510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k063425

B. Purpose for Submission:
New Device

C. Analyte:
Immunoglobulin E (IgE)

D. Type of Test:
Quantitative, Nephelometry

E. Applicant:
Dade Behring, Inc.

F. Proprietary and Established Names:
Dimension Vista™ IgE Flex® reagent cartridge
Dimension Vista™ Protein 1 Calibrator
Dimension Vista™ Protein 1 Control L
Dimension Vista™ Protein 1 Control M
Dimension Vista™ Protein 1 Control H

G. Regulatory Information:

1. Regulation section:
   21CFR §866.5510- Immunoglobulin A, G, M, D, and E immunological test system
   21CFR §862.1150- Calibrator
   21CFR §862.1660- Quality control material, assayed and unassayed
2. Classification:
   Class II
3. Product Code:
   DGC- IgE, Antigen, Antiserum, Control
   JIX- Calibrator, multi-analyte mixture
   JJY- Multi-analyte controls
4. Panel
   Immunology (82)

H. Intended Use:

1. Intended use(s):
   Dimension Vista™ IGE Flex® reagent cartridge: The IGE method is an in vitro diagnostic test for the quantitative determination of Immunoglobulin E in human serum, heparinized plasma or EDTA plasma on the Dimension Vista® System. Measurements of IGE aid in the diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings.
   Dimension Vista™ Protein 1 Calibrator: PROT1 CAL is an in vitro diagnostic product for the calibration of the C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods on the Dimension Vista® System.

Dimension Vista™ Protein 1 Controls L, M and H: PROT1 CON L, M, and H are assayed intra-laboratory quality controls for assessment of precision and analytical bias in the determination of C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods on the Dimension Vista® System.

2. Indication(s) for use:
   Same as above
3. Special condition for use statement(s):
   Prescription use only
4. Special instrument Requirements:
   Dimension Vista® System

I. Device Description:

Dimension Vista™ IGE Flex® reagent cartridge: IGE Flex® reagent cartridge consists of three reagents: IgE Reagent consists of polystyrene particles coated with monoclonal antibodies to human IgE. IGE Supplement Reagent 1 consists of phosphate buffer, polyethylene glycol, and sorbitan monolaureate. IGE Supplement Reagent 2 consists of mouse immunoglobulin in a phosphate buffer.

Dimension Vista ™ Protein 1 Calibrator:
PROT1 CAL is a multi-analyte, liquid, human serum based product containing C3 complement (C3), C4 complement (C4), immunoglobulin A (IGA), immunoglobulin E (IGE) immunoglobulin G (IGG), immunoglobulin M (IGM), and prealbumin (PREALB)

Dimension Vista ™ Protein 1 Control L, M and H:
PROT1 CON L, M and H are multi-analyte, liquid, human serum based products containing C3 complement (C3), C4 complement (C4), immunoglobulin A (IGA), immunoglobulin E (IGE), immunoglobulin G (IGG), immunoglobulin M (IGM), and prealbumin (PREALB)

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) numbers:

Dade Behring N Latex IgE mono assay	k991787
Dade Behring N Protein Standard SL	k012470
Dade Behring N/T Protein Control SL	k012468

2. Comparison with predicate:

Dimension Vista™ IgE Flex ® regent cartridge

Similarities		
Item	Device	Predicate
Intended Use	For the quantitative determination of Immunoglobulin E in human serum, heparinized plasma or EDTA plasma on the Dimension Vista® System.	For the quantitative in vitro determination of IgE in human serum, EDTA and heparinized plasma by means of particle enhanced immunonephelometry using the BN Systems
Indications for Use	Measurements aid in the	Same

Similarities		
Item	Device	Predicate
	diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings.	
Method	Immunonephelometry	Same
Measurement type	Quantitative	Same
Capture antibody	Mouse monoclonal	Mouse monoclonal
Reportable range	18- 1150 IU/mL	Same
Matrices	Serum, heparin plasma (Li and Na), and EDTA plasma	Same

Differences		
Item	Device	Predicate
Instrument system	Dimension Vista® System	BN ProSpec® System
Stability: opened	21 days	4 weeks

Dimension Vista ™ Protein 1 Calibrator

Similarities		
Item	Device	Predicate
Intended Use	For the calibration of the C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods on the Dimension Vista® System	For establishment of reference curves for the determination of [26 specific analytes] on the BN Systems, as well as of IgM, C3c, ceruloplasmin and Ig/L-chains (types kappa and lambda) by radial immunodiffusion (RID) using Partigen plates.
Composition	Pooled Human sera	Same
Reagent Preparation	Liquid, Ready-for-Use	Same
Traceability	2nd IRP 75/502	Same

