SIEMENS

N Latex FLC kappa

N FLC KAPPA

N Latex FLC lambda

N FLC LAMBDA

Revision bar indicates update to previous version.

BN II System / BN ProSpec® System / Atellica® CH Analyzer

Warning: The result of the FLC kappa or FLC lambda in a given specimen determined with assays and/or instrument platforms 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. The values of FLC kappa or FLC lambda on BN systems and on Atellica® CH Analyzer should not be used interchangeably.

If, in the course of serially monitoring a patient, the assay method used for determining the FLC kappa and FLC lambda levels is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

Intended Use

N Latex FLC kappa and lambda are *in-vitro* diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma. N Latex FLC kappa and lambda assays are used:

- as an aid in the diagnosis and monitoring of multiple myeloma (MM) on the BN Systems and Atellica® CH Analyzer.
- as an aid in the diagnosis of immunoglobulin light-chain amyloidosis (AL) on the Atellica® CH Analyzer.
- as an aid in the diagnosis and monitoring of immunoglobulin light-chain amyloidosis (AL) on the BN Systems.
- as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems.

Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.

Precaution:

- The performance of N Latex FLC kappa and lambda has not been thoroughly studied in IgM and Light Chain MGUS patients due to the low prevalence of these subtypes.
- Patients with decreased renal function may have elevated FLC kappa and FLC lambda[1].
- Sample populations excluded MGUS populations that were further diagnosed with a disease/disorder in subsequent testing with another medical device such as human immunodeficiency virus, hepatitis, and chronic lymphocytic leukemia. Thus, because the samples were enriched the specificity of the test may be inflated.

Summary and Explanation

In a normal immune response complete immunoglobulin molecules are built, composed of two identical heavy chains (α, γ, μ, δ, ϵ) and two identical light chains (κ, λ). The type of immunoglobulin (IgA, IgG, IgM, IgD, IgE) is defined by the heavy chain, which is combined with either kappa or lambda light chains. A single plasma cell produces one type of heavy chain, and one type of light chain, which are assembled and secreted into the plasma. Compared to the amount of heavy chains produced by each plasma cell clone, a slight excess of light chains is always produced and released into the blood stream as unbound or free light chains (FLC). Thus, in healthy individuals, the majority of light chains exists in bound form as complete immunoglobulins, and only few FLC circulate. While FLC kappa circulate as monomers of about 22.5 kD the FLC lambda form dimers of about 45 kD. Both FLCs are eliminated by the kidney, and, due to the different molecular size, the glomerular filtration rate is higher for FLC kappa compared to FLC lambda, resulting in a mean FLC kappa/lambda ratio of 0.6 in plasma, compared to a plasma ratio for a total light chains of about 2.

Monoclonal gammopathy typically goes along with a grossly increased production of one specific immunoglobulin, and an excess production of the specific FLC involved. As a result, either the plasma level of FLC kappa or that of FLC lambda is elevated, and the ratio FLC kappa/lambda is either increased or decreased compared to the reference range. The determination of FLC in serum is part of recent international recommendations for diagnosis and monitoring multiple myeloma[2–6] and immunoglobulin light-chain amyloidosis (AL)[8–12].

Principle of the Method

BN Systems:

Polystyrene particles coated with 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.

Atellica® CH Analyzer:

Polystyrene particles coated with antibodies to human free light chains, type kappa or lambda, respectively, are agglutinated when mixed with samples containing FLC. Monitoring the agglutination by measuring the increase in turbidity, a concentration curve is obtained. The actual change in absorbance is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

Reagents

Note: FLC kappa and FLC lambda can be used on the Atellica® CH Analyzer.
Siemens Healthcare Diagnostics provides an Application Sheet for Atellica® CH Analyzer. The Application Sheet contains analyzer / assay specific handling and performance information which may differ from that provided in these Instructions for Use. In this case, the information contained in the Application Sheet supersedes the information in this Instructions for Use. Please also consult the instruction manual of the instrument manufacturer!

