510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K171742

B. Purpose for Submission:

New device on two previously cleared instruments

C. Measurand:

Kappa (κ) Free Light Chain (FLC)
Lambda (λ) Free Light Chain (FLC)

D. Type of Test:

Nephelometry, quantitative

E. Applicant:

Siemens Healthcare Diagnostics Products GmbH

F. Proprietary and Established Names:

N Latex FLC Kappa assay
N Latex FLC Lambda assay
N FLC Standard SL
N FLC Control SL1 & SL2

G. Regulatory Information:

1. Regulation section:

   21 CFR § 866.5550 – Immunoglobulin (light chain specific) immunological test system
   21 CFR § 862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

   Class II, test systems

3. Product code:

   DFH, Kappa, antigen, antiserum, control
   DEH, Lambda, antigen, antiserum, control

4. Panel:

   Immunology (82)

H. Intended Use:

1. Intended uses:

   N Latex FLC Kappa and N Latex FLC Lambda assays

   In-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis of multiple myeloma (MM) and amyloidosis (AL).

   N FLC Supplementary Reagent

   Supplementary reagent for the immunonephelometric determination of free light chains (FLC), type kappa and type lambda on BN Systems. A mixture of both supplementary reagents is used to suppress interference by rheumatoid factors and human anti-mouse antibodies (HAMA).

   N FLC Standard SL

   Establishment of reference curves for the determination of free light chains (FLC), type kappa and type lambda on the BN Systems.

   N FLC Control SL1 and SL2

   The N FLC Controls SL1 and SL2 are for use as assayed accuracy controls and precision controls in the determination of free light chains (FLC), type kappa and type lambda by immunonephelometry with the BN Systems.

2. Indications for use:

   Same as Intended Uses

3. Special conditions for use statements:

   For prescription use only

Warning: The result of the FLC Kappa or FLC Lambda in a given specimen determined with assays and or instrument plarforms from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the FLC Kappa or FLC Lambda assay used. Values obtained with different assay methods cannot be used interchangeably.

4. Special instrument requirements:

   BN II (K943997) and BN ProSpec® Systems (K001647)

I. Device Description:

The N Latex FLC Kappa and N Latex FLC Lambda assays are comprised of the following reagents in liquid form:

N latex FLC reagents: Consist of suspension of polysterene particles coated with monoclonal antibodies (mouse) to either human FLC Kappa or human FLC Lambda; conjugate of S-adenosyl-cysteine/porcine thyreoglobin (<0.1 g/L); conjugate of S-adenosyl-L-homocysteine hydrolase (<100 U/mL); dithiothreitol (<0.5 g/L). Preservative: Sodium azide (<1 g/L)

N FLC Supplementary Reagents A and B: N FLC Supplementary Reagent A contains mouse immunoglobulin in buffered solution and N FLC Supplementary Reagent B: consist of a buffered salt solution containing detergent. Preservatives in both Supplemntary reagents: Sodium azide (<1 g/L).

N FLC Standard SL: Contains human free light chains proteins, human serum albumin and protease inhibitors.

N FLC Controls SL1 and SL2: contains human free light chain proteins, human serum albumin and protease inhibitors.

J. Substantial Equivalence Information:

1. Predicate device names and 510(k) numbers:

   The Binding Site Freelite® Human Kappa Free Kit for use on the Siemens BN™ II - K031016

   The Binding Site Freelite® Human Lambda Free Kit for use on the Siemens BN™ II - K031016

2. Comparison with predicate:

Kappa and Lambda Reagents:

Similarities		
Item	Device N Latex FLC Kappa N Latex FLC Lambda	Predicate Freelite® Human Kappa Free and Freelite® Human Lambda Free kits on the Siemens BN™II
Analyte	Kappa: Kappa FLC Lambda: Lambda FLC	Same
Measurement	Quantitative	Same
Detection Method	Nephelometric	Same

