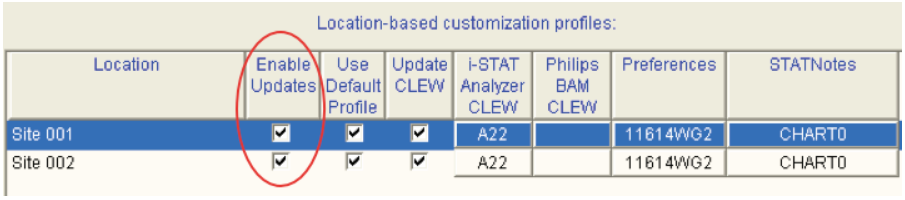
1. Click on **Main - Open Administration Function - Customization.**



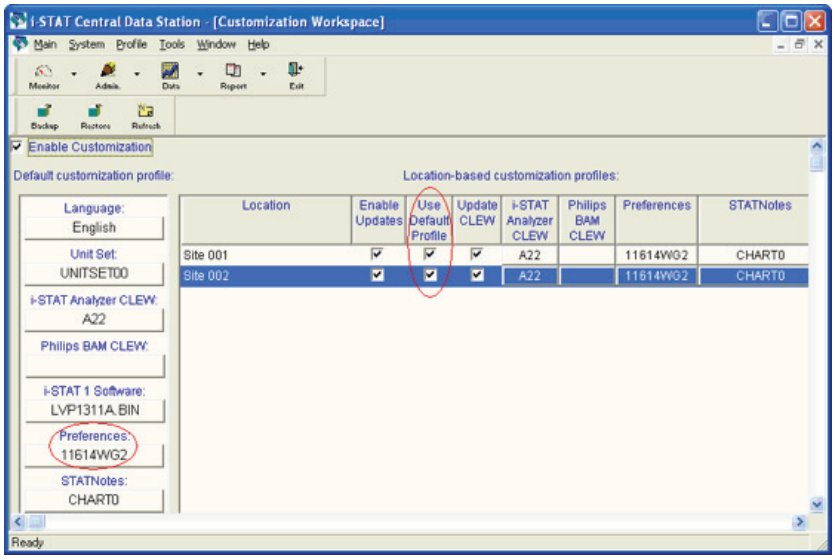
2. Type in your password and click **OK**. The default password is the word istat.
   Note: Abbott Point of Care recommends changing the default password.

3. Make sure the "**Enable Customization**" box has a check mark in it.

Also, make certain that the "**Enable Updates**" box is checked for the particular location to which this i-STAT 1 Analyzer is assigned.

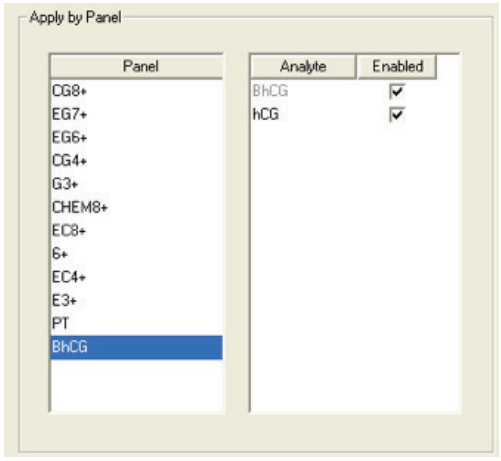


4. If the location where this handheld is assigned has a check mark under the **Use Default Profile** column, double click on the alphanumeric code under **Preferences** in the **Default Customization Profile** column. Otherwise, double click on the alphanumeric code under **Preferences** for the specific location to which this handheld is assigned.

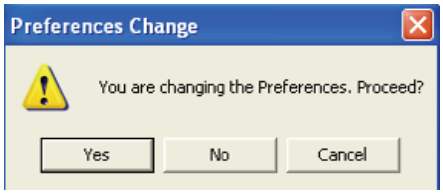


5. Once the **Preferences** screen opens, click on the "**Analyte Enable**" tab.

6. In the **Apply by Panel** section of the screen, select BhCG in the **Panel** column. The default setting has qualitative hCG enabled. To disable the qualitative hCG result, click the box beside the hCG analyte in the **Enable** column to clear the check mark. *OR* To enable the qualitative hCG result, check the box beside the hCG analyte in the **Enable** column.



