510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k081161

B. Purpose for Submission:
Urine sample matrix is added to existing devices. In addition, a pre-reaction step is added to modify the cerebrospinal fluid assay.

C. Measurand:
Immunoglobulin IgG

D. Type of Test:
Quantitative, Nephelometry

E. Applicant:
Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:
Dimension Vista® System Immunoglobulin G Flex® Reagent Cartridge
Dimension Vista® Protein 1 Calibrator
Dimension Vista® Protein 3 Control

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CFN: Method Nephelometric, Immunoglobulins (G, A, M)	Class II, Devices	21 CFR § 866.5510, Immunoglobulins A, G, M, D, and E Immunological test system.	Immunology (82)
JIX: Calibrator, Multi-analyte Mixture	Class II, Calibrator	21 CFR § 862.1150, Calibrator	Chemistry (75)
JJY: Multi-analyte Controls, All kinds (Assayed and Unassayed)	Class I, Quality Control Material	21 CFR § 862.1660, QC material (Assayed and Unassayed	Chemistry (75)

H. Intended Use:

1. Intended use(s):
Dimension Vista® System Immunoglobulin G Flex® reagent cartridge:
The IGG method is an *in vitro* diagnostic test for the quantitative measurement of immunoglobulin G in human serum, heparinized plasma, cerebrospinal fluid (CSF) and urine on the Dimension Vista® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

Dimension Vista® System Protein 1 Calibrator (PROT1 CAL):
PROT1 CAL is an *in vitro* diagnostic product for the calibration of the Dimension Vista® System for: α_1 -Acid Glycoprotein (A1AG), α_1 -Antitrypsin (A1AT), β_2-Microglobulin

(B2MIC), C3 Complement (C3), C4 Complement (C4),Ceruloplasmin (CER), Haptoglobin (HAPT), Hemopexin (HPX), Homocysteine (HCYS), Immunoglobulin A (IgA), Immunoglobulin E (IgE), Immunoglobulin G (IgG) [serum/ plasma], (IgG-C) [cerebrospinal fluid], (IgG-U) [urine], Immunoglobulin G Subclass 1 (IgG1), Immunoglobulin G Subclass 2 (IgG2), Immunoglobulin G Subclass 3 (IgG3), Immunoglobulin G Subclass 4 (IgG4), Immunoglobulin M (IGM), Prealbumin (PREALB), Retinol Binding Protein (RBP), soluble Transferrin Receptor (STFR), and Transferrin (TRF).

Dimension Vista® System Protein 3 Control (PROT3 CON):
PROT3 CON is an assayed, low level intralaboratory quality control for assessment of precision and analytical bias on the Dimension Vista® System in the determination of α_1-Microglobulin(A1MIC), specialty Albumin (sALB)*, Immunoglobulin G (IgG -C)*, Immunoglobulin U (IgG -U)** and Microalbumin (MALB).
* For Cerebrospinal fluid (CSF)
**For urine

2. Indication(s) for use:
   Same an Intended Use.
3. Special conditions for use statement(s):
   For Prescription only.
4. Special instrument requirements:
   Dimension Vista® Analyzer (k051087)

I. Device Description:

Dimension Vista® System Immunoglobulin G Flex® reagent cartridge carton contains 2 cartridges (12 wells/cartridge). Wells 1 through 8 contain buffers and polyethylene glycol. Wells 9 through 12 contain liquid rabbit polyclonal antisera to human IgG. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 1 Calibrator carton contains 6 vials with 2 mL per vial, with multi-analyte, liquid human serum based product containing A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, IgA, IgE, IgG, IgM, PREALB, RBP, STRF, TRF, IgG1, IgG2, IgG3, IgG4 and HCYS. Reagent is in ready-to-use liquid form.

