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

A. 510(k) Number:

k163418

B. Purpose for Submission:

New device

C. Measurand:

Total beta human chorionic gonadotropin (βhCG) in human serum

D. Type of Test:

Quantitative chemiluminescent immunoassay

E. Applicant:

Diazyme Laboratories

F. Proprietary and Established Names:

Diazyme DZ-Lite Total βhCG Test System
DZ-Lite 3000 Plus Chemiluminescence Analyzer

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1155 Human chorionic gonadotropin test system

   21 CFR 862.2160 Discrete photometric chemistry analyzer for clinical use

2. Classification:

   Class II (21 CFR 862.1155)
   Class I (21 CFR 862.2160)

3. Product code:

   DHA, System, Test, Human Chorionic Gonadotropin
   JJE, Analyzer, Chemistry (Photometric, Discrete), For Clinical Use

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indication for use below.

2. Indication(s) for use:

   The Diazyme DZ-Lite Total βhCG Test System is comprised of the DZ-Lite Total βhCG assay, calibrator set and control set, using a paramagnetic particle, chemiluminescent immunoassay test method. The test system is intended for in vitro diagnostic use on Diazyme Chemiluminescent Analyzers for the quantitative determination of total beta-human chorionic gonadotropin (total βhCG) in human serum. The test system is intended for use as an aid in the early detection of pregnancy.

   The Diazyme DZ-Lite 3000 Plus Chemiluminescent Analyzer is intended for determination of various analyte concentrations in human specimens, and is intended for in vitro diagnostic use in a clinical laboratory.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Performance characteristics studies were conducted on the Diazyme DZ-Lite 3000 Plus Chemiluminescence Analyzer.

I. Device Description:

The Diazyme DZ-Lite Total βhCG Test System consists of magnetic microbeads coated with anti-hCG monoclonal antibody, TRIS buffer containing bovine serum albumin (BSA), anti-hCG monoclonal antibody labeled with N-(4-Aminobutyl)-N-ethylisoluminol (ABEI), and 0.9% NaCl containing BSA diluent. Low and high calibrators consist of bovine serum and hCG antigen.

The Diazyme DZ-Lite 3000 Plus Analyzer is a microcomputer controlled, random and

continuous access analyzer that includes an external computer. This computer stores the system user interface software and allows the operator to interface through a touch-screen monitor. The DZ-Lite 3000 Plus analyzer uses immunoassays that utilize magnetic particle solid phase and chemiluminescent detection for the quantitative, semi-quantitative, or qualitative determination of various analyte concentrations found in human body fluids.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Beckman Dxi Access Total βhCG Assay

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

   k130020

3. Comparison with predicate:

Similarities		
Item	Candidate Device Diazyme DZ-Lite Total βhCG Test System	Predicate Beckman Dxi Access Total βhCG Assay k130020
Intended Use	The Diazyme DZ-Lite Total βhCG Test System Assay is a chemiluminescent immunoassay intended for use for the quantitative determination of total beta-human chorionic gonadotropin (total βhCG) in human serum. The assay is intended for use as an aid in the early detection pregnancy.	Same
Type of Test	Quantitative	Same
Specimen Type	Serum	Serum and plasma
Technology	Sandwich Immunoassay	Same
Format	Chemiluminescent assay on closed system analyzer	Same
Method	Automated	Same
Calibration	Utilizes a stored calibration curve	Same
Standardization	WHO 5th International	Same

Similarities		
Item	Candidate Device Diazyme DZ-Lite Total βhCG Test System	Predicate Beckman Dxi Access Total βhCG Assay k130020
	Reference Standard, 07/364	

Differences		
Item	Candidate Device Diazyme DZ-Lite Total βhCG Test System	Predicate Beckman Dxi Access Total βhCG Assay k130020
Assay Range	2.8 - 5000 mIU/mL	0.6 - 1350 mIU/mL
Calibrator Levels	Two levels	Six levels