7. Click **OK** and answer **YES** to the question about changing the preferences.



8. Download the handheld(s) to the CDS from a downloader in the location to which the handheld is assigned. This action will upload the chosen customization features into the handheld. Repeat step 8 for all handhelds from the same location to be customized. To customize handhelds from other locations for the same features, return to step 1 of this section.

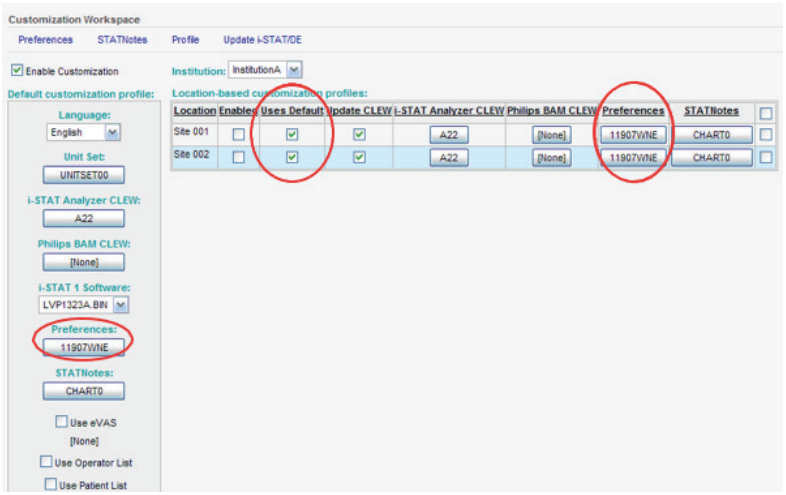
C. Customizing the Analyzer to Disable or Enable the Qualitative β-hCG Result Using i-STAT/DE

1. Access the Customization Workspace
   - RALS-Plus Users:
     – Within the RALS-Plus application, pick **i-STAT** from the drop-down menu.
     – Click on **Device Customization**.
   - PrecisionWeb Users:
     – Enter the DE i-STAT Customization Workspace.

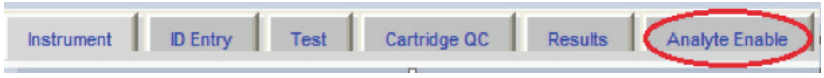
2. Make sure the "**Enable Customization**" box has a check mark in it.

Also, make certain that the **Enabled** box is checked for the particular location to which the i-STAT 1 Analyzer is assigned.

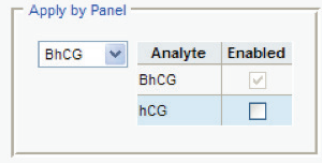
3. If the location where this handheld is assigned has a check mark under **Uses Default**, under the **Default customization profile**: column, double click the alphanumeric code under **Preferences**. Otherwise, double click the alphanumeric code under the **Preferences** column for the specific location to which this handheld is assigned.



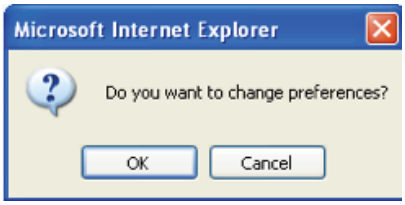
4. Once the **Preferences** window opens, click on the A**nalyte Enable** tab.



5. In the **Apply by Panel** section of the screen, select BhCG in the **Panel** column. The default setting has qualitative hCG enabled. To disable the qualitative hCG result, click the box beside the hCG analyte in the **Enable** column to clear the check mark. *OR* To enable the qualitative hCG result, check the box beside the hCG analyte in the **Enabled** column.



6. Click **OK** and answer **OK** to the question about changing the Preferences.



7. Download the handheld(s) to the Data Manager from a downloader in the location to which the handheld is assigned. This action will upload the chosen customization features into the handheld. Repeat step 7 for all handhelds from the same location to be customized. To customize handhelds from other locations for the same features, return to step 1 of this section.

