

K070900

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

NOV 30 2007

- A. 510(k) Number:**
k070900
- B. Purpose for Submission:**
New analyzer
- C. Measurand:**
Immunoglobulins, Kappa (κ) free light chains and Lambda (λ) free light chains
- D. Type of Test:**
Quantitative, Nephelometry or turbidimetry
- E. Applicant:**
The Binding Site, Ltd.
- F. Proprietary and Established Names:**
FREELITE™ Human Kappa Free Kit for use on Roche COBAS® INTEGRA
400/400*plus*
FREELITE™ Human Lambda Free Kit for use on Roche COBAS® INTEGRA
400/400*plus*
- G. Regulatory Information:**
- Regulation section:
21 CFR § 866.5550, Immunoglobulin (light chain specific) immunological test system
 - Classification:
Class II
 - Product codes:
DFH - Kappa, antigen, antiserum, control
DEH - Lambda, antigen, antiserum, control
 - Panel:
Immunology (82)
- H. Intended Use:**
- Intended use(s):
The FREELITE™ Human Kappa Free kit is intended for the quantitation of Kappa free light chains in serum on the Roche COBAS INTEGRA 400 and 400*plus*. Measurement of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.

The FREELITE™ Human Lambda Free kit is intended for the quantitation of Lambda free light chains in serum on the Roche COBAS INTEGRA 400 and 400*plus*. Measurement of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.

2. Indication(s) for use:
Same as Intended use.
3. Special conditions for use statement(s):
For prescription only.
4. Special instrument requirements:
Roche COBAS® INTEGRA 400/400*plus*

I. Device Description:

The FREELITE™ Human Kappa and Lambda Free kit contains polyclonal monospecific antibody coated onto polystyrene latex, a standard, two controls (high and low polyclonal kappa or lambda free light chain), and supplementary reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):
FREELITE™ Human Kappa Free Kit for use on Dade Behring Nephelometer™ II
FREELITE™ Human Lambda Free Kit for use on Dade Behring Nephelometer™ II
2. Predicate K number(s):
k010440 (Kappa)
k010441 (Lambda)
3. Comparison with predicate:

| Similarities | | |
|--|--|-----------|
| Item | Device | Predicate |
| Indication for Use | Measurement of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings | Same |
| Controls | Human sera containing polyclonal free light chain, in stabilized liquid form, contain 0.099% sodium azide, 0.1% EACA, 0.01% benzamidine. Packaged in glass vials | Same |
| Stability/ storage of unopened reagent | 2-8°C until expiry date | Same |

| Differences | | |
|-------------|---|---------------------------------------|
| Item | Device | Predicate |
| Instrument | Roche COBAS INTEGRA 400 and 400 <i>plus</i> | Dade Behring Nephelometer II (BN™ II) |
| Technology | Turbidimetry | Nephelometry |
| Assay times | 8.3 minutes | 18 minutes |

| Differences | | |
|-----------------------------------|--|--|
| Item | Device | Predicate |
| Cuvettes | Disposable | Washable |
| Sample matrix | Serum | Serum and urine |
| Sample dilution | 1:10 | 1:100 |
| Kappa or Lambda Latex Reagent | Supplied in Nalgene plastic bottles. Transferred to C-Pack prior to assay. | Supplied in Nalgene plastic bottles. No transfer prior to assay. |
| Supplementary Reagent | Type 116 Latex buffer containing Sodium Azide (NaN ₃) 0.099%. Type 265 PEG solution can be added for optimizing reaction if required. Supplied in Nalgene plastic bottles. Transferred to C-Pack prior to assay. | Type 49 Distilled water containing Sodium Azide (NaN ₃) 0.099%. Type 265 PEG solution can be added for optimizing reaction if required. Packaged in glass vials. |
| Opened reagent Storage/ stability | 2-8°C up to 1 month | 2-8°C up to 3 months |
| Measuring range | κ: 2.9 – 127 mg/L (1:10) λ: 5.2 – 139 mg/L (1:8) | κ: 5.9 – 190 mg/L (1:100) λ: 8.1 – 260 mg/L (1:100) |
| Sensitivity (serum) | κ: 0.6 mg/L (1:2) λ: 1.3 mg/L (1:2) | κ: 0.3 mg/L (1:5) λ: 0.4 mg/L (1:5) |
| Linearity | κ: $y = 1.003x - 0.937$, $r = 0.99$ λ: $y = 1.004x - 1.123$, $r = 1.0$ | κ: $y = 0.98x + 0.83$, $r = 0.99$ λ: $y = 0.99x - 0.63$, $r = 1.0$ |

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

CLSI (NCCLS) EP5-A: Evaluation of Precision Performance of Clinical Chemistry Approved Guideline.