Reagent	Description	Storage	Stability once opened/ reconstituted
N Latex FLC kappa N FLC KAPPA N Latex FLC lambda N FLC LAMBDA			
N Latex FLC kappa N FLC KAPPA REAGENT	Suspension of polystyrene particles coated with monoclonal antibodies (mouse) to human FLC kappa. Preservative: Sodium azide < 1 g/L	2–8 °C See expiry date on the label.	Four weeks if stored at 2–8 °C securely capped immediately after use and if contamination (e.g. by microorganisms) is precluded. Do not freeze the reagent.
N Latex FLC lambda N FLC LAMBDA REAGENT	Suspension of polystyrene particles coated with monoclonal antibodies (mouse) to human FLC lambda. Preservative: Sodium azide < 1 g/L		

On-board stability:
A minimum of 5 days, at 8 hours per day, or a comparable period of time.

Note: On-board stability may vary, depending on the system used and laboratory conditions. For further details, refer to the respective BN System Assay Protocol documents or Atellica® CH Analyzer Application Sheet.

Warnings and Precautions

For *in-vitro* diagnostic use only.

For laboratory professional use.

Safety data sheets (MSDS/SDS) available on siemens-healthineers.com/sds.

CAUTION!
Federal (USA) law restricts this device to sale by or on the order of licensed healthcare professionals.

CAUTION! POTENTIAL BIOHAZARD
Each donor or donor unit was tested and found to be negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus (HBV) and hepatitis C virus (HCV) using either tests that are CE marked or FDA approved for this purpose. Because no known test can offer complete assurance of the absence of infectious agents, all human derived products should be handled with appropriate caution.

CAUTION!
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with all government requirements.

Preparation of the Reagents

N Latex FLC kappa and **N Latex FLC lambda** are liquid reagents and can be used on the BN Systems without additional preparation. Shake carefully to mix before first use.

For use on the Atellica® CH Analyzer, refer to the respective Application Sheet.

Materials provided

REF	Contents		
OPJA07	N Latex FLC kappa N FLC KAPPA	3 ×	1.7 mL
OPJB07	N Latex FLC lambda N FLC LAMBDA	3 ×	2.1 mL

Materials required but not provided

Item	Description
REF OPJC05	N FLC Supplementary Reagent
REF OPJD05	N FLC Standard SL
REF OPJE05	N FLC Control SL1
REF OPJF05	N FLC Control SL2
REF OQUB21[a]	Cleaner SCS, (for N FLC LAMBDA)
REF OUMT65[a]	N Diluent
REF OVLE21[a]	BN II Evaporation Stoppers (optional)
	BN II System, BN ProSpec® System, Atellica® CH Analyzer

Additional materials and supplies are described in your BN System's Instruction Manual. Refer also to the Application Sheet for use on the Atellica® CH Analyzer.

[a] Material required only for use on BN II System and BN ProSpec® System.

Specimens

Suitable samples are human serum and EDTA-plasma, either as fresh as possible (stored no more than four days at 2 to 8 °C) or stored frozen. The samples can be stored frozen (at –20 °C or below) for up to six months if they are frozen within 24 hours after collection and if repeated freeze-thaw cycles are avoided. Serum samples must have completely coagulated and, after centrifugation, must not contain any particles or traces of fibrin. Lipemic samples, or frozen samples which became turbid after thawing, must be clarified by centrifugation (10 minutes at approximately 15 000 x g) prior to testing.

Procedure

Notes

BN Systems:

1. Consult your BN System's Instruction Manual for details regarding operation of the instrument.
2. For a BN II or BN ProSpec® System reagents and samples stored at 2 to 8 °C can be placed directly on the analyzer.

Atellica® CH Analyzer:

Before use on the Atellica® CH Analyzer, reagents need to be transferred into system specific containers. For details and further information refer to the system specific Application Sheet.

Assay protocols for the BN Systems

BN Systems:

The assay protocols for serum and plasma are given in the BN System Assay Protocol documents and the software of the instrument. All steps are performed automatically by the system.