Performing Patient Analysis

1. Press ⏻ to turn on handheld.
2. Press 2 for i-STAT cartridge.
3. Follow handheld prompts
4. Scan the lot number on the cartridge portion pack.
    - Position barcode 3 – 9 inches from scanner window on the handheld
    - Press and hold SCAN to activate the scanner
    - Align the red laser light so it covers the entire barcode
    - The handheld will beep when it reads the barcode successfully
5. Continue normal procedures for preparing the sample, filling, and sealing the cartridge
6. Push the sealed cartridge into the handheld port until it clicks into place. Wait for the test to complete.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Special Precautions

The i-STAT Total β-hCG cartridge requires a minimum sample volume of 17 µL to fill. Reported results will not be impaired by excess amounts beyond this requirement. However, excess blood or plasma will be present at the inlet of the cartridge and caution should be observed in handling the cartridge to minimize biohazard exposure.

Maintaining Sample Integrity

The i-STAT Total β-hCG test requires the use of heparinized whole blood or plasma samples collected in plastic syringes or evacuated tubes containing lithium or sodium heparin, filled to capacity.

Samples collected with the above mentioned anticoagulant are to be tested within 30 minutes after collection. Remix thoroughly before testing.

Known Interfering substances

The use of whole blood or plasma samples containing other anticoagulants such as EDTA, oxalate and citrate will cause deactivation of the alkaline phosphatase, resulting in decreased β-hCG readings.

PROCEDURE

For a detailed description of the procedure, refer to the i-STAT 1 System Manual.

Material Provided

i-STAT Total β-hCG cartridges

Materials Required but not Provided

i-STAT 1 Analyzer

02R29-01, 02R29-02, 02R29-03 i-STAT Total β-hCG Controls

05P59-04 i-STAT Total β-hCG Calibration Verification Material

Quality Control Procedures

On receipt of new cartridges, verify that the transit temperatures were satisfactory using the four-window temperature indicator strip included in the shipping container. For each lot of cartridges received, use a representative number of cartridges to analyze multiple levels of i-STAT Total β-hCG Controls for use on the i-STAT System using any verified i-STAT 1 Analyzer.* These controls should also be used to verify cartridge performance when storage conditions are in question.

*This is not a manufacturer's system instruction; it is a suggestion to comply with federal, state and local guidelines regarding quality control.

For additional information on Quality Control of the i-STAT System, refer to the 'Quality Control" section of the i-STAT 1 System Manual.

Proficiency Testing Recommendation

Proficiency Provider	Survey Title	Additional Information or Recommendations
College of American Pathologists (CAP) 325 Waukegan Road Northfield, IL 60093-2750 800-323-4040 or 847-832-7000 www.cap.org	CAP C Survey for General Chemistry and Therapeutic Drug Monitoring	The CAP C survey is a quantitative survey comprised of five liquid serum specimens. The only i-STAT cartridge that the C survey is recommended for is the i-STAT Total β-hCG cartridge.
	hCG, Serum (Immunology)	Qualitative/Quantitative Survey comprised of five liquid serum specimens.
American Proficiency Institute (API) 1159 Business Park Drive Traverse City, MI 49686 800-333-0958 www.api-pt.com	HCG, Quantitative: • Catalog #409 (5 serum samples) • Catalog #D09-Verification Program (5 serum samples)	For use with the i-STAT Total β-hCG cartridge.
WSLH Proficiency Testing (WSLH PT) 465 Henry Mall Room 402 Madison, WI 53706 800-462-5261 www.wslhpt.org	i-STAT β-hCG, Quantitative -Item # PT01310 (5 samples, 3x/yr) -Item # PT0326-QE product i-STAT β-hCG, Qualitative -Item # PT01480 or PT01495 (5 samples, 3x/yr) -Item # PT0490-QE product	Chemistry/Endocrinology/ Therapeutic Drugs (CET) for quantitative serum hCG reporting.

RESULTS

The test measures the hcg amount-of-substance concentration in plasma or the plasma fraction of whole blood (dimension IU/L) for *in vitro* diagnostic use.