L. Test Principle:

The concentration of a soluble antigen is nephelometrically or turbidimetrically measured by the addition of the test sample to a solution containing the appropriate antibody in a reaction vessel or cuvette. A beam of light is passed through the cuvette and as the antigen-antibody reaction proceeds, the light passing through the cuvette is scattered increasingly as insoluble immune complexes are formed. The antibody in the cuvette is in excess so the amount of immune complex formed is proportional to the antigen concentration. In nephelometry the light scatter is monitored by measuring the light intensity at an angle away from incident light, whilst in turbidimetry light scatter is monitored by measuring the decrease in intensity of the incident beam of light. A series of calibrators of known antigen concentration are assayed initially to produce a calibration curve of measured light scatter versus antigen concentration. Samples of unknown antigen concentration can then be assayed and the results read from the calibration curve.

The sensitivity of nephelometric or turbidimetric assays can be increased by the use of particle enhancement. This entails linking the antibody to a suitably sized particle that increases the relative light-scattering signal of the antigen-antibody reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The study was carried out by testing three samples with different concentrations of kappa or lambda light chains using three different reagent lots on one analyzer. The study was performed over 21 working days, with two runs per day. Results are summarized below:

| Kappa Precision | Within run | | Between-run | | Between-day | | Total Precision | |
|--------------------------|------------|-----|-------------|-----|-------------|-----|-----------------|-----|
| | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Low (mean 5.99 mg/L) | 0.35 | 5.8 | 0.16 | 2.7 | 0.22 | 3.6 | 0.44 | 7.4 |
| Medium (mean 18.72 mg/L) | 0.40 | 2.1 | 0.51 | 2.7 | 0.60 | 3.2 | 0.88 | 4.7 |
| High (mean 95.64 mg/L) | 1.38 | 1.4 | 1.68 | 1.8 | 2.01 | 2.1 | 2.97 | 3.1 |

| Lambda Precision | Within run | | Between-run | | Between-day | | Total Precision | |
|-------------------------|------------|-----|-------------|-----|-------------|-----|-----------------|-----|
| | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Low (mean 7.72 mg/L) | 0.17 | 2.3 | 0.19 | 2.5 | 0.29 | 3.7 | 0.39 | 5.0 |
| Medium (mean 27.0 mg/L) | 0.18 | 0.7 | 0.21 | 0.8 | 0.42 | 1.5 | 0.50 | 1.9 |
| High (mean 99.2 mg/L) | 0.72 | 0.7 | 0.73 | 0.7 | 1.60 | 1.6 | 1.90 | 1.9 |

b. *Linearity/assay reportable range:*

Linearity was confirmed using serial dilutions of polyclonal samples. The regression plot equations where y is the measured level of free chain concentration and x the theoretical concentration were:

$$y = 1.003x - 0.937 \text{ (mg/L), } r = 0.99 \text{ for } \kappa \text{ chains}$$

$$y = 1.004x - 1.123 \text{ (mg/L), } r = 1.00 \text{ for } \lambda \text{ chains}$$

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

No reference standards are available for these analytes. A calibrator and two controls are provided with each kit. No changes were made from previous cleared submission.

