

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

k082503

**B. Purpose for Submission:**

New device

**C. Measurand:**

Immunoglobulins, Kappa ( $\kappa$ ) light chains and Lambda ( $\lambda$ ) light chains

**D. Type of Test:**

Quantitative, Nephelometry

**E. Applicant:**

Siemens Healthcare Diagnostics

**F. Proprietary and Established Names:**

Dimension Vista® KAPPA Flex® reagent cartridge

Dimension Vista® LAMBDA Flex® reagent cartridge

Dimension Vista® Protein 1 Calibrator

Dimension Vista® Protein 1 Control L

Dimension Vista® Protein 1 Control M and H

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.5550, Immunoglobulin (Light Chain Specific) Immunological Test system

21 CFR 862.1150 - Calibrator

21 CFR 862.1660 - Quality Control Material (Assayed and Unassayed)

2. Classification:

Class II, Devices and Calibrator

Class I, Quality Control Material

3. Product code:

DEH - lambda, antigen, antiserum, control

DFH - kappa, antigen, antiserum, control

JIX- Calibrator, multi-analyte mixture

JJY- Multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

Immunology (82) and Clinical Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

Dimension Vista® KAPPA Flex® reagent cartridge:

The KAPPA method is an in vitro diagnostic test for the quantitative measurement of immunoglobulin light chains, type kappa in human serum and plasma on the Dimension Vista® Systems. Measurements of the various amounts of the different types of light chains aid in the diagnosis of multiple myeloma (cancer of antibody-forming cells), lymphocytic neoplasms (cancer of lymphoid tissue), Waldenstrom's macroglobulinemia (increased production of large immunoglobulins), and connective tissue diseases such as rheumatoid arthritis or systemic lupus erythematosus in conjunction with other laboratory and clinical

findings.

Dimension Vista® LAMBDA Flex® reagent cartridge:

The LAMBDA method is an in vitro diagnostic test for the quantitative measurement of immunoglobulin light chains, type lambda in human serum and plasma on the Dimension Vista® Systems. Measurements of the various amounts of the different types of light chains aid in the diagnosis of multiple myeloma (cancer of antibody-forming cells), lymphocytic neoplasms (cancer of lymphoid tissue), Waldenstrom's macroglobulinemia (increased production of large immunoglobulins), and connective tissue diseases such as rheumatoid arthritis or systemic lupus erythematosus in conjunction with other laboratory and clinical findings.

Dimension Vista® PROT 1 CAL:

PROT1 CAL is an in vitro diagnostic product for the calibration of the Dimension Vista® Systems for: a1-Acid Glycoprotein (A1AG), a1-Antitrypsin (A1AT), a2 -macroglobulin (A2MAC), b2 -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, IGG-C\*, IGG-U\*\*), Immunoglobulin G subclass 1 (IGG1), Immunoglobulin G subclass 2 (IGG2), Immunoglobulin G subclass 3 (IGG3), Immunoglobulin G subclass 4 (IGG4), Immunoglobulin light chains type kappa (KAPPA), Immunoglobulin light chains type lambda (LAMBDA), Immunoglobulin (IGM), Prealbumin (PREALB), Retinol Binding Protein (RBP), soluble Transferrin Receptor (STFR), Transferrin (TRF)

\*For cerebrospinal fluid

\*\* For urine

Dimension Vista® Protein 1 Control L:

PROT1 CON L is an assayed, low level, intra-laboratory quality control for assessment of precision and analytical bias on the Dimension Vista® Systems in the quantitative determination of: a1-Acid Glycoprotein (A1AG), a1-Antitrypsin (A1AT), a2 -Macroglobulin (A2MAC), C3 Complement (C3), C4 Complement (C4), Ceruloplasmin (CER), Haptoglobin (HAPT), Hemopexin (HPX), Homocysteine (HCYS), Immunoglobulin A (IGA), Immunoglobulin E (IGE), Immunoglobulin G (IGG), Immunoglobulin G subclass 1 (IGG1), Immunoglobulin G subclass 2 (IGG2), Immunoglobulin G subclass 3 (IGG3), Immunoglobulin G subclass 4 (IGG4), Immunoglobulin light chains type kappa (KAPPA), Immunoglobulin light chains type lambda (LAMBDA), Immunoglobulin M (IGM), Prealbumin (PREALB), Retinol Binding Protein (RBP), specialty Albumin (sALB\*), soluble Transferrin Receptor (STFR) and Transferrin (TRF).

