August 23, 2018

The Binding Site Group Ltd
Andrea Thomas
Regulatory Affairs Officer
8 Calthorpe Road Edgbaston
Birmingham, B15 1QT Gb

Re: K173732
Trade/Device Name: Optilite Freelite Mx Kappa Free Kit, Optilite Freelite Mx Lambda Free Kit
Regulation Number: 21 CFR 866.5550
Regulation Name: Immunoglobulin (light chain specific) immunological test system
Regulatory Class: Class II
Product Code: DFH, DEH
Dated: July 26, 2018
Received: July 31, 2018

Dear Andrea Thomas:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to 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 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kelly Oliner -S

For
Lea Carrington, Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K173732

Device Name
Optilite Freelite Mx Kappa Free Kit (LK016.M.OPT.A)

Optilite Freelite Mx Lambda Free Kit (LK018.M.OPT.A)

Indications for Use *(Describe)*
The Optilite Freelite Mx Kappa Free Kit is intended for the quantitative in vitro measurement of Kappa free light chains in serum and urine using the Binding Site Optilite analyser. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.

The Optilite Freelite Mx Lambda Free Kit is intended for the quantitative in vitro measurement of Lambda free light chains in serum and urine using the Binding Site Optilite analyser. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Optilite Freelite Mx Kappa Free Kit and Optilite Freelite Lambda Free Submission Summary

Date prepared: 23rd August 2018

A. 510(k) Number:
K173732

B. Purpose for Submission:
Addition of a urine matrix and an addition of a 1+0 sample dilution to a cleared IVD assay (K150658)

C. Measure and:

Kappa (κ) free light chains and Lambda (λ) free light chains

D. Type of Test:
Quantitative, Turbidimetry

E. Applicant:
The Binding Site Group, Ltd.
Contact person: Andrea Thomas
Address: 8 Calthorpe Road, Birmingham, B15 1QT, United Kingdom
Contact number: +44(0)121 456 9500

F. Proprietary and Established Names:
Optilite® Freelite Mx™ Kappa Free Kit
Optilite® Freelite Mx™ Lambda Free Kit

G. Regulatory Information:

1. Regulatory 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

   Panel:
   Immunology (82)

H. Intended Use:

1. Intended use(s):
   The Optilite Freelite Mx Kappa Free Kit is intended for the quantitative *in vitro* measurement of Kappa free light chains in serum and urine using the Binding Site Optilite analyser. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and

connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.

The Optilite Freelite Mx Lambda Free Kit is intended for the quantitative *in vitro* measurement of Lambda free light chains in serum and urine using the Binding Site Optilite analyser. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.

Indication(s) for use:

Same as intended use.

2. Special conditions for use statement(s):
For prescription use only.

Warning: The kappa free light chain results for a given specimen determined with assays from different manufacturers or on different systems 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 kappa free light chain assay used. Values obtained with different assays or systems cannot be used interchangeably. If, in the course of serially monitoring a patient, the assay or system used for determining kappa free light chain levels is changed, additional sequential testing should be carried out. Prior to changing assay or system, the laboratory **MUST** confirm baseline values for patients being serially monitored

Warning: The lambda free light chain results for a given specimen determined with assays from different manufacturers or on different systems 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 lambda free light chain assay used. Values obtained with different assays or systems cannot be used interchangeably. If, in the course of serially monitoring a patient, the assay or system used for determining lambda free light chain levels is changed, additional sequential testing should be carried out. Prior to changing assay or system, the laboratory **MUST** confirm baseline values for patients being serially monitored.

Special instrument requirements:

Optilite Analyser (Indiko) (K110035)

I. Device Description:

The Optilite Freelite Mx Kappa Free Kit is comprised of the following reagents:

Latex Reagent: Sheep anti-Human Kappa (polyclonal monospecific) antibody (F(ab')2 fragment) bound to 200nm polystyrene latex particles. In 0.033M Glycine buffered saline pH8 (containing Sodium Azide (0.033%), Proclin (0.05%), Benzamidine (0.01%) and EACA (0.1%) as preservative plus BSA (0.033%)

Calibrator and Controls: Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, 0.1% EACA and 0.01% benzamidine as preservatives.