Differences		
Item	Device	Predicate
Indication for use	*In-vitro* diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda, in human serum and EDTA plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis of multiple myeloma (MM) and amyloidosis (AL).	This kit is intended for the quantitation of kappa free light chains or lambda free light chains in serum and urine on the Siemens BN™ II. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.
Sample type	Serum and EDTA plasma	Serum and urine
Detection Antibody	Kappa: Monoclonal mouse anti-human FLC kappa antibody onto polysterene particles Lambda: Monoclonal mouse anti-human FLC lambda antibody onto polysterene particles	Kappa: Polyclonal sheep anti-human kappa antibody coated onto latex particles Lambda: Polyclonal sheep anti-human lambda antibody coated onto latex particles

Differences		
Item	Device	Predicate
Analytical Measuring ranges (Calibrator lot dependent):	Kappa: 3.4 – 110 mg/L Lambda: 1.9 – 60 mg/L	Kappa: 5.9 – 190 mg/L Lambda: 5.0 – 160 mg/L
Instrument System	Siemens BN II and BN ProSpec Systems	Siemens BN II
Reference Interval	Kappa: 8.24 – 28.90 mg/L Lambda: 9.10 – 32.60 mg/L Ratio: 0.53 – 1.51	Kappa: 3.30 to 19.40 mg/L Lambda: 5.71 to 26.30 mg/L Ratio: 0.26 – 1.65

Calibrators:

Similarities		
Item	Device N Latex FLC Standard SL for the BN Systems	Predicate Human Kappa Free Standard and Human Lambda Free Standard on the Siemens BN™II
Number of Levels	One	Same
Reference material	Internal reference preparation	Same

Differences		
Item	Device N Latex FLC Standard SL for the BN Systems	Predicate Human Kappa Free Standard and Human Lambda Free Standard on the Siemens BN™II
Indication for use	Establishment of reference curves for the determination of free light chains (FLC), type kappa and type lambda on the BN Systems.	Used for the establishment of reference curves for the determination of Freelite® Kappa and Lambda light chains on the BN II System.
Matrix	Consists of a stabilized liquid containing human free light chain proteins, human serum albumin and protease inhibitors. Contains	Consists of human sera that contain kappa free light chain and lambda free light chain respectively. They are

Differences		
Item	Device N Latex FLC Standard SL for the BN Systems	Predicate Human Kappa Free Standard and Human Lambda Free Standard on the Siemens BN™II
	sodium azide (<1 g/L) as a preservative.	supplied in a stabilized liquid form and contain 0.099% sodium azide, 0.1% E- amino-n-caproic acid (EACA) and 0.01% benzamidine as preservatives.
Volume	3 x 1.0 mL	2 x 1.0 mL
Analytical values (Control lot dependent)	Kappa: 22 mg/L Lambda: 32 mg/L	Kappa: 19.99 mg/L Lambda: 16.21 mg/L

Controls:

Differences		
Item	Device N FLC Control SL 1 N FLC Control SL 2	Predicate Human Kappa Free Control, Human Kappa Free High Control, Human Lambda Free Control and Human Lambda Free High Control
Indications for Use	The N FLC Controls SL1 and SL2 are for use as assayed accuracy controls and precision controls in the determination of free light chains (FLC), type kappa and type lambda by immunonephelometry with the BN Systems.	Used as quality controls for the Freelite® Kappa and Lambda assays on the Siemens BN II
Matrix	Controls are stabilized liquids containing human free light chain proteins, human serum albumin and protease inhibitors. The concentration of the free light chains (FLC), type kappa and type lambda is	Controls consist of human sera that contain kappa free light and lambda free light chain. They are supplied in a stabilized liquid form and contain 0.099% sodium azide, 0.1% E-amino- n-caproic