\*For serum and plasma

Dimension Vista® Protein 1 Control M and H:

PROT1 CON M and PROT1 CON H are assayed, mid-level and high level,

intralaboratory quality controls for assessment of precision and analytical bias on the Dimension Vista® System in the quantitative determination of: a2-Acid Glycoprotein (A1AG), a1 -Antitrypsin (A1AT), a2-Macroglobulin (A2MAC), b2 - 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), Immunoglobulin G Subclass 1 (IGG1), Immunoglobulin G subclass 2 (IGG2), Immunoglobulin G subclass 3 (IGG3), Immunoglobulin G subclass 4 (IGG4), Immunoglobulin light chains type kappa (KAPPA), Immunoglobulin light chains type lambda (LAMBDA), Immunoglobulin M (IGM), Prealbumin (PREALB), Retinol Binding Protein (RBP), soluble Transferrin Receptor (STFR), specialty Albumin (sALB) and Transferrin (TRF).

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® Systems

#### **I. Device Description:**

Dimension Vista® System Kappa and Lambda Flex reagent consists of 2 Flex cartridges per carton. Each cartridge consists of reagents contained in 12 segregated wells in a plastic cartridge. Wells 1 through 4 contain buffers and polyethylene glycol. Wells 5 through 10 are empty and available for use by the instrument for other assays, and wells 11 and 12 contain liquid rabbit polyclonal antisera to human Immunoglobulin/L-chains, type kappa or lambda, respectively.

Dimension Vista® System Protein 1 Calibrator , Protein 1 Control L, and Protein 1 Control M and H each consists of six 2.0 ml vials, respectively.

#### **J. Substantial Equivalence Information:**

1. Predicate K numbers and device name(s):  
k860894 N Antisera to Human Immunoglobulin/L-chains  
k012470 N Protein Standard SL  
k012468 N/T Protein Control SL
2. Comparison with predicate:

| <b>Similarities:</b> |  |           |
|----------------------|--|-----------|
| Item                 | Device   | Predicate |
| Intended Use: Kappa  | In vitro diagnostic reagents for the quantitative measurement of immunoglobulin light chains, type kappa in human serum  | Same      |
| Intended Use: Lambda | In vitro diagnostic reagents for the quantitative measurement of immunoglobulin light chains, type lambda in human serum | Same      |
| Method               | Immunonephelometry   | Same      |

| <b>Similarities:</b> |                                       |           |
|----------------------|---------------------------------------|-----------|
| Item                 | Device                                | Predicate |
| Measurement          | Quantitative                          | Same      |
| Capture Antibody     | Rabbit Polyclonal                     | Same      |
| Reagents             | Reagents are liquid and ready for use | Same      |

| <b>Differences:</b>  |   |   |
|----------------------|---|---|
| Item                 | Device  | Predicate   |
| Analyzer:            | Dimension Vista® Systems                          | BN Prospec® System  |
| Sample type:         | Human serum and plasma.                           | Serum only  |
| Stability (On board) | Sealed: 90 days<br>Open: 21 days for wells 1 - 12 | Sealed: 4 weeks (+2 to +8 °C);<br>Open: 5 days at 8 hours each (maximum 40 hours) |

### PROT 1 CALIBRATOR

| <b>Similarities:</b>              |  |           |
|-----------------------------------|--|-----------|
| Item                              | Device   | Predicate |
| Intended Use: Calibrator/standard | Dimension Vista® PROT 1 CAL is an in vitro diagnostic product for the calibration of various protein methods including the KAPPA and LAMBDA methods. | Same      |
| Form                              | Liquid human serum based.  | Same      |
| Traceability                      | Protein reference: ERM®- DA470 (CRM470)  | Same      |
| Composition                       | Ready-to-use   | Same      |
| Level                             | One  | Same      |
| Storage                           | 2-8 °C   | Same      |

