

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

A. 510(k) Number:

K033811 (bundled)

B. Analyte:

kappa (κ) free light chain, lambda (λ) free light chain

C. Type of Test:

Quantitative (*nephelometry*)

D. Applicant:

The Binding Site, Ltd.

E. Proprietary and Established Names:

FREELITE[®] Human Kappa Free Kit for use on the Olympus AU[™] series diagnostic test kits

FREELITE[®] Human Lambda Free Kit for use on the Olympus AU[™] series diagnostic test kits

F. Regulatory Information:

1. Regulation section:
21 CFR § 866.5550, Immunoglobulin (light chain specific) immunological test system.
2. Classification:
Class II
3. Product Codes:
DFH [Kappa (κ)]; DEH [Lambda (λ)]
4. Panel:
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G. Intended Use:

1. Intended use(s):
The FREELITE[®] Human kappa (κ) free and the FREELITE[®] Human Lambda (λ) free kits is used to determine the concentration of these light chains in serum and urine on the Olympus AU[™] series diagnostic test kits. (*The kits are sold separately.*)
2. Indication(s) for use:
The quantitation of κ and λ free light chains "...aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosis."

3. Special condition for use statement(s):
Not applicable.
4. Special instrument Requirements:
The test kits are used on the Olympus AU™ series diagnostic test kits.

H. Device Description:

Each FREELITE® kit contains the specific anti-free light chain antibody, i.e., either anti-κ or anti-λ, and the reagents needed for assaying serum and urine samples. (*Each kit is sold separately.*)

I. Substantial Equivalence Information:

1. Predicate device name(s):
FREELITE® BNII test kits.
2. Predicate K number(s):
K010440 AND K010441
3. Comparison with Predicate:
The kits in this submission are identical to those in the predicate devices. The only difference is that the kits will be used in another test system.

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

Not applicable.

K. Test Principle:

The concentration of the soluble antigen is assessed by nephelometry. The test sample is mixed with the appropriate antibody in a solution inside a cuvette. As the antigen-antibody complex forms, a beam of light is passed through the cuvette. The degree of scattering of this light increases with the increase in the concentration of insoluble immune complexes. An excess of antibody is placed in the cuvette so that the amount of immune complex formed is proportional to the antigen concentration. Measurement of the light intensity at an angle away from the incident light is used to monitor the light scattering. A Calibration curve of measured light scatter vs. antigen concentration is generated using a series of Calibrators of known antigen concentration, and the results read from this curve for samples of unknown antigen concentration.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. Precision/Reproducibility:
Repetitive assays of clinical sera at three different concentration levels, i.e., low, medium, and high, were performed, i.e., 10 measurements made on one day run for within run precision, and 10 separate assays using the same batch of antisera for between run precision. The data summarized below show consistent results across all three levels with an acceptable percentage Coefficient of Variation (%CV).

Within run Precision:

Level	Kappa (κ) [mg/mL]			Lambda (λ) [mg/mL]		
	1	2	3	1	2	3
Mean	22.05	40.83	153.26	31.43	66.10	183.09
%CV	1.97	1.24	1.89	1.64	0.77	6.79

Between run Precision:

Level	Kappa (κ) [mg/mL]			Lambda (λ) [mg/mL]		
	1	2	3	1	2	3
Mean	22.23	41.35	135.38	29.63	62.92	177.91
%CV	5.78	5.17	6.02	5.43	4.92	4.51

- b. *Linearity/assay reportable range:*
Linearity for the Olympus Freelite assays (covalent liquid latex) was confirmed using serially diluted samples covering the lower part of the measuring range, samples at the higher measuring range and at the neat concentration. The regression plot equations where y is the measured level of free chain concentration and x the theoretical concentration were:

$$y = 0.98 x + 1.68 \text{ (mg/mL), } r = 1.00, \text{ for } \kappa \text{ chains (1:10 dilution)}$$

$$y = 1.08 x - 2.97 \text{ (mg/mL), } r = 0.98, \text{ for } \lambda \text{ chains (1:10 dilution)}$$

- c. *Traceability (controls, calibrators, or method):*
Not applicable for the purpose of this submission.
- d. *Detection limit:*
The sensitivity attained is shown below:

	Serum (1:5)	Urine (neat)
Both κ and λ	3.0 mg/L	0.6 mg/L

- e. *Analytical specificity*
Measurement of purified whole immunoglobulins, i.e., IgG, IgA, and IgM, were used to demonstrate analytical specificity for both test kits using control sera consisting of 53mg κ /L or 24mg λ /L at 1:10 dilution).