Similarities/Differences		
Item	Candidate Device DZ-Lite 3000 Plus Chemiluminescence Analyzer	Predicate Beckman UniCel DxI 800 Access Immunoassay System k023764
Intended Use	The Diazyme DZ-Lite 3000 Plus Analyzer is a microcomputer controlled, random and continuous access analyzer that includes an external computer. This computer stores the system user interface software and allows the operator to interface through a touch-screen monitor. The DZ-Lite 3000 Plus analyzer uses immunoassays that utilize magnetic particle solid phase and chemiluminescent detection for the quantitative, semi-quantitative, or qualitative determination of various analyte concentrations found in human body fluids. The DZ-Lite 3000 Plus analyzer is an in vitro diagnostic device for use in	Similar

Similarities/Differences		
Item	Candidate Device DZ-Lite 3000 Plus Chemiluminescence Analyzer	Predicate Beckman UniCel DxI 800 Access Immunoassay System k023764
	the clinical laboratory.	
Detection System	Chemiluminescent	Same
Principle of Operation	Chemiluminescence using magnetic particle solid phase and chemiluminescent tracer	Same
Sample Aspiration	Directly from sample tube in the sample bay of the analyzer	Same
Sample Identification	Bar-coded sample tubes read directly by the analyzer bar code reader	Same

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

CLSI CA28-A3 Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory: Approved Guideline-Third Edition, 3rd Edition

CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods-Approved Guideline-Second Edition, 2nd 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, 3rd Edition

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition, 2nd Edition

L. Test Principle:

The Diazyme DZ-Lite Total βhCG Test System is a sandwich chemiluminescence immunoassay. A specific mouse anti-hCG monoclonal antibody is coated on the magnetic beads; another monoclonal antibody is labeled with an isoluminol derivative.

After addition of serum sample, calibrator, or controls to the microbead-antibody conjugate, the mixture is incubated at 37 °C allowing hCG present in samples, calibrator, or controls to bind to the monoclonal antibody on the bead. After a washing step, the isoluminol derivative labeled antibody conjugate reacts with hCG already bound to the magnetic beads to form sandwich complexes. After precipitation in a magnetic field and removal of the supernatant, another wash cycle is performed. Subsequently, the starter 1+2 is added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier within 3 seconds as Relative Light Units, which is proportional to the concentration of total βhCG present in samples.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were conducted using three lots of Diazyme DZ-Lite Total βhCG Test System reagent and two DZ-Lite 3000 Plus Chemiluminescence Analyzers. Six levels of pooled human serum specimens and three levels of hCG controls were tested on each analyzer for each lot of reagent. Samples and controls were tested with 2 runs per day, 2 replicates per run over 20 working days.

Results from multiple lots were similar on the two different analyzers. Results from the three lots on one representative analyzer are provided in the table below.

Sample	Mean (N=240)	Within-Run		Between-Run		Between-day		Between-Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum 1	25.6	0.7	2.6%	0.4	1.7%	0.7	2.8%	1.1	4.1%	1.1	4.2%
Serum 2	57.4	1.5	2.6%	0.7	1.3%	1.5	2.6%	2.0	3.6%	2.2	3.9%
Serum 3	473.2	16.4	3.5%	13.8	2.9%	14.8	3.1%	26.0	5.5%	26.0	5.5%
Serum 4	1821.9	79.8	4.4%	16.0	0.9%	46.6	2.6%	94.3	5.2%	93.7	5.1%
Serum 5	2374.5	99.3	4.2%	54.9	2.3%	52.0	2.2%	124.7	5.2%	124.8	5.3%
Serum 6	4289.2	123.1	2.9%	43.0	1.0%	91.5	2.1%	158.9	3.7%	159.3	3.7%
Control 1	5.6	0.3	5.3%	0.2	3.3%	0.3	4.6%	0.4	7.8%	0.4	7.8%
Control 2	38.7	1.0	2.6%	0.4	1.0%	0.6	1.7%	1.3	3.2%	1.3	3.3%
Control 3	275.9	4.9	1.8%	3.1	1.1%	4.7	1.7%	7.5	2.7%	7.5	2.7%

b. Linearity/assay reportable range:

High range linearity was established by preparing ten sample dilutions with concentrations from 0.3 - 5186.3 mIU/mL by mixing different proportions of a sample with a high hCG concentration with a normal serum sample without detectable hCG. The samples were tested with the Diazyme DZ-Lite Total βhCG Test System on two analyzers in triplicate with one lot of hCG reagent. The results for high range linearity are

shown in the table below.

Levels	Recovery				Expected Recovery	Error	% Recovery
	Rep 1	Rep 2	Rep 3	Mean			
Level 0	0.3	0.1	0.1	0.1	0.0	-0.1	NA
Level 1	554.4	548.1	561.2	554.6	523.8	-30.8	106%
Level 2	998.5	1030.4	1043.4	1024.1	1047.5	23.4	98%
Level 3	1624.2	1564.0	1639.0	1609.1	1571.3	-37.8	102%
Level 4	1990.0	2012.3	2064.6	2022.3	2095.0	72.7	97%
Level 5	2688.6	2531.8	2719.8	2646.7	2618.8	-28.0	101%
Level 6	2926.5	3135.4	3022.8	3028.2	3142.5	114.3	96%
Level 7	3747.8	3585.6	3761.3	3698.3	3666.3	-32.0	101%
Level 8	3924.1	4158.2	4030.4	4037.6	4190.0	152.4	96%
Level 9	4791.5	4473.8	4375.7	4547.0	4713.8	166.8	96%
Level 10	5186.3	5258.1	5268.1	5237.5	5237.5	0	100%

The expected values were plotted against the recovered hCG values. Linear regression gave the following equation:

$y = 0.9786x + 19.528$, $R^2 = 0.9984$

Mid-range linearity was established by preparing 11 sample dilutions with concentrations ranging from 0 - 541.6 mIU/mL by mixing different proportions of a sample with high hCG concentration with a sample with hCG-free serum. Samples were tested in triplicate.

Levels	Recovery				Expected Recovery	Error	% Recovery
	Rep 1	Rep 2	Rep 3	Mean			
Level 11	0	0	0	0	0.00	0.0	0.00%
Level 10	51.8	54.3	55.2	53.7	53.70	0.0	0.08%
Level 9	100.6	102.3	103.8	102.3	107.40	-5.1	-4.79%
Level 8	150.9	151.6	160.3	154.3	161.10	-6.8	-4.24%
Level 7	205.7	204.3	211.0	207.0	214.80	-7.8	-3.62%
Level 6	260.9	260.8	275.7	265.8	268.50	-2.7	-1.01%
Level 5	308.3	309.5	310.7	309.5	322.20	-12.7	-3.95%
Level 4	364.4	364.7	368.8	366.0	375.90	-9.9	-2.64%
Level 3	418.6	423.2	416.2	419.4	429.60	-10.2	-2.38%
Level 2	484.2	483.2	491.3	486.2	483.30	2.9	0.60%
Level 1	541.6	542.0	527.4	537.0	537.00	0.0	0.00%

The expected and recovered hCG were plotted, and gave the following linear regression equation:

$y = 0.9975x - 4.083$, $R^2 = 0.992$

Low range linearity was established by preparing 12 sample dilutions with concentrations ranging from 0.35 to 85.19 mIU/mL by mixing different proportions of a sample with high hCG concentration with a sample with low-level hCG. The samples were tested in triplicate. The data support an analytical measuring range of 2.8 - 5000 mIU/mL.