| <b>Differences:</b> |  |   |
|---------------------|--|---|
| Item                | Device   | Predicate   |
| Quantity            | Six 2.0 ml vials   | Three 1.0 ml vials  |
| Stability (opened)  | 9 days   | 14 days   |
| Constituents        | Dimension Vista® PROT 1 CAL contains: α1-acid glycoprotein, α1-antrypsin, α2 – macroglobulin, β2-microglobulin, C3 complement, C4 complement, ceruloplasmin, haptoglobin, hemopexin, homocysteine, immunoglobulins A, E, G, subclass 1, subclass 2, subclass 3, subclass 4, light chains kappa, light chains lambda, and M, prealbumin, retinol binding protein, soluble transferrin receptor and transferrin. | N Protein Standard SL contains: α1-acid glycoprotein, α1-antrypsin, albumin, α2 – macroglobulin, β2-microglobulin, C3 Complement, C4 complement, ceruloplasmin, haptoglobin, hemopexin, homocysteine, immunoglobulins A, E, G, subclass 1, subclass 2, subclass 3, subclass 4, light chains kappa, light chains lambda, and M, prealbumin, retinol binding protein, soluble transferrin receptor and transferrin. |

**PROT 1 CONTROLS (Low, Medium, and High)**

| <b>Similarities:</b> |  |           |
|----------------------|--|-----------|
| Item                 | Device   | Predicate |
| Intended Use:        | Dimension Vista® PROT 1 CON L, M and H are assayed inter-laboratory controls for the assessment of precision and analytical bias on automated systems. | Same      |
| Form:                | Liquid, human based material ready for use.  | Same      |
| Storage              | 2-8 °C   | Same      |

| <b>Differences:</b> |  |  |
|---------------------|--|--|
| Item                | Device   | Predicate  |
| Analyte:            | <p>Dimension Vista® PROT 1 CON L, is a low level multianalyte control containing: <math>\alpha</math>1-antrypsin, <math>\alpha</math>2 – macroglobulin, albumin, C3 Complement, C4 complement, ceruloplasmin, haptoglobin, hemopexin, homocysteine, immunoglobulins A, E, G, subclass 1, subclass 2, subclass 3, subclass 4, M, prealbumin, retinol binding protein, soluble transferrin receptor and transferrin.</p> <p><u>Dimension Vista® PROT 1 CON M and H</u> are mid and high level controls respectively containing: <math>\alpha</math>1-acid glycoprotein, <math>\alpha</math>1-antrypsin, <math>\alpha</math>2 – macroglobulin, albumin, <math>\beta</math>2-microglobulin, C3 Complement, C4 complement, ceruloplasmin, haptoglobin, hemopexin, ferritin, immunoglobulins A, E, G, subclass 1, subclass 2, subclass 3, subclass 4, light chains kappa, light chains lambda, and M, prealbumin, retinol binding protein, soluble transferrin receptor and transferrin.</p> | N Protein Controls SL L, M and H are low, mid and high level controls respectively. They are multianalyte controls containing $\alpha$ 1-acid glycoprotein, $\alpha$ 1-antrypsin, $\alpha$ 2 – macroglobulin, albumin, $\beta$ 2-microglobulin, C3 Complement, C4 complement, ceruloplasmin, haptoglobin, hemopexin, ferritin, immunoglobulins A, E, G, subclass 1, subclass 2, subclass 3, subclass 4, light chains kappa, light chains lambda, and M, prealbumin, retinol binding protein, soluble transferrin receptor and transferrin. |
| Stability (opened)  | 9 days   | 14 days  |
| Quantity            | Six 2.0 ml vials   | Three 1.0 ml vials   |

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

CLSI EP5-A2: Evaluation of Precision Performance of Clinical Chemistry

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures - A Statistical Approach.

EP09-A2 Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline

CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation

Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material

**L. Test Principle:**

Proteins contained in human body fluids form immune complexes in an immuno-chemical 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:*

Precision testing for the KAPPA and LAMBDA methods were performed using two human serum, two plasma pools, and three levels of Dimension Vista ® Protein 1 Controls, over twenty days according to CLSI/NCCLS EP5-A2, at a single site, using a single instrument, single reagent lot and two operators. On each day of testing, each sample was run in duplicate, in two separate runs. Serum and plasma pools for both methods were established at levels that encompassed approximately 15% - 85% of the analytical measuring range for each method. The serum and plasma pools with high concentrations were prepared by spiking a native pool with purified antigen.