Differences		
Item	Device N FLC Control SL 1 N FLC Control SL 2	Predicate Human Kappa Free Control, Human Kappa Free High Control, Human Lambda Free Control and Human Lambda Free High Control
	calibrated against standard preparations and is lot-dependent. The controls contain sodium azide (<1 g/L) as a preservative.	acid (EACA) and 0.01% benzamidine as preservatives.
Volume	SL1: 3 vials x 1.0 mL SL2: 3 vials x 1.0 mL	1 vial x 1.5 mL for each level of control: 2 levels of Kappa Free controls levels of Lambda Free controls
Assigned Values (lot dependent)	Level 1: Kappa: 13 mg/L Lambda: 13 mg/L Level 2: Kappa: 32 mg/L Lambda: 32 mg/L	Human Kappa Free Control: 14.90 mg/L Human Kappa Free High Control: 30.10 mg/L Human Lambda Free Control: 27.7 mg/L Human Lambda Free High Control: 55.10 mg/L

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

CLSI EP05-A3 "Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Third Edition".

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

CLSI EP07-A2 "Interference Testing in Clinical Chemistry, Approved Guideline - Second Edition".

CLSI EP09-A3 "Measurement Procedure Comparison and Bias Estimation using Patient samples, Approved Guideline - third Edition".

CLSI EP17-A2 "Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition"

CLSI C28-A3C "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition".

L. Test Principle:

The FLC test systems are based upon the principles of particle-enhanced immunonephelometry. Polystyrene particles coated with monoclonal antibodies to human free light chains, type kappa or lambda, respectively, are agglutinated when mixed with samples containing FLC. These aggregates 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:

1. Analytical performance:

All results met the manufacturer's pre-determined acceptance criteria.

a. Precision/Reproducibility:

The precision of the N Latex FLC Kappa and N Latex FLC Lambda FLC assays were evaluated according to the Clinical and Laboratory Standards Institute (CLSI) EP5-A3 guideline. Serum samples were obtained from commercial sources and samples with values close to normal, abnormal and very abnormal analyte levels were pooled to achieve target concentrations spanning the linear range of each FLC assay. In the study, the tests were performed on three levels of serum specimens, and two levels of controls. These specimens included one sample within 25% of the cutoff/upper limit of normal for FLC Kappa and FLC Lambda. Testing was performed on three BN II and three BN ProSpec® instruments with two replicates per run, two runs per day using one lot of the assay-specific reagents. The precision data was analyzed according to three-way nested ANOVA and the results of mean (mg/L) and %CV are summarized below:

N Latex FLC Kappa on three BN II Systems

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	11.43	0.20	1.75	0.20	1.74	0.07	0.58	0.27	2.34	0.39	3.45
S2	25.54	0.43	1.68	0.32	1.26	0.23	0.88	0.52	2.04	0.78	3.06
S3	81.31	1.91	2.35	1.28	1.58	1.84	2.26	0.95	1.17	3.10	3.81
C1	14.60	0.32	2.17	0.20	1.39	0.21	1.41	0.51	3.47	0.66	4.55
C2	37.49	0.64	1.71	0.62	1.66	0.61	1.62	0.57	1.52	1.22	3.26

N Latex FLC Lambda on three BN II Systems

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	10.91	0.17	1.59	0.36	3.27	0.00	0.00	0.47	4.27	0.61	5.60
S2	27.84	0.35	1.24	0.51	1.85	0.22	0.79	1.72	6.18	1.84	6.61
S3	44.46	0.66	1.49	0.68	1.52	0.29	0.66	2.90	6.52	3.06	6.89
C1	13.83	0.23	1.65	0.29	2.09	0.20	1.44	0.56	4.07	0.70	5.07
C2	37.70	0.45	1.20	0.78	2.07	0.66	1.74	2.33	6.18	2.58	6.85

