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White Paper

Implementation of N Latex Free Light Chain Kappa and Lambda into Routine Practice

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Implementation of N Latex Free Light Chain Kappa and Lambda into Routine Practice

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Contents

Implementation of N Latex Free Light Chain Kappa and Lambda into Routine Practice

Established in 2005, Lancashire Teaching Hospitals NHS Foundation Trust was the first trust in the country to be awarded teaching hospital status. It is one of the largest and highest-performing trusts in the country, providing district general hospital services to 370,000 people in Preston and Chorley, and specialist care to 1.5 million people across Lancashire and South Cumbria.

The Lancashire and Lakeland Immunology Service based at the Royal Preston Hospital is a regional immunology department processing around 260,000 samples per year for autoimmunity, immunochemistry, allergy, and cellular immunology.

Over 2000 requests per year were being routinely processed for serum free light chains using The Binding Site FREELITE methods on the Roche COBAS INTEGRA 400 plus analyzer. The Siemens launch of N Latex free light chain (FLC) Kappa and Lambda methods offered an alternative, and the decision was taken to evaluate the benefits of the Siemens methods on the Siemens BN ProSpec® nephelometry system.

The Siemens N Latex FLC methods on the BN ProSpec System demonstrated:

- Good clinical concordance between the two methods, with few discrepant results
- That a period of patient rebaselining is required to convert methods, as with all tumour markers
- Good correlation with immunofixation electrophoresis (IFE) and good assay characteristics in terms of accuracy, precision, interfering factors, and no antigen-excess issues detected
- Improved operator ease of use and increased kit efficiency through flexible kit configuration
- Streamlined laboratory service through random-access capability and elimination of the requirement to manually check new patient samples for antigen excess

Following a 3-month period of reporting both The Binding Site FREELITE and Siemens N Latex FLC results, Royal Preston Hospital converted their FLC service over to the Siemens N Latex FLC methods.

Siemens would like to thank the laboratory staff at Royal Preston Hospital for evaluating the N Latex FLC methods and sharing the data obtained in the study for publication in this paper.

During this evaluation, Royal Preston Hospital also participated in a multicenter study comparing the N Latex and FREELITE methods across four UK laboratories using Siemens BN ProSpec, Siemens BN™ II and Roche COBAS INTEGRA 400 plus analyzers. This study was published in the Annals of Clinical Biochemistry in 2013.[1]

Background

The determination of serum FLC kappa and lambda in patients with plasma-proliferative disorders has been part of the guidelines for detection and monitoring of multiple myeloma and related disorders since 2009.[2] It is widely accepted and proven that FLC determination provides prognostic information and assists in monitoring therapy success.

Siemens Healthcare Diagnostics launched N Latex FLC Kappa and Lambda methods on the BN II and BN ProSpec Systems in 2011. Prior to this, despite several technical drawbacks that have been reported with FREELITE methods,[3,4] these were the most widely adopted applications on BN II and BN ProSpec Systems.

Recent clinical studies[5,6] have reported N Latex FLC results to demonstrate good clinical concordance with FREELITE, with some differences in measurement of concentrations. These studies conclude that N Latex FLC monoclonal antibody-based assays were developed with good performance characteristics such as batch-to-batch reproducibility, antigen-excess security, and high precision.

Since the availability of the N Latex FLC methods, many BN II and BN ProSpec System laboratories worldwide have chosen to adopt these Siemens methods.

Method

The evaluation at the Royal Preston Hospital was performed in two phases: 1) initial assay evaluation and 2) extended evaluation.

The focus for the initial assay evaluation was to determine the N Latex assay performance characteristics, including comparison with IFE. Comparative analysis was performed with FREELITE, including external quality assurance (EQA) samples, to determine the clinical utility in the diagnosis and management of monoclonal gammopathies.

