October 29, 2021

Siemens Healthcare Diagnostics Products GmbH
Kerstin Koenigs
Official Correspondent
Emil-von-Behring-Str. 76
Marburg, 35041 Germany

Re: K201496
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 29, 2021
Received: August 2, 2021

Dear Kerstin Koenigs:

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 (Katelin) 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)*
K201496

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.

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

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: K201496

1. Submitter

Siemens Healthcare Diagnostics Products GmbH
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Date of Preparation:	October 20, 2021

2. Device Information

Trade Name:	N Latex FLC kappa N Latex FLC lambda
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

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) and immunoglobulin light-chain amyloidosis (AL) and as an aid in the evaluation of Monoclonal Gammopathy of Undetermined Significance (MGUS). Monitoring of immunoglobulin light-chain amyloidosis (AL) and evaluation of MGUS are cleared for use only on the BN Systems.

The N Latex 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 free light chains. 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 originally cleared under K171742. The purpose for this submission is to add monitoring of immunoglobulin light-chain amyloidosis (AL), on the BN Systems, to the intended use.

5. Intended Use / Indications for Use

<u>N Latex FLC kappa and N Latex FLC lambda assays</u>

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.

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

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 may have elevated FLC kappa and FLC lambda (Jacobs et al. N Latex FLC serum free light-chain assays in patients with renal impairment. Clin Chem Lab Med 2013, DOI 10.1515/cclm-2013-0864).
- 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.

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 Latex FLC kappa and lambda assays versus The Binding Site (TBS) Freelite Human Kappa Free Kit and Lambda Free Kit assays (predicate devices) is provided in the table below.

Comparison of Technological Characteristics

	Predicate Devices **The Binding Site** Freelite® Human Kappa Free Kit and Freelite® Human Lambda Free Kit on the Siemens BN II K031016	**Proposed Devices** **Siemens Healthcare BN Systems** N Latex FLC kappa N Latex FLC lambda K171742, K182098, 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 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.
Sample Type	Human serum and urine	Human serum and EDTA plasma
Units	mg/L	Same
Technology	Nephelometry Polystyrene particles coated with polyclonal monospecific antibodies	Nephelometry Polystyrene particles coated with monoclonal antibodies
Traceability	Internal reference preparation	Internal Reference Plasma Pool
Calibrators	One level	Same

	Predicate Devices **The Binding Site** Freelite® Human Kappa Free Kit and Freelite® Human Lambda Free Kit on the Siemens BN II K031016	**Proposed Devices** **Siemens Healthcare BN Systems** N Latex FLC kappa N Latex FLC lambda K171742, K182098, K193047
Instrument System	Siemens BN II System	Siemens BN II and BN ProSpec Systems
Analytical Measuring Range (Calibrator lot dependent)	Kappa: 5.9 to 190 mg/L Lambda: 5.0 to 160 mg/L	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 – 28.90 mg/L lambda: 9.10 – 32.60 mg/L Ratio: 0.53 to 1.51

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 immunoglobulin light-chain amyloidosis (AL).
See submissions K171742, K182098 and K193047 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 immunoglobulin light-chain amyloidosis (AL) patients

The Latex FLC assays were evaluated on BN II Systems in a multi-center study to evaluate performance in monitoring immunoglobulin light-chain amyloidosis (AL) patients. N Latex FLC kappa and lambda assays were compared to Freelite Kappa and Lambda assays (predicate

devices) in a method comparison analysis. In addition, both methods were compared to the patient's "clinical response", taking into account all available clinical and laboratory information.

For each of the comparisons these three evaluation modes were applied to all immunoglobulin light-chain amyloidosis (AL) data sets, respectively:

- Evaluation Mode 1[1]
- Evaluation Mode 2[2]
- Evaluation Mode 3[3-4]

Response evaluation was done by comparing changes between the initial sample draw and each consecutive blood draw independently, applying the rules as outlined in the table below.

Therapy Response Criteria

NCCN Response Criteria	Serum M Protein / IFE	Evaluation Mode 1	Evaluation Mode 2	Evaluation Mode 3
CR (Complete Response)	Serum and Urine IFE negative	FLC levels and ratio normal	FLC levels and ratio normal	FLC levels and ratio normal
VGPR (Very Good Partial Response)	n/a	Reduction in the dFLC to <40 mg/L	Reduction in the dFLC to <40 mg/L	Reduction in the dFLC to <40 mg/L
PR (Partial Response)	n/a	dFLC ≥ 50 mg/L A greater than 50% reduction in the initial dFLC value	dFLC ≥ 50 mg/L A greater than 50% reduction in the initial dFLC value	dFLC ≥ 50 mg/L 1. A greater than 50% reduction in the initial dFLC value 2. For patients with an initial dFLC value of less than 50 mg/L a low FLC response is indicated if dFLC < 10 mg/L*
SD (Stable Disease)	n/a	Less than a PR	Less than a PR	Less than a PR
PD (Progressive Disease)	From CR, any detectable monoclonal protein From PR, 50% increase in serum M protein to > 0.5g/dL or 50% increase in urine M protein to > 200 mg/dL	From CR, abnormal FLC ratio (light chain must at least double) From PR, Serum FLC increase of ≥ 50% to iFLC > 100 mg/L	From CR, abnormal FLC ratio (light chain must at least double) From PR, Serum FLC increase of ≥ 50% to dFLC > 50 mg/L	From CR, abnormal FLC ratio (light chain must at least double) From PR, Serum FLC increase of ≥ 50% to dFLC > 20 and 20% increase of baseline

* Note:-For dFLC <50 it is considered low-dFLC response and based on this citation[3] the sponsors combined partial response with low-dFLC response.