Establishment of the Reference Curve

BN Systems:

Reference curves are generated by multi-point calibration. Serial dilutions of N FLC Standard SL are automatically prepared by the instrument using N Diluent. The reference curve is valid for six weeks and can be used beyond this period of time as long as controls with corresponding method-dependent target values, e. g. N FLC Control SL1 and N FLC Control SL2, are reproduced within their respective range. If a different lot of reagent is used, a new reference curve must be generated. The exact measuring range depends upon the concentration of the protein in each lot of N FLC Standard SL. For typical figures refer to the BN System Assay Protocol documents.

Atellica® CH Analyzer:

Before use on the Atellica® CH Analyzer, N FLC Standard SL needs to be transferred into system specific containers. For details and further information refer to the system specific Application Sheet.

Assay of Specimens

BN Systems:

Samples are automatically diluted 1:100 with N Diluent for N Latex FLC kappa and 1:20 for N Latex FLC lambda by the BN System. If the results obtained are outside the measuring range, the assay can be repeated using a higher or lower dilution of the sample. Refer to the BN System's Instruction Manual for information on repeat measurements using other dilutions.

Atellica® CH Analyzer:

For details and further information refer to the system specific Application Sheet.

Internal Quality Control

Assay N FLC Control SL1 and N FLC Control SL2 after each establishment of a reference curve, the first use of a reagent vial as well as with each run of serum or plasma samples. The controls are assayed and evaluated as for patient samples. The assigned values and ranges are listed in the Table of Assigned Values of the respective control. Follow government regulations or accreditation requirements for quality control frequency.

Note: Before use on the Atellica® CH Analyzer, N FLC Control SL1 and N FLC Control SL2 need to be transferred into system specific containers. For details and further information refer to the system specific Application Sheet.

If the result of a control is outside the range, the determination must be repeated. If the repeated determination confirms the deviation, a new reference curve should be established. Do not release patient results until the cause of deviation has been identified and corrected.

Results

Evaluation is performed automatically in mg/L or in a derived unit selected by the user on the BN System. Additionally, the software of the BN Systems offers the calculation of the κ/λ quotient.

The Atellica® CH Analyzer determines the result using the calculation scheme described in the online help. The system reports results in mg/L, depending on the units defined when setting up the assay. Additionally, the software offers the calculation of the κ/λ quotient.

Limitations of the Procedure

No interference was detected in serum samples for concentrations of rheumatoid factors up to 2 000 IU/mL, of triglycerides up to 5 g/L, of bilirubin (conjugated) up to 1 025 µmol/L, of bilirubin (unconjugated) up to 618 µmol/L, of free hemoglobin up to 10 g/L and of total protein up to 143 g/L on the BN Systems. For Atellica® CH Analyzer specific interference refer to the system specific Application Sheet. No interference to commonly used drugs is known.

Turbidity and particles in the samples may interfere with the assay. Therefore, samples containing particles must be centrifuged prior to testing. Lipemic or turbid samples which cannot be clarified by centrifugation (10 minutes at approximately 15 000 x g) must be excluded from the assay.

Patient samples may contain heterophilic antibodies that could react in immunoassays to give a falsely elevated or depressed result[7]. This assay has been designed to minimize interference from heterophilic antibodies. No significant effect on the performance of the N Latex FLC kappa and lambda assays with HAMA up to 15.47 mg/L were observed on the BN Systems. Refer to the system specific Application Sheet for Atellica® CH Analyzer. Nevertheless, complete elimination of this interference from all patient specimens cannot be guaranteed.

Excessively elevated monoclonal immunoglobulin concentrations might have the potential to suppress the reaction of anti-FLC antibodies with free light chain molecules. In addition, other conditions may cause lower FLC concentrations, e.g., bi-clonal after therapy, polymerization of lambda chains, etc. If results do not fit to previous ones, or to results of other tests (e.g., serum and urine protein electrophoresis, immunofixation, differential blood cell count) and/or to the clinical situation, it is recommended to re-analyze the sample in a higher sample dilution. Such samples may also not dilute in a linear fashion. Refer to the BN System's Instruction Manual for information on additional dilution schemes. Refer to the system specific Application Sheet for Atellica® CH Analyzer.