On-board stability studies were tested at 0, 4, 8, 13, 17, 24, 31, 38 day intervals. Stability results over the testing period meet the acceptance criteria of $\pm 20\%$ differences.

d. *Detection limit:*

Analytical sensitivity was determined by assaying ten replicates of two samples with concentrations close to the lowest calibration points. The analytical sensitivity claims were: 0.6 mg/L for kappa and 1.3 mg/L for lambda.

e. *Analytical specificity:*

Interference study: the table below shows common substances that could interfere with this method. Samples were run in triplicate. Minimum interferences were observed except for 15.5% difference with Rheumatoid factor on kappa antiserum. The package insert states the information below.

| Interferent | Concentration | % Difference | |
|-------------------|---------------|--------------|-------------|
| | | κ (15 mg/L) | λ (18 mg/L) |
| Bilirubin | 200.0 mg/L | -9.4 | -1.7 |
| Haemoglobin | 5.7 g/L | 8.2 | 3.8 |
| Intralipid | 0.2% | 1.3 | |
| | 0.5% | | -1.9 |
| Rheumatoid factor | 320.0 I.U. | 15.5 | |
| | 480.0 I.U. | | 3.3 |

f. Assay cut-off:

Refer to Expected values.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 132 serum samples were tested on the Freelite Kappa and Lambda Roche Cobas Integra 400/400plus and Freelite Kappa and Lambda Dade Behring BNII assays. Fifty (50) samples were normal adult sera and 82 samples were abnormal adult sera (58 known/suspected multiple myeloma (<80 mg/dL to >1000 mg/dL) and 24 systemic lupus erythematosus). The differences observed between the two assays were likely due to different test parameters and kinetics of reaction. The data including regression analysis results were as follows:

| Samples | Kappa | Lambda |
|------------------------|------------------------|------------------------|
| Normal Sera (n = 50) | | |
| Range (mg/L) | 5-24 mg/L | 3-19 mg/L |
| Deming regression | $y=0.932x + 1.472$ | $y=1.08x - 1.09$ |
| R ² | R ² =0.9168 | R ² =0.9351 |
| Clinical Sera (n = 82) | | |
| Range (mg/L) | 0.4-1,900 mg/L | 1-18,700 mg/L |
| Deming regression | $y=0.90x + 23.54^*$ | $y=0.892x + 50.06$ |
| R ² | 0.9316 | 0.9673 |

*Two markedly high monoclonal values (5000 and 120000 mg/L) were excluded from calculation.

b. Matrix comparison:

Not applicable,

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:

The reference range table provided below were from 282 normal subjects aged

from 20 – 90 years which were assayed using Binding Site FREELITE Kappa and Lambda Free kits on BN II™ (Katzmann, JA et al. 2002 Clin Chem 48: 1437 – 1444).

| Normal adult serum | Mean conc. | Median conc. | 95 th percentile range |
|--------------------|--------------|--------------|-----------------------------------|
| Free Kappa | 8.36 (mg/L) | 7.30 (mg/L) | 3.30 - 19.40 (mg/L) |
| Free Lambda | 13.43 (mg/L) | 12.40 (mg/L) | 5.71 - 26.30 (mg/L) |
| | Mean | Median | Total range |
| Kappa/Lambda Ratio | 0.63 | 0.60 | 0.26 - 1.65 |

In addition, the package insert includes the following statements:

- 1.) “The ranges provided have been obtained from a limited number of samples and are intended for guidance purposes only. Wherever possible it is strongly recommended that local ranges are generated.”

- 2.) “In order to demonstrate equivalence of the normal range obtained with the BNII and INTEGRA assays, 50 normal samples from UK donors aged 20 – 60 years were assayed on both BN and INTEGRA FREELITE kits”. Results of regression analysis were:
 Kappa assay
 $(\text{INTEGRA}) = 0.932(\text{BNII}) + 1.472, R^2 = 0.9168;$
 Lambda assay
 $(\text{INTEGRA}) = 1.08(\text{BNII}) - 1.09, R^2 = 0.9351$

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.

P. Other Supportive Device and Instrument Information:

I. Comparative study with predicate:

The original data submitted had several different scale unit measurements and could not be analyzed. The applicant was asked to re-submit the method comparison analysis with the same scale unit increments for appropriate analysis. In addition, the applicant was asked to provide the line data in tabulated format with results in descending order and identified with the disease condition.