Precision for serum: Kappa

| Material    | Mean  |        | Standard Deviation mg/dL [g/L] (% CV) |        |       |            |        |       |
|-------------|-------|--------|---------------------------------------|--------|-------|------------|--------|-------|
|             | mg/dL | [g/L]  | Repeatability                         |        |       | Within-Lab |        |       |
| PROT1 CON L | 158   | [1.58] | 2.6                                   | [0.03] | (1.6) | 4.6        | [0.05] | (2.9) |
| PROT1 CON M | 202   | [2.02] | 4.8                                   | [0.05] | (2.4) | 6.6        | [0.07] | (3.3) |
| PROT1 CON H | 307   | [3.07] | 5.2                                   | [0.05] | (1.7) | 8.8        | [0.09] | (2.9) |
| Serum pool  | 87    | [0.87] | 1.5                                   | [0.02] | (1.7) | 2.4        | [0.02] | (2.8) |
| Serum pool  | 821   | [8.21] | 14.9                                  | [0.15] | (1.8) | 23.0       | [0.23] | (2.8) |
| Plasma pool | 197   | [1.97] | 4.5                                   | [0.05] | (2.3) | 4.8        | [0.05] | (2.4) |
| Plasma pool | 326   | [3.26] | 5.9                                   | [0.06] | (1.8) | 7.3        | [0.07] | (2.2) |

Precision for serum: Lambda

| Material    | Mean  |        | Standard Deviation mg/dL [g/L] (% CV) |        |       |            |        |       |
|-------------|-------|--------|---------------------------------------|--------|-------|------------|--------|-------|
|             | mg/dL | [g/L]  | Repeatability                         |        |       | Within-Lab |        |       |
| PROT1 CON L | 86    | [0.86] | 4.2                                   | [0.04] | (4.9) | 5.1        | [0.05] | (5.9) |
| PROT1 CON M | 116   | [1.16] | 6.1                                   | [0.06] | (5.3) | 6.7        | [0.07] | (5.8) |
| PROT1 CON H | 175   | [1.75] | 8.2                                   | [0.08] | (4.7) | 9.3        | [0.09] | (5.3) |
| Serum pool  | 52    | [0.52] | 2.7                                   | [0.03] | (5.2) | 3.0        | [0.03] | (5.8) |
| Serum pool  | 345   | [3.45] | 13.9                                  | [0.14] | (4.0) | 15.6       | [0.16] | (4.5) |
| Plasma pool | 126   | [1.26] | 6.8                                   | [0.07] | (5.4) | 7.3        | [0.07] | (5.8) |
| Plasma pool | 204   | [2.04] | 7.1                                   | [0.07] | (3.5) | 8.2        | [0.08] | (4.0) |

Additional performance data for the PROT1 Controls and calibrator are available in the decision summaries for k081249 and k081161.

*b. Linearity/assay reportable range:*

Kappa: The reportable range for the Kappa method [28 - 910 mg/dL (0.28 - 9.10 g/L)] was determined, according to the CLSI EP-6-A, by serially diluting a human serum sample with an original value of 975 mg/dL (9.75 g/L) with System Diluent. Five replicates were run at each level. The observed value represents the mean of six replicates. The bias was determined at each level.

Lambda: The reportable range for the Lambda method [19 - 415 mg/dL (0.19 - 4.15 g/L)] was determined by serially diluting a human serum sample with a value of 446 mg/dL (4.46 g/L) with System Diluent according to the CLSI EP-6-A. Five replicates were run at each level. The observed values represented the mean of six replicates. The bias was determined at each level.

|        | Sample Range<br>(mg/dL) | Slope | Y-intercept<br>(mg/dL) | Correlation<br>coefficient<br>(R <sup>2</sup> ) | % Bias<br>(mean absolute) | n  |
|--------|-------------------------|-------|------------------------|---|---------------------------|----|
| Kappa  | 28 – 910                | 1.004 | - 3.2                  | 0.997   | - 5.2 to +6.7%<br>(3.1%)  | 14 |
| Lambda | 18.7 - 447              | 0.992 | - 2.3                  | 0.997   | - 3.6 to +7.5%<br>(3.7%)  | 13 |

