May 23, 2025

The Binding Site Group Ltd
Jolanta Wolff
Regulatory Affairs Project Manager
8 Calthorpe Road
Edgbaston
Birmingham, B15 1QT
United Kingdom

Re: K250549
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: February 24, 2025
Received: February 25, 2025

Dear Jolanta Wolff:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ying Mao -S

Ying Mao, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K250549

Device Name
Optilite® Freelite Mx Kappa Free Kit;
Optilite® Freelite Mx Lambda Free Kit

Indications for Use *(Describe)*

Optilite® Freelite Mx Kappa Free Kit:
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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted in conjunction with other laboratory and clinical findings.

Optilite® Freelite Mx Lambda Free Kit:
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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted 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.

510(k) SUMMARY (as per 21 CFR 807.92)

This 510(k) Summary of Safety and Effectiveness information is being submitted in accordance with the requirements of the Safe Medical Device Act 1990 and 21 CFR 807.92.

510(k) Number:	K250549
Type of 510(k):	Original, Traditional 510(k)
Purpose of Submission:	Modification to a previously cleared device
Date of Preparation:	24 February 2025, revised on 23 May 2025

1 SUBMITTER / APPLICANT:

The Binding Site Ltd
8 Calthorpe Road, Edgbaston, Birmingham, B15 1QT, GB

Correspondent/ Contact:	Jolanta Wolff, MBA Regulatory Affairs Project Manager
Phone:	+44 121 456 9500

2 DEVICE INFORMATION:

Proprietary Name:	Optilite® Freelite Mx™ Kappa Free Kit Optilite® Freelite Mx™ Lambda Free Kit
Measurand:	Kappa (κ) free light chains (FLC) Lambda (λ) free light chains (FLC)
Type of Test:	Quantitative, immunoturbidimetry

Regulatory information:

Regulation section:	21 CFR 866.5550, Immunoglobulin (light chain specific) immunological test system
Classification:	Class II
Product Code(s):	DFH – Kappa antigen, antiserum, control DEH – Lambda antigen, antiserum, control
Review Panel:	IM - Immunology (82)

3 PREDICATE DEVICES AND 510(k) NUMBERS

Freelite® Human Kappa Free Kit for use on the Siemens BN™II - K040009
Freelite® Human Lambda Free Kit for use on the Siemens BN™II - K040009

4 DEVICE DESCRIPTION

4.1 Test Principle

No modification is made to the principle of operation for the Optilite® Freelite Mx Kappa and Lambda Free Kits cleared in K173732 and K150658.

The determination of soluble antigen concentration by turbidimetric methods involves the reaction with specific antiserum to form insoluble complexes. When light is passed through the suspension formed a portion of the light is transmitted and focused onto a photodiode by an optical lens system. The amount of transmitted light is indirectly proportional to the specific protein concentration in the test sample. Concentrations are automatically calculated by reference to a calibration curve stored within the instrument.

4.2 Special conditions for use statement(s):

This product is for in vitro diagnostic prescription use only.

The kappa (or 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 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.
Interpretation of results:
Guidelines and consensus recommendations for the diagnosis and monitoring of multiple myeloma and AL amyloidosis have been published by the International Myeloma Working Group (IMWG) and National Cancer Comprehensive Network (NCCN). Evaluation of patients with MGUS is also included in guidelines published by IMWG and NCCN. These include FLC testing, with the reference values for FLC based on Freelite Mx assay results. Guidelines are included in the bibliography. However, clinicians should refer to the most current versions available as they may be updated.
Limitations:

- Turbidity, particles and haemolysis may interfere with the assay. Samples that are visibly turbid or containing particles should be centrifuged prior to testing (ref CLSI – C56-A). Highly lipaemic or turbid samples that cannot be clarified should not be used. Unexpected results should be confirmed using an alternative assay method.
- Diagnosis cannot be made and treatment must not be given on the basis of Kappa free light chain measurements alone. Clinical history and other laboratory findings must be taken into account.
- This assay has not been established for use with the paediatric population.

4.3 Special Instrument requirements

Automated Optilite® Analyser

4.4 Kit Reagents and composition

The devices in this submission have not materially changed since originally cleared under K150658.

Materials provided in the Optilite Freelite Mx Kappa Free kit:

- Optilite Kappa Free Mx Reagent
- Optilite Kappa Free Mx Calibrator
- Optilite Kappa Free High Mx Control
- Optilite Kappa Free Low Mx Control

Materials provided in the Optilite Freelite Mx Lambda Free kit:

- Optilite Lambda Free Mx Reagent
- Optilite Lambda Free Mx Calibrator
- Optilite Lambda Free High Mx Control
- Optilite Lambda Free Low Mx Control

Reagents composition:

- *Latex Reagent*: Consisting of polyclonal monospecific antibody coated onto polystyrene latex. Supplied in stabilised liquid form. Preservatives: 0.1% E-amino-n-caproic acid (EACA) and 0.01% benzamidine, 0.05% ProClin.
- *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.