Applicant re-submitted the data in 10 different graphs: five graphs for kappa and five graphs for lambda. The five different kappa graphs depicted: (a) all normal samples; (b) all abnormal samples; (c) abnormal samples >1000 mg/dL; (d) abnormal samples 80-1000 mg/dL; and (e) abnormal samples <80 mg/dL. The five different lambda graphs depicted: (a) all normal samples; (b) all abnormal samples; (c) abnormal samples >997 mg/dL; (d) abnormal samples 80 - 997 mg/dL; and (e) abnormal samples <80 mg/dL.

After the initial analysis, the applicant was asked to recalculate the Kappa comparative clinical study calculations (n =82) excluding two samples with extreme values (5000 and 12,000 mg/L). The Deming regression equation improved from $y = 0.77x + 45.85$ to $y = 0.90x + 23.54$ after the two extreme values were excluded.

II. Package Insert (P.I.):

Major revisions were made to both the Kappa and Lambda package inserts.

1. Intended Use statement: No 'urine' samples were provided for the study. The 'urine' sample claim was omitted from the Intended Use statement in both Kappa and Lambda P.I.
2. Comparative study section:
 - a) Major errors were found in this section. It appears that the P.I. data were from the predicate device P.I. with 'immunofixation electrophoresis (IFE)' comparative data. The data in this section did not match the 'nephelometric' data submitted in the file. Major corrections were made to clearly present the 'nephelometric' comparative data.
 - b) Applicant was asked to delete the 'Kappa/Lambda Ratio Range' column and rows from the Comparative Study Table. Reviewer checked the normal ratio and the numbers appeared to be comparable. The 'Kappa/Lambda Ratio Range' data are depicted below:

| | Kappa/Lambda Ratio Range |
|----------------------|--------------------------|
| Normal Sera (n = 50) | |
| Range (mg/L) | 0.74-2.29 |
| Deming regression | $y=0.91x + 0.18$ |

| | Kappa/Lambda Ratio Range |
|------------------------|--------------------------|
| R ² | 0.79 |
| Clinical Sera (n = 82) | |
| Range (mg/L) | 0.0007-4000 |
| Deming regression | y=0.955x + 8.571 |
| R ² | 0.994 |

3. Precision study: No line data for precision studies were submitted. Line data were asked to be provided for both the within run and between run precision on the Kappa and Lambda studies. Line data were received.
4. Linearity study: Erroneous data were submitted for the Kappa and Lambda linearity studies. Corrections were made and re-submitted.
5. Interference study: Slight interference with Rheumatoid factor on the Kappa and Lambda kits were observed. The following statement have been included in the P.I.:

Kappa and Lambda Limitation section: “Possible interference due to the presence of rheumatoid factor can also occur.

Kappa Interference section: “Slight interference (+15.1% difference) by 320 IU/mL rheumatoid factor has been demonstrated using a 15mg/L free kappa serum sample”.

Lambda Interference section: “Minimal interference (+3.3% difference) by 480 IU/mL rheumatoid factor has been demonstrated using an 18mg/L free lambda serum sample”.

6. Limitation section of both Kappa and Lambda P.I.: Applicant was asked to clarify that the results in this assay may not be interchangeable depending on the platform and kinetics of reaction used. The new information in the ‘Limitation section’ states: “Monoclonal light chains may not demonstrate identical reaction kinetics on different instruments. Whilst abnormal results are expected on all platforms, the numerical values will not always be directly comparable”
7. Interpretation of Serum Free Light Chain Results section: This section was misleading and was subsequently excluded. One literature support from The Binding Site, Inc. was insufficient for the claims listed in this section. A consensus in literature was strongly preferred to support the claims listed below. Since the applicant could not provide additional literature, the following statements were asked to be deleted:
 - “Abnormal kappa/lambda ratios support the diagnosis of a monoclonal gammopathy and require an appropriate tissue biopsy. Borderline elevated kappa/lambda ratios occur with renal impairment and may require appropriate renal function tests.
 - Low concentration of kappa, lambda or both indicates bone marrow function

- impairment.
- Elevated concentrations of both kappa and lambda with a normal kappa/lambda ratio may be due to the following:
 - Renal impairment (common)
 - Over-production of polyclonal free light chains from inflammatory conditions (common)
 - Biclonal gammopathies of different free light chain types (rare)
 - Elevated concentrations of both kappa and lambda with an abnormal kappa/lambda ratio suggest a combination of monoclonal gammopathy and renal impairment.

