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

**A. 510(k) Number:**
k051915

**B. Purpose for Submission:**
Add a new platform/analyzer.

**C. Measurand:**
Kappa free light chains and lambda free light chains

**D. Type of Test:**
Nephelometric or turbidimetric, quantitative

**E. Applicant:**
The Binding Site, Ltd.

**F. Proprietary and Established Names:**
Freelite™ Human Kappa Free kit for use on Bayer ADVIA 1650 Analyzer
Freelite™ Human Lambda Free kit for use on Bayer ADVIA 1650 Analyzer

**G. Regulatory Information:**

1. Regulation section:
   21 CFR § 866.5550, Immunoglobulin (light chain specific) immunological test system
2. Classification:
   Class II
3. Product code:
   DFH, Kappa, antigen, antiserum, control
   DEH, Lambda, antigen, antiserum, control
4. Panel:
   IM (82)

**H. Intended Use:**

1. Intended use(s):
   The Binding Site FREELITE™ Human Kappa or Lambda Free kit is intended for the quantitation of kappa free light chains or lambda free light chains in serum on the Bayer ADVIA 1650 Analyzer. Measurement of the various amounts of the different types of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphatic neoplasms, Waldenstrom's microglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus.
2. Indication(s) for use:
   Same as intended use.
3. Special conditions for use statement(s):
   For prescription use only.
4. Special instrument requirements:
   Bayer ADVIA 1650 Analyzer

**I. Device Description:**
The FREELITE Human Kappa or Lambda kit consists of a latex reagent (polystyrene beds coated with monospecific antibody), a standard, a high control, a low control

and a supplementary reagent.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   The Binding Site (TBS) Freelite BN II kit and TBS Bayer ADVIA Freelite assays.
2. Predicate 510(k) number(s):
   k010440 and k010441
3. Comparison with predicate:
   Please fill in comparison tables

| **Similarities** | | |
|---|---|---|
| Item | Device | Predicate |
| Intended use | Quantitation of kappa free light chains or lambda free light chains in serum | Same |
| Indication for use | Aids in the diagnosis and monitoring of multiple myeloma, lymphatic neoplasms, Waldenstrom's microglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus. | Same |
| Methodology | Nephelometric & Turbidimetric | Same |
| Calibration procedure | Same | Same |

| **Differences** | | |
|---|---|---|
| Item | Device | Predicate |
| Analyzer | Bayer Advia 1650 | Dade Behring Nephelometer II |

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

None referenced

**L. Test Principle:**

The FREELITE Human Kappa kits and FREELITE human Lambda kits are nephelometric or turbidimetric assays. The test sample is added to a solution containing the appropriate antibody in a reaction vessel. A beam of light is passed through the vessel and as the antigen–antibody reaction proceeds, the light passing through is increasingly scattered as insoluble immune complexes are formed. The

amount of immune complex formed is proportional to the antigen concentration in the test sample. In nephelometry, the light scatter is monitored by measuring the light intensity at an angle away from incident light beam. A series of calibrators of known antigen concentration are assayed to construct a calibration curve which will be used for determining the antigen concentration of test samples.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

   Analytical studies were performed at the Bayer Diagnostics facility at New Bury, Berks, UK.

   *a. Precision/Reproducibility:*

   Three pooled sera containing free kappa and free lambda at three different levels were used for this study. Each sample was run ten times to generate within run precision. For between run precision the samples were run in singlicate on ten separate assay runs using the same batch of antisera. Results are summarized below:

| | Kappa | | | Lambda | | |
|---|---|---|---|---|---|---|
| Within-run precision | Level 1 | Level 2 | Level 3 | Level 1 | Level 2 | Level 3 |
| Mean (mg/mL) | 9.39 | 17.41 | 40.72 | 9.67 | 23.00 | 73.03 |
| SD | 0.61 | 0.48 | 0.95 | 0.61 | 1.48 | 1.33 |
| %CV | 6.51 | 2.72 | 2.34 | 6.28 | 6.42 | 1.81 |
| Between-run precision | | | | | | |
| Mean (mg/mL) | 9.60 | 18.20 | 40.68 | 11.20 | 23.96 | 77.14 |
| SD | 0.48 | 0.35 | 1.05 | 0.79 | 0.69 | 2.28 |
| %CV | 4.98 | 1.91 | 2.59 | 7.07 | 2.90 | 2.96 |

   *b. Linearity/assay reportable range:*

   Three serum samples with high concentrations of free kappa and free lambda were serially diluted with saline to 1/516 to cover the assay measuring ranges (3.74- 56.2 mg/mL for Kappa, and 7-93.4 mg/mL for Lambda). Each diluted sample was assayed in duplicate and the assays were run at the normal sample dilutions of 1/5 for Kappa and 1/8 for Lambda on Bayer Advia 1650.

| | Kappa | Lambda |
|---|---|---|
| Sample 1 | $y = 1.0115x + 0.2859$<br>$r^2 = 0.9975$ | $y = 0.9964x - 1.1026$<br>$r^2 = 0.9981$ |
| Sample 2 | $y = 0.9993x + 0.0585$<br>$r^2 = 0.9996$ | $y = 1.0099x – 1.1441$<br>$r^2 = 0.9994$ |
| Sample 3 | $y = 1.0022x + 0.2726$<br>$r^2 = 0.999$ | $y = 1.0043x - 0.0966$<br>$r^2 = 0.9999$ |

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

   No reference standard or method available.

   Stability was determined by testing three kit lots of Freelite Kappa and Lambda were tested at 0 and 12 months. At each stage a calibration curve was

run with kit controls and internal reference standard. Acceptance criteria for control results and internal standard were set to be within ± 20% of the assigned value. An acceptable working calibration curve was obtained at each time point tested (0 and 12 months). All the control results obtained were within the acceptable range of ± 20% of the assigned value. The results showed stability for at least 12 months from the date of manufacture when stored at 2-8 °C.

*d. Detection limit:*
Not performed for purpose of this submission.

*e. Analytical specificity:*
Interference was assessed by spiking high concentrations of triglycerides (0.5%), hemoglobin (1,3and 5 mg/mL) and bilirubin (200mg/mL). Saline was added as a control for comparison. All assays were run in triplicate. No significant interference was observed in the case of triglycerides and bilirubin. However, some interference was observed for hemoglobin concentrations at and above 3mg/mL.

*f. Assay cut-off:*
Not performed for purpose of this submission.

2. Comparison studies:

*a. Method comparison with predicate device:*
Comparison of Binding site's (TBS) Bayer Advia Freelite Kappa and TBS Freelite Kappa BNII assays were performed using 77 serum samples (30 normals, 27 myeloma patient samples and 20 other clinical conditions [not specified] collected from various hospitals in U.K). All samples were stored at -20°C prior to assay. The regression plot gave a gradient close to unity (0.976). A slope of 0.976 and a correlation coefficient $r^2 = 0.9481$. The y-intercept was high (19.83 mg/mL) and is said to be due to some myeloma samples. Overall the data show comparabilty between the current and the predicate Kappa kits. For comparison of TBS Bayer Advia Freelite Lambda and TBS Freelite Lambda BNII kits, the regression plot gave a gradient very close to unity (1.012) and a correlation coefficient $r^2 = 0.9681$ and a relatively high y-intercept of 6.264 mg/mL. The results show an acceptable comparison with the predicate device.

*b. Matrix comparison:*
No comparison was performed since the sample matrices are the same.

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:
Not applicable for this submission.

**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.