*c. Traceability, Stability, Expected values (controls, calibrators, or methods):*

The calibrator and control are traceable to protein reference preparation ERM®-DA470 (CRM 470). The values are assigned based on the process presented by Lievens et al. Medical and Technical Usefulness of Measurement of Kappa and lambda Immunoglobulin Light Chains in Serum with an M-component” J. Clin. Chem. Clin. Biochem. Vol. 27, 1989 pp 519 – 523. The equation to determine the concentrations was developed from the percentage of each IgG subclass vs. the Ig class concentration, the ratio of relative molecular masses of the two Ig light chains vs. the total and the kappa and lambda concentration ratio within each subclass. A master calibrator is value assigned for IgG, IgA, and IgM vs. the ERM®-DA470. Commercial lot values are assigned vs. the master lot and the values are calculated according to the following equations: [kappa] = [IgG] \*0.1983 + [IgA]\*0.171 + [IgM]\*0.0975 and [lambda] = [IgG] \*0.1054 + [IgA]\*0.1206 + [IgM]\*0.0305.

*d. Detection limit:*

Limit of Quantitation (LoQ) was established using a testing protocol outlined in CLSI EP17-A Section 5.1 and a total analytical error of 30% based on precision and recovery performance of the method. Three test samples were tested at each concentration; three replicates per sample were tested per run, for each of five runs. Testing was performed in one day with a single reagent lot, calibrator lot, instrument and operator. The LoQ for Kappa was determined to be 7.0 mg/dL ( 0.07 g/L) and Lambda was determined to be 4.8

mg/dL (0.048 g/L) using the calculations described previously.

e. *Analytical specificity:*

Interference Studies:

Test samples were prepared by spiking the potential interferent into serum. Kappa concentrations ranged from 169 to 780 mg/dL (1.69 g/L to 7.80 g/L) and Lambda concentrations ranged from 168 to 368 mg/dL (1.68 to 3.68 g/L). Interference testing was performed according to CLSI/NCCLS EP7-A2 to determine the effect of various endogenous and exogenous substances on the Dimension Vista® KAPPA and LAMBDA assays. For all interferents except RF 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 had been added. A percent bias exceeding 10% was considered to be interfering.

| Analyte | Substance tested | Substance conc. (mg/dL) | Kappa (mg/dL) | Bias (%) |
|---------|------------------|-------------------------|---------------|----------|
| Kappa   | Hemoglobin       | 1000                    | 169           | +10      |
|         | (hemolysate)     |                         | 779           | +1       |
|         | Bilirubin        | 60                      | 172           | -1       |
|         | Unconjugated     |                         | 780           | 0        |
|         | Bilirubin        | 60                      | 17.2          | 0        |
|         | Conjugated       |                         | 78.0          | +1       |
| Lambda  | Hemoglobin       | 1000                    | 36.8          | 0        |
|         | (hemolysate)     |                         | 16.5          | +6       |
|         | Bilirubin        | 60                      | 16.8          | -1       |
|         | Unconjugated     |                         | 36.8          | +3       |
|         | Bilirubin        | 60                      | 16.7          | -1       |
|         | Conjugated       |                         | 35.7          | 0        |

To evaluate interference from rheumatoid factors interference, samples which had elevated RF concentrations and samples with no detectable RF concentration were used to prepare samples for the study. For Kappa elevated RF values were in the range 726 - 871.5 IU/mL; for Lambda the RF values were in the range 726 -521.5 IU/mL. 1+1 mixture of samples with high concentrations of RF were prepared and the KAPPA and LAMBDA assays concentrations determined in replicates of five on the Dimension® Vista System. The resulting percent bias was less than 10% indicating no interference was observed. The following substances were determined to not interfere with the kappa and lambda assays.

