510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k090594

B. Purpose for Submission:
Device modification (Expanded lower measuring range)

C. Measurand:
Immunoglobulin A (IgA) and Immunoglobulin M (IgM)

D. Type of Test:
Quantitative, Nephelometry

E. Applicant:
Siemens Healthcare Diagnostic Products GmbH

F. Proprietary and Established Names:
Dimension Vista® Immunoglobulin A Flex® reagent cartridge (IGA)
Dimension Vista® Immunoglobulin M Flex® reagent cartridge (IGM)

G. Regulatory Information:
1. Regulation section:
   21 CFR § 866.5510 - Immunoglobulins A, G, M, D, and E Immunological Test System.
2. Classification:
   Class II
3. Product code:
   CFN, Method Nephelometric, Immunoglobulins (G, A, M)
4. Panel:
   Immunology (82)

H. Intended Use:
1. Intended use(s):
   Dimension Vista® IgA Flex® Reagent Cartridge:
   The IgA method is an *in vitro* diagnostic test for the quantitative measurement of Immunoglobulin A in human serum and heparinized plasma by means of nephelometry on the Dimension Vista® System. Measurements of IgA aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.
   Dimension Vista® IGM Flex® reagent cartridge:
   The IgM method is an *in vitro* diagnostic test for the quantitative measurement of Immunoglobulin M in human serum and heparinized plasma by means of nephelometry on the Dimension Vista® System. Measurements of IgM aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.
2. Indication(s) for use:
   Same as Intended Use
3. Special conditions for use statement(s):
   For prescription use only.
4. Special instrument requirements:
   Dimension Vista Integrated System® (k051087)

I. Device Description:

Dimension Vista® System IgA Flex® reagent cartridge carton contains 2 cartridges (12 wells per cartridge) with rabbit polyclonal antiserum to human IgA, phosphate buffer and polyethylene glycol. All reagents are liquid and ready to use

Dimension Vista® System IgM Flex® reagent cartridge carton contains 2 cartridges (12 wells per cartridge) with rabbit polyclonal antiserum to human IgM, phosphate buffer and polyethylene glycol. All reagents are liquid and ready to use

J. Substantial Equivalence Information:

1. Predicate device name(s):
   N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) Assay
2. Predicate 510(k) number(s):
   k042735
3. Comparison with predicate:
   Dimension Vista® System IGA:

Similarities		
Item	Device	Predicate
Intended Use	Aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	Same
Methodology	Nephelometry	Same
Storage Conditions	+ 2-8°C	Same
Standardization	Traceable to IFCC/BCR/CAP CRM 470	Same
Antibody	Rabbit polyclonal	Same
Components	Controls and Calibrator are sold separately	Same

Differences		
Item	Device	Predicate
Analyte	IgA	IgG, IgA and IgM
Sample types	Serum, lithium and sodium heparin plasma	Serum and plasma (EDTA, heparin)
Reportable range	0.063 – 7.5 g/L	0.06 – 8.0 g/L
Instrument	VISTA® systems	BN™ systems

N Antiserum to Human IgM

Similarities		
Item	Device	Predicate
Intended Use	Aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	Same

Similarities		
Item	Device	Predicate
Methodology	Nephelometry	Same
Storage Conditions	+2-8°C	Same
Standardization	Traceable to IFCC/BCR/CAP CRM 470	Same
Reportable range	0.053-6.40 g/L	Same
Antibody	Rabbit polyclonal	Same
Components	Controls and Calibrator are sold separately	Same

Differences		
Item	Device	Predicate
Analyte	IgM	IgA, IgG and IgM
Sample types	Serum, lithium and sodium heparin plasma	Serum and plasma (EDTA, heparin)
Instrument	VISTA® systems	BN™ systems

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

CLSI/NCCLS Standards:

EP5-A2: Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition

EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline

EP9-A2: Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline – Second Edition

EP17-A: Protocol for Determination of Limits of Detection and Limits of Quantitation

Guidance Documents:

Draft Guidance Document for 510(k) Submission of Immunoglobulins A, G, M, D, and E Immunoglobulin System In Vitro Devices

L. Test Principle:

Proteins contained in human body fluids form immune complexes in an immunochemical reaction with specific antibodies. These complexes scatter a beam of light passed through the 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:*

   Reproducibility testing was performed in accordance with CLSI EP5-A2, using ANOVA method. Specimens at each level were analyzed in duplicate, twice a day, for 20 days, (n=80).

