510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k070552

B. Purpose for Submission:
New Device

C. Analyte:
Ferritin

D. Type of Test:
Semi-quantitative, Chemiluminescence

E. Applicant:
Dade Behring, Inc.

F. Proprietary and Established Names:
Dimension Vista™ (FERR) Flex® reagent cartridge
Dimension Vista™ LOCI 4 Calibrator

G. Regulatory Information:

1. Regulation section:
   21CFR §866.5340 Ferritin immunological test system
   21CFR §862.1150 Calibrator
2. Classification:
   Class II
3. Product Code:
   DBF-Ferritin, antigen, antiserum, control
   JIT-Calibrator, secondary
4. Panel:
   Immunology (82)
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   Dimension Vista™ (FERR) Flex® reagent cartridge- The FERR method is an in vitro diagnostic device for the quantitative measurement of ferritin in human serum and plasma (lithium or sodium heparin, and EDTA) on the Dimension Vista® System. Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, such as hemochromatosis (Iron overload) and iron deficiency anemia.

   The Dimension Vista™ LOCI 4 Calibrator is an in vitro diagnostic device intended to be used to calibrate the ferritin (FERR) assay on the Dimension Vista™.
2. Indication(s) for use:
   Same as intended use.
3. Special condition for use statement(s):
   Prescription use only
4. Special instrument Requirements:

Dimension Vista® System

I. Device Description:

Dimension Vista™ FERR Flex® reagent cartridge assay is a homogeneous, sandwich chemiluminescent immunoassay using LOCI ™ reagents: Sensibeads (bead reagent coated with streptavidin and containing a photosensitizer dye), Chemibeads (bead reagent coated with murine anti-ferritin monoclonal antibody and containing a chemiluminescent dye), and a biotinylated murine anti-ferritin monoclonal antibody fragment. Buffers, preservatives and stabilizers are also included in the cartridge.

Dimension Vista™ LOCI 4 Calibrator is a five level, liquid calibrator kit consisting of 10 vials (two vials for each level). The product matrix is 6% bovine serum albumin with buffer, stabilizer, and preservatives. Levels A through E contains ferritin at the following target concentrations: A~0 ng/mL, B~26 ng/mL, C~ 210 ng/mL, D~ 1050 ng/mL, E ~2000 ng/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dimension® Ferritin Flex® reagent cartridge
   Dimension ® Ferritin calibrator
2. Predicate K number(s):
   k963498
   k983548
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
	Dimension Vista™ Ferritin Flex ® reagent cartridge (K6440)	Dimension® Ferritin Flex® reagent cartridge (RF440)
Intended Use	The FERR method is an in vitro diagnostic device for the quantitative measurement of ferritin in human serum and plasma (lithium or sodium heparin, and EDTA) on the Dimension Vista® System.	The Ferritin Flex® reagent cartridge used on the Dimension® clinical chemistry system with the heterogeneous immunoassay module is an in vitro diagnostic test intended to quantitatively measure ferritin in serum and heparinized plasma.
Indications for Use	Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, such as hemochromatosis (Iron overload) and iron deficiency anemia.	Same
Measurement type	Quantitative	Same

Similarities		
Item	**Device**	**Predicate**
	Dimension Vista™ Ferritin Flex ® reagent cartridge (K6440)	Dimension® Ferritin Flex® reagent cartridge (RF440)
Capture antibody	Mouse monoclonal	Same
Reference intervals	Males 26-388 ng/mL Females 8-252 ng/mL All adults 8-388 ng/mL	Same
Stability: Sealed & On-board	30 days	Same
Differences		
Item	**Device**	**Predicate**
Instrument	Dimension Vista ® System	Dimension® Clinical Chemistry System
Solid phase	Chemibeads and Sensibeads	Ferritin antibody coated chromium dioxide particles
Conjugate reagent	None	β galactosidase labeled anti-ferritin monoclonal antibody
Substrate	None	Chlorophenol red-β-d-galactopyranoside
Detection method	Chemiluminescence	Colorimetric
Measurement absorbance	680 and 612 nm	577 and 700 nm
Sample type	Serum, heparinized and EDTA plasma	Serum, heparinized plasma
Sample size	2 µL	40 µL
Measuring Range	0.5 ng/mL- 2000 ng/mL	1-1000 ng/mL
Stability: Open	7 days for wells 1-12	Varies from 3-10 days

Similarities		
Item	**Device**	**Predicate**
	Dimension Vista™ LOCI 4 Calibrator	Dimension ® Ferritin Calibrator
Intended Use	To calibrate the ferritin method	Same
Composition	Ferritin from human liver in bovine serum albumin	Same
Reagent Preparation	Liquid, Ready-to-use	Same
Traceability	WHO, 3rd IS 94/572	Same
Levels	1 without ferritin, 4 with different concentrations of ferritin	Same

Stability	30 days at 2-8°C	Same
Differences		
Item	**Device**	**Predicate**
Analytes	Multi-analyte	Ferritin
Instrument system	Dimension Vista ® System	Dimension® Clinical Chemistry System
Storage	Frozen -10 to -20°C	Refrigerated -2 to-8°C

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

CLSI Evaluation of Precision Performance of Clinical Devices; Approved Guideline: EP5-A2, CLSI Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline EP9-A2, CLSI Interference Testing in Clinical Chemistry; Approved Guideline EP7-A2. CLSI Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline EP6-A.