Differences		
Item	Device	Predicate
Analytes	C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin	IgG, IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgE, C3c, C4, transferrin, albumin, α_1-antitrypsin,

Differences		
Item	Device	Predicate
	E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB)	α_2-macroglobulin, haptoglobulin, α_1-acid glycoprotein, prealbumin, hemopexin, ceruloplasmin, retinol binding protein, Ig Light chain kappa, Ig Light chain lambda, soluble transferrin receptor, ferritin, β_2-microglobulin and total protein, IgM, C3c, ceruloplasmin and Ig/L-chains (types kappa and lambda).
Instrument system	Dimension Vista® System	BN Systems
Stability: Open	9 days 2-8ºC	14 days 2-8ºC

Dimension Vista ™ Protein 1 Control L, M and H

Similarities		
Item	Device	Predicate
Intended Use	Assayed intra-laboratory quality controls for the assessment of precision and analytical bias in the determination of C3 complement (C3), C4 complement (C4), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods on the Dimension Vista™ System.	Assayed accuracy controls for accuracy and precision controls in the determination of [26] human serum proteins by immunonephelometry with the BN Systems, by immunoturbidimetry with the TurbiTime System and by radial immunodiffusion (RID) with Partigen plates.
Composition	Pooled human sera	Same
Reagent Preparation	Liquid, Ready to use	Same
Concentration Range	Low, Medium and High	Same

Differences		
Item	Device	Predicate
Analytes	C3 complement (C3), C4	IgG, IgG1, IgG2, IgG3,

Differences		
Item	Device	Predicate
	complement (C4), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin M (IGM), and Prealbumin (PREALB) methods.	IgG4, IgA, IgM, IgE, C3c, C4, transferrin, albumin, α_1-antitrypsin, α_2-macroglobulin, haptoglobulin, α_1-acid glycoprotein, prealbumin, hemopexin, ceruloplasmin, retinol binding protein, Ig Light chain kappa, Ig Light chain lambda, soluble transferrin receptor, ferritin, β_2-microglobulin and total protein.
Instrument system	Dimension Vista® System	BN Systems and the TurbiTime System
Stability Open	days 2-8ºC	14 days 2-8ºC

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

CLSI Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline: EP5-A, CLSI Interference Testing in Clinical Chemistry; Approved Guideline EP7-A2.

L. Test Principle:

Polystyrene particles coated with antibodies specific to human IgE are aggregated when mixed with samples containing IgE. These aggregates scatter a beam of light passed through a sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility: Precision testing was done in accordance with CLSI Approved Guideline EP5-A2. Controls (PROT1 CON L, M, and H) and six samples (4 derived from serum pools and 2 derived from plasma pools), representing IgE concentrations across the measuring range and near the clinical decision points, were analyzed in duplicate, for 20 days, two times per day. The repeatability and within-lab standard deviations (SD) and percent coefficient of variation (% CV) were calculated. Repeatability imprecision was $\leq$3.5%, and within-lab imprecision was $\leq$7.0%.

Material	Mean IU/mL	Repeatability		Within-Lab	
		SD	%CV	SD	%CV
PROT1 CON L	52.1	1.7	3.3	3.6	7.0
PROT1 CON M	187.6	4.9	2.6	10.2	5.4
PROT1 CON H	449.4	10.8	2.4	25.7	5.7

Material	Mean IU/mL	Repeatability		Within-Lab	
		SD	%CV	SD	%CV
Serum pool	15.7	0.2	1.3	0.3	1.8
Serum pool	16.9	0.2	1.1	0.3	1.6
Serum pool	64.0	2.2	3.5	4.0	6.2
Serum pool	889.8	16.3	1.8	41.7	4.7
Plasma pool	54.2	1.7	3.2	3.0	5.6
Plasma pool	223.9	5.6	2.5	12.5	5.6

b. *Linearity/assay reportable range*: Linearity across the assay measuring range (18 - 1150 IU/mL) was confirmed by testing a calibrator with a high concentration of immunoglobulin E. The calibrator was serially diluted with System Diluent in 5, approximately two-fold increments. The range of IgE values in the study was 14.7 to 1368.7 IU/mL. Each dilution was tested in replicates of three. Data were analyzed using linear regression analysis. The acceptance criteria for confidence intervals around the slope (0.9 and 1.1) and correlation coefficient ($\geq$0.95) were met. Regression analysis of theoretical concentration versus measured concentration produced the following results:

Slope	**Intercept**	**R**	**n**
0.951	14.490	0.996	21

The method used to fit the linear regression line was Passing-Bablok. Recovery of protein reference material 2nd IRP 75/502 ranged from 98.7 – 100.6 % with a mean recovery of 100.0 %.