- Accuracy: Nine EQA samples were tested for both FLC methods and IFE to evaluate how well the samples correlated. As there is no international standard for the assay, this was difficult to evaluate.
- Precision: Pools of sera were created, including a normal pool, kappa pools of low, medium, and high values, and lambda pools of medium and high values. Result reproducibility in the pools was evaluated
- Recovery: Three serum samples were serially diluted 10-fold in phosphate-buffered solution (1/10, 1/100, 1/1000 and 1/10,000) and assay performance evaluated
- Interference: Normal and pathological samples with WHO/NIBSC rheumatoid reference reagent (25 IU/L), in-house patient sera with high rheumatoid factor (245 IU/L), LIQUICHECK paediatric quality control containing high bilirubin (300 µmol/L), and an in-house highly haemolysed patient serum were tested. The samples were then tested on both assays to determine the impact of these interfering factors.
- Antigen excess: A very-high-kappa known myeloma patient (97,859.60 mg/L on Integra) and high lambda sample (1488.40 mg/L on Integra) were tested on the BN ProSpec System using the N Latex FLC assay to confirm that the BN ProSpec System recognized very high value for kappa and lambda and diluted the sample appropriately to obtain a valid result.
- Clinical utility: Patients with known myeloma/malignancy background and patients with nonspecific clinical background were tested by both assays, and a direct comparison was performed on the interpretation of results obtained using the two assays. One-third of the patients recruited were either known myeloma patients or were being investigated for myeloma.

The initial assay evaluation concluded that:

- Assay characteristics were good, with no problems seen with accuracy, precision, and interfering factors and no antigen-excess issues detected.
- Results correlated well with IFE.
- Comparative analysis was good between manufacturers, but it was felt that an extended evaluation was required, testing more samples.

The focus for the extended evaluation was to analyze all FLC patient and EQA sample requests on both methods for a 3-month period to further evaluate the clinical utility of the N Latex FLC methods. The results from this phase of the evaluation are outlined below.

Results

FLC Kappa Correlation Siemens N Latex vs. FREELITE

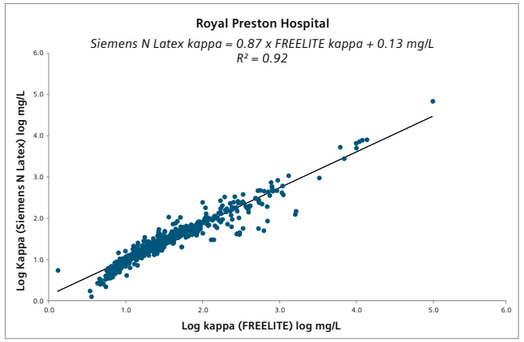

Figure 1. FLC kappa correlation for Siemens N Latex versus The Binding Site FREELITE on a log scale.

FLC Lambda Correlation Siemens N Latex vs. FREELITE

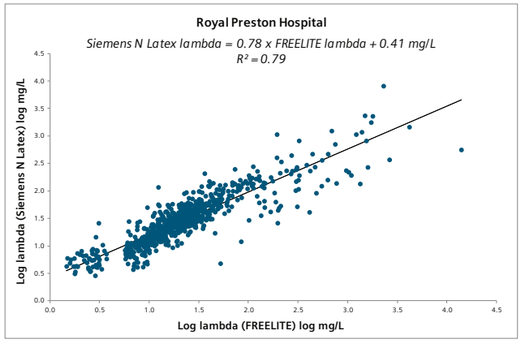

Figure 2. FLC lambda correlation for Siemens N Latex versus The Binding Site FREELITE on a log scale.

Table 1. FLC kappa concordance table for Siemens N Latex (reference range 6.7–22.4 mg/L) versus The Binding Site FREELITE (reference range 3.3–19.4 mg/L).

		FREELITE					
	Kappa	**<3.3 mg/L Low**	**3.3–19.4 mg/L Normal**	**>19.4 mg/L High**			
N Latex	**<6.7 mg/L Low**	1	42	0	**Different:**	115	16%
	6.7–22.4 mg/L Normal	0	236	68	**Identical:**	611	84%
	>22.4 mg/L High	0	5	374	**Total:**	726	

Table 2. FLC lambda concordance table for Siemens N Latex (reference range 8.3–27.0 mg/L) versus The Binding Site FREELITE (reference range 5.7–26.3 mg/L).