Reportable Range

The i-STAT Total β-hCG test will report 5.0 IU/L to 2000.0 IU/L. Samples below the reportable range will display "<5.0 IU/L" on the handheld. Samples above the reportable range will display ">2000.0 IU/L" on the handheld.

Qualitative Interpretation of Results

The default setting on the handheld is a display of the quantitative β-hCG value as well as a qualitative interpretation of the β-hCG test result. The handheld can be customized to disable or enable the qualitative β-hCG interpretation.

Quantitative β-hCG Result	Qualitative β-hCG Interpretation*	Handheld Display
β-hCG ≤ 5.0 IU/L	Negative	hCG QUAL (-)
5.0 < β-hCG < 25.0 IU/L	Indeterminate	hCG QUAL ( )
β-hCG ≥ 25.0 IU/L	Positive	hCG QUAL (+)

If enabled, qualitative interpretations will always be displayed with quantitative values.

***Note:** The Qualitative β-hCG Interpretation displayed on the i-STAT 1 analyzer screen is based on the quantitative β-hCG result **prior** to rounding. Thus, due to rounding, a Quantitative β-hCG result of 5.0 IU/L may be displayed with a Qualitative β-hCG result of either Negative (-) or Indeterminate ( ). Similarly, a Quantitative β-hCG result of 25.0 IU/L may be displayed with a Qualitative β-hCG result of either Indeterminate ( ) or Positive (+).

LIMITATIONS OF THE PROCEDURE

The i-STAT Total β-hCG test is intended for use in the early detection of pregnancy only and should not be performed for any other purpose. For diagnostic purposes, hCG results should always be used in conjunction with other data, e.g., patient's medical history, symptoms, results of other tests, clinical impressions, etc. The i-STAT Total β-hCG test results should always be used and interpreted only in the context of the overall clinical picture.

End-users may obtain individual result > 15% negative bias for plasma samples when hCG concentrations are >5 IU/L.

Elevated hCG levels have been associated with some abnormal physiological states such as gestational trophoblastic disease and nontrophoblastic neoplasms.[2,3] Results of this test should not be used in the diagnosis of these abnormal states. Persistent low levels of hCG (e.g., <50 IU/L) may be present one to five years preceding malignant gestational trophoblastic disease.[4] There have been reports of people receiving unnecessary medical treatment and surgery, including chemotherapy and hysterectomy, when hCG results were used in the diagnosis of abnormal states.

Detection of low levels of hCG does not rule out pregnancy.[5] Because hCG values double approximately every 48 hours in a normal pregnancy,[5] patients with low levels of hCG should be resampled and retested after 48 hours.

Specimens from peri- or post-menopausal women may elicit weak positive results due to low hCG levels unrelated to pregnancy. With a weak positive result, it is good laboratory practice to resample and retest after 48 hours.

Because of the high degree of sensitivity of the test, positive results during the initial days after conception may later be negative due to natural termination of the pregnancy. Natural termination occurs in 22% of clinically unrecognized pregnancies and 31% of pregnancies overall.[6] It is good laboratory practice to resample and retest weak positive results after an additional 48 hours.

Interfering substances (such as heterophilic antibodies, non-specific proteins, or hCG-like substances) may falsely depress or falsely elevate results.[5,7,8] These interfering substances may cause false results over the entire range of the test, not just at low levels. While this product contains reagents that minimize the effect of these interferents and QC algorithms designed to detect their effects, the possibility of interference causing erroneous results should be evaluated carefully in cases where test results are inconsistent with clinical information. In these cases results should be confirmed by an alternate hCG method.[9]

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 demonstrate either falsely elevated or falsely depressed results when tested with test kits which employ mouse monoclonal antibodies.[10,11] These specimens should not be tested with the i-STAT Total β-hCG test.

Unknown interferences from medications may affect results.

Hook effect: No significant hook effect detected in samples up to 300,000 IU/L.

Partially clotted samples can result in elevated hCG results as well as quality check codes. To prevent clotting in samples collected in heparinized tubes, the sample should be inverted gently at least 10 times to ensure even dissolution of the heparin anticoagulant.

Grossly hemolyzed samples can cause a decreased alkaline phosphatase activity, resulting in decreased detection of hCG or quality check codes.