c. *Traceability (controls, calibrators, or method):*
The Calibrator is referenced to the second international reference preparation for human serum IgE, 2nd IRP 75/502. Detailed description of the value assignments for Calibrator and Controls was provided.

d. *Detection limit:*
Analytical sensitivity was determined by assaying analyte-free System Diluent 20 times and determining the mean value plus two SDs: 0.953 IU/mL. Package insert states the limit of detection represents the lower limit of the reportable range and is reported as 3.6 IU/mL.

e. *Analytical specificity:*

i. Interference Studies: Interference testing was performed according to CLSI EP7-A2, to determine the effect of various endogenous and exogenous substances on the Dimension Vista™ IgE assay. For the following interferents, the percent bias was determined by testing a control sample without the interferent and comparing it to the value obtained from a test sample to which the potential interferent was added: bilirubin (conjugated and unconjugated, 60 mg/dL), hemoglobin (1000 mg/dL), creatinine (30 mg/dL), albumin (6 g/dL), urea (500 mg/dL), cholesterol (500 mg/dL), uric acid (20 mg/dL). Sample concentrations represented the lowest and highest clinical decision points ~15 IU/mL and ~260- 310 IU/mL. Interference (<9%) was within the acceptance criteria ±10%. Triglyceride interference

was evaluated by testing five samples containing known amount of triglyceride and comparing the results to the same sample after centrifugation. The study demonstrated that clarified samples produced the same results as original samples (% CV < 6%) but did not demonstrate that assay performance is not affected by triglycerides since the baseline IgE concentrations in these samples without triglycerides were not known. A statement that lipemic samples should be avoided was placed in the specimen handling section. Additionally, 41 potentially interfering drugs were also assayed and shown to exhibit minimal interference (<10%).

ii. Cross-reactivity with autoimmune antibodies common to other systemic autoimmune diseases was not tested.

iii. Antigen Excess: The effect of antigen excess was evaluated using a serum sample with a high concentration of IgE (above the assay range). No prozone effect was observed up to at least 34,327 IU/mL. Samples whose values exceed 1150 IU/mL using the initial 1:20 dilution are reported as "exceeds assay range" to alert the user to repeat the assay using a higher dilution.

f. Assay cut-off:

See Expected Values.

2. Comparison studies:

a. Method comparison with predicate device:

Information regarding age and clinical status of the samples are not available. The Dimension Vista™ IGE assay was compared to the Dade Behring N Latex IgE mono assay on the BN ProSpec ® System by evaluating 68 serum and 52 plasma samples with concentrations ranging from 18.2 IU/mL to 1126.5 IU/mL. Regression analysis of these results yielded the following results:

Comparative Method	Slope (95% CI)	Y-Intercept IU/mL (95% CI)	Correlation Coefficient r	n
IGE on the BN ProSpec®	1.041 (1.034-1.046)	0.151 (0.899-1.092)	0.999	120

b. Matrix comparison:

Ten matched samples of serum, EDTA, lithium heparin and sodium heparin plasma containing concentrations of IgE spanning the measuring range (25.88 to 923.73 IU/mL), were assayed and compared. Regression analysis between the four matrices yielded the following information:

% recovery vs. serum		Slope (95%CI)	Y-Intercept (IU/mL)	Correlation Coefficient	n
Lithium heparin plasma	Mean = -0.6% (Range = -6.4%-7.5%)	1.04 (1.00-1.08)	-14.31	0.998	10
Sodium heparin plasma	Mean = 1.6% (Range = -1.7%-8.0%)	1.02 (0.986-1.06)	-3.38	0.998	10

EDTA	Mean = -0.5% (Range = -6.5%-4.5%)	1.02 (0.991-1.04)	-7.93	0.999	10

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.
5. Expected values/Reference range:

Neonates	< 1.5 IU/mL
Infants in first year of life	< 15 IU/mL
Children (1 - 5 years)	< 60 IU/mL
Children (6 - 9 years)	< 90 IU/mL
Children (10 - 15 years)	< 200 IU/mL
Adults	< 100 IU/mL

These reference values were established using an EIA method in a comprehensive study (448 children, 200 adults) conducted in Europe. In clinically healthy adult subjects, IgE levels exhibit a wide distribution range and do not follow a normal distribution.
IgE concentrations in children are highly dependent on age. Adult values are achieved at about 7 to 10 years of age. Higher values occur at about 10 to 15 years of age. Concentrations of up to approximately 100 IU/mL in adults can be considered the upper limit of the reference range.

N. Proposed Labeling:

The labeling is sufficient and 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.