Reviewer asked the applicant to omit the above misleading claims due to the following reasons:

- (a) The listed statements in the 'Interpretation of Serum Free Light Chain Results (sub-section 11.2) on how to use the results for different pathological conditions were incomplete and could be misleading which could cause adverse outcomes. The Serum Free Light Chain tests are not stand-alone tests.
- (b) It is not a standard clinical practice to diagnose or rule out pathological conditions based on one laboratory test. Other clinical and laboratory findings are required.
- (c) One of the essential factors in monoclonal gammopathy determination is the clonality of the M (monoclonal) protein. The FREELITE™ Kappa and Lambda free light chain kits nor the serum electrophoresis do not measure heavy chains, therefore, it is not possible for either test mentioned in this section to rule out monoclonal gammopathy.
- (d) Elevated concentration levels of kappa and/or lambda light chains and abnormal κ/λ ratios have also been observed in conditions other than monoclonal gammopathy.
- (e) Wordings used to the effect that abnormal Serum Free Light Chain Results and Ratio Results could 'support diagnosis monoclonal gammopathy and require an appropriate biopsy'; or that borderline results could 'occur with renal impairment; or that low concentrations 'indicates bone marrow function impairment' statements need justification and additional literature support.
- (f) The user should be provided with a listing of all scenarios on how to appropriately interpret the results of Kappa and Lambda Serum Free Light Chains and the κ/λ ratio from low, marginal to high results. It has to be a clear and thorough guide for the users to use in order to prevent adverse outcomes on false negative or false positive interpretations.
- (g) Revision of the statements in the 'Serum Free light chain and ratio' result interpretation section' should include other clinical and laboratory findings which are required and to address the following scientific articles compiled by the reviewer:
 - i. Bakshi N et al. [Am J Clin Path 2005] reported 11 out of 23 cases with high FLC κ/λ ratio to be false positives for monoclonal gammopathy

- (MCG) and 4 out of 10 cases with low FLC κ/λ ratio were false negatives for MCG.
- ii. Bakshi N et al. [Am J Clin Path 2005] mentioned detecting “22 cases with M proteins by CZE that had normal κ/λ ratios”.
 - iii. Bakshi N et al [Am J Clin Path 2005] reported that “the FLC ratio can be abnormal in non-neoplastic B-cell proliferative disorders (chronic immune stimulation, e.g. SLE polyangiitis, Sjögren syndrome, hepatitis B) or asymptomatic cases”.
 - iv. Tate J et al [Clin Chem 2003] reported that the ‘use of Free Light Chain measurements alone cannot differentiate some groups of patients with monoclonal gammopathy from healthy individuals’.
 - v. Bradwell A et al. [Clin Chem 2001] stated that “ratios might be normal in early disease or during clinical remission, and increased polyclonal FLC concentrations will mask low concentrations of monoclonal FLC. In addition, biclonal gammopathies of different FLC types could produce normal κ/λ ratios although the concentrations of both molecules might be increased”.
 - vi. Kyle et al [NEJM 2002] observed that unrelated patient conditions could affect the FLC κ/λ ratio determinations and results, e.g. some effects in cases with idiopathic thrombocytopenic purpura and vasculitis cases
 - vii. Munshi N [Blood 2005] mentioned that renal function changes and the light chain short life could affect the FLC κ/λ ratio determinations and results.
 - viii. Munshi N [Blood 2005] recommended that ‘levels of Free Light Chains need to be interpreted carefully, taking into consideration the κ/λ ratio’.

III. Statistics:

1. Recommendations from Dr. Shanti Gomatam were followed as listed below:

- (a) Two samples with extreme values (5000 and 12,000 mg/L) were excluded from the kappa comparative clinical study calculations (n =82). Reviewer explained that in clinical setting, patients with these results would be automatically treated as clinically indicated. The Deming regression improved from ‘ $y = 0.77x + 45.85$ ’ to ‘ $y = 0.90x + 23.54$ ’ after the two extreme values were excluded.
- (b) The applicant was asked to explain the differences of the two instrument versions ‘Integra 400’ and ‘Integra 400*plus*’. Although all data were generated from ‘Integra 400*plus*’, the submitted file documents only referred to ‘Integra 400’. The applicant explained that the current instrument version available is the ‘Integra 400*plus*’. The difference between the two instruments is that the computer is an integral part of the 400 analyzer, but a separate entity from the 400*plus* analyzer. The printout

states Integra 400 for both 400 and 400*plus* versions.