The i-STAT Total β-hCG test has been characterized in whole blood samples with hematocrit levels up to 55% PCV. Imprecision (CV) and bias exceeding 10% have been observed for samples with hematocrit levels above 50% PCV.

The handheld must remain on a level surface with the display facing up during testing. Motion of the handheld during testing can increase the frequency of suppressed results or quality check codes. A level surface includes running the handheld in the downloader/recharger.

The frequency of suppressed results is affected by atmospheric pressure. Suppressed result rates may increase with higher elevations (decreased barometric pressure) and may become persistent if testing is performed at more than 7500 feet (2286 meters) above sea level. Where unavailability of results is unacceptable, Abbott Point of Care recommends having an alternate test method available.

When testing whole blood, prior to filling the i-STAT Total β-hCG cartridge, invert the blood collection tube and inspect for red cell sedimentation. If sedimentation is observed, continue mixing by repeated inversion until the sedimentation is no longer apparent. Samples from β-hCG positive patients or patients undergoing hormone therapy may have higher erythrocyte sedimentation rates (ESR) which, if not tested immediately, could cause visible red cell sedimentation at the bottom of the collection tube.[12,13]

EXPECTED VALUES

Because hCG is normally synthesized and secreted by cells of the placenta or its precursor, levels of the hormone in normal, non-pregnant pre-menopausal individuals are low to undetectable.[14] Concentrations of hCG measured in the sera of non-pregnant individuals, as reported in the literature, are < 5 IU/L.[15,16,17,18]

Total β-hCG concentrations were measured in lithium heparinized blood and plasma samples collected from 123 apparently healthy non-pregnant females ≥ 18 and < 40 years, and 125 apparently healthy non-pregnant females > 40 years, using the i-STAT Total β-hCG test.

The median, range and 95th percentile with 95% confidence intervals for the two age groups were calculated. The median and range were also reported for the subjects ≥ 40 years based on menopausal status. Menopausal status was defined as 12 months since last menses and was self-reported by subjects. The observed results are presented 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 y	125	125	124	0	0 – 9.6	4.5 [4.0 , 5.4]
≥ 40 y, pre-menopausal	68	68	68	0	0 – 2.5	--
≥ 40 y post-menopausal	57	57	56	1.5	0 – 9.6	--

Each facility should establish it's own reference ranges to assure proper representation of specific populations.

The concentration of hCG rises rapidly during the first weeks of pregnancy, approximately doubling every two days. Therefore, values of total β-hCG between 5 IU/L and 25 IU/L may be indicative of early pregnancy.[19] However, these results must always be evaluated in the context of the clinical situation, the date of the last menstrual period, pelvic examination, and other clinical findings or diagnostic modalities[20] (see Limitations of Procedure section above). When borderline results between 5 IU/L and 25 IU/L are encountered, or β-hCG results do not match clinical context, re-test β-hCG 48 hours later.[19,21] Levels of hCG >25 IU/L are indicative of early pregnancy.[17] Values for hCG generally peak during the first trimester and decline slowly throughout the remainder of the pregnancy.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The i-STAT Total β-hCG test is designed to have total imprecision ≤ 10% CV for concentrations above 14 IU/L, or a standard deviation (SD) of 1.4 IU/L for concentrations ≤ 14 IU/L in blood and plasma. Two separate studies were each performed at the Point-of-Care. The first study, using hCG spiked blood, was performed at each of three sites . One of four target levels was prepared each day over four consecutive days, with a unique donor for each preparation. Seven analyzers were used per site, and three replicates were run per analyzer, per sample.