N Latex FLC Kappa on three BN ProSpec Systems

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	11.03	0.27	2.47	0.00	0.00	0.09	0.80	0.50	4.56	0.58	5.24
S2	25.05	0.47	1.88	0.27	1.08	0.09	0.37	1.21	4.84	1.33	5.32
S3	79.04	1.78	2.25	1.84	2.33	0.00	0.00	5.50	6.96	6.07	7.68
C1	14.19	0.39	2.78	0.22	1.55	0.13	0.94	0.57	4.03	0.74	5.22
C2	36.33	0.70	1.92	0.87	2.39	0.00	0.00	1.69	4.66	2.03	5.58

N Latex FLC Lambda on three BN ProSpec Systems

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	10.87	0.27	2.52	0.00	0.00	0.12	1.12	0.36	3.27	0.47	4.28
S2	27.27	0.67	2.46	0.29	1.05	0.00	0.00	0.76	2.78	1.05	3.86
S3	44.69	0.96	2.15	0.64	1.43	0.00	0.00	1.76	3.84	2.11	4.17
C1	13.82	0.27	1.94	0.27	1.97	0.00	0.00	0.23	1.64	0.44	3.22
C2	37.09	0.69	1.87	0.79	2.14	0.00	0.00	0.15	0.41	1.07	2.87

The lot-to-lot reproducibility of the N Latex FLC Kappa and N Latex FLC Lambda FLC assays were evaluated according to the CLSI EP5-A3 guideline. Serum samples were obtained from commercial sources and samples with values close to normal, abnormal and very abnormal analyte levels were pooled to achieve target concentrations spanning the linear range of each FLC assay. In the study, the tests were performed on three levels of serum specimens, and two levels of controls. These specimens included one sample within 25% of the cutoff/upper limit of normal for FLC Kappa and FLC Lambda. Testing was performed on one BN II and one BN ProSpec® instruments with two replicates per run, two runs per day using three lots of the assay-specific reagents. The results of mean (mg/L) and %CV are summarized below:

Three Lots of N Latex FLC Kappa on one BN II System

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	11.66	0.17	1.49	0.17	1.44	0.04	0.30	0.70	5.99	0.74	6.35
S2	25.91	0.38	1.46	0.34	1.32	0.00	0.00	0.90	3.48	1.04	4.00
S3	82.35	1.51	1.84	1.87	2.27	0.98	1.19	3.52	4.27	4.37	5.31
C1	14.39	0.23	1.62	0.09	0.62	0.00	0.00	0.61	4.21	0.66	4.55
C2	37.40	0.47	1.26	0.60	1.59	0.00	0.00	1.95	5.20	2.09	5.58

Three Lots of N Latex FLC Lambda on one BN II System

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	10.30	0.14	1.37	0.14	1.39	0.11	1.02	0.85	8.25	0.88	8.54
S2	26.35	0.34	1.30	0.32	1.23	0.14	0.52	1.55	5.90	1.63	6.19
S3	41.59	0.65	1.57	0.29	0.70	0.46	1.10	3.83	9.22	3.93	9.44
C1	13.07	0.22	1.70	0.25	1.88	0.00	0.00	0.87	6.63	0.93	7.10
C2	35.13	0.42	1.18	0.68	1.93	0.00	0.00	2.06	5.88	2.21	6.30

Three Lots of N Latex FLC Kappa on one BN ProSpec System

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	11.18	0.34	2.92	0.00	0.00	0.15	1.26	0.85	7.20	0.93	7.87
S2	26.15	0.60	2.29	0.31	1.18	0.00	0.00	1.19	4.55	1.37	5.23
S3	81.79	1.94	2.37	1.76	2.15	0.00	0.00	5.44	6.66	6.04	7.39
C1	14.88	0.43	2.87	0.45	3.01	0.00	0.00	0.89	6.00	1.09	7.30
C2	37.93	0.70	1.85	1.12	2.96	0.00	0.00	2.22	5.85	2.58	6.81