Dimension Vista® System Protein 3 Control carton contains 4 vials with 1 mL per vial, with multi-analyte, polygeline and rabbit albumin based product containing urinary α_1-A1AG and serum albumin and IgG of human origin. Reagent is in lyophilized form.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Beckman Coulter IMMAGE® Immunochemistry System Urine Immunoglobulin G
   N Antisera to Human Immunoglobulins on the BN Systems (IgG, IgA, and IgM)
   Dade Behring Dimension Vista® System Protein 1 Calibrator
   Dade Behring Dimension Vista® System Protein 3 Control
2. Predicate 510(k) number(s):
   k951635 (Beckman Coulter IMMAGE®)
   k042735 (N Antisera on the BN Systems)

k073561 (Dade Behring Dimension Vista Calibrator, Control)

3. Comparison with predicates:
   To demonstrate correlation and equivalent performance between the new device and predicate Beckman Coulter IMMAGE® Immunochemistry System Urine Immunoglobulin G for urine sample matrix:

Similarities		
Item	New Device	Predicate Device
Technology	Nephelometric	Same
Storage conditions	Refrigerate at 2-8ºC until expired	Same
Components	Calibrators and Controls are sold separately	Same

Differences		
Item	New Device	Predicate
Intended Use/Indication for Use: Reagent IgG Antisera	Dimension Vista™ IgG Flex® reagent cartridge: The IgG method is an *in vitro* diagnostic test for the quantitative measurement of Immunoglobulin G in human serum, heparinized plasma, cerebrospinal fluid (CSF) and urine on the Dimension Vista™ System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	IGU reagent, when used in conjunction with IMMAGE® Immunochemistry Systems and Urine Protein Calibrator, is intended for the quantitative determination of Urine Immunoglobulin G (IGU) in human urine by rate nephelometry.
Sample type	Serum, heparinized plasma and CSF	Urine only
Analyzer	Dimension Vista® System	IMMAGE ® Immunochemistry Systems
Measuring ranges	Serum/ plasma: 0.14-4.0 g/dL Undiluted CSF: 0.44-12.3 mg/dL Urine: 0.44-5.0 mg/dL	Urine: 0.3-6.0 mg/dL
IgG antisera mammal source	Rabbit polyclonal	Processed goat sera

To demonstrate correlation and equivalent performance between the new device and predicate N Antisera to Human Immunoglobulins on the BN Systems (IgG, IgA, and IgM) for the addition of a pre-reaction step to the IGG-C assay:

Similarities		
Item	New Device	Predicate Device
Technology	Nephelometric	Same
IgG antisera mammal source	Rabbit polyclonal	Same
Storage conditions	Refrigerate at 2-8ºC until expired	Same
Components	Calibrators and controls are sold separately	Same
Expected values	≤ 3.40 mg/dL	Same

Differences		
Item	New Device	Predicate
Intended Use/Indication for Use: Reagent IgG Antisera	Dimension Vista™ IgG Flex® reagent cartridge: The IgG method is an *in vitro* diagnostic test for the quantitative measurement of Immunoglobulin G in human serum, heparinized plasma, cerebrospinal fluid (CSF) and urine on the Dimension Vista™ System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.	*In vitro* diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA, and IgM) in human serum, heparinized and EDTA plasma as well as IgG in cerebrospinal fluid (CSF) by means of immunonephelometry on the BN Systems.
Sample type	Serum, plasma (lithium heparin), CSF and urine	Serum, plasma (EDTA; lithium heparin) and CSF
Measuring ranges	Undiluted CSF: 0.44-12.3 mg/dL	Undiluted CSF: 0.36-11.5 mg/dL
Analyzer	Dimension Vista® System	BN™ Systems

To demonstrate correlation and equivalent performance between the new device and predicate Dimension Vista® System Protein 1 Calibrator and Protein 3 Control to include IGG-U (IGG in urine):

Similarities		
Item	New Device	Predicate Device
Calibrator material source	Human serum	Same
Control material source	Human serum and rabbit albumin	Same
International Reference standard material	Traceable to ERM® DA 470 (CRM 470)	Same
Storage conditions	Refrigerate at 2-8ºC until expired	Same