| Substance        | Test Concentration | SI Units    |
|------------------|--------------------|-------------|
| Acetaminophen    | 20 mg/dL           | 1328 µmol/L |
| Amikacin         | 15 mg/dL           | 256 µmol/L  |
| Ammonium heparin | 3 U/mL             | 3000 U/L    |
| Ampicillin       | 5.3 mg/dL          | 152 µmol/L  |
| Ascorbic acid    | 5 mg/dL            | 284 µmol/L  |



|                        |            |             |
|------------------------|------------|-------------|
| Caffeine               | 6 mg/dL    | 308 µmol/L  |
| Carbamazepine          | 3 mg/dL    | 127 µmol/L  |
| Chloramphenicol        | 5 mg/dL    | 155 µmol/L  |
| Chlordiazepoxide       | 1 mg/dL    | 33.3 µmol/L |
| Chlorpromazine         | 0.2 mg/dL  | 6.27 µmol/L |
| Cholesterol            | 500 mg/dL  | 12.9 mmol/L |
| Cimetidine             | 2 mg/dL    | 79.2 µmol/L |
| Creatinine             | 30 mg/dL   | 2652 µmol/L |
| Dextran                | 6000 mg/dL | 1500 µmol/L |
| Diazepam               | 0.5 mg/dL  | 17.6 µmol/L |
| Digoxin                | 5 ng/mL    | 6.15 nmol/L |
| Erythromycin           | 6 mg/dL    | 81.6 µmol/L |
| Ethanol                | 400 mg/dL  | 86.8 mmol/L |
| Ethosuximide           | 25 mg/dL   | 1770 µmol/L |
| Furosemide             | 6 mg/dL    | 181 µmol/L  |
| Gentamicin             | 12 mg/dL   | 151 µmol/L  |
| Ibuprofen              | 50 mg/dL   | 2425 µmol/L |
| Immunoglobulin G (IgG) | 5 g/dL     | 50 g/L      |
| Lidocaine              | 1.2 mg/dL  | 51.2 µmol/L |
| Lithium chloride       | 2.3 mg/dL  | 3.2 mmol/L  |
| Lithium heparin        | 3 U/mL     | 3000 U/L    |
| Nicotine               | 0.1 mg/dL  | 6.2 µmol/L  |
| Penicillin             | 5 U/mL     | 25000 U/L   |
| Pentobarbital          | 8 mg/dL    | 354 µmol/L  |
| Phenobarbital          | 10 mg/dL   | 431 µmol/L  |
| Phenytoin              | 5 mg/dL    | 198 µmol/L  |
| Primidone              | 4 mg/dL    | 183 µmol/L  |
| Propoxyphene           | 0.2 mg/dL  | 4.91 µmol/L |
| Protein, Albumin       | 6 g/dL     | 60 g/L      |
| Rheumatoid Factors     | 726 IU/mL  | 726 IU/mL   |
| Salicylic acid         | 60 mg/dL   | 4.34 mmol/L |
| Sodium heparin         | 3 U/mL     | 3000 U/L    |
| Theophylline           | 4 mg/dL    | 95 µmol/L   |
| Urea                   | 500 mg/dL  | 83.3 mmol/L |
| Uric acid              | 20 mg/dL   | 1190 µmol/L |
| Valproic acid          | 50 mg/dL   | 3467 µmol/L |

*Hook Effect:*

No hook effect up to 500 mg/dL (50.00 g/L) and 271.6 mg/dL (27.16 g/L) was observed for kappa and lambda, respectively when using the Dimension Vista® System Kappa and Lambda Flex reagent.

*f. Assay cut-off:*

Not Applicable.

2. Comparison studies:

*a. Method comparison with predicate device:*

Method comparison testing was run on each de-identified patient serum samples containing measurable amounts of Ig/L-chain kappa and lambda were used in this study according to CLSI EP9-A2 using single determinations. , The only sample criteria were that there was sufficient sample volume for testing and that mentioned above. Aliquots were stored at -20°C until tested on the device and the predicate device.

