November 1, 2018

Siemens Healthcare Diagnostics Products GmbH
Christine Perkins
Regulatory Specialist
Emil-von-Behring-Str. 76
Marburg, DE 35041

Re: K182098
Trade/Device Name: N Latex FLC kappa assay, N Latex FLC lambda assay
Regulation Number: 21 CFR 866.5550
Regulation Name: Immunoglobulin (light chain specific) immunological test system
Regulatory Class: Class II
Product Code: DFH, DEH
Dated: August 2, 2018
Received: August 3, 2018

Dear Christine Perkins:

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,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology
and Hematology Devices
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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)*
K182098

Device Name
N Latex FLC kappa and N Latex FLC lambda

Indications for Use *(Describe)*

In-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis and monitoring of multiple myeloma (MM) and as an aid in the diagnosis of amyloidosis (AL) in conjunction with other laboratory and clinical findings.
The response category assignment of Complete Response for the monitoring of MM is reliant upon the combination of clinical history and other tests including protein electrophoresis, immunofixation and bone marrow, imaging and urine assessments.

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.

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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: K182098

1. Submitter

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Date of Preparation:	August 29, 2018

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

4. Device Description / Test Principle

In-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis and monitoring of multiple myeloma (MM) and as an aid in the diagnosis of amyloidosis (AL) in conjunction with other laboratory and clinical findings.
The response category assignment of Complete Response for the monitoring of MM is reliant upon the combination of clinical history and other tests including protein electrophoresis, immunofixation and bone marrow, imaging and urine assessments.

The FLC test systems are based upon the principles of particle-enhanced immunonephelometry. Polystyrene particles coated with monoclonal antibodies to human free light chains, type kappa or lambda, respectively, 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 have not materially changed since clearance under K171742. The purpose for this submission is to add monitoring of multiple myeloma (MM) to the intended use.

5. Intended Use / Indications for Use

N Latex FLC kappa and N Latex FLC lambda assays

In-vitro diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis and monitoring of multiple myeloma (MM) and as an aid in the diagnosis of amyloidosis (AL) in conjunction with other laboratory and clinical findings.
The response category assignment of Complete Response for the monitoring of MM is reliant upon the combination of clinical history and other tests including protein electrophoresis, immunofixation and bone marrow, imaging and urine assessments.

N FLC Supplementary Reagent

Supplementary reagent for the immunonephelometric determination of free light chains (FLC), type kappa and type lambda on BN Systems. A mixture of both supplementary reagents is used to suppress interference by rheumatoid factors and human anti-mouse antibodies (HAMA).

Special Conditions for Use:

For prescription use only.

Special instrument requirements:

BN II (K943997) and 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 N Latex FLC kappa and N Latex FLC lambda assays versus The Binding Site (TBS) Freelite Human Kappa Free and Lambda Free assays (predicates) is provided in the table below.

Comparison of Technological Characteristics

	Proposed Devices **Siemens Healthcare BN Systems** N Latex FLC kappa N Latex FLC lambda	**Predicate Devices** **The Binding Site** Freelite® Human Kappa Free and Freelite® Human Lambda Free kits on the Siemens BN™II K031016
Indications for Use	*In-vitro* diagnostic reagents for the quantitative determination of free light chains (FLC), type kappa or type lambda in human serum and EDTA-plasma by means of particle-enhanced immunonephelometry using the BN Systems. FLC measurements are used as an aid in the diagnosis and monitoring of multiple myeloma (MM) and as an aid in the diagnosis of amyloidosis (AL) in conjunction with other laboratory and clinical findings. The response category assignment of Complete Response for the monitoring of MM is reliant upon the combination of clinical history and other tests including protein electrophoresis, immunofixation and bone marrow, imaging and urine assessments.	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.
Sample Type	Human serum and EDTA plasma	Human serum and urine
Units	mg/L	Same
Technology	Nephelometry Polystyrene particles coated with monoclonal antibodies	Nephelometry Polystyrene particles coated with polyclonal monospecific antibodies
Traceability	Internal Reference Plasma Pool	Internal reference preparation
Calibrators	One level	Same
Instrument System	Siemens BN II and BN ProSpec Systems	Siemens BN II

	Proposed Devices **Siemens Healthcare BN Systems** N Latex FLC kappa N Latex FLC lambda	**Predicate Devices** **The Binding Site** Freelite® Human Kappa Free and Freelite® Human Lambda Free kits on the Siemens BN™II K031016
Analytical Measuring Range (Calibrator lot dependent)	kappa: 3.4 to 110 mg/L lambda: 1.9 to 60 mg/L	Kappa: 5.9 to 190 mg/L Lambda: 5.0 to 160 mg/L
Reference Interval	kappa: 8.24 – 28.90 mg/L lambda: 9.10 – 32.60 mg/L Ratio: 0.53 to 1.51	Kappa: 3.30 to 19.40 mg/L Lambda: 5.71 to 26.30 mg/L Ratio: 0.26 to 1.65

The differences between the predicate devices and proposed reagents do not result in a change to the intended use, the indications for use, or the safety and efficacy when used according to the product labeling.