Differences		
Item	New Device	Predicate
Intended Use/Indication for Use: Calibrator	The PROT 1 CAL is an *in vitro* diagnostic product for the calibration of the Dimension Vista® System for: A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, HCYS, IgA, IgE, IgG [serum/ plasma], (IgG-C) [cerebrospinal fluid], and (IgG-U) [urine], IgG1, IgG2, IgG3, IgG4, IgM, PREALB, RBP, STFR and TRF	The PROT 1 CAL is an *in vitro* diagnostic product for the calibration of the Dimension Vista® System for: A1AG, A1AT, B2MIC, C3, C4, CER, HAPT, HPX, HCYS, IgA, IgE, IgG [serum/ plasma] and (IgG-C) [cerebrospinal fluid], IgG1, IgG2, IgG3, IgG4, IgM, PREALB, RBP, STFR and TRF
Control	PROT3 CON is an assayed, low level intralaboratory quality control for assessment of precision and analytical bias on the Dimension Vista® System in the determination of A1MIC, sALB*, IgG-C*, IgG-U**, and MALB. *For CSF; **For urine	PROT3 CON is an assayed, low level intralaboratory quality control for assessment of precision and analytical bias on the Dimension Vista® System in the determination of A1MIC, sALB*, IgG-C* and MALB. *For CSF

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

Standard Document:
CLSI/NCCLS, EP 9-A2: Method Comparison
CLSI/NCCLS, EP 5-A2: Precision Performance of Quantitative Measurement
CLSI/NCCLS, EP 7-A: Interference Testing
CLSI/NCCLS, EP 6-A: Linearity of Quantitative Measurement
Guidance Document:
OIVD/ DIHD Guidance Document Number 785: 510(k) Submission for IgA,G,M,D,E Immunological System IVD (9/1/1992)
OIVD Guidance Document Number 2231: For Industry and FDA Staff: Assayed and Unassayed Control Material (6/7/2007)

L. Test Principle:

Proteins contained in human body fluids react with specific antibodies in the reagent, to form immune complexes in an immunochemical reaction. These complexes in the reaction mixture cause the scatter of a beam of light passed through the samples. The intensity of the scattered light is proportional to the concentration of IgG 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:
   For urine:

Reproducibility testing was done in accordance with CLSI document EP5-A2. The intra-assay reproducibility was determined by testing two samples in duplicate twice a day for 20 days. The samples included two human source urine pools (1.0 mg/dL and 4.4 mg/dL), and one Protein 3 control (2.3 mg/dL). The urine pools had %CV of 1.62% and 2.22%; Protein 3 control 4.66%.

The inter-assay reproducibility was determined by testing the same three samples in duplicate twice a day for 20 days. The urine pools had %CV of 7.64% and 3.55%; Protein 3 control 6.71%. The data are summarized below:

Material	Mean	Intra-assay		Inter-assay	
		SD	%CV	SD	%CV
Urine pool low	1.0 mg/dL	0.0159	1.62	0.0751	7.64
Urine pool high	4.4 mg/dL	0.0996	2.22	0.1549	3.55
PROT 3 CON	2.3 mg/dL	0.1047	4.66	0.1508	6.71

For CSF:
Reproducibility testing was done in accordance with CLSI document EP5-A2. The intra-assay reproducibility was determined by testing two samples in duplicate twice a day for 20 days. The samples included two human source CSF pools (1.1 mg/dL and 11.4 mg/dL). Both CSF pools had %CV of 2.73%.

The inter-assay reproducibility was determined by testing the same two samples in duplicate twice a day for 20 days. The CSF pools had %CV of 3.99% and 3.72%. The data are summarized below:

Material	Mean	Intra-assay		Inter-assay	
		SD	%CV	SD	%CV
CSF pool 1	1.1 mg/dL	0.0293	2.73	0.0428	3.99
CSF pool 2	11.4 mg/dL	0.3105	2.73	0.4224	3.72

b. *Linearity/assay reportable range:*
For Urine:
Linearity across the assay range was confirmed by testing a human urine sample with high concentration (51.7 mg/L) of IgG. This sample was serially diluted 11 times with System Diluent down to the lower detectable measuring range (4.88 mg/L). Each dilution was tested in replicates of five. Data were analyzed in accordance to CLSI EP06-A and EP17-A. Percent recovery was calculated using the formula: (Mean of test/expected concentration) x 100. All dilutions met the acceptance criteria of 85 to 115%. The linear regression analysis was performed. Data showed a regression equation y = -0.542055+1.028992, r^2=0.999591.

Reportable range for IgG-U device was set at 4.4-50 mg/L.