Levels	Recovery				Expected Recovery	Error	% Recovery
	Rep 1	Rep 2	Rep 3	Mean			
Level 1	0.35	0.33	0.45	0.38	0.40	-0.02	-5.00%
Level 2	3.71	3.73	3.58	3.67	4.37	-0.70	-15.93%
Level 3	8.11	7.88	8.23	8.07	8.73	-0.66	-7.57%
Level 4	17.06	16.51	14.97	16.17	17.46	-1.29	-7.40%
Level 5	26.23	27.93	25.35	26.51	26.19	0.32	1.21%
Level 6	34.90	35.01	35.03	34.98	34.92	0.06	0.16%
Level 7	41.03	43.46	43.72	42.74	43.65	-0.91	-2.09%
Level 8	51.76	53.68	54.46	53.30	52.38	0.92	1.75%
Level 9	61.15	62.93	60.84	61.64	61.11	0.53	0.86%
Level 10	69.24	70.24	68.42	69.30	69.85	-0.55	-0.78%
Level 11	80.79	81.71	79.52	80.67	78.58	2.09	2.66%
Level 12	85.19	90.46	84.48	86.70	87.71	-1.01	-1.15%

The expected and recovered hCG were plotted, and gave the following linear regression equation:

$y = 1.0109x - 0.5423$, $R^2 = 0.9991$

On-board Dilution Recovery

Verification studies were performed to determine the sample recovery after a 1:10 dilution is performed automatically by the DZ-Lite 3000 Plus Chemiluminescence Analyzer. Seven serum samples with beta-hCG concentrations between 5,000 and 50,000 mIU/mL as determined by the predicate device were tested with the Diazyme DZ-Lite Total βhCG Test System reagent using the automatic 1:10 dilution of the analyzer and two lots of reagents. The percent differences for the diluted specimen versus the expected concentration were within 10%. The dilution study results support the sponsor's labeling claims that samples with beta-hCG above 5,000 mIU/mL may be diluted 1:10 on-board the analyzer to obtain results up to 50,000 mIU/mL.

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

Traceability:

The calibrators for the Diazyme DZ-Lite Total βhCG Test System are traceable to WHO hCG 5th International Standard 07/364.

Stability:

Stability protocols and acceptance criteria for accelerated, real-time, and on-board studies for the reagent were reviewed and found to be acceptable. The results support the reagent shelf life of 18 months when stored at 2 - 8°C.

d. Detection limit:

Limit of blank:

The limit of blank was determined by running 60 replicates of blank samples with three lots of Diazyme DZ-Lite Total βhCG Test System reagent over at least 3 days on one DZ-Lite 3000 Plus analyzer. The limit of blank was calculated as the mean of the 57th and 58th ranked values. The highest value of the three lots was the limit of blank. The limit of blank was determined to be 0.307 mIU/mL.

Limit of detection:

Low hCG concentration samples were prepared from five serum samples diluted with a normal serum pool without detectable hCG. These samples were tested with three lots of Diazyme DZ-Lite Total βhCG Test System reagent on the DZ-Lite 3000 Plus in three runs with four replicates per run over three days. The LOD was calculated as the LOB + (1.645 * (SD of LOD samples)) for each lot tested. The LOD was assigned based on the highest value of hCG for the three reagent lots, and was determined to be 0.615 mIU/mL.

Limit of quantitation:

Five serum samples were diluted with hCG negative serum samples to target concentrations of 0.5, 2, 4, 6.5, and 8 mIU/mL. The diluted serum samples were tested with three lots of Diazyme DZ-Lite Total βhCG Test System reagent on the DZ-Lite 3000 Plus Chemiluminescence Analyzer with 12 replicates per run over three days. The assay LOQ claimed by the sponsor is 1.5 mIU/mL based on total error goals of bias at 15.5% and CV of 12.3%.

e. Analytical specificity:

Serum pools containing hCG concentrations of approximately 5, 60, 200, and 400 mIU/mL were spiked with various endogenous substances and therapeutic drugs, and tested in triplicate. No significant interference (< ±10%) was observed up to the concentrations summarized below.