Reaction Buffer: Containing 0.099% sodium azide as a preservative.

The Optilite Freelite Mx Lambda Free Kit is comprised of the following reagents:

Latex Reagent: Sheep anti-Human Lambda (polyclonal monospecific) Free antibody (F(ab')2 fragment) bound to 200nm polystyrene latex particles. In 0.033M Glycine buffered saline pH8 (containing Sodium Azide (0.033%), Proclin (0.05%), Benzamidine (0.01%) and EACA (0.1%) as preservatives plus BSA (0.1665%))

Calibrator and Controls: Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, 0.1% EACA and 0.01% benzamidine as preservatives.

Reaction Buffer: Containing 0.099% sodium azide as a preservative.

Note - In Optilite Freelite kits, the latex reagent and reaction buffer are supplied in a single wedge with a chamber for each fluid. They are therefore labelled as a single component *Optilite Kappa Free Mx Reagent* or *Optilite Lambda Free Mx Reagent*.

J. Substantial Equivalence Information:

1. Predicate device names and predicate 510(k) number:
   Freelite® Human Kappa Free Kit for use on the Siemens BN™II (K) and Freelite® Human Lambda Free Kit for use on the Siemens BN™II (K040009)

2. Comparison with predicate:

Similarities		
Item	**Test Device (Optilite)**	**Predicate (BNII)**
Assay type	Quantitative	Same
Intended Use (Kappa)	Quantitation of kappa free light chains in serum and urine. It is intended to aid in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.	Same
Intended Use (Lambda)	Quantitation of lambda free light chains in serum and urine. It is intended to aid in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinaemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.	Same
Analyte	Kappa Free Light Chains Lambda Free Light Chains	Same
Detection Antibody	LK016.M.OPT.A: Sheep anti-human kappa antibody ($F(ab)_2$ fragment) bound to latex particles LK018.OPT.A: Sheep anti-human kappa antibody ($F(ab)_2$ fragment) bound to latex particles	Same
Calibration	The Optilite analyser produces a calibration curve by performing multiple dilutions of a single calibrator fluid	Same
Traceability	Internally produced master calibrator	Same
Sample Matrix	Serum and Urine	Same
Open Vial Stability	3 months	3 months

Differences		
Item	**Device**	**Predicate (BNII)**
Instrument	Optilite	Siemens BNII Systems
Test Method	Turbidimetric	Nephelometric
Adult Reference Interval	Free Kappa: 32.90 mg/L* Free Lambda: 3.79 mg/L* * 97.5th Percentile (one sided reference interval)	Free Kappa: 1.35 – 24.19 mg/L Free Lambda: 0.24 – 6.66 mg/L Kappa/Lambda Ratio: 2.04 – 10.37 Reference intervals taken from predicate product inserts.
Measuring Range and Dilutions (Kappa)	1+0: 0.3 – 12.65 mg/L 1+1: 0.6 – 25.3 mg/L **1+9: 2.9 – 127 mg/L (Std. dil.)** 1+99: 29 – 1270 mg/L 1+999: 290 – 12700 mg/L 1+4999: 1450 – 63500 mg/L	1/1: 0.06 – 1.9 mg/L 1/5: 0.3 – 9.5 mg/L 1/20: 1.2 – 38.0 mg/L **1/100: 5.9 – 190 mg/L (Std. dil.)** 1/400: 23.6 – 760 mg/L 1/2000: 118 – 3800 mg/L 1/8000: 472 – 15200 mg/L
Measuring Range and Dilutions (Lambda)	1+0: 0.74 – 17.4 mg/L 1+1: 1.3 – 34.7 mg/L **1+7: 5.2 – 139 mg/L (Std. dil.)** 1+79: 52 – 1390 mg/L 1+799: 520 – 13900 mg/L 1+7999: 5200 – 139000 mg/L	1/1: 0.05 – 1.6 mg/L 1/5: 0.25 – 8.0 mg/L 1/20: 1.0 – 32.0 mg/L **1/100: 5.0 – 160 mg/L (Std. dil.)** 1/400: 20.0 – 640 mg/L 1/2000: 100 – 3200 mg/L 1/8000: 400 – 12800 mg/L
On Board Stability	30 days	None quoted

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

CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

CLSI EP7-A2 Interference Testing in Clinical Chemistry, Approved Guideline - Second Edition.