7. Performance Data

Performance Data: Extended indication for monitoring of MM. See original submission (K171742) 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 Specificity and Sensitivity
- Method comparison to Predicate Devices

7.1 Performance data for monitoring of MM patients

The Latex FLC assays were evaluated on BN II Systems in a multi-center study to evaluate performance in monitoring multiple myeloma (MM) patients. The following studies were performed in support of an MM monitoring claim:

<u>Comparison to Clinical Status</u>

Therapy response was evaluated according to IMWG FLC criteria considering IFE and serum FLC measurements. Response categories were determined for FLC testing by N Latex FLC and Freelite, respectively. The response levels obtained by the two different test systems were compared to the clinical response level provided by the physician in charge within the Case Report Form (CRF). Relative agreement between the clinical responses (including further

information in addition to serum testing) and the response level applying the IMWG FLC response scheme by either using N Latex FLC or the predicate device were calculated and compared.

		Clinical Status		
		Progression	No Progression	Total
Change in N Latex FLC	Positive*	12	9	21
	Negative**	35	335	370
	Total	47	344	391
Clinical Sensitivity: 26%*** (12/47) (95% CI: 13.9% – 40.3%) Clinical Specificity: 97% (335/344) (95% CI: 95.1%– 98.8%)				

*Positive: ≥25% rd_dFLC and d_dFLC ≥100 mg/L
**Negative: <25% rd_dFLC and d_dFLC FLC <100 mg/L
*** For the predicate device similar data were obtained when compared to clinical status.

Results of N Latex FLC Kappa and N Latex FLC Lambda assays in combination with IFE results were used to assign a response category and compared to the clinical assessment according to the table below:

Response Category	**Response Criteria based on N Latex FLC and IFE Results**	**Clinical Assessment based on IMWG**
Good Response	FLC ratio normal and IFE negative*	sCR
		CR
Moderate Response	≥ 50 to ≥ 90% reduction of rd_dFLC**	VGPR
		PR
Stable Disease	50% reduction to 25% increase of rd_dFLC	SD
Progressive Disease	≥ 25% increase of rd_dFLC AND increase of d_dFLC*** ≥ 100 mg/L	PD

*Applies only to MM population
**rd_dFLC = (dFLC t2 – dFLC t1)/ dFLC t1
***d_dFLC = dFLC t2 – dFLC t1 (with 'dFLC = iFLC – ni FLC')

Definitions:

- t1 = time point 1; t2 = time point 2
- rd = relative difference
- iFLC = involved FLC; niFLC = not involved FLC;
- Relative change of involved FLC: rd_iFLC = (iFLC t2 – iFLC t1)/ iFLC t1
- Relative change of difference between both FLC: dFLC = iFLC – niFLC

The performance of N Latex FLC kappa and FLC lambda in combination with IFE compared to the clinical assessment is summarized in the following table:

Response based on N Latex FLC results	**Clinical Assessment**				
	Good Response	Moderate Response	Stable Disease	Progressive Disease	Total
Good Response	21	3	6	1	31
Moderate Response	10	104	38	16	168
Stable Disease	3	24	126	18	171
Progressive Disease	0	0	9	12	21
Total	**34**	**131**	**179**	**47**	**391**
Agreement	**62%**	**79%**	**70%**	**26%**	**67%**

Discordance results:

- The response criteria established by clinicians are often based on multiple factors besides FLC results, therefore FLC results alone might lead to a different classification.

Comparison to Predicates

Therapy response was evaluated according to the International Myeloma Working Group (IMWG) FLC criteria considering IFE and serum FLC measurements alone.

The performance of N Latex FLC kappa and FLC lambda assays were also compared to the predicate devices based on the disease response categories describe above.

In this retrospective clinical study, all samples were tested with the N Latex FLC kappa and lambda assays and with the predicate device. The performance of N Latex FLC kappa and N Latex FLC lambda assays compared to the predicate devices based on the same disease response category is summarized as follows:

Response based on N Latex FLC results	**Response Based on Freelite Results**				
	Good Response	Moderate Response	Stable Disease	Progressive Disease	Total
Good Response	27	2	0	1	31
Moderate Response	0	66	15	0	81
Stable Disease	0	13	238	7	258
Progressive Disease	0	0	5	16	21

Total	**27**	**81**	**259**	**24**	**391**
Agreement	**100%**	**81%**	**92%**	**67%**	**89%**

Comparison to Predicates using Follow-up Graphs

Patients were monitored and tested using N Latex FLC kappa and lambda and Freelite Kappa and Lambda after initiation of the first therapy phase and at intervals of ≥ three weeks with a total of at least four collections. Two graphs each were established for the 102 patients included in the study, one using lin/lin and one using log/log scaling.

While N Latex FLC assays and Freelite Kappa and Lambda assays react in the same manner and follow a parallel response, they do not always agree in the magnitude of concentration. For this reason, different FLC assays cannot be used interchangeably (as stated in the sponsor's package insert).

8. Proposed Labeling

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

9. Conclusion

The N Latex FLC kappa and lambda assays with the expanded intended use to include monitoring of multiple myeloma patients are substantially equivalent to the legally marketed predicate devices FDA cleared under K031016.

END OF SUMMARY