For CSF:
Linearity across the assay range was confirmed by testing a human CSF sample with

high concentration (134 mg/L) of IgG. This sample was serially diluted 13 times with System Diluent down to the lower detectable measuring range (6.63 mg/L). Each dilution was tested in replicates of four or five. Data were analyzed in accordance to CLSI EP06-A and EP17-A. Percent recovery was calculated using the formula: (Mean of test/expected concentration) x 100. All dilutions met the acceptance criteria of 85 to 115%. The linear regression analysis was performed. Data showed a regression equation y = -0.244353+0.9993525, r^2=0.999112.

Reportable range for IgG-CSF device was set at 4.4-123 mg/L.

Antigen Excess Effect:
The possibility of antigen excess occurring when using the device was evaluated with urine and CSF samples above the assay range. The samples were analyzed on the Dimension Vista™ instrument, indicating no antigen excess effect up to 5200 mg/L for CSF and 5770 mg/L for urine.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The calibrator and controls are traceable to the reference material ERM® DA 470 (CRM 470).
Stability
The expiration date claims for the reagents are as follows:
Unopened reagent cartridges and closed vials:
Dimension Vista™ IgG Flex® reagent cartridge (IGG) – 24 months
Dimension Vista™ Protein 1 Calibrator – 24 months
Dimension Vista™ Protein 3 Control – 24 months
On-board Instrument products:
Dimension Vista™ IgG Flex® reagent sealed wells – 90 days
Dimension Vista™ IgG Flex® open well reagent cartridge – 21 days
Dimension Vista™ Protein 1 Calibrator open vial – 9 days
Dimension Vista™ Protein 3 Control open vial – 14 days

d. *Detection limit:*
Detection limit (4.4 mg/L) represents the lower limit of the reportable range of urine IgG. The analytical sensitivity is defined as the minimal detectable level of analyte, which can be distinguished from zero. The value was calculated as the mean value of fifteen replicates of three urine samples and system diluent. It was determined to be 4.47 mg/L.

e. *Analytical specificity:*
Interference testing was performed according to CLSI document EP7-A2. No significant interference for urine sample matrix was observed in the presence of the following interferents: Hemoglobin up to 115 mg/dL; Bilirubin (unconjugated) up to 2 mg/dL; Bilirubin (conjugated) up to 2.4 mg/dL.
No significant interference for CSF sample matrix was observed in the presence of the following interferents:
Hemoglobin up to 1000 mg/dL; Bilirubin (unconjugated) up to 60 mg/dL; Bilirubin (conjugated) up to 60 mg/dL

Non-interfering substances section of the device package insert provides a list of 37 drugs and other exogenous substances that do not interfere with the assay at the concentrations indicated for CSF sample matrix and 14 for urine sample matrix.

f. Assay cut-off:
Not applicable.

2. Comparison studies:
   a. Method comparison with predicate device:
   For Urine:
   The table below shows the comparison of 53 urine samples ranging from 4.7-49.4mg/L IgG that were tested with the Dimension Vista™ IgG assay and the predicate Beckman Coulter IMMAGE® Immunochemistry Systems Urine Immunoglobulin G assay. Results were analyzed by Passing-Bablok regression analysis and are summarized below:

	N	Slope (95% CI)	Intercept (95%CI)	R
Dimension Vista™ vs. Beckman Coulter IMMAGE®	53	1.035 (0.977, 1.105)	0.23 (-0.748, 0.916)	0.976

   For CSF:
   The table below shows the comparison of 104 CSF samples ranging from 5.3-116mg/L IgG that were tested with the Dimension Vista™ IgG assay and the predicate BNProSpec® System. Results were analyzed by Passing-Bablok regression analysis and are summarized below:

	N	Slope (95% CI)	Intercept (95%CI)	R
Dimension Vista™ vs. BN ProSpec® System	104	0.956 (0.940, 0.974)	0.392 (-0.874, 0.075)	0.994

   b. Matrix comparison:
   Not applicable.

3. Clinical studies:
   a. Clinical Sensitivity and specificity:
   Not applicable.
   b. Other clinical supportive data (when a. is not applicable):
   Not applicable.

4. Clinical cut-off:
   Not applicable.

5. Expected values/Reference range:
   A literature reference was used for the IGG Urine expected value of <9.60 mg/L (Hofmann W, Guder WG. A diagnostic programme for quantitative analysis of proteinuria. J Clin Chem Clin Biochem 1989; 27:589-600). This was confirmed by performing a Reference Interval transference study.

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.