Dimension Vista IgA
To assess precision of the extended lower assay range, two low serum pool samples (0.09 g/L and 0.22 g/L) were evaluated. Precision results were summarized below:

| Material | Mean | | Standard Deviation mg/dL [g/L] (% CV) | | | | | |
	mg/dL	[g/L]	Repeatability			Within-Lab		
Serum pool low	9.0	[0.09]	0.2	[0.002]	(2.5)	0.3	[0.003]	(2.9)
Serum pool low	22.0	[0.22]	0.3	[0.003]	(1.5)	0.4	[0.004]	(1.7)

Dimension Vista IgM
To assess precision of the extended lower assay range, two low serum pool samples (0.093 g/L and 0.176 g/L) were evaluated. Results are summarized below:

| Material | Mean | | Standard Deviation mg/dL [g/L] (% CV) | | | | | |
	mg/dL	[g/L]	Repeatability			Within-Lab		
Serum pool low	9.3	[0.093]	0.2	[0.002]	(1.9)	0.2	[0.002]	(2.0)
Serum pool low	17.6	[0.176]	0.4	[0.004]	(2.3)	0.4	[0.004]	(2.5)

b. *Linearity/assay reportable range:*
Data were analyzed in accordance to CLSI EP06-A.
Linearity across the lower extended range was confirmed by testing one human serum sample containing 1.42g/L IgA and one human serum sample containing 0.42g/L IgM. Each sample was serially diluted 12 times. Each dilution was tested in replicates of five. All dilutions met the acceptance criteria of 15% or less difference between the measured and expected concentrations.
The IgA new extended range is 0.063 g/L to 7.50 g/L
The IgM new extended range is 0.053 g/L to 6.40 g/L

Hook Effect:
Same as k061338 (IgA) and k061845 (IgM).
c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Same as k061338 (IgA) and k061845 (IgM)
d. *Detection limit:*
Data were analyzed according to EP17-A with allowable total error of 30%.
The Limit of Quantitation (LOQ) is the lowest amount of analyte that can be quantitatively determined within a defined total error. The value was calculated as the mean value of fifteen replicates of three human serum samples and sample diluent. The Limit of Quantitation (LoQ) was determined to be 0.063 g/L for IgA and 0.053 g/L for IgM.
e. *Analytical specificity:*
Same as k061338 (IgA) and k061845 (IgM).
f. *Assay cut-off:*
Not applicable.

2. Comparison studies:
   a. *Method comparison with predicate device:*
      The method comparison studies for both Flex cartridges were done according to EP9-A2. To support the extended range, the Dimension Vista® IgA and IgM assays were compared to N Antiserum to Human IgA and N Antiserum to Human IgM, respectively, on the BN ProSpec® System. Serum samples at the extended low end of the assay range with concentrations ranging from 0.062 to 0.246 g/L (IgA) and 0.052 to 0.200 g/L (IgM). Regression analysis of these results yielded the following equations:

Dimension Vista	n	Slope (95%CI)	Intercept (g/L) (95%CI)	Correlation Coefficient r	Correlation Coefficient r^2
IgA	28	1.000 (1.000, 1.000)	0.000 (0.000, 0.000)	0.992	0.983
IgM	26	1.023 (0.967, 1.122)	0.004 (-0.004, 0.008)	0.989	0.979

   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:
   IgA and IgM data were provided in original 510(k) submissions k061338 and k061845 respectively.
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.