Results from each site are represented below.*

POC Site 1

Target Concentration	n	Min (IU/L)	Max (IU/L)	Mean (IU/L)	SD	SD, 95% CI	%CV	%CV, 95% CI
5 IU/L	21	3.9	6.5	5.2	0.81	0.62, 1.17	15.45	11.80, 22.38
25 IU/L	21	23.0	28.4	24.8	1.44	1.10, 2.08	5.80	4.43, 8.38
Mid range	21	804.1	1072.4	935.5	60.69	44.76, 94.22	6.49	4.79, 10.07
High range	21	1891.2	2323.1	2039.8	111.61	84.65, 163.84	5.47	4.15, 8.03

POC Site 2

Target Concentration	n	Min (IU/L)	Max (IU/L)	Mean (IU/L)	SD	SD, 95% CI	%CV	%CV, 95% CI
5 IU/L	21	4.3	5.6	5.0	0.39	0.30, 0.56	7.71	5.89, 11.14
25 IU/L	21	28.5	34.8	30.5	1.87	1.43, 2.71	6.14	4.69, 8.87
Mid range	21	866.5	1128.3	1008.1	55.65	41.72, 83.59	5.52	4.14, 8.29
High range	21	1474.3	1850.8	1641.0	105.81	80.02, 156.20	6.45	4.88, 9.52

POC Site 3

Target Concentration	n	Min (IU/L)	Max (IU/L)	Mean (IU/L)	SD	SD, 95% CI	%CV	%CV, 95% CI
5 IU/L	21	4.4	6.0	5.0	0.42	0.32, 0.61	8.51	6.48, 12.38
25 IU/L	21	25.0	32.6	27.9	1.97	1.41, 3.25	7.04	5.05, 11.65
Mid range	21	753.5	955.9	842.5	50.55	35.99, 84.79	6.00	4.27, 10.06
High range	21	1553.5	2064.4	1816.4	132.52	96.86, 209.70	7.30	5.33, 11.54

The second study using four levels of spiked plasma was performed over five days at three different sites. Five replicates of each level were tested on five analyzers at each site. Within-day and within-site imprecision are represented below.

Plasma Reproducibility at the Point-of-Care*

Target Concentration	n	Min	Max	Mean	Within-Day		Within-Site		Overall	
		IU/L	IU/L	IU/L	SD	%CV	SD	CV	SD	CV
5 IU/L	75	0.0	7.1	5.5	0.75	13.61	0.88	16.05	1.03	18.7
25 IU/L	75	21.9	27.2	24.3	1.26	5.16	1.26	5.16	1.26	5.18
Mid range	75	1038.5	1277.1	1155.7	49.76	4.31	50.77	4.39	53.08	4.59
High range	75	1636.1	2249.8	1874.5	104.95	5.60	104.95	5.60	111.11	5.93

* Representative data; results in individual laboratories may vary from these data.

Method Comparison

Quantitative

Method comparison data were collected using CLSI guideline EP9-A2.[22] Blood samples were collected at the point-of-care at four external clinical sites in heparinized evacuated tubes and analyzed in duplicate on the i-STAT System. The blood collection tubes were sent to the laboratory and the plasma portion was separated from the red cells. The plasma portion was tested in duplicate on both the i-STAT System and the ARCHITECT system.

A weighted Deming regression analysis was performed using the first replicate result from each sample. In the method comparison table, n is the number of specimens in the first data set, and Sxx and Syy refer to estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively. Sy.x is the standard error of the estimate, and r is the correlation coefficient.

Method comparison results will vary from site to site due to differences in sample handling, comparative method calibration and other site specific variables.

Quantitative Method Comparison: i-STAT vs Abbott Architect (IU/L)

	i-STAT (Whole Blood) vs ARCHITECT (Fresh Plasma)	i-STAT (Fresh Plasma) vs ARCHITECT (Fresh Plasma)
n	134	134
Slope	0.95	1.02
Intercept	2.39	-0.22
Sy.x	0.131	0.105
Syy	7.3%	5.4%
Sxx	3.2%	3.2%
r	0.99	0.99
Xmin	8.2	6.3
Xmax	1624.4	1948.8

Qualitative

Qualitative results from clinical samples gathered in the method comparison studies were analyzed for concordance with the Abbott Architect. Samples producing results below 5.0 IU/L or above 2000.0 IU/L were included in the data set.