Interference (*)

Substance	Kappa (κ)		Lambda (λ)	
	Conc.	% Int *	Conc.	% Int *
Bilirubin	200 mg/L	- 4.8	200mg/L	- 1.6
Hemoglobin	1g/L	+ 5.9	3g/L	+ 8.9
Chyle	1930 [#]	- 10.7	1930 [#]	+ 0.77

[#] formazine turbidity units

As shown above, interference of the substances tested was minimal. The values reported in this submission are consistent with the results of similar studies reviewed for clearance of K010440 and K010441.

f. *Assay cut-off.*

The approximate measuring ranges when using a 1: 10 sample dilution are 6 - 150mg/L for κ free light chains, and 8.1 -260 mg/L for λ free light chains.

g. *Stability.*

Results from two stability studies were submitted to support modifications to the storage times for both kits. The stability of Free Kappa and Free Lambda Freelite® Olympus kits was established by testing three lots of each at the time of manufacture and at 3, 6, 9 and 12 months at recommended storage conditions. The results provide reasonable assurance that the kits are stable for up to 12 months at the recommended storage conditions. In addition, the stability of partially used kits stored for five months was assessed. Based on the percentage difference in the values obtained at t_0 and after storage the reagents are stable for up to five months after opening when stored at 2–8°C.

2. Comparison studies:

a. *Method comparison with predicate device:*

The applicant submitted the results of a study where they tested samples from normal subjects and from disease state samples with both the Olympus AU™ and the BNII assays to establish equivalence. The data, including regression analysis results, are summarized below:

κ free light chains*

Sample Type	N	BNII		Olympus AU™		Y intercept	slope	r
		Low	Max.	Low	Max			
Normal serum	100	4.10	31.20	8.03	34.56	21.18mg/L	0.95	0.95
SLE**	8	13.9	44.7	18.02	29.64			
κ myeloma	28	12.75	2615.00	17.44	2637.00			
λ myeloma	25	0.12	29.15	0.90	16.5			

* Normal adult serum ranges were established for BNII.

** System lupus erythemoatosus

λ free light chains*

Sample Type	N	BNII		Olympus AU™		Y intercept	slope	r
		Low	Max.	Low	Max			
Normal serum	100	6.06	34.30	9.87	37.38	11.75mg/L	0.88	0.99
SLE**	8	18.00	68.35	15.16	66.25			
κ myeloma	40	30.50	3917.50	25.52	3133.00			
λ myeloma	28	0.84	20.87	3.25	23.08			

* Normal adult serum ranges were established for BNII.

** System lupus erythemoatosus

Normal Urine Ranges (Olympus AU™) [N=16 healthy adults]

	Free κ (mg/mL)	Free λ (mg/mL)	κ/λ ratio (mg/mL)
Mean conc.	6.06	2.88	2.10
Median conc.	3.45	2.22	1.86
95 Percentile Range	0.35 – 20.30	0.52 – 6.82	0.99 – 3.62

Conclusion from these studies: The r values obtained for the serum samples were 0.95 and 0.99, which suggest that the linear regression analyses provides reasonable estimates of the slope and y intercept. The data provide reasonable assurance of comparable performance of the FREELITE® kits with both systems. However, it should be noted that some level of systematic error (SE) is detected when comparisons are made at the concentration limits that border the 95 Percentile ranges (normal serum range) for both types of free chains.

- b. *Matrix comparison:*
Established in original device clearance.
- 3. Clinical studies:
 - a. *Clinical sensitivity:*
(Established in original device clearance.)
 - b. *Clinical specificity:*
(Established in original device clearance.)
 - c. *Other clinical supportive data (when a and b are not applicable):*
Not applicable.
- 4. Clinical cut-off:
See comments to items L.1.f above and N.5 below.
- 5. Expected values/Reference range:
The expected values and reference ranges for both free κ and free λ chains in adult serum were established for the FREELITE® BNII. The applicant provided data in this submission to establish comparable performance of the kits in the BNII and Olympus AU™ series assays, and that the established ranges are applicable to use of the kits in the new device. The device labeling contains a statement alerting the user that these ranges “...have been obtained from a limited number of samples and are intended for guidance purposes only.” The manufacturer recommends in the labeling that users generate local ranges.

M. Conclusion:

A single 510K statement [as required in 21 CFR 807.93 (a)], a 510(k) Truthful and Accurate statement [as required by 21 CFR 807.87(k)], and a single copy of the Indications for Use statement [as required by 21 CFR § 807.92 (a) (5)] were provided for both test kits.

The purpose of this 510(k) was to seek clearance to market the FREELITE® Human

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Kappa and Lambda Free Kit for use on the Olympus AU™ series diagnostic test kits. The data submitted in this 510(k) substantiate a good level of agreement between the results obtained with both test kits and confirms the level of performance previously demonstrated for the FREELITE® BNII test (K040441). Based on the review of the information provided each FREELITETM kit performs equally in both the Olympus AU™ and the predicate device in the assessment of the concentration of either Kappa or Lambda free light chains for those conditions specified in the Indications for Use statement. Therefore, the applicant provided acceptable supporting evidence to establish substantial equivalence.