L. Test Principle:

The FERR method is a homogenous, sandwich chemiluminescent immunoassay. Ferritin in a sample is incubated with biotinylated murine monoclonal and beads that are coated with anti-ferritin mouse monoclonal and containing a chemiluminescent dye (Chemibeads) to form a particle/ferritin/biotin-antibody sandwich. A second set of beads (Sensibeads), coated with streptavidin and containing a photosensitizer dye is added and bind to the biotin to form bead-pair immunocomplexes. The sample is illuminated at 680nm, generating a single oxygen from the Sensibeads that diffuses into the Chemibeads and triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct indication of the ferritin concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision testing was done in accordance with CLSI Approved Guideline EP5-A2. Three serum pools and one plasma sample representing the measuring range were analyzed in duplicate, twice a day, for 20 days. Two commercially available controls were also evaluated. The standard deviation (SD) and coefficient of variation (%CV) for repeatability and within-lab precision are reported below. Overall repeatability was greater than 98% and within-lab reproducibility was greater than 96%.

	Mean	Repeatability		Within-lab	
	(ng/mL)	SD	%CV	SD	%CV
Anemia Control Level 1	6.2	0.11	1.7	0.24	3.8
Control Level 2	161.1	2.02	1.3	3.72	2.3
Serum Pool 1	8.8	0.16	1.8	0.31	3.5
Serum Pool 2	436.4	5.58	1.3	14.33	3.3
Serum Pool 3	1696.3	27.18	1.6	57.44	3.4
Plasma Pool	9.0	0.16	1.8	0.28	3.1

b. Linearity/assay reportable range:

The linear range of the assay (0.5 – 2000 ng/mL) was confirmed by testing five replicates of each dilution (7 total) prepared from a patient serum sample, as described in CLSI protocol EP-6-A. Ferritin concentrations in the sample ranged from 0.0 to 2136.6 ng/mL. The mean of the observed values for each dilution were plotted versus the expected values. Least squares regression analysis generated the following data:

Slope	Y-intercept (ng/mL)	Correlation Coefficient	n
1.00	2.1 ng/mL	1.00	35

Recovery studies were also performed using six serum samples with ferritin concentrations ranging from 4.5 - 151 ng/mL. Samples were spiked with 10 ng/mL of ferritin. The percent recovery ranged from 87% to 104% with a mean recovery of 95%.

c. *Traceability (controls, calibrators, or method):*
Value assignments for the calibrators are made from a master pool that is referenced to the WHO standard for ferritin 3rd IS 94/572.

d. *Detection limit:*
The limit of blank was determined from the mean of 20 replicates of the zero-level calibrator plus 2 standard deviations. The value obtained was 0.13 ng/mL. The limit of blank claim is 0.5 ng/mL.

e. *Analytical specificity:*

i. Interference studies: Interference testing was performed according to CLSI Approved Guideline EP7-A2 to determine the effect of various exogenous substances of the Dimension Vista™ FERR method. Minimal interference (<10%) was observed when pooled human serum samples representing two concentrations of ferritin (20 ng/mL and 502.7 ng/mL) containing the following interferents were compared to a control without interferent: hemoglobin (500 mg/dL), unconjugated bilirubin (20 mg/dL), conjugated bilirubin (60 mg/dL), Intralipid (3000 mg/dL) rheumatoid factor (510 IU/mL). An additional panel of 41 exogenous substances were evaluated for interference and were shown to exhibit minimal interference (<10%).

ii. Cross-reactivity
Not applicable.

iii. Antigen excess- The effect of antigen excess in the Dimension Vista™ FERR assay was evaluated using the zero-level calibrator spiked with 250,000 ng/mL of human ferritin. The test result was reported as "exceeds assay range." Samples greater than 2000 ng/mL are reported as exceeding assay range.

f. *Assay cut-off:*
See Expected values/reference range.

2. Comparison studies:

a. *Method comparison with predicate device:*

CLSI Approved Guideline for Method Comparison and Bias Estimation Using Patient Samples; EP9-A2 was followed. The Dimension Vista™ FERR method on the Dimension Vista™ System was compared to the predicate Dimension® Ferritin Flex® reagent cartridge on the Dimension® RxL instrument by assaying 158 serum samples with concentrations ranging from 4.4 ng/mL to 1573.3 ng/mL on both systems and comparing the results. Ordinary least squares linear regression statistics are as follows:

Comparative Method	Slope	Y-Intercept (ng/mL)	Correlation coefficient (r)	N
Dimension RxL System	1.01	1.48ng/mL	0.996	158

Passing-Bablok non-parametric linear regression analysis yielded the following statistics: Slope 1.02 (95% CI: 1.00 to 1.03), Y-intercept -0.95 (95% CI -1.81 to -0.47).

b. Matrix comparison:

Ten matched serum, Na-heparin plasma, Li-heparin plasma, EDTA-plasma samples containing ferritin concentrations ranging 5.3 -1978.5 ng/mL, were assayed and compared. Least squared regression analysis demonstrated that there was no significant bias between the two matrices and yielded the following statistics:

Sample type compared to serum	Slope	Y-intercept	Correlation coefficient
Na-heparin plasma	1.03	-2.1	1.00
Li-heparin plasma	1.01	-4.0	1.00
EDTA-plasma 1.00	1.00	-4.6	1.00

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:
   See Expected values/reference range
5. Expected values/Reference range:
   The reference intervals were transferred from those previously obtained using the predicate Dimension® system. They represent the central 95% of results determined from a population of healthy adults (n=296; 118 males, and 178 females). The original determination and transference were done in accordance with protocol CLSI C28-A2, How to Define and Determine Reference Intervals in the Clinical Laboratory. Pediatric samples were not evaluated.

Sample	95% Reference Interval
Males	26-388 ng/mL
Females	8-252 ng/mL
All adults	8-388 ng/mL

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.