Siemens Healthcare Diagnostics has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. User defined modifications are not supported by Siemens as they may affect performance of the system and assay results. It is the responsibility of the user to validate modifications to these instructions or use of the reagents on analyzers other than those included in Siemens Application Sheets or these Instructions for Use.

These assays were not evaluated in samples from IgD or IgE multiple myeloma patients for diagnosis or monitoring.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

Due to matrix effects, inter-laboratory survey samples and control samples may yield results that differ from those obtained with other methods. It may therefore be necessary to assess these results in relation to method-specific target values.

Test results are not interchangeable with results obtained from other assay methods.

Reference Intervals

The 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:

	2.5^{th}–97.5^{th} percentile
FLC kappa	8.24–28.9 mg/L
FLC lambda	9.10–32.6 mg/L

The calculation of the κ/λ ratios resulted in 0.88 (0.53 to 1.51) (median, 1.0^{st} – 99.0^{th} percentile).

Nevertheless, each laboratory should determine its own reference intervals since values may vary depending on the individual population studied.

This reference interval was confirmed on the Atellica® CH Analyzer by determining 150 serum samples of apparently healthy adults.

Result interpretation

Interpretation of diagnostic and monitoring results of multiple myeloma and immunoglobulin light-chain amyloidosis (AL); and evaluation of monoclonal gammopathy of undetermined significance (MGUS)

The International Myeloma Working Group (IMWG)[8] and National Cancer Comprehensive Network (NCCN)[10,11] guidelines have consensus recommendations for the diagnosis and monitoring (hematological response categories) for multiple myeloma and immunoglobulin light-chain amyloidosis, which include FLC kappa and FLC lambda tests. Similarly, the IMWG[8,12] and NCCN[10] guidelines have recommendations to evaluate patients with MGUS that include FLC kappa and FLC lambda tests. These clinical tests are to be used in conjunction with a patient's history, physical exam, other clinical and radiological results, overall patient fitness, and consent to treat the patient looking at the totality of the data. All relevant guidelines[8–14] are in the references below, however, they may change and the treating clinician should be cognizant of any updates to these guidelines.

Specific Performance Characteristics

For Atellica® CH Analyzer specific Performance Characteristics refer to the system specific Application Sheet.

Sensitivity

BN Systems:

Limit of Quantitation (LoQ)

A typical LoQ for N Latex FLC kappa and N Latex FLC lambda was determined on the BN II and BN ProSpec® Systems in consistency with CLSI guideline EP17-A2[15]. The limit of quantitation is the lowest concentration of analyte that can be quantitatively determined with stated accuracy.

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.

Limit of Blank (LoB)

All results measured on blank samples for the LoB study yielded results below the measuring range for both assays.

Limit of Detection (LoD)

Since LoD is calculated using LoB, the Limit of Detection is undetermined.

Atellica® CH Analyzer:

For the respective sensitivity data refer to the system specific Application Sheet.

Assay Range

BN Systems:

The typical analytical measuring range (AMR) for N Latex FLC kappa on BN Systems is 3.4 to 110 mg/L. For N Latex FLC lambda the typical AMR is 1.9 to 60 mg/L. Linearity of FLC kappa and FLC lambda was evaluated according to CLSI EP06–A[16] guideline.

If samples are above or below the AMR the systems allows automatic re-dilutions of the samples in higher or lower steps for a re-measurement.

Atellica® CH Analyzer:

For the respective ranges refer to the system specific Application Sheet.

Specificity

N Latex FLC kappa and N Latex FLC lambda are specific for the respective protein.

Precision

The precision of the N Latex FLC kappa and N Latex FLC lambda FLC assays were evaluated according to Clinical and Laboratory Standards Institute EP5-A3[17] 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 (S1 – S3), and two levels of controls (C1, C2). 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 three lots of the assay-specific reagents. The precision data was analyzed according to three-way nested ANOVA and the results of mean (mg/L) and Coefficient of Variation [CV (%)] are summarized below:

N Latex FLC: One lot of assay-specific reagents on three BN II instruments

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total Precision	
		SD[b] (mg/L)	CV[c] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
kappa											
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
lambda											
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