		FREELITE					
	Lambda	**<5.7 mg/L Low**	**5.7–26.3 mg/L Normal**	**>26.3 mg/L High**			
N Latex	**<8.3 mg/L Low**	50	38	1	**Different:**	183	25%
	8.3–27.0 mg/L Normal	6	239	16	**Identical:**	543	75%
	>27.0 mg/L High	0	122	254	**Total:**	726	

Table 3. FLC ratio concordance table for Siemens N Latex (reference range 0.31–1.56) versus The Binding Site FREELITE (reference range 0.26–1.65).

		FREELITE					
	Ratio	**<0.26 Low**	**0.26–1.65 Normal**	**>1.65 High**			
N Latex	**<0.31 Low**	58	29	0	**Different:**	120	17%
	0.31–1.56 Normal	3	402	84	**Identical:**	602	83%
	>1.56 High	0	4	142	**Total:**	722	

Data analysis

The concentration range of FLC kappa and lambda spans several potencies; levels can be below 1 mg/L or higher than 10 mg/L. In order to illustrate the correlation of the entire range, a logarithmic scale has been applied.

The comparison data for the extended evaluation demonstrates good correlation between the N Latex FLC and FREELITE assays.

A higher correlation is observed between FLC kappa (R2 0.92) compared to FLC lambda (R2 0.79).

When applying the reference ranges specified by each manufacturer, the concordance tables show an 84% agreement for FLC kappa, 75% agreement for FLC lambda, and 83% agreement for the FLC ratio between the N Latex FLC and FREELITE assays.

In general, N Latex lambda measures 10% higher than FREELITE, pushing more of these patients into the monoclonal increase or abnormal classification groups. However, of the 122 patients that demonstrated high N Latex lambda but normal FREELITE lambda, 95 reported normal ratios. This is also reflected in the higher agreement for FLC ratio between the N Latex FLC and FREELITE assays. The International Myeloma Working Group recommends a panel of serum protein electrophoresis, serum IFE, and serum FLC kappa and lambda assays for screening monoclonal gammopathies. Complying with this testing algorithm shows no difference in the final diagnosis for these patients.

Conclusion

The Siemens N Latex FLC methods demonstrate good clinical concordance with The Binding Site FREELITE assay, with few discrepant results.

Where differences were seen, complying with the testing strategy recommended by the International Myeloma Working Group identified any discrepant results, so there was no difference in the final diagnosis for these patients.

Slight differences in actual concentration are expected when comparing assays with the monoclonal (Siemens N Latex FLC) versus polyclonal (The Binding Site FREELITE) antibody approach. Changing over to the Siemens N Latex FLC method therefore requires a period of rebaselining patients.

Siemens N Latex FLC methods deliver improved efficiency and substantial cost savings through flexible kit configuration, antigen-excess security, and random-access capability, all of which help to streamline laboratory processes. Running FLC samples and managing the laboratory workload is simplified for the operator and laboratory management.

References:

1. RJ Lock, et al. A multicentre study comparing two methods for serum free light chain analysis. Ann Clin Biochem. 2013;50:255-259.
2. Dispenzieri A, Kyle R, Merlini G, Miguel JS, Ludwig H, Hajek R, et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. Leukemia. 2009;23:215-24.
3. Tate JR, Mollee P, Dimeski G, Carter AC, Gill D. Analytical performance of serum free light-chain assay during monitoring of patients with monoclonal light-chain diseases. Clin Chem Acta. 2007;376:30-6.
4. Briand PY, Decaux O, Caillon H, Grosbois B, Le TA, Guenet L. Analytical performance of the serum free light chain assay. Clin Chem Lab Med. 2010;48:73-9.
5. te Velthuis H, Knop I, Stam P, van den Broek M, Klaasse Bos H, Hol S, et al. N Latex FLC – new monoclonal high performance assays for the determination of free light chain κ and λ. Clin Chem Lab Med. 2011;49:1323-32.
6. Hoedemakers RMJ, et al. Clinical comparison of new monoclonal antibody-based nephelometric assays for free light chain kappa and lambda to polyclonal antibody-based assays and immunofixation electrophoresis. Clin Chem Lab Med. 2012;50(3):489-495.