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach.

CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition.

CLSI C28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory.

L. Test Principle:

Evaluating the concentration of a soluble antigen (e.g. Kappa free light chains) by turbidimetry involves 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. Light scatter is monitored by measuring the decrease in intensity of the incident beam of light. The antibody in the cuvette is in excess so the amount of immune complex formed is proportional to the antigen concentration. 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

Kappa

The within-run, between-run, between-day and between-instrument precision were determined by testing four urine sample pools over 21 days with two runs per day using one reagent lot on three analysers. Results are summarised below.

Sample	Mean	Within Run		Between Run		Between Day		Between Instrument		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	5.49	0.28	5.1	0.10	1.8	0.30	5.4	0.35	6.3	0.42	7.6
2	33.08	0.70	2.1	1.61	4.9	2.08	6.3	0.55	1.7	2.72	8.2
3	99.16	3.12	3.1	4.56	4.6	4.29	4.3	2.62	2.7	6.99	7.1
4	179.12	5.16	2.9	5.11	2.9	13.89	7.8	12.88	7.2	15.68	8.8

Lambda

The within-run, between-run, between-day and between-instrument precision were determined by testing five urine sample pools over 23 days with two runs per day using one reagent lot on three analysers. Results are summarised below.

Sample	Mean	Within Run		Between Run		Between Day		Between Instrument		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	4.48	0.11	2.5	0.22	4.9	0.27	4.8	0.05	1.1	0.33	7.3
2	7.19	0.35	4.8	0.37	5.1	0.36	5.1	0.48	6.7	0.62	8.7
3	54.37	1.22	2.2	3.17	5.8	2.88	5.3	3.25	6.0	4.45	8.2
4	109.27	5.19	4.8	4.39	4.0	5.72	5.2	4.45	4.1	8.89	8.1
5	133.46	4.09	3.1	3.66	2.7	10.11	7.6	11.62	8.7	11.50	8.6

b. *Linearity/assay reportable range:*

A linearity study was performed following CLSI document Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. The linearity of the Kappa Free and Lambda Free assays have been confirmed using serially diluted urine samples to cover the standard measuring ranges of 2.9 – 127mg/L (Kappa) and 5.2 – 139mg/L (Lambda) respectively. The results demonstrated that the kappa free and lambda free assays are linear over the ranges of 2.383–142.687mg/L (Kappa) and 3.87 – 160.02mg/L (Lambda) with deviation from linearity ≤ 10%.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Traceability: Internally produced master calibrator

Stability: Not applicable. On board, open vial and real time stability was evaluated in K150658.

d. *Detection limit:*
The analytical sensitivity was determined in accordance with CLSI EP17-A and was carried out using both serum and urine matrices. The Limit of Blank was based on 60 determinations of blank samples (analyte depleted serum and urine at a low analyte concentration) and was estimated at the 95th percentile of the distribution. The Limit of Detection was calculated from the LoB and the combined SD of the five LoQ samples. The LoQ was calculated from five independent samples (Serum samples: samples diluted with analyte depleted serum and Urine samples: in house urine at low analyte concentration which was then pooled with an in house urine with a higher analyte concentration) to achieve a concentration close to the bottom of the measuring range) tested twelve times over five days. The tabulated summary of results is shown below:

	LoB	**LoD**	**LoQ**
Kappa Free (Serum)	0.195mg/L	0.224mg/L	0.330mg/L
Kappa Free (Urine)	0.210mg/L	0.232mg/L	0.330mg/L
Lambda Free (Serum)	0.285mg/L	0.393mg/L	0.740mg/L
Lambda Free (Urine)	0.080mg/L	0.184mg/L	0.740mg/L

e. Analytical specificity:

Interference:

Interferences were assessed according to CLSI EP7-A2 by testing a single urine sample for the Kappa Free assay and the Lambda Free assay. Samples were prepared with an analyte concentration around the reference limit of each assay. Each sample was made up using urine from a healthy adult donor and urine from a kappa or lambda myeloma patient. Samples containing interferents were compared to matched control samples which contained no interferent. The mean results from the spiked samples must be within 10% of the mean of the control samples.

