March 2, 2022

Siemens Healthcare Diagnostics Products GmbH
Martina Pfeiff
Regulatory Affairs Manager
Emil-von-Behring Str. 76
Marburg, 35041
Germany

Re: K212379
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: July 30, 2021
Received: August 2, 2021

Dear Martina Pfeiff:

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)*
K212379

Device Name
N Latex FLC kappa and 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 immunoglobulin light-chain amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer.
• as an aid in the monitoring of immunoglobulin light-chain amyloidosis (AL) on the BN Systems.
• as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems and Atellica® CH Analyzer.
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.

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510(k) Summary per 21 CFR 807.92
Type of 510(k): Traditional 510(k)

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: **K212379**

1. Submitter

Siemens Healthcare Diagnostics Products GmbH
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35041 Marburg, Germany

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Email : martina.pfeiff@siemens-healthineers.com
Phone: +49 (174) 3319336
Date of Preparation: July 30, 2021

2. Device Information

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

3. Legally Marketed Unmodified / Predicate Devices

Cleared for use on Siemens' BN Systems under K201496 on October 29, 2021 as an aid in the monitoring of amyloidosis (AL) on the BN Systems.

Trade Name	Common/Usual Name	Classification	Product Code	Panel	FDA clearance
N Latex FLC kappa	Immunoglobulin (light chain specific) immunological test system	Class II per 21CFR 866.5550	DFH	Immunology (82)	K171742 K182098 K193047 K201496
N Latex FLC lambda	Immunoglobulin (light chain specific) immunological test system	Class II per 21CFR 866.5550	DEH	Immunology (82)	K171742 K182098 K193047 K201496

4. Device Description / Test Principle of the Modified Device

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) on the BN Systems and Atellica® CH Analyzer; as an aid in the monitoring of amyloidosis (AL) on the BN Systems and as an aid in the evaluation of MGUS on the BN Systems.

The FLC test systems on the Atellica® CH Analyzer are based upon the principles of particle-enhanced turbidimetry. Polystyrene particles coated with antibodies to human free light chains, type kappa or lambda, respectively, are agglutinated when mixed with samples containing FLC. Monitoring the agglutination by measuring the increase in turbidity, a concentration curve is obtained. The actual change in absorbance 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 since clearance under K171742. Later clearances dealt with the intended use claims. The purpose for this submission is to add an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) claim, on the Atellica® CH Analyzer to the intended use.

5. Intended Use / Indications for Use

N Latex FLC kappa and N Latex FLC lambda assays

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 immunoglobulin light-chain amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer.
- as an aid in the monitoring of immunoglobulin light-chain amyloidosis (AL) on the BN Systems.
- as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems and Atellica® CH Analyzer.

Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.

6. Special Conditions for Use Statements

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 monitoring a patient, the assay method used for determining serial levels of the FLC kappa and FLC lambda is changed, the laboratory MUST perform additional testing to confirm baseline values prior to changing assays.

Precaution:

- 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 (e.g. chronic kidney disease) 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.

7. Special instrument requirements:

Atellica® CH Analyzer (K151767)
BN II System (K943997)
BN ProSpec® (K001647)

8. Technological characteristics

Similarities and Differences to the predicate:

A comparison of the similarities and differences between the proposed Atellica® CH N Latex FLC assays versus the BN Systems' N Latex FLC assays (predicates):

Table 8.-1: Similarities and Differences of Technologies between the BN Systems and the Atellica® CH Analyzer