(c) All statement referring to Mayo Clinic trials were deleted.

(d) The 'urine' sample claim was deleted from the device P.I.

IV. Summary of additional comments:

1. Reviewer performed data search on previously cleared three 510 (k)'s on Kappa and Lambda Free Light Chains with the same Intended Use. The clinical data were comparable to these two new devices. The results of these tests are not stand-alone results but will be used in conjunction with other laboratory/clinical findings. Treatment of patients will depend on clinical indications. Major revisions were made in the two final P.I. versions with additional specific limitation comments, clear statistical information, and deletions of various claims.
2. The confidence interval of intercept and slope in the comparative 50 normal sera studies were as follows:
Kappa 95% CI Intercept = 0.4259 to 2.5183 and Slope = 0.8505 to 1.0134.
Lambda 95% CI Intercept = -2.0419 to -0.1533 and Slope = 1.0017 to 1.1676.

Q. Administrative Information:

1. Applicant contact information:
 - a. *Name of applicant:*
The Binding Site, Inc.
 - b. *Mailing address:*
P.O. Box 11712
Birmingham B14 4ZB, UK
 - c. *Phone #:*
+44 (0) 121-436-1000
310-449-1399
 - d. *Fax #:*
+44 (0) 121-430-7061
310-449-1394
 - e. *E-mail address (optional):*
info@bindingsite.co.uk
jhgeller@aol.com
 - f. *Contact:*
Jay H. Geller
2. Review documentation:
 - a. All required administrative paperwork was included in the submission: Indications for Use statement, Truthful and Accurate statement and a 510 (k) Summary.
 - b. Chronology
03/30/07 Date of submission

04/02/07 Received in DMC and letter sent for missing User fee
 04/09/07 Received by reviewer
 05/14/07 Telephone Hold letter for additional information
 05/23/07 Extension letter request
 05/25/07 DMC granted extension up to 8/13/07
 07/17/07 Preliminary e-responses received by reviewer
 07/27/07 Supplement # S1 received in DMC
 07/30/07 Supplement # S1 received in DIHD
 07/31/07 Supplement # S1 received by reviewer
 08/14/07 Statistician consult request
 08/15/07 Brief meeting with Statistician Dr. S. Gomatam
 08/28/07 Applicant information on alternate TBS contact scientist
 08/29/07 Teleconference with Dr. S. Gomatam
 08/30/07 Received Stat review Dr. S. Gomatam
 08/30/07 Consult with Dr. M. Chan
 08/30/07 Clarification and P.I. revision requests
 08/31/07 Applicant re-submitted unreadable graphs via email
 08/31/07 Applicant unavailable to respond to issues until next week
 08/31/07 Telephone hold for additional information
 09/05/07 Update on applicant availability after 9/20/07
 09/21/07 Preliminary e-responses received by reviewer
 09/21/07 New reference literature emailed to reviewer
 09/26/07 Clarification questions emailed to applicant
 09/27/07 DMC due date grace period emailed to applicant's inquiry
 09/28/07 Consult with Dr. M. Chan
 09/28/07 Additional clarification questions emailed to applicant
 10/22/07 Supplement # S2 received in DMC
 10/23/07 Supplement # S2 received in DIHD
 10/24/07 Supplement # S2 received by reviewer
 10/25/07 Consult with Dr. M. Chan
 10/25/07 Corrections to uncorrected Kappa P.I. emailed to applicant
 10/26/07 Received corrected Kappa P.I.
 11/05/07 Consult with Dr. M. Chan on two P.I.'s
 11/05/07 Corrections to P.I. emailed to applicant
 11/06/07 Applicant unavailable to respond in a week
 11/06/07 Telephone hold for two P.I. modifications
 11/27/07 Preliminary P.I. corrected versions emailed to reviewer
 11/27/07 Consult with Dr. M. Chan
 11/27/07 Clarification question emailed to applicant
 11/28/07 Clarification response emailed to reviewer
 11/28/07 Revisions on two P.I.s emailed to applicant
 11/29/07 Corrected final versions of two P.I.s emailed to reviewer
 11/29/07 Consult with Dr. M. Chan
 11/29/07 Acceptance of two final P.I. versions emailed to applicant
 11/30/07 Supplement #3: Two final P.I.s received in DMC & by reviewer
 11/30/07 SE decision