[b] Standard deviation
[c] Coefficient of variation

N Latex FLC: One lot of assay-specific reagents on three BN ProSpec® instruments

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total Precision	
		SD[d] (mg/L)	CV[e] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
kappa											
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
lambda											
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	4.71

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total Precision	
		SD[d] (mg/L)	CV[e] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
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

[d] Standard deviation
[e] Coefficient of variation

N Latex FLC: Three lots of assay-specific reagents on one BN II instrument

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD[f] (mg/L)	CV[g] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
kappa											
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
lambda											
S1	10.30	0.14	1.37	0.143	1.39	0.11	1.02	0.85	8.25	0.879	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

[f] Standard deviation
[g] Coefficient of variation

N Latex FLC: Three lots of assay-specific reagents on one BN ProSpec® instrument

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD[h] (mg/L)	CV[i] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
kappa											
S1	11.80	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
lambda											
S1	10.79	0.363	3.36	0.000	0.00	0.140	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

ID	Mean (mg/L)	Within-Run		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD[h] (mg/L)	CV[i] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
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	1.71	0.40	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

[h] Standard deviation
[i] Coefficient of variation

Antigen Excess

On the BN Systems, no high-dose hook effect was observed as false negative when samples up to 27 100 mg/L for FLC kappa and up to 57 300 mg/L for FLC lambda were tested.

Method Comparison

152 serum samples from patients with monoclonal gammopathy were assayed by immunofixation (IFE), with N Latex FLC on the BN systems and in parallel with another commercially available particle-enhanced immunonephelometric method (comparison method).

Table 1: Method Comparison
N Latex FLC kappa versus Comparison Method

N Latex FLC kappa ⇓ / Comparison Method ⇒	< 3.3 mg/L	3.3 - 19.4 mg/L	> 19.4 mg/L	total N
< 8.24 mg/L	**6**	**11**	**0**	17
8.24 - 28.9 mg/L	**3**	**23**	**6**	32
> 28.9 mg/L	**0**	**1**	**102**	103
total N	9	35	108	152

overall agreement rate: 131 / 152 = **86.2 %**

Table 2: Method Comparison
N Latex FLC lambda versus Comparison Method

N Latex FLC lambda ⇓ / Comparison Method ⇒	< 5.7 mg/L	5.7 - 26.3 mg/L	> 26.3 mg/L	total N
< 9.10 mg/L	**16**	**10**	**0**	26
9.10 - 32.6 mg/L	**6**	**23**	**2**	31
> 32.6 mg/L	**0**	**10**	**85**	95
total N	22	43	87	152

overall agreement rate: 124 / 152 = **81.6 %**

Table 3: Method Comparison

N Latex FLC ratio versus Comparison Method

N Latex FLC Ratio ⇓ \ Comparison Method ⇒	< 0.26	0.26 - 1.65	> 1.65	total N
< 0.53	**47**	**10**	**0**	57
0.53 - 1.51	**0**	**11**	**5**	16
> 1.51	**0**	**0**	**79**	79
total N	47	21	84	152

overall agreement rate: 137 / 152 = **90.1 %**

115 were tested positive in immunofixation (IFE) for light chains (56 positive for type kappa, 55 positive for type lambda, 4 positive for types kappa and lambda). The positive agreement with IFE of N Latex FLC kappa, N Latex FLC lambda and N Latex FLC ratio was 100 % (60/60), 96.6 % (57/59) and 94.8 % (109/115), respectively. The corresponding positive agreement for comparison method kappa, comparison method lambda and comparison method ratio was 98.3 % (59/60), 94.9 % (56/59) and 89.6 % (103/115), respectively.

Method Comparison with predicate device

219 samples were tested on the BN systems with Siemens N Latex FLC kappa and N Latex FLC 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 Bablok)	95 % CI[j] (Slope)	Y-Intercept (Passing Bablok)	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

[j] Confidence Interval

Clinical Sensitivity and Specificity

A total of 342 samples were included in the clinical validation study for the N Latex FLC kappa and lambda assays on the BN systems. This validation set included 96 samples from Multiple Myeloma patients, 83 samples from AL patients and 163 samples from non-myeloma patients with various clinical conditions: 24 polyclonal immunoglobulin stimulation; 16 Chronic Kidney Disease (CKD) and 123 other clinical conditions.