Kappa

No significant assay interference effects were observed when the samples were tested with substances at the concentrations given below.

Substance	Concentration
Ascorbic Acid	200 mg/L
Albumin	5 g/L
Bilirubin	100 mg/L
Bortezomib	6 mg/mL
Cyclophosphamide	330 mg/mL
Digoxin	0.375 µg/mL
Haemoglobin	240 mg/L
Penicillin	75 mg/L
Phenytoin	15 mg/L
Theophylline	150 mg/L

Lambda

No significant assay interference effects were observed when the samples were tested with substances at the concentrations given below.

Substance	Conc.
Ascorbic Acid	200 mg/L
Albumin	5 g/L
Bilirubin	100 mg/L
Bortezomib	3.6 mg/mL
Cyclophosphamide	330 mg/mL
Digoxin	0.375 µg/mL
Haemoglobin	250 mg/L
Penicillin	75 mg/L
Phenytoin	15 mg/L
Theophylline	150 mg/L

Cross reactivity:

No significant cross reaction was observed during testing for the predicate device. The specificity of the antisera is unchanged.

Antigen Excess Detection:
The possibility of antigen excess occurring when using the device on the Optilite analyser was evaluated in K150658

Assay cut-off:
Not applicable. Refer to expected values of reference range.

2. Comparison studies:
   a. *Method comparison with predicate device:*

Kappa Free:
A comparison study was performed by analysing 165 urine samples (including 86 with analyte levels below the reference limit) using the Optilite Freelite Mx Kappa Free kit and an alternative commercially available assay. Passing Bablok regression analysis generated the following results:

y = 1.02x – 0.21 (mg/L) (y = Optilite; x = predicate analyser)
correlation coefficient r = 0.992

Lambda Free:
A comparison study was performed by analysing 115 urine samples (including 59 with analyte levels below the reference limit) using the Optilite Freelite Mx Lambda Free kit and an alternative commercially available assay. Passing Bablok regression analysis generated the following results:

y = 1.11x – 0.27 (mg/L) (y = Optilite; x = predicate analyser)
correlation coefficient r = 0.947

   b. *Matrix comparison:* Not applicable.

3. Clinical studies:
   a. *Clinical Sensitivity/clinical specificity:*

Kappa (2X2):

		Predicate Assay		
		+	-	**Total**
Test Assay	+	78	1	79
	-	8	79	87
	Total	86	80	**166**

Agreement	**Percentage**	**95% Confidence Interval**
Positive	90.7%	82.7% to 95.2%
Negative	98.8%	93.3% to 99.8%
Overall	94.6%	90.0% to 97.1%

Lambda (2X2):

		Predicate Assay		
		+	-	**Total**
Test Assay	+	56	0	56
	-	20	92	112
	Total	76	92	**168**

Agreement	**Percentage**	**95% Confidence Interval**
Positive	73.7%	62.8% to 82.3%
Negative	100.0%	96.0% to 100.0%
Overall	88.1%	92.3% to 92.2%

b. Other clinical supportive data (when a. is not applicable):
Not applicable.

4. Clinical cut-off: Not applicable

5. Expected values/Reference range:

Normal adult urine	**Mean (mg/L)**	**Median (mg/L)**	**Reference Limit (mg/L) (97.5th Percentile)**
Kappa free	7.64	4.54	32.90
Lambda free	1.03	0.74	3.79

N. Proposed Labelling:
The labelling 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.