	Predicate **Siemens Healthcare** **BN Systems** N Latex FLC kappa N Latex FLC lambda (K171742, K182098, K193047, K201496)	**Proposed** **Siemens Healthcare** **Atellica® CH Analyzer** **Modified Devices** N Latex FLC kappa N Latex FLC lambda
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 kappaand 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 immunoglobulin light-chain amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer. •as an aid in the monitoring of immunoglobulin light-chain amyloidosis (AL) on the BN Systems. •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.	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 immunoglobulin light-chain amyloidosis (AL) on the BN Systems and Atellica® CH Analyzer. •as an aid in the monitoring of immunoglobulin light-chain amyloidosis (AL) on the BN Systems. •as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) on the BN Systems and Atellica® CH Analyzer. Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.
SampleType	Human serum and EDTA plasma	Same
Reagent Packaging	3 x 1 mL	Same
Reagent Handling	Bottles placed directly on system	Reagents poured into reagent containers
Units	mg/L	Same

	Predicate **Siemens Healthcare** **BN Systems** N Latex FLC kappa N Latex FLC lambda (K171742, K182098, K193047, K201496)	**Proposed** **Siemens Healthcare** **Atellica® CH Analyzer** **Modified Devices** N Latex FLC kappa N Latex FLC lambda
Detection Method	Nephelometry	Turbidimetry
Measurement	Quantitative	Same
Detection Antibody	Monoclonal mouse anti-human FLC kappa Monoclonal mouse anti-antibody FLC lambda	Same
Reagent Composition	Polystyrene particles coated with monoclonal antibodies	Same
Traceability	Internal Reference Plasma Pool	Same
Calibrators	One level	Same
Calibration Interval	42 days	Same
Analytical Measuring Range	Typical range: kappa: 3.4 to 110 mg/L lambda: 1.9 to 60 mg/L (Calibrator lot value dependent)	kappa: 3.91 to 60 mg/L lambda: 5.47 to 70 mg/L (Independent of Calibrator lot value)
Reference Interval	kappa: 8.24 to 28.90 mg/L lambda: 9.10 to 32.60 mg/L Ratio: 0.53 to 1.51	Same

Results of FLC measurements should always be interpreted in conjunction with other laboratory and clinical findings.

The purpose of the modification to the proposed device is to add the aid in evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS) to the intended use for the reagent application on the Atellica® CH Analyzer.

7. Summary of Design Control Activities

A risk analysis was performed with risks identified. Mitigation of risk to acceptable levels was achieved through verification activities summarized below.

7.1 Risk Analysis

Risk analysis was performed according to the ISO14971:2019 standard, Medical Devices – Application of Risk Management to Medical Devices. The change to the N Latex FLC kappa and N Latex FLC lambda assays, previously cleared for use on the BN Systems, is to add the aid in evaluation of MGUS to the intended use. The reagents used for both systems are identical in composition, packaging and labeling.

Each difference was analyzed, and its effect identified. Severity and probability were estimated by risk class. Risks were mitigated to the acceptable degree.

7.2. Verification Activities

Based on the results of the risk analysis, verification activities were identified, pertinent studies were determined and acceptance criteria established.

The test methods and acceptance criteria used to demonstrate comparability between N Latex FLC kappa and lambda on the Atellica® CH Analyzer and N Latex FLC kappa and lambda on the BN ProSpec System are presented in section 7.3.
Reagent and application specific performance claims established in K171742 and K182098 for the reagent application on the BN systems and K190879 for the reagent application on the Atellica® CH Analyzer are not affected by the change to the intended use of the reagent and remain unchanged for K193047 and for this submission.

7.3. Performance Studies

7.3.1 Method comparison study

Summary of the protocol:

A Method comparison study designed according to CLSI EP09c: *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition* was conducted internally at the Siemens Healthcare Diagnostics Products GmbH site in Marburg, Germany.
Method comparison data from K190879 was extended by inclusion of samples derived from MGUS patients in order to show equivalency for the new intended use population between the predicate the N Latex FLC kappa and N Latex FLC lambda assays on the BN ProSpec System and the candidate device the N Latex FLC kappa and N Latex FLC lambda assays on the Atellica® CH Analyzer.