Clinical sensitivity and specificity summary of the N Latex FLC kappa and lambda Ratio for Multiple Myeloma are shown in the table below:

		Clinical Diagnosis of Multiple Myeloma		
		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 % Confidence Interval: 89.8 to 98.4 %)

Clinical Specificity: 96.9 % (95 % Confidence Interval: 93.0 to 98.7 %)

Clinical sensitivity and specificity summary of the N Latex FLC kappa and lambda Ratio for AL are shown in the table below:

		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 % Confidence Interval: 73.7 to 89.7 %)

Clinical Specificity: 96.9 % (95 % Confidence Interval: 93.0 to 98.7 %)

For MGUS evaluation, the study was performed using 121 MGUS samples (89 Non-IgM, 21 IgM and 11 LC MGUS) and 102 polyclonal immunostimulation samples (confirmed with SPEP/SIFE). The result showed positive rate of 50.4 % (61/121) for all MGUS samples tested and negative rate of 90.2 % (92/102) for non-MGUS samples.

Limitation:

Sample populations were excluded from MGUS populations, if the plasma cell dyscrasias were related to other disorders.

Interferences

The N Latex FLC kappa and lambda assays were evaluated for interference on BN Systems according to CLSI guideline EP7-A2[18]. Following concentrations of listed endogenous and exogenous substances were found to cause no interference up to the indicated concentrations:

Interferent	**No Interference up to...**
Acetamidophenol	1 324 µmol/L
Acetylsalicylic acid	3.62 µmol/L
Amikacin	136.8 µmol/L
Aminophylline Hydrate (Theophylline)	222 µmol/L
Ascorbic acid	342 µmol/L
Bilirubin conjugated	1 025 µmol/L
Bilirubin unconjugated	618 µmol/L
Caffeine	308 µmol/L
Carbamazepine	127 µmol/L
Chloramphenicol	155 µmol/L
Chlordiazepoxide	33.3 µmol/L
Chlorpromazine	6.3 µmol/L
Cimetidine	79.2 µmol/L
Creatinine	5 mg/dL
Dexamethasone	1.53 µmol/L
Dextran	60 g/L
Dextropropoxyphene	4.91 µmol/L
Diazepam	18 µmol/L

Interferent	No Interference up to...
Digoxin	7.8 nmol/L
Erythromycin	81.6 µmol/L
Ethanol	100 mg/dL
Ethosuximide	1 770 µmol/L
Furosemide	181 µmol/L
Gentamicin	21 µmol/L
Hemoglobin	10 g/L
Heparin Ammonium Salt	3 000 U/L
Heparin Lithium Salt	3 000 U/L
Heparin Sodium Salt	3 000 U/L
Ibuprofen	2 425 µmol/L
Lidocaine	51.2 µmol/L
Lithium Chloride	3.2 mmol/L
Melphalan	4 000 ng/mL
Nicotine	6.2 µmol/L
Penicillin	161 µmol/L
Pentobarbital	354 µmol/L
Phenytoin	198 µmol/L
Primidone	183 µmol/L
RF	2 000 IU/mL
Total Protein	143 g/L
Triglycerides	5 g/L
Urea	42.9 mmol/L
Uric acid	1.4 mmol/L
Valproic acid	3 467 µmol/L

Note: The values cited for specific performance characteristics of the assays represent typical results and are not to be regarded as specifications for the N Latex FLC kappa or N Latex FLC lambda.

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Definition of Symbols

The following symbols may appear on the product labeling:

	Do not reuse		Use By
LOT	Batch Code	REF	Catalogue Number
	Caution, consult accompanying documents		Manufacturer
EC REP	Authorized representative in the European Community		Contains sufficient for <n> tests
	Biological Risks	IVD	*In Vitro* Diagnostic Medical Device
	Temperature Limitation		Consult instruction for Use
	Non-sterile		CE mark
CONTENTS	Contents		Reconstitution volume
LEVEL	Level		Keep away from sunlight and heat


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