3. Substantial Equivalence Discussion:

| | Yes | No |
|--|-----|---------------------------------------|
| 1. Same Indication Statement? | X | If YES = Go To 3 |
| 2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness? | | If YES = Stop NSE |
| 3. Same Technological Characteristics? | X | If YES = Go To 5 |
| 4. Could The New Characteristics Affect Safety Or Effectiveness? | | If YES = Go To 6 |
| 5. Descriptive Characteristics Precise Enough? | | X If NO = Go To 8 If YES = Stop SE |
| 6. New Types Of Safety Or Effectiveness Questions? | | If YES = Stop NSE |
| 7. Accepted Scientific Methods Exist? | | If NO = Stop NSE |
| 8. Performance Data Available? | X | If NO = Request Data |
| 9. Data Demonstrate Equivalence? | X | Final Decision: SE |

Note: See

http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4148/FLOWCHART%20DECISION%20TREE%20.DOC for Flowchart to assist in decision-making process. Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

- a. *Explain how the new indication differs from the predicate device's indication:*
- b. *Explain why there is or is not a new effect or safety or effectiveness issue:*
- c. *Describe the new technological characteristics:*
- d. *Explain how new characteristics could or could not affect safety or effectiveness:*
- e. *Explain how descriptive characteristics are not precise enough:*

It is necessary to see the assay's analytical performance as well as comparison to the predicate device. For this reason, descriptive characteristics alone would not be adequate to address agency concerns.

- f. *Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:*

g. *Explain why existing scientific methods can not be used:*

h. *Explain what performance data is needed:*

The performance data in support of substantial equivalence include the following: method comparison, precision/reproducibility, analytical sensitivity and specificity, linearity, and stability.

i. *Explain how the performance data demonstrates that the device is or is not substantially equivalent:*

The analytical performance data presented correlated with the performance of the predicate device and therefore demonstrate that the device is substantially equivalent to the marketed device.

R. Reviewer Name and Signature:


Therese B. Datiles



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 30 2007

The Binding Site, Ltd.
c/o Mr. Jay H. Geller
East Tower, Suite 600
2425 West Olympic Blvd.
Santa Monica, CA 90404

Re: k070900

Trade/Device Name: FREELITE™ Human Lambda Free Kit for use on Roche COBAS®
INTEGRA 400/400 plus
FREELITE™ Human Kappa Free Kit for use on Roche COBAS®
INTEGRA 400/400 plus

Regulation Number: 21 CFR 866.5550

Regulation Name: Immunoglobulin (light chain specific) immunological test system

Regulatory Class: Class II

Product Code: DFH, DEH

Dated: November 29, 2007

Received: November 30, 2007

Dear Mr. Geller:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set

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forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,



Robert L. Becker, Jr., M.D., Ph.D.

Director

Division of Immunology and Hematology Devices

Office of In Vitro Diagnostic Device Evaluation and Safety

Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K070900

Device Name: FREELITE® Human Kappa Free Kit for use on the Roche COBAS® INTEGRA 400/400 plus Analyzer

Indications for Use: For the quantitation of kappa free light chains in serum on the Roche COBAS INTEGRA 400 and 400plus. Measurement of the various amounts of the different types of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.


Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K070900

Prescription Use
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE
OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Attachment K /

Indications for Use

510(k) Number (if known): K070900

Device Name: FREELITE® Human Lambda Free Kit for use on the Roche COBAS® INTEGRA 400/400 plus Analyzer

Indications for Use: For the quantitation of lambda free light chains in serum on the Roche COBAS INTEGRA 400 and 400plus. Measurement of the various amounts of the different types of light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.

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Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k): K070900

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use _____
(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE
OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Attachment K 2