Kappa: There were 66 serum samples tested for the initial method comparison testing. In addition, there were 27 serum samples run for the extended range high and 24 serum samples for the extended range low study. Lambda: There were 66 serum samples tested for the initial method comparison testing. In addition, there were 26 serum samples run for the extended range high and 23 serum samples run for the extended range low. The distribution among the sample population in the initial assay range method comparison is as follows:

Sample Distribution Kappa Method Comparison

| Sample range mg/dL (g/L)  | % of samples | Representative Population        |
|---------------------------|--------------|----------------------------------|
| <170 (1.70)               | 21           | Below expected range             |
| ≥170 < 370 (≥1.70 <3.70)  | 29           | Expected Range                   |
| ≥370 < 640 (≥3.70 < 6.40) | 29           | Above expected range             |
| ≥640 < 870 (≥6.4 <8.70)   | 21           | Upper portion of measuring range |

Sample Distribution Lambda Method Comparison

| Sample range mg/dL (g/L)  | % of samples | Representative Population        |
|---------------------------|--------------|----------------------------------|
| <90 (<0.9)                | 18           | Below expected range             |
| ≥90 < 210 (≥0.9 <2.1)     | 36           | Expected Range                   |
| ≥210 < 310 (≥2.10 < 3.10) | 31           | Above expected range             |
| ≥310 < 410 (≥3.1<4.10)    | 15           | Upper portion of measuring range |

Passing-Bablok regression analysis was used to analyze the data for the initial measuring range and the extended high and low values.above.

|        | Dilution | Approx conc. Range (g/L) | Slope | Y-intercept (mg/dL) | Correlation coefficient (R <sup>2</sup> ) | N = |
|--------|----------|--------------------------|-------|---------------------|---|-----|
| Kappa  |          | 0.3 – 9.0                | 1.105 | -4.2                | 0.998                                     | 66  |
|        | 1:5      | 0.08 – 0.28              | 1.102 | -1.0                | 0.986                                     | 24  |
|        | 1:100    | 8.0 – 35.0               | 1.158 | -1.690              | 0.986                                     | 27  |
| Lambda |          | 0.2 – 4.3                | 1.045 | -1.5                | 0.993                                     | 66  |
|        | 1:5      | 0.05 – 0.17              | 1.000 | -0.003              | 0.984                                     | 23  |
|        | 1:100    | 4.0 – 32.0               | 1.059 | -0.729              | 0.950                                     | 26  |

b. *Matrix comparison:*

In addition to the method comparison studies done using serum on the Dimension Vista® System and the BN Prospec® System, a separate study was done using matched serum and plasma samples on the Dimension Vista® System. In this study, matched samples of serum, lithium heparin, sodium heparin and EDTA were tested on the Dimension Vista® System. The % recovery of immunoglobulin light chains kappa type, and the % recovery of immunoglobulin light chains lambda type for each plasma type was determined versus serum and a regression analysis was done for each plasma type versus serum. The acceptance criteria were for a correlation coefficient of  $\geq 0.950$  and for a median of the normalized differences  $< 7\%$ .

|        | Compared to serum | Slope | Y-intercept (mg/dL) | Correlation coefficient ( $R^2$ ) | n  |
|--------|-------------------|-------|---------------------|-----------------------------------|----|
| Kappa  | Li. heparin       | 0.98  | 0.05                | 0.998                             | 13 |
|        | Na heparin        | 0.98  | 0.04                | 0.998                             | 13 |
|        | EDTA              | 0.99  | -0.04               | 1.000                             | 13 |
| Lambda | Li. heparin       | 1.02  | -0.02               | 1.000                             | 10 |
|        | Na heparin        | 1.00  | 0.00                | 1.000                             | 10 |
|        | EDTA              | 0.98  | 0.00                | 1.000                             | 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:

Not Applicable

5. Expected values/Reference range:

The concentration of Ig/L-chain kappa and lambda in healthy individuals is below the detection limit for this method (less than 7.0 mg/dL ( 0.07 g/L) and Lambda was determined to be 4.8 mg/dL (0.048 g/L) and is based on the following literature reference: Dati F., Lammers, M., Adam, A, Sondag, D., and Stienen, L. *Referenzwerte für 18 Plasmaproteine am Berhring- Nephelometer-System*. The range was adjusted for standardization to the international reference preparation ERM-DA470 and confirmed by performing a reference interval transference study following the NCCLS/CLSI Guideline C28-A2.

**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.