July 14, 2021

Siemens Healthcare Diagnostics Products GmbH
Sanja Matern
Regulatory Affairs Manager
Emil-von-Behring-Str. 76
Marburg, 35041 De

Re: K193047
Trade/Device Name: N Latex FLC kappa, N Latex FLC lambda
Regulation Number: 21 CFR 866.5550
Regulation Name: Immunoglobulin (light chain specific) immunological test system
Regulatory Class: Class II
Product Code: DFH, DEH
Dated: October 2, 2020
Received: October 5, 2020

Dear Sanja Matern:

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/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 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 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, Ph.D.
Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K193047

Device Name
N Latex FLC kappa, N Latex FLC lambda

Indications for Use *(Describe)*
N Latex FLC kappa and lambda are in-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma. N Latex FLC kappa and lambda assays are used:
• as an aid in the diagnosis and monitoring of multiple myeloma (MM) on the BN Systems and Atellica® CH Analyzer,
• as an aid in the diagnosis of amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer,
• as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems.

Results of FLC 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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary per 21 CFR 807.92

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

The assigned 510(k) number is: **K193047**

1. Submitter

Siemens Healthcare Diagnostics Products GmbH

Emil-von-Behring-Str. 76

35041 Marburg, Germany

Contact:	Sanja Matern
Email:	sanja.matern@siemens-healthineers.com
Phone:	+49 176 34939948
Date of Preparation:	July 12, 2021

2. Device Information

Trade Name:	N Latex FLC kappa assay
	N Latex FLC lambda assay
Common or Usual Name:	Light Chain immunological test system
Classification Name:	Immunoglobulin (light chain specific) immunological test system per 21CFR 866.5550
Product Code:	DFH (kappa)
	DEH (lambda)
Regulatory Class:	II
510(k) Review Panel:	Clinical Immunology (82)

3. Predicate Devices

The Binding Site Freelite® Human Kappa Free Kit for use on the

Siemens BN™ II - K031016

The Binding Site Freelite® Human Lambda Free Kit for use on the

Siemens BN™ II - K031016

Even though TBS' Freelite assays are cited as predicate devices in this submission, they do not contain an MGUS evaluation claim in the product package insert intended use statement. Siemens has received guidance from FDA in an email dated October 5, 2018, stating that Siemens may use the Freelite assays as predicate devices with the understanding that FDA will determine Substantial Equivalence based on clinical performance.

4. Device Description / Test Principle

The N Latex FLC (free light chain) assays are in vitro diagnostic reagents for the quantitative determination of free light chains, type kappa or type lambda, in human serum and EDTA plasma by means of particle-enhanced immunoassay determination. Used in conjunction with other clinical and laboratory findings, FLC measurements are used as an aid in the diagnosis and monitoring of multiple myeloma (MM), as an aid in the diagnosis of amyloidosis (AL) and on the BN Systems, as an aid in the evaluation of MGUS.

Polystyrene particles coated with antibodies to human free light chains, type kappa or lambda, are agglutinated when mixed with samples containing FLC. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

The devices in this submission are not materially changed from those cleared under K171742. The purpose for this submission is to add evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) to the intended use.

5. Intended Use / Indications for Use

N Latex FLC kappa and lambda are in-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma. N Latex FLC kappa and lambda assays are used:

• as an aid in the diagnosis and monitoring of multiple myeloma (MM) on the BN Systems and Atellica® CH Analyzer,

• as an aid in the diagnosis of amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer,

• as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems.
Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.

Special Conditions for Use:

For prescription use only.

The result of the FLC kappa or FLC lambda in a given specimen determined with assays and/or instrument platforms from different manufacturers 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 FLC kappa or FLC lambda assay used. Values obtained with different assay methods cannot be used interchangeably. The values of FLC kappa or FLC lambda on BN systems and on Atellica® CH Analyzer should not be used interchangeably.

If, in the course of serially monitoring a patient, the assay method used for determining the FLC kappa and FLC lambda levels is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

- Precautions:
- The performance of N Latex FLC kappa and lambda has not been thoroughly studied in IgM and Light Chain MGUS patients due to the low prevalence of these subtypes.
- Patients with decreased renal function may have elevated FLC Kappa and FLC Lambda.
- Sample populations excluded MGUS populations that were further diagnosed with a disease/disorder in subsequent testing with another medical device such as human immunodeficiency virus, hepatitis, and chronic lymphocytic leukemia. Thus, because the samples were enriched the specificity of the test may be inflated.

Special instrument requirements:

BN II (K943997)

BN ProSpec Systems (K001647)

6. Technical Characteristics

Similarities and Differences to the Predicate

A comparison of the similarities and differences between the proposed Siemens Healthcare Latex FLC kappa and lambda assay versus The Binding Site (TBS)

Freelite Human Kappa Free and Lambda Free assays (predicates) is provided in the table below.