5 INTENDED USE/ INDICATIONS FOR USE:

5.1 Intended use:

Same as indications for use.

5.2 Indications for use:

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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted 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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted in conjunction with other laboratory and clinical findings.

6 PERFORMANCE CHARACTERISTICS

6.1 Similarities and Differences to the Predicate:

A comparison of the similarities and differences between the proposed Optilite Freelite Mx Kappa and Lambda Free Kits and the predicate Freelite Human Kappa and Lambda Free Kit for use on the Siemens BN™II, provided in Table 1 as follows:

Table 1. Technological similarities and differences.

Similarities		
Item	**(Proposed Device)** **Optilite Freelite Mx Kappa Free Kit** **Optilite Freelite Mx Lambda Free Kit** **(K250549)**	**(Predicate Device)** **Freelite® Human Kappa Free Kit for use on the Siemens BN™II** **Freelite® Human Lambda Free Kit for use on the Siemens BN™II** **(K040009)**
Assay type	Quantitative	same
Analyte	Kappa Free Light Chains Lambda Free Light Chains	same
Calibration	The Optilite analyser produces a calibration curve by performing multiple dilutions of a single calibrator fluid	same
Detection antibody	Kappa: Sheep anti-human kappa antibody (F(ab)2 fragment) bound to latex particles Lambda: Sheep anti-human kappa antibody (F(ab)2 fragment) bound to latex particles	same
Adult Reference Interval (Serum)	Serum (95 Percentile Range): Kappa: 3.30 – 19.40mg/L Lambda: 5.71 – 26.30mg/L Ratio: 0.26 – 1.65mg/L	same
Specimen Type	Serum and Urine	same
Calibrator Traceability	Internal Reference Master Calibrator	same

Differences		
Item	**(Proposed Device)** **Optilite Freelite Mx Kappa Free Kit** **Optilite Freelite Mx Lambda Free Kit** **(K250549)**	**(Predicate Device)** **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)**
Intended use	**Kappa:** 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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted in conjunction with other laboratory and clinical findings. **Lambda:** 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 in serum and urine 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); and in serum aids in the evaluation of monoclonal gammopathy of undetermined significance (MGUS). Results of the free light chain measurements should always be interpreted in conjunction with other laboratory and clinical findings.	**Kappa:** This kit is intended for the quantitation of kappa free light chains in serum and urine on the Siemens BN™II. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings. **Lambda:** This kit is intended for the quantitation of lambda free light chains in serum and urine on the Siemens BNII. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.
Instrument	Optilite Analyser	Siemens BN™II Systems
Measuring Range (Kappa)	1+0: 0.3 – 12.7 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 (urine only) 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 (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 (urine only) 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
Adult Reference Interval (Urine)	Kappa: ≤32.90mg/L* Lambda: ≤3.79mg/L* * 97.5th Percentile (one sided reference interval)	Kappa: 1.35 – 24.19 mg/L Lambda: 0.24 – 6.66 mg/L Kappa/Lambda Ratio: 2.04 – 10.37 (95 Percentile Range)

This submission is to add a claim for evaluation of MGUS to the intended use statement (in serum). The differences between the predicate and proposed device do not result in a change to the safety and efficacy when used according to the product labeling.

6.2 Performance Data:

Refer to submission K173732 and K150658 for previously documented analytical performance studies.

6.3 Clinical Performance data for evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS)

MGUS is a plasma cell dyscrasia characterised by the presence of a monoclonal protein (M-protein) in the serum of asymptomatic individuals who do not meet the diagnostic criteria for multiple myeloma (MM), AL amyloidosis, Waldenström's macroglobulinaemia (WM), lymphoproliferative disorders, plasmacytoma or related conditions. [1]
The clinical evaluation studies included testing of samples from patients with clinically confirmed MGUS and from disease control subjects (non-MGUS patients) with the Optilite Freelite Mx Kappa Free Kit, and the Optilite Freelite Mx Lambda Free Kit, and assessing the concordance of the test results with the clinical truth of the patient. The testing investigated the performance of Freelite Mx test results in MGUS and disease controls (non-MGUS) at single time points (Study 1); and the monitoring performance of Freelite Mx test results measured on serial samples from patients with stable and progressive MGUS (Study 2).