Three Lots of N Latex FLC Lambda on one BN ProSpec System

Sample	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
S1	10.79	0.36	3.36	0.00	0.00	0.14	1.30	0.766	7.10	0.86	7.97
S2	27.24	0.64	2.34	0.62	2.27	0.00	0.00	0.83	3.06	1.22	4.47
S3	44.11	1.02	2.30	0.79	1.79	0.00	0.00	3.09	7.01	3.35	7.59
C1	13.89	0.24	1.17	0.04	2.90	0.00	0.00	0.65	4.67	0.80	5.76
C2	37.12	0.68	1.83	1.29	3.48	0.00	0.00	0.97	2.61	1.75	4.72

b. Linearity/assay reportable range:

The studies were performed following the CLSI EP06-A guideline. The linearity of this assay has been demonstrated using test specimens diluted serially in Kappa or Lambda depleted plasma or serum to yield 13 levels within the claimed assay range. Serum and EDTA plasma specimens from healthy donors from a blood bank (one donor each for Kappa EDTA plasma and serum and one donor each for Lambda EDTA plasma and serum) were spiked with purified polyclonal FLC Kappa and FLC Lambda and subsequently diluted with FLC depleted serum or plasma until concentrations of FLC Kappa and FLC Lambda were below the initial measuring range. The diluted samples were measured in three independent measurements. The approximate measuring range of the N Latex FLC Kappa at initial dilution of 1:100 is 3.4–110 mg/L and the approximate measuring range of the N Latex FLC Lambda at initial dilution of 1:20 is 1.9–60 mg/L.

Tabulated summary of linearity studies:

FLC Assay	Instrument	Sample type	Range Tested (mg/L)	Linearity regression data	95% CI (Slope)	95% CI (Y-Intercept)
Kappa	BN II	EDTA Plasma	1.5–122.0	Y=1.0176x +0.000	0.99963 – 1.03560	N/A
Kappa	BN II	Serum	1.5–120.0	Y=1.0120x +0.000	1.00181 – 1.02220	N/A
Kappa	BN ProSpec	EDTA Plasma	1.7–139.0	Y=1.0154x +0.000	0.99800 – 1.03274	N/A
Kappa	BN ProSpec	Serum	1.5–117.0	Y=0.9872x +0.000	0.96239 – 1.01197	N/A
Lambda	BN II	EDTA Plasma	1.2–94.7	Y=1.0439x +0.000	1.02283 – 1.06494	N/A
Lambda	BN II	Serum	0.9–75.1	Y=1.0528x +0.000	1.03675 – 1.06884	N/A
Lambda	BN ProSpec	EDTA Plasma	0.9–72.2	Y=1.0451x +0.000	1.02165 – 1.06860	N/A
Lambda	BN ProSpec	Serum	0.9–73.4	Y=1.0323x +0.000	1.02088 – 1.04381	N/A

High Dose Hook Effect:

No high dose hook effect was observed with FLC Kappa samples up 27,100 mg/L or with FLC Lambda samples up to 57,300 mg/L.

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

Traceability:

In the absence of an international reference standard, the calibration of the assay is traceable to an internally assigned master calibrator.

Stability:

Shelf-life, opened-vial, on-board BN Prospec and on-board BN II studies were performed on the N Latex FLC Kappa and FLC Lambda Reagent, on the N Latex FLC Standard SL, on the N Latex FLC Control SL1 and SL2 and on the N Latex FLC Supplementary Reagent A and B. All results met stability acceptance criteria and the product stability claims are listed in the table below:

	Shelf Life (unopened)	Opened	On-board BN ProSpec	On-Board BN II
N Latex FLC Kappa Reagent	18 months	4 weeks	2 weeks	Not stored on board
N Latex FLC Lambda Reagent	18 months	4 weeks	2 weeks	Not stored on board
N Latex FLC Standard SL	12 months	42 days	Not stored on board	Not stored on board
N Latex FLC Control SL1 and SL2	12 months	28 days	14 days	Not stored on board
N Latex FLC Supplementary Reagent A	18 months	A/B Mixed 4 weeks	A/B Mixed 2 weeks	Not stored on board
N Latex FLC Supplementary Reagent A	18 months			

d. Detection limit:

Limit of Quantitation (LoQ):

The limit of quantitation (LoQ) for N Latex FLC Kappa and N Latex FLC Lambda was determined on the BN II and BN ProSpec® Systems according to the CLSI EP17- A2 guideline. The limit of quantitation is the lowest concentration of analyte that can be quantitatively determined with stated accuracy.
All results measured on blank samples for the Limit of Blank (LoB) study yielded results below the measuring range for both assays. Since Limit of Detection (LoD) is calculated using LoB, the Limit of Detection is undetermined.
LoQ on BN Systems: FLC Kappa: 0.195 mg/L and FLC Lambda: 0.532 mg/L. The total error was found to be below 11 % for both methods.

e. Analytical specificity:

The N Latex FLC Kappa and FLC Lambda assays were evaluated for interference on BN Systems according to the CLSI EP07-A2 guideline. No interferences were observed with the following tabulated lists of endogenous and exogenous substances with their corresponding concentration labels as shown below:

Interference Study	
Interferent (Endogenous and Exogenous)	Concentration level
RF	2000 IU/mL
Hemoglobin	10 g/L
Bilirubin conjugated	1025 µmol/L
Bilirubin unconjugated	618 µmol/L
Triglycerides	5 g/L
Total Protein	143 g/L
Amikacin	136.8 µmol/L
Acetamidophenol	1324 µmol/L
Ascorbic Acid	342 µmol/L
Caffeine	308 µmol/L
Creatinine	5 mg/dL
Erythromycin	81.6 µmol/L
Acetylsalicylic Acid	3.62 µmol/L
Dextran	60 g/L
Carbamazepine	127 µmol/L
Ethosuximide	1770 µmol/L
Ibuprofen	2425 µmol/L
Lidocaine	51.2 µmol/L
Penicillin	161 µmol/L
Urea	42.9 mmol/L

Uric Acid	1.4 mmol/L
Valproic Acid	3467 µmol/L
Dexamethasone	1.53 µmol/L
Cimetidine	79.2 µmol/L
Chlorpromazine	6.3 µmol/L
Ethanol	100 mg/dL
Digoxin	7.8 nmol/L
Furosemide	181 µmol/L
Phenytoin	198 µmol/L
Primidone	183 µmol/L
Nicotine	6.2 µmol/L
Chlordiazepoxide	33.3 µmol/L
Diazepam	18 µmol/L
Pentobarbital	431 µmol/L
Dextropropoxyphene	4.91 µmol/L
Heparin Ammonium Salt	3000 U/L
Heparin Lithium Salt	3000 U/L
Heparin Sodium Salt	3000 U/L
Gentamicin	21 µmol/L
Lithium Chloride	3.2 mmol/L
Aminophylline Hydrate (Theophylline)	222 µmol/L
Chloramphenicol	155 µmol/L
Melphalan	4000 ng/mL

Human Anti-Mouse Antibody (HAMA):

No HAMA interferent was observed in both FLC Kappa and FLC Lambda assays with HAMA samples up to 15.47 mg/L. The Package Insert states: *"Nevertheless, complete elimination of this interference from all patient specimens cannot be guaranteed."*

f. Assay cut-off:

See expected values/reference range.

2. Comparison studies:

a. Method comparison with predicate device:

219 samples were tested with the Siemens N Latex FLC Kappa and Lambda assays and the results were compared to the results of the predicate devices. A total of 96 MM and a total of 83 AL serum samples spanning the dynamic range of one or both assays were used in this study. In addition, samples from 24 donors with polyclonal

immunoglobulin stimulation and 16 with Chronic Kidney Disease (CKD) were included. 216 of these samples yielded quantitative values in both kappa assays and 218 in both lambda assays.