Qualitative Method Comparison: i-STAT Whole Blood vs Abbott ARCHITECT

	Architect plasma				
i-STAT whole blood		Positive	Indeterminate	Negative	Total
	Positive	188	1**	0	189
	Indeterminate	0	12	2**	14
	Negative	0	1**	108	109
	Total	188	14	110	312

Qualitative Method Comparison: i-STAT Plasma vs Abbott ARCHITECT

	Architect plasma				
i-STAT plasma		Positive	Indeterminate	Negative	Total
	Positive	188	0	0	188
	Indeterminate	1**	13	2**	16
	Negative	0	1**	108	109
	Total	189	14	110	313

****Quantitative Values (IU/L) of Discordant Points**

Blood	
i-STAT	Architect
5.8	4.89
5.3	4.84
< 5.0	5.78
26.0	24.44
Plasma	
i-STAT	Architect
6.2	4.89
5.2	4.84
< 5.0	5.78
24.2	28.85

Analytical Specificity

The i-STAT Total β-hCG test is specific for the β subunit (free and intact) of hCG. The following were tested and found to have an insignificant effect on the measured β-hCG.

Crossreactant	Concentration	Crossreactivity (%)
LH	450 IU/L	< 10%
FSH	300 IU/L	< 10%
TSH	100 mIU/L	< 10%

Limit of Quantitation, Limit of Detection, Limit of Blank

The Limit of Quantitation (LOQ), Limit of Detection (LOD), and Limit of Blank (LOB) were all estimated (as per CLSI guideline EP17-A[23]) to be below the lower end of the reportable range, 5 IU/L.

Recovery

A dilution recovery study was performed using heparinized whole blood and plasma samples from six donors. For each donor, the original negative sample and β-hCG spiked samples were prepared with WHO 5th IS (07/364) in either heparinized whole blood or heparinized plasma to approximately 2000 IU/L. The spiked samples were diluted using unspiked whole blood or plasma and tested in a minimum of ten cartridges. A series of nine levels were generated for each donor. For samples with hcg concentrations >5 IU/L, the individual recovery results for whole blood 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. End-users may obtain individual result > 15% negative bias for plasma samples when hCG concentrations are >5 IU/L.

Percent recovery results were pooled across each hCG concentration.

Summary Recovery Performance, Whole Blood

Level	Expected Mean (IU/L)	Observed Mean (IU/L)	% Recovery or Absolute Bias
1	1936.4	1974.6	102.0 %
2	972.7	989.3	101.7 %
3	644.8	677.4	105.1 %
4	484.2	509.5	105.2 %
5	242.2	261.4	107.9 %
6	121.3	128.2	105.7 %
7	60.6	62.9	103.8 %
8	24.3	26.6	109.5 %
9	5.1	5.8	0.7 IU/L

Summary Recovery Performance, Plasma

Level	Expected Mean (IU/L)	Observed Mean (IU/L)	% Recovery or Absolute Bias
1	1972.6	1811.5	91.8 %
2	986.5	895.5	90.8 %
3	657.5	622.1	94.6 %
4	493.3	475.0	96.3 %
5	246.9	234.1	94.8 %
6	123.5	109.2	88.4 %
7	61.8	54.5	88.2 %
8	24.8	22.6	91.0 %
9	5.3	4.5	0.8 IU/L

Interference Testing

Interference studies were based on CLSI guideline EP7-A2.[24] The following substances were found to have no significant effect (less than 10%) on the i-STAT Total β-hCG test when added to a plasma pool containing approximately 40 IU/L of β-hCG, at the concentrations indicated:

Compound	Test Level (µmol/L unless otherwise indicated)
Acetyl Salicylic Acid	3620
Acetaminophen	1660
Albumin	60 g/L
Allopurinol	294
Ampicillin	152
Ascorbic Acid	342
Atenolol	37.6
Bilirubin	342
Caffeine	308
Captopril	23
Chloramphenicol	155
Cholesterol	13 mmol/L
Diclofenac	169
Digoxin	6.53
Dopamine	5.87
Enalaprilat	0.86
Erythromycin	81.6
Furosemide	181
Hemoglobin	2 g/L
Ibuprofen	2425
Isosorbide dinitrate	636
Triglycerides	37 mmol/L
Nicotine	6.2
Nifedipine	1156
Phenytoin	198
Propranolol	7.71
Salicylic acid	4340
Sodium Heparin	90 U/mL
Theophylline	222
Uric Acid	1.4 mmol/L
Verapamil	4.4
Warfarin	65.2

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