Interferent	Concentration
Ascorbic Acid	20 mg/dL
Bilirubin	20 mg/dL
Bilirubin Conjugated	20 mg/dL
Hemoglobin	1000 mg/dL

Rheumatoid Factor	200 IU/mL
Triglycerides	3000 mg/dL
Luteinizing Hormone	250,000 mIU/L
Follicle-Stimulating Hormone	500,000 mIU/L
Human Growth Hormone	100 ng/mL
Thyroid-Stimulating Hormone	200 mIU/L
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	20 mg/dL
Atropine	20 mg/dL
Caffeine	20 mg/dL
EDTA	80 mg/dL
Ethanol	1%
Gentisic Acid	20 mg/dL
Glucose	2000 mg/dL
Salicylic Acid	20 mg/dL

Hook effect:

Samples with hCG concentrations up to 1.5 million mIU/mL was prepared by spiking human beta hCG antigen to a pool of normal human serum, and were tested with the candidate Diazyme DZ-Lite Total βhCG Test System. No evidence of a high dose hook effect was observed in the study for hCG concentrations up to 1.5 million mIU/mL.

f. Assay cut-off:

Not applicable; this is a quantitative assay.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 142 serum samples tested in singlet were performed with the candidate Diazyme DZ-Lite Total βhCG Test System and the predicate Beckman Access Total hCG assay (k130020). The sample values ranged from 5.2 - 5394 mIU/mL on the predicate device, and 5.2 - 4652 mIU/mL on the candidate device. The results are summarized in the table below.

Parameter	Deming Regression
n	142
Slope	0.939
95% CI	0.912 to 0.965
Intercept	-18.53
95% CI	-78.83 to 41.77
Correlation Coefficient(R^2)	0.9718

b. Matrix comparison:

Not applicable.

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 135 apparently healthy, non-pregnant women ≤ age 50, and 139 healthy women over age 50 were used. The reference interval was calculated using the nonparametric method according to CLSI C28-A3, and was determined to be 0.05 - 0.85 mIU/mL for women ≤ age 50, and 0.1 - 4.4 mIU/mL for women over age 50.

N. Instrument Name:

Diazyme DZ-Lite 3000 Plus Chemiluminescence Analyzer

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 sample area. If the samples that are being used do not have an associated barcode, then sample ID's must be manually entered into the user software.

4. Specimen Sampling and Handling:

   The DZ-Lite Total βhCG assay is for use with serum samples.

5. Calibration:

   The Diazyme DZ-Lite Total βhCG Test System on DZ-Lite 3000 Plus Chemiluminescence Analyzer utilizes a RFID card that is preprogrammed with a reagent lot specific master curve and is supplied with each kit. The master curve consists of ten levels of concentration points. The mean reactive light units at each level with corresponding hCG concentration are used to make the Diazyme DZ-Lite Total βhCG Test System master curve. When RFID card is scanned with the RFID scanner imbedded in the DZ-Lite 3000 Plus Chemiluminescence Analyzer, the lot specific master calibration curve is automatically utilized for the assay test. RFID cards are programmed at the manufacturer site. The assay lot specific master calibration curve is generated by experimental data. The master calibrators are traceable to WHO hCG 5th International standard 07/364.

   Two levels of calibrator are also included in each kit. Via measurement of two levels of the working calibrators, the predefined master curve in the RFID card is adjusted to a new lot-specific working curve for calculation of hCG concentrations in the specimens.

6. Quality Control:

   Quality control can be performed using Diazyme DZ-Lite hCG controls. Controls should be run at least once per day, once per kit, and after calibration. Control intervals should be adjusted to match each individual laboratory's requirements. Values should fall within established ranges and if not, laboratories should establish guidelines corrective

measures.

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

The software documentations were reviewed and found to be acceptable. The firm provided documentation to support the devices were designed, developed, and remain under good software lifecycle processes.

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.