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:

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Classification</th>
<th>Regulation Section</th>
<th>Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIX: Calibrator, Multi-analyte Mixture</td>
<td>Class II, Calibrator</td>
<td>21 CFR § 862.1150, Calibrator</td>
<td>Chemistry (75)</td>
</tr>
<tr>
<td>JJY: Multi-analyte Controls, All kinds (Assayed and Unassayed)</td>
<td>Class I, Quality Control Material</td>
<td>21 CFR § 862.1660, QC material (Assayed and Unassayed)</td>
<td>Chemistry (75)</td>
</tr>
</tbody>
</table>

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: $\alpha_1$-Acid Glycoprotein (A1AG), $\alpha_1$-Antitrypsin (A1AT), $\beta_2$-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 α1-
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 as 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, STFR, 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 α1-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)
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:

<table>
<thead>
<tr>
<th>Similarities</th>
<th>New Device</th>
<th>Predicate Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology</td>
<td>Nephelometric</td>
<td>Same</td>
</tr>
<tr>
<td>Storage conditions</td>
<td>Refrigerate at 2-8ºC until expired</td>
<td>Same</td>
</tr>
<tr>
<td>Components</td>
<td>Calibrators and Controls are sold separately</td>
<td>Same</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Differences</th>
<th>New Device</th>
<th>Predicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intended Use/Indication for Use: Reagent IgG Antisera</td>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Sample type</td>
<td>Serum, heparinized plasma and CSF</td>
<td>Urine only</td>
</tr>
<tr>
<td>Analyzer</td>
<td>Dimension Vista® System</td>
<td>IMMAGE® Immunochemistry Systems</td>
</tr>
<tr>
<td>Measuring ranges</td>
<td>Serum/ plasma: 0.14-4.0 g/dL</td>
<td>Urine: 0.3-6.0 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Undiluted CSF: 0.44-12.3 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urine: 0.44-5.0 mg/dL</td>
<td></td>
</tr>
<tr>
<td>IgG antisera mammal source</td>
<td>Rabbit polyclonal</td>
<td>Processed goat sera</td>
</tr>
</tbody>
</table>

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

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

### Differences

<table>
<thead>
<tr>
<th>Item</th>
<th>New Device</th>
<th>Predicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intended Use/Indication for Use: Reagent IgG Antisera</td>
<td>Dimension Vista™ IgG Flex® reagent cartridge: The IgG method is an <em>in vitro</em> 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.</td>
<td><em>In vitro</em> 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.</td>
</tr>
<tr>
<td>Sample type</td>
<td>Serum, plasma (lithium heparin), CSF and urine</td>
<td>Serum, plasma (EDTA; lithium heparin) and CSF</td>
</tr>
<tr>
<td>Measuring ranges</td>
<td>Undiluted CSF: 0.44-12.3 mg/dL</td>
<td>Undiluted CSF: 0.36-11.5 mg/dL</td>
</tr>
<tr>
<td>Analyzer</td>
<td>Dimension Vista® System</td>
<td>BN™ Systems</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Item</th>
<th>New Device</th>
<th>Predicate Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibrator material source</td>
<td>Human serum</td>
<td>Same</td>
</tr>
<tr>
<td>Control material source</td>
<td>Human serum and rabbit albumin</td>
<td>Same</td>
</tr>
<tr>
<td>International Reference standard material</td>
<td>Traceable to ERM® DA 470 (CRM 470)</td>
<td>Same</td>
</tr>
<tr>
<td>Storage conditions</td>
<td>Refrigerate at 2-8ºC until expired</td>
<td>Same</td>
</tr>
</tbody>
</table>
### Differences

<table>
<thead>
<tr>
<th>Item</th>
<th>New Device</th>
<th>Predicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intended Use/Indication for Use: Calibrator</td>
<td>The PROT 1 CAL is an <em>in vitro</em> 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</td>
<td>The PROT 1 CAL is an <em>in vitro</em> 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</td>
</tr>
<tr>
<td>Control</td>
<td>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</td>
<td>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</td>
</tr>
</tbody>
</table>

**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:**

**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:

<table>
<thead>
<tr>
<th>Material</th>
<th>Mean</th>
<th>SD</th>
<th>%CV</th>
<th>SD</th>
<th>%CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine pool low</td>
<td>1.0 mg/dL</td>
<td>0.0159</td>
<td>1.62</td>
<td>0.0751</td>
<td>7.64</td>
</tr>
<tr>
<td>Urine pool high</td>
<td>4.4 mg/dL</td>
<td>0.0996</td>
<td>2.22</td>
<td>0.1549</td>
<td>3.55</td>
</tr>
<tr>
<td>PROT 3 CON</td>
<td>2.3 mg/dL</td>
<td>0.1047</td>
<td>4.66</td>
<td>0.1508</td>
<td>6.71</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Material</th>
<th>Mean</th>
<th>SD</th>
<th>%CV</th>
<th>SD</th>
<th>%CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF pool 1</td>
<td>1.1 mg/dL</td>
<td>0.0293</td>
<td>2.73</td>
<td>0.0428</td>
<td>3.99</td>
</tr>
<tr>
<td>CSF pool 2</td>
<td>11.4 mg/dL</td>
<td>0.3105</td>
<td>2.73</td>
<td>0.4224</td>
<td>3.72</td>
</tr>
</tbody>
</table>

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, r²=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  |
      |---|----------------|-------------------|----|
      | 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  |
      |---|----------------|-------------------|----|
      | 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.