Kit	N	Sample Range N Latex FLC mg/L	Slope (Passing Bablock)	95% CI (Slope)	Y-Intercept (Passing Babloc)	95% CI (Y-Intercept)	R^2
FLC Kappa	216	1.38 – 13,400	0.794	0.742 – 0.852	2.112	1.134 – 2.785	0.889
FLC Lambda	218	0.924 – 24,300	1.170	1.014– 1.318	2.163	0.723 – 3.881	0.950

b. Matrix comparison:

Matrix comparison studies were performed between serum and EDTA plasma on 44 samples. Results are as follows:

Serum versus EDTA Plasma FLC Kappa Summary				
N=44	Regression	Passing Bablock Slope (95% CI)	PB Intercept (95% CI)	Median Difference
Serum vs EDTA	r = 0.98	1.014 (0.967 – 1.036)	- 0.791 (-1.250 – 0.050)	-3.5%

Serum versus EDTA Plasma FLC Lambda Summary				
N=44	Regression	Passing Bablock Slope (95% CI)	PB Intercept (95% CI)	Median Difference
Serum vs EDTA	r = 0.99	1.050 (1.005 – 1.094)	- 1.10 (-1.91 – -0.19)	-1.0%

3. Clinical studies:

a. Clinical Sensitivity and specificity:

A total of 342 samples were included in the clinical validation study for the N Latex FLC Kappa and Lambda assay. This validation set included 96 samples from MM patients, 83 samples from AL patients and 163 samples from non-myeloma patients with various clinical conditions: 24 samples from polyclonal immunoglobulin stimulation patients; 16 samples from CKD patients & 123 samples from other

clinical condition patients.

For MM, a total of 259 samples were included in the clinical validation study for the N Latex FLC Kappa and Lambda assay. This validation set included 96 samples from Multiple Myeloma patients, and 163 samples from non-myeloma patients with various clinical conditions.

Clinical sensitivity and specificity summary of the N Latex FLC Kappa and Lambda Ratio for MM are shown in the table below (using the FLC Kappa and Lambda Ratio Reference Interval of 0.53–1.51 as cut-off):

		Clinical Diagnosis of MM		
		Positive	Negative	Total
N Latex FLC Kappa and Lambda Ratio	Positive	92	5	97
	Negative	4	158	162
	Total	96	163	259

Clinical Sensitivity: 95.8% (95% CI: 89.8 – 98.4%)
Clinical Specificity: 96.9% (95% CI: 93.0 – 98.7%)

For AL, a total of 246 samples were included in the clinical validation study for the N Latex FLC Kappa and Lambda assay. This validation set included 83 samples from AL Amyloidosis patients, and 163 non-AL Amyloidosis samples from patients with various clinical conditions.

Clinical sensitivity and specificity summary of the N Latex FLC Kappa and Lambda Ratio for AL are shown in the table below (using the FLC Kappa and Lambda Ratio Reference Interval of 0.53–1.51 as cut-off):

		Clinical Diagnosis of AL		
		Positive	Negative	Total
N Latex FLC Kappa and Lambda Ratio	Positive	69	5	74
	Negative	14	158	172
	Total	83	163	246

Clinical Sensitivity: 83.1% (95% CI: 73.7 – 89.7%)
Clinical Specificity: 96.9% (95% CI: 93.0 – 98.7%)

b. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

Reference intervals were determined from a US-population of 201 apparently healthy subjects. The reference intervals were calculated nonparametrically and represent the central 95 % range of the population.

The following reference intervals apply for serum and plasma samples from healthy adults:
FLC Kappa: 8.24 – 28.9 mg/L (2.5^{th} – 97.5^{th} percentile)
FLC Lambda: 9.10 – 32.6 mg/L (2.5^{th} – 97.5^{th} percentile)
FLC Kappa/ Lambda Ratio: 0.53 – 1.51 (median 1.0st – 99.0^{th} percentile)

The Package Insert states: "*Nevertheless, each laboratory should determine its own reference intervals since values may vary depending on the individual population studied.*"

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.