6.3.1 Evaluation of MGUS and disease controls (non-MGUS) at single time points (Study 1)

6.3.1.1 <u>Determination of Positive Rate Ratio</u>

Freelite Mx Kappa:Lambda Ratio – Positive Rate (%) in MGUS

A retrospective study was performed using a total of 229 MGUS samples from patients with clinically confirmed MGUS. The clinical diagnostic criteria that the clinicians used to establish the clinical truth of all samples included in the study as 'MGUS positive' was confirmed with each site. The diagnostic criteria and classification for MGUS and related plasma-cell disorders, as practiced clinically, fulfilled, but was not limited to, the criteria outlined by the 'International Myeloma Working Group (IMWG)' consensus. All samples were tested for free light chain (FLC) Kappa and Lambda levels with the Optilite Freelite Mx Kappa and Lambda Free kits on the Optilite Analyser. The Kappa:Lambda ratios were calculated for each sample. The result of the device was compared to the clinical diagnosis for each sample.
The test result for MGUS positive or negative were based on the following definitions:

- Test positive (Freelite Mx Positive = Abnormal): FLC Kappa:Lambda ratio was outside the reference interval (0.26-1.65) for intact immunoglobulin MGUS; the FLC Kappa:Lambda ratio was outside the reference interval (0.26-1.65) and the involved FLC level was above the reference interval (Kappa 3.30-19.40 mg/L and Lambda 5.71-26.30 mg/L) for LC-MGUS.
- Test negative (Freelite Mx Negative = Normal): FLC Kappa:Lambda ratio was within the reference interval (0.26-1.65).

Light chain MGUS (LC-MGUS), is a subset of MGUS in which the monoclonal protein produced consists of only immunoglobulin free light chains. The published definition of LC-MGUS is *"an abnormal FLC ratio with complete lack of IgH expression, plus elevation in the appropriate involved FLC"* [2], and was evaluated as part of this study to demonstrate the

capability of the Freelite Mx Kappa and Lambda Free assays to detect this subgroup of MGUS patients.
Obtained positive rate ratio with 95% confidence interval has been summarized in Table 2 below:

Table 2. Summary Table - Freelite Mx Kappa:Lambda Ratio – Positive Rate (%).

Disease group	n/N =	Obtained Positive Rate (%)
All MGUS positive	129/229	56.3
Light chain MGUS	10/10	100.0
Non-light chain only MGUS	119/219	54.3

Freelite Mx Kappa:Lambda Ratio - Positive Rate (%) in MGUS by isotype

The cohort of 229 MGUS samples included: 173 non-IgM MGUS, 24 IgM MGUS, 22 biclonal,10 light chain MGUS. The distribution of the cohort with confirmed M component isotype in MGUS samples and the number and percentage of test positive samples are summarised in Table 3 as follows:

Table 3. MGUS isotype, number in study and abnormal by Freelite Mx.

MGUS type	N	n (n/N%) Freelite Mx positive
Non-IgM MGUS (all)	**173**	**95 (54.9%)**
IgG κ	74	47 (63.5%) >1.65
IgG λ	61	20 (32.8%) <0.26 3 (4.9%) >1.65 23 (37.7%) total FLC abnormal
IgA κ	21	15 (71.4%) >1.65 1 (4.8%) <0.26 16 (76.2%) total FLC abnormal
IgA λ	15	9 (60.0%) <0.26
IgD κ	0	0
IgD λ	0	0
λ band (not free light chain) with no obvious corresponding heavy chain*	2	0
IgM MGUS (all)	**24**	**10 (41.7%)**
IgM κ	20	9 (45.0%) >1.65
IgM λ	4	1 (25.0%) <0.26
LC-MGUS (all)	**10**	**10 (100%)**
κ	5	5 (100%)
λ	5	5 (100%)
Biclonal	22	2 (9.1%) <0.26 12 (54.5%) >1.65 14 (63.6%) total abnormal
Total	**229**	**129 (56.3%)**

* These samples have been categorized as non-IgM MGUS based on associated IFE and FLC results generated for these samples.

6.3.1.2 Determination of Negative Rate Ratio

Freelite Mx Kappa:Lambda Ratio – Negative rate (%)in Disease Controls (non-MGUS)

A retrospective study was performed using a total of 136 samples. These samples were from patients with polyclonal hypergammaglobulinemia confirmed by study testing (total IgG/IgA/IgM and serum IFE), with supporting clinical information for example, diagnosis of hepatitis, systemic lupus erythematosus. All samples were tested for free light chain (FLC) Kappa and Lambda levels with the Optilite Freelite Mx Kappa and Lambda Free kits on the Optilite Analyser. The Kappa:Lambda ratios were calculated for each sample. The result of the device was compared to the clinical truth for each sample.

Negative rate ratio with 95% confidence interval for non-MGUS samples was determined; refer to Table 4 as follows:

Table 4. Freelite Mx Kappa:Lambda Ratio - Negative Rate (%).

