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

A. 510(k) Number:
k063754

B. Purpose for Submission:
New device

C. Measurand:
Human Chorionic Gonadotropin (hCG)

D. Type of Test:
Quantitative immunoassay

E. Applicant:
Dade Behring, Inc.

F. Proprietary and Established Names:
Dimension Vista BHCG Flex reagent cartridge
Dimension Vista BHCG calibrator

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1155 Human chorionic gonadotropin test system
   21 CFR §862.1150 Calibrators
2. Classification:
   Class II
3. Product code:
   DHA Human chorionic gonadotropin (HCG) test system
   JIT Calibrator
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See Indication(s) for use.
2. Indication(s) for use:
   Method: The BHCG method is an in vitro diagnostic assay for the quantitative measurement of total Beta (β) human chorionic gonadotropin: both the intact hCG dimer and the free β subunit of the human chorionic gonadotropin hormone in human serum and plasma on the Dimension Vista system. Measurements of β human chorionic gonadotropin are used for the early detection of pregnancy.

   Calibrator: The BHCG calibrator is an in vitro diagnostic product for the calibration of the Beta Human Chorionic Gonadotropin method for the Dimension Vista System.
3. Special conditions for use statement(s):
   Prescription use only.
4. Special instrument requirements:
   For use on the Dimension Vista Clinical Chemistry system.

I. Device Description:

The Dimension Vista™ BHCG Flex® reagent cartridge is an *in vitro* diagnostic device that consists of prepackaged, liquid reagents in a plastic twelve well cartridge for use on the Dade Behring Dimension Vista™ clinical chemistry system for the quantitative determination of total beta human chorionic gonadotropin levels in serum and plasma. The flex cartridge contains antibody-labeled beads, streptavidin-labeled beads and biotinylated antibody.

The Dimension Vista™ BHCG Calibrator is a liquid product containing human chorionic gonadotropin in a bovine calf serum matrix with stabilizers and preservatives. The kit consists of twelve vials, two each of six levels containing 2.0 mL per vial for level A, 1.0 mL per vial for levels B, C, D, and E, 1.5 mL per vial for level F.

All human source material was tested by FDA-approved methods for HIV-1/2, HBsAg, and HCV and found to be negative.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dimension Human Chorionic Gonadotropin (HCG) method and calibrator
2. Predicate 510(k) number(s):
   k970387; k970396
3. Comparison with predicate:
   Dimension Vista BHCG Flex assay:

Similarities		
	Predicate device	**Proposed device**
Sample type	Serum and plasma	same
Reportable range	1-1000 mIU/mL	same
Analytical sensitivity	≤ 1 mIU/mL	same

Differences		
	Predicate device	**Proposed device**
Assay type	Photometric immunoassay	Chemiluminescent immunoassay
Sample volume	40 µL	2 µL

Calibrator:

Similarities		
	Predicate device	**Proposed device**
Analyte	Human urine chorionic gonadotropin	same
Storage temperature	2-8°C	same

Differences		
	Predicate device	**Proposed device**
Form	Lyophilized	Liquid
Matrix	Equine serum	Bovine calf serum
Volume	10 vials, 2 at each levels, reconstituted volume 2 mL for each level	12 vials, 2 at each level, 2.0 mL per vial for level A, 1.0 mL per vial for levels B, C, D, and E, 1.5 mL per vial for level F
Levels	5 levels (0, 25, 155, 522, 1120 mIU/mL)	6 levels (0, 14, 28, 160, 550, 1100 mIU/mL)

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

Standard:

WHO Standard for HCG, 4th IS, 75/589

Guidance:

CLSI Documents:

• *User Evaluation of Precision Performance of Clinical Chemistry Devices: Approved Guideline* (EP5-A2)

• *Interference Testing in Clinical Chemistry: Approved Guideline* (EP7-A2)

• *Method Comparison and Bias Estimation using Patient Samples: Approved Guideline* (EP9-A2)

L. Test Principle:

The Dimension Vista BHCG Flex assay is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI technology. The LOCI reagents include two synthetic bead reagents and a biotinylated anti-βhCG monoclonal antibody fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a second anti-βhCG monoclonal antibody and contains chemiluminescent dye. Sample is incubated with chemibeads and biotinylated antibody to form a bead-βhCG-biotinylated antibody sandwich. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680nm generates singlet oxygen from the Sensibeads which diffuses to the Chemibeads and triggers a chemiluminescent reaction. The resulting chemiluminescent signal is measured at 612nm and is directly proportional to the free and intact β human chorionic gonadotropin concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   To evaluate precision, the within-lab and repeatability of the Dimension Vista BHCG Flex assay was calculated using the CLSI EP5-A2 method. Two serum pools and one control were tested in duplicate during two runs per day over 20 days. The results were as follows:

		Repeatability		Within-Lab	
Sample	Mean (mIU/mL)	SD (mIU/mL)	% CV	SD (mIU/mL)	% CV
Low pool	25	0.6	2.6	0.7	2.8
High pool	417	5.9	1.4	8.5	2.0
Control 1	5	0.2	3.2	0.2	3.6

b. *Linearity/assay reportable range:*
The reportable range for this assay is 1-1000 mIU/mL. Linearity across this range was established by pooling four serum samples with high β-hCG concentrations and diluting with water. The eleven samples/dilutions all recovered within 10% of the expected value.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Stability: Shelf life for this calibrator is 12 months. Product is stored at 2-8 °C throughout the testing cycle and tested at the following time intervals: months 0, ¼, 1, 2, 3, 4, 6, 8, 10, 12, 13. The control/reference material is the same lot stored at -20°C and tested at the same frequency. The test calibrator material values are recovered versus the calibrations with the control material. Recovery versus time is monitored and percent change over time is determined. Acceptance criteria are changes in value ≤ 2 SD for Level 1 and less than 5% for Levels 2-6.
Open well stability and on board stability testing protocols for the flex cartridges and the acceptance criteria were described and found to be acceptable.
Traceability and Value Assignment: The calibrator master pools are made by adding quantities of purified hCG into bovine calf serum with preservatives. The master lot (5 levels) is stored at -20°C and values are assigned by using the Dimension Vista clinical chemistry instrument and referenced to the WHO standard for HCG, 4th IS, 75/589. Commercial lots of the calibrator are produced by addition of analyte to bovine calf serum. The concentration of each level of the commercial calibrator lots is verified by using an instrument calibrated with the master pools. The final bottle values for each level of the commercial lot are assigned using three instruments by testing N > 40 replicates.

d. *Detection limit:*
Analytical sensitivity (or limit of the blank) was determined by assaying twenty consecutive replicates of the analyte free (0 level) calibrator on the Dimension Vista BHCG Flex assay. The sensitivity was then calculated by multiplying the standard deviation by two and adding it to the absolute value of the mean. The limit of the blank was calculated to be 0.0425 mIU/mL, but the analyzer does not report a reading less than 1.0 mIU/mL.

e. *Analytical specificity:*
Cross reactivity: Thyroid stimulating hormone (TSH), luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, and human growth hormone (hGH) were spiked into serum to evaluate cross-reactivity. No detectable cross-reactivity was observed for 2500 µIU/mL TSH, 1000

mIU/mL LH, 1000 mIU/mL FSH, 1000 ng/mL prolactin, and 500 ng/mL hGH.

Interference: The Dimension Vista BHCG Flex assay was evaluated for interference using CLSI Document EP7-A2 as a guideline. Hemoglobin (1000 mg/dL), Bilirubin (conjugated and unconjugated at 60 mg/dL) and Lipids (3000 mg/dL) did not affect the performance of the assay when 25 mIU/mL bhCG was tested. The sponsor defines interference as results exceeding +/-10% of the expected value. Other substances, including various prescription and over-the-counter drugs, were tested and shown not to interfere with this assay.

Hook effect: Hook effect was evaluated using samples containing β-hCG concentrations ranging from 0 - 3,000,000 mIU/mL. Samples consisted of Scripps hCG antigen spiked into bovine calf serum material. The results demonstrated that samples with hCG concentrations up to 3,000,000 mIU/mL do not give results within the assay measuring range.

Concentration mIU/mL	Signal (LOCI Counts)	Observed Results mIU/mL
14	79.99	14
29	158.61	29
169	928.20	178
582	2835.89	576
1173	5336.26	above assay range
5000	12448.93	above assay range
6000	18110.76	above assay range
15000	19568.23	above assay range
30000	No signal obtained	above assay range/above cutoff value
60000	No signal obtained	above assay range/above cutoff value
300000	No signal obtained	above assay range/above cutoff value
750000	18923.28	above assay range
1500000	16757.50	above assay range
3000000	14617.38	above assay range

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The Dimension Vista BHCG Flex assay was compared to the predicate device using CLSI Document EP9-A2 as a guideline for the method comparison study. Ninety nine serum samples with β-hCG values ranging from 1-980 mIU/mL were split and run on the predicate device (Dade Behring Dimension Human Chorionic Gonadotropin method) and the proposed device (Dade

Behring Dimension Vista BHCG method).
Regression statistics:
Slope = 0.94
Intercept = 4.6 mIU/mL
Correlation Coefficient = 0.99

b. Matrix comparison:

Fifty-two matched serum and lithium heparin plasma samples were tested on the Dimension Vista BHCG Flex assay. Samples above the assay range were diluted with reagent grade water, as recommended in the product labeling. (The same dilution factor was used for both the serum and lithium heparin plasma matched pair.)
Regression statistics:
Slope = 0.95
Intercept = 2.3 mIU/mL
Correlation coefficient = 0.998

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 was determined by a study performed by the sponsor using samples from a population of healthy adults:
Non-pregnant females, ages 18-62: 1-3 mIU/mL (n=123)
Adult males, ages 19-67: < 1 mIU/mL (n=130)

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.