Comparison of Technological Characteristics	**Predicate Devices** **The Binding Site** **Freelite® Human Kappa Free Freelite® Human Lambda Free on Siemens BN™II** **(K031016)**	**Proposed Device** **Siemens Healthcare BN Systems** **N Latex FLC kappa N Latex FLC lambda** **(K193047)**
Indications for Use	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, Waldenstrom'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 BN™ II. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom'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.	N Latex FLC kappa and lambda are in-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma. N Latex FLC kappa and lambda assays are used: • as an aid in the diagnosis and monitoring of multiple myeloma (MM) on the BN Systems and Atellica® CH Analyzer, • as an aid in the diagnosis of amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer. • as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems. Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.
Sample Type	Human serum and urine	Human serum and EDTA plasma
Units	mg/L	Same

Comparison of Technological Characteristics	Predicate Devices The Binding Site Freelite® Human Kappa Free Freelite® Human Lambda Free on Siemens BN™II (K031016)	Proposed Device Siemens Healthcare BN Systems N Latex FLC kappa N Latex FLC lambda (K193047)
Detection Mode	Nephelometry	Same
Measurement	Quantitative	Same
Detection Antibody	Polyclonal mouse anti-human FLC Kappa Polyclonal mouse anti-antibody FLC Lambda	Monoclonal mouse anti-human FLC kappa Monoclonal mouse anti-antibody FLC lambda
Reagent Composition	Polystyrene particles coated with polyclonal antibodies	Polystyrene particles coated with monoclonal antibodies
Traceability	Internal reference preparation	Internal reference plasma pool
Calibrators	One level	Same
Instrument System	Siemens BN II System	Siemens BN II and BN ProSpec Systems
Analytical measuring range	Kappa: 5.9 to 190 mg/L Lambda: 5.0 to 160 mg/L	Typical range: kappa: 3.4 to 110 mg/L lambda: 1.9 to 60 mg/L
Reference Interval	Kappa: 3.30 to 19.40 mg/L Lambda: 5.71 to 26.30 mg/L Ratio: 0.26 to 1.65	kappa: 8.24 to 28.9 mg/L lambda: 9.10 to 32.6 mg/L Ratio: 0.53 to 1.51

This submission is to add a claim for evaluation of MGUS to the intended use statement.

7. Performance Data

Performance data is provided for the extended indication for evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS). See submissions K171742 and K182098 for previously documented analytical and clinical studies:

- Precision and Reproducibility
- Linearity / Assay Measuring Range
- Antigen Excess
- Stability

- Detection Capabilities
- Analytical Specificity / Interferences
- Expected Values
- Clinical Sensitivity / Specificity for MM and AL diagnosis and MM monitoring claims
- Method comparison to the Predicate Devices for MM and AL diagnosis and MM monitoring claims

7.1 Performance data for evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) patients

The Latex FLC assays were evaluated on BN II Systems in a multi-center study to evaluate performance to support a claim for the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) patients. The following studies were performed in support of the proposed claim

7.1.1 Aid in Evaluation of MGUS

Concordances were evaluated using clinically defined samples including a panel of samples from patients with defined MGUS diagnosis and a panel of samples from patients with the diagnosis of polyclonal immunostimulation to evaluate for MGUS.

7.1.1.1 MGUS Concordance

The cohort of MGUS samples consisted of 121 samples (89 Non-IgM, 21 IgM and 11 LC MGUS).

N Latex FLC κ/λ Ratio Concordance

Disease Group	N =	Concordance Obtained (%)
MGUS	121	50.4

In order to demonstrate the capability of N Latex FLC to detect this subgroup of MGUS patients, the group of LC MGUS samples was evaluated separately using the currently defined criteria:

LC MGUS is defined as an abnormal FLC-Ratio with complete lack of IgH (Heavy-Chain) expression, plus an elevation in the appropriate involved FLC. The following table contains the % concordance for the LC MGUS evaluated population:

LC MGUS Disease Group Concordance

Disease Group	N=	Positive for both criteria	Positive for one criterion	Concordance obtained (%)
LC MGUS	11	10	1	90.9

7.1.1.2 Polyclonal Immunostimulation Concordance

Evaluation used a panel of samples from patients with the diagnosis of polyclonal immunostimulation to evaluate for MGUS.

The cohort of polyclonal immunostimulation samples consisted of 102 specimens.

N Latex FLC κ/λ Ratio Concordance

Disease Group	N =	Concordance obtained (%)
Polyclonal Immunostimulation	102	90.2

7.1.2 Evaluation of MGUS patients

Patients initially diagnosed for MGUS were evaluated over different time periods. At least 4 sample draws at various time intervals were obtained from each participant. The overall population consisted of 61 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).

7.1.2.1 MGUS Stable Cohort

Evaluation criteria: Agreement of the N Latex FLC results with the clinical diagnosis of MGUS was defined if the two following criteria were both fulfilled:

a) The κ/λ ratio must be within the reference interval of 0.53 – 1.51 at the time of the last draw
b) Two consecutive assessments did not show a relative change of ≥ 25% for the involved free light chain (iFLC)

Results in Stable Patient Cohort

Disease Group	N =	Agreement with clinical (%)
Stable MGUS	61	98.4

7.1.2.2 Progressive Cohort

Evaluation criteria: Agreement of the N Latex results with a change in clinical diagnosis of MGUS to MM defined if the two following criteria were both fulfilled:

The κ/λ ratio must be outside the reference interval of 0.53 – 1.51 at the time of clinical MM diagnosis

Two consecutive assessments must show a relative change of ≥ 25% for the involved light chain (iFLC).

Results in Progressive Patient Cohort

Disease Group	N =	Agreement with clinical (%)
Progressive MGUS	4	75.0

8. Proposed Labeling

The labeling is adequate and satisfies the requirements of 21 CFR Part 809.10.

9. Conclusion

The completed studies demonstrate that the N Latex FLC kappa and lambda assays can be used to evaluate Monoclonal Gammopathy of Undetermined Significance (MGUS).

END OF SUMMARY