Clinical performance studies were performed for the predicate which has been recently cleared under K193047.
For MGUS evaluation, the study was performed using 121 MGUS samples (89 Non-IgM, 21 IgM and 11 LC MGUS) and 102 polyclonal immunostimulation samples (confirmed with SPEP/ SIFE). The result showed positive rate of 50.4 % (61/121) for all MGUS samples tested and negative rate of 90.2 % (92/102) for non-MGUS samples.

Summary of the Results:

The correlation between the assays is summarized below.

Table 7.3.1-1: Acceptance criteria Method comparison study

Method	Acceptance Criteria
N Latex FLC kappa and N Latex FLC lambda on Atellica® CH Analyzer vs N Latex FLC kappa and N Latex FLC lambda on BN ProSpec System	**Pearson correlation coefficient:** r ≥ 0.95 **Slope** : 0.9 - 1.1 **Predicted bias:** • ≤ +/- 10% at lower limit reference interval • ≤ +/- 10% at upper limit reference interval **Number of samples**: n ≥ 160

Table 7.3.1-2: Results Method comparison study

Method	N	Sample range N Latex FLC mg/L	Slope (Passing Bablok)	95% CI (Slope)	Y Intercept (Passing Bablok)	95% CI (Y-intercept)	Pearson correlation coefficient
Acceptance criteria	**≥ 160**	**N/A**	**0.9 - 1.1**	**N/A**	**N/A**	**N/A**	**r ≥ 0.95**
N Latex FLC kappa	212 *	1.29- 550	0.995	0.982 – 1.02	0.119	-0.223 - 0.346	0.983
N Latex FLC lambda	202 **	1.85 – 710	0.914	0.887 – 0.939	0.112	-0.252 - 0.525	0.970
Acceptance criteria fulfilled	**yes**	**N/A**	**yes**	**N/A**	**N/A**	**N/A**	**yes**

*including 38 MGUS samples
**including 35 MGUS samples

Table 7.3.1-3: Predicted Bias Analysis- Method comparison study

Method	Lower Limit of Reference Interval [mg/L]	PredictedBias [%]	Upper Limit of Reference Interval [mg/L]	PredictedBias [%]
Acceptance criteria	--	**≤ +/- 10**	--	**≤ +/- 10**
N Latex FLC kappa	8.24	0.93	28.9	-0.10
N Latex FLC lambda	9.10	-7.60	32.6	-8.56
Acceptance criteria fulfilled	--	**yes**	--	**yes**

Table 7.3.1-4: Results Method comparison study (MGUS patients only)

Method	N	Sample range N Latex FLCmg/L	Slope (Passing Bablok)	95% CI (Slope)	Y Intercept (Passing Bablok)	95% CI (Y-intercept)	Pearson correlation coefficient
N Latex FLC kappa	38	6.61 - 345	0.966	0.930 – 1.00	0.645	-0.207 - 1.19	0.977
N Latex FLC lambda	35	8.52 - 181	0.841	0.750 – 0.934	0.123	-1.69 - 2.69	0.970

Table 7.3.1-5: Predicted Bias Analysis- Method comparison study (MGUS patients only)

Method	Lower Limit of Reference Interval [mg/L]	Predicted Bias [%]	Upper Limit of Reference Interval [mg/L]	Predicted Bias [%]
N Latex FLC kappa	8.24	4.33	28.9	-1.18
N Latex FLC lambda	9.10	-15.7	32.6	-16.9

8. Comments on Substantial Equivalency

The reagents for the proposed devices and the cleared devices are identical in composition, labeling and packaging. Comparative testing was performed, and the results obtained demonstrate substantial equivalent performance.

The use of these reagents on another instrument platform with a different measuring technology, i.e., nephelometry versus turbidimetry, does not affect safety and efficacy when used according to the product labeling.

9. Conclusion

The modified devices, N Latex FLC kappa and lambda on the Atellica® CH Analyzer, are substantially equivalent to the predicate devices based on intended use, design, and basic scientific principle and performance.

Results from the risk analysis and design control activities with comparative testing support a substantial equivalence decision.

END OF SUMMARY