Disease group	n/N =	Obtained Negative Rate (%)
Disease Controls (Non-MGUS)	125/136	91.9

6.3.2 Evaluation of MGUS progression (Study 2)

Another retrospective study was performed using a total of 185 samples from 49 MGUS patients with clinically determined stable or progressive status. Up to 4 individual sample draws, taken at various time intervals, were tested from each patient for the stable cohort and up to 6 for the progressive MGUS cohort. All samples were tested for free light chain (FLC) Kappa and Lambda levels with the Optilite Freelite Mx Kappa and Lambda Free kits on the Optilite analyser. The Kappa:Lambda ratios were calculated for each sample. The result of the device was compared to the clinical diagnosis for each sample. The study population consisted of 45 patients with clinically stable MGUS diagnosis (stable cohort) and 4 patients that demonstrated a progressive clinical status by converting from MGUS to MM (progressive cohort).

Evaluation criteria: There are no published guidelines relating to the interpretation of consecutive FLC results for MGUS patients. Therefore, for the purpose of the device evaluation only, results were evaluated as stable and progressive MGUS based on the clinical diagnosis provided with the samples and Optilite Freelite Mx FLC testing performed during the study, per definitions as follows:

- FLC stable: Stable MGUS defined as < 25% increase in the concentration of the involved FLC in two assessments taken at least 6 months +/- 2 months apart where possible. This analysis included MGUS patients with and without abnormal FLC Kappa:Lambda ratio.

- FLC progressive: Progressive MGUS defined as the FLC Kappa:Lambda ratio outside of the reference interval of 0.26-1.65, and an increase of ≥ 25% in the concentration of the involved light chain at or preceding the diagnosis of MM, compared to a previous sample taken at least 6 months +/- 2 months where possible.

Free light chain results criteria, specifically the 25% change, was adapted from IMWG guidelines for multiple myeloma [3].

6.3.2.1 MGUS stable and progressive

Results have been categorized as clinical positive or negative based on the clinical diagnosis and evaluated as test positive or negative based on the results of the Freelite Mx testing performed during the study. The percentage of patients who are considered stable or progressive based on their FLC results among the patients with clinically stable or progressive disease was calculated as follows:

Stable MGUS patients:

((Number of stable patients test positive / total number of stable patients) x 100)

Table 16. Study 2, stable MGUS test positive cases

Disease group	No. of patients (n/N)	Test positive patients (%)
Stable MGUS	43/45	95.6

Progressive MGUS patients:

((Number of progressive patients test positive / total number of progressive patients) x 100)

Table 17. Study 2, progressive MGUS test positive cases

Disease group	No. of patients (n/N)	Test positive patients (%)
Progressive MGUS	2/4	50.0

The distribution of the confirmed M component isotype (by IFE) in the stable and progressive MGUS samples are shown in Table 18.

Table 18. MGUS isotype, number and abnormal result by Freelite Mx in study 2

Isotype breakdown		
MGUS type	**N**	**n (n/N%) Freelite Mx positive at first blood draw**
Non-IgM MGUS (all) abnormal	**39**	**24 (61.5%)**
IgG κ	20	15 (75%) >1.65
IgG λ	14	6 (42.9%) <0.26
IgA κ	2	2 (100%) >1.65
IgA λ	3	1 (33.3%) <0.26
IgM MGUS (all) abnormal	**6**	**3 (50%)**
IgM κ	4	3 (75%) >1.65
IgM λ	2	0 (0%) <0.26
Biclonal	**4**	3 (75%) >1.65 0 (0%) <0.26
Total	**49**	**29 (59.2%)**

7 Conclusion:

The differences between the predicate and proposed device do not raise safety or efficacy questions when used according to the product labelling. Clinical Performance testing is part of the submission to support the clinical claims. The completed clinical performance studies demonstrate that the Optilite Freelite Mx Kappa and Lambda Free Kits assays can be used as an aid to evaluate Monoclonal Gammopathy of Undetermined Significance (MGUS). The studies generated successful results where all pre-defined acceptance criteria were met, therefore, supporting the extension of the claim to aid in evaluation of MGUS, and the products safety and effectiveness in this regard.

8 Bibliography

1. Rajkumar, S.V., et al., *International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma.* Lancet Oncol., 2014. **15**: p. e538-e548.
2. Dispenzieri, A., et al., *Prevalence and risk of progression of light-chain monoclonal gammopathy of undetermined significance: a retrospective population-based cohort study.* Lancet, 2010. **375**(9727): p. 1721-1728.
3. Kumar, S., et al., *International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma.* Lancet Oncol, 2016. **17**(8): p. e328-46.

END OF SUMMARY