The following studies were performed in support of an immunoglobulin light-chain amyloidosis (AL) monitoring claim:

Comparison to Predicate Devices

For comparison of the five response criteria (CR (Complete Response), VGPR (Very Good Partial Response), PR (Partial Response), SD (Stable Disease), PD (Progressive Disease)) three evaluation modes were applied to all immunoglobulin light-chain amyloidosis (AL) data sets. Siemens favors using evaluation mode 2.

Response categories were determined for free light chain testing by Siemens Healthcare N Latex FLC and TBS Freelite Kappa Free and Lambda Free. Response evaluation was done by comparing changes between the initial sample draw and each consecutive blood draw independently. The response levels obtained by the two different test systems were compared in 5x5 contingency tables and relative agreement calculated.

Agreement of N Latex FLC versus Freelite (Evaluation Mode 1)

Response Criteria based on N Latex FLC results	Response Criteria based on Freelite results					
	Complete Response	**VGPR**	**Partial Response**	**Stable Disease**	**Progressive Disease**	**Total**
Complete Response	49	3	1	0	0	**53**
VGPR	19	48	9	2	0	**78**
Partial Response	0	5	15	5	1	**26**
Stable Disease	6	2	1	55	4	**68**
Progressive Disease	0	0	1	4	11	**16**
Total	**74**	**58**	**27**	**66**	**16**	**241**

Agreement Rate and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 1)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Agreement Rate	66.2%	82.8%	55.6%	83.3%	68.8%
95% CI Bootstrap	51.6 – 83.6%	70.3 – 92.3%	21.4 – 71.4%	77.4 – 96.7%	47.4 – 92.3%

Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 1)

	Result (n / Total)	95% CI Bootstrap
PPA	68.8% (11/16)	47.4 – 92.3%
NPA	97.8% (220/225)	96.8 – 100.0%

Agreement of N Latex FLC versus Freelite (Evaluation Mode 2)

Response Criteria based on N Latex FLC results	Response Criteria based on Freelite results					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	49	3	0	0	0	**52**
VGPR	17	45	14	3	0	**79**
Partial Response	0	5	15	4	1	**25**
Stable Disease	6	2	2	54	1	**65**
Progressive Disease	0	0	2	3	15	**20**
Total	**72**	**55**	**33**	**64**	**17**	**241**

Agreement Rate and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 2)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Agreement Rate	68.1%	81.8%	45.5%	84.4%	88.2%
95% CI Bootstrap	53.6 – 86.3%	67.4 – 91.1%	15.0 – 60.0%	76.5 – 95.4%	70.0 – 100.0%

Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 2)

	Result (n / Total)	95% CI Bootstrap
PPA	88.2% (15/17)	70.0 – 100.0%
NPA	97.8% (219/224)	95.9 – 99.6%

Agreement of N Latex FLC versus Freelite (Evaluation Mode 3)

Response Criteria based on N Latex FLC results	Response Criteria based on Freelite results					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	50	2	0	0	0	**52**
VGPR	19	48	7	2	1	**77**
Partial Response	0	5	15	4	1	**25**
Stable Disease	6	2	3	54	0	**65**
Progressive Disease	0	0	1	3	18	**22**
Total	**75**	**57**	**26**	**63**	**20**	**241**

Agreement Rate and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 3)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Agreement Rate	66.7%	84.2	57.7	85.7%	90.0%
95% CI Bootstrap	52.0 – 83.9%	71.2 – 93.3%	23.1 – 76.0%	77.0 – 96.1%	77.8 – 100.0%

Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) and 95% Confidence Intervals of N Latex FLC versus Freelite (Evaluation Mode 3)

	Result (n / Total)	95% CI Bootstrap
PPA	90.0% (18/20)	77.8 – 100.0%
NPA	98.2% (217/221)	96.3 – 99.6%

Comparison to Clinical Status

For comparison of the five response criteria (CR (Complete Response), VGPR (Very Good Partial Response), PR (Partial Response), SD (Stable Disease), PD (Progressive Disease)) three evaluation modes were applied to all immunoglobulin light-chain amyloidosis (AL) data sets. Siemens favors using evaluation mode 2.

Response categories were determined for free light chain testing by Siemens Healthcare N Latex FLC and TBS Freelite Kappa Free and Lambda Free, respectively. Response evaluation was done by comparing changes between the initial sample draw and each consecutive blood draw independently.

The response levels obtained by the two different test systems were compared to the clinical response level provided by the physician taking into account all available clinical and laboratory information. Relative agreement between the clinical response (including further information in addition to serum testing) and the response level applying the clinical response criteria by either using N Latex FLC or the predicate device were calculated, also using 5x5 contingency tables, and compared.

Immunoglobulin light-chain amyloidosis (AL): Concordance Rate N Latex FLC Kappa and Lambda versus Clinical Status

Concordance of N Latex FLC versus Clinical Status (Evaluation Mode 1)

Response Criteria based on N Latex FLC results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	19	8	10	6	1	**44**
VGPR	15	40	11	8	1	**75**
Partial Response	0	4	15	6	1	**26**
Stable Disease	0	4	17	35	5	**61**
Progressive Disease	0	0	3	4	9	**16**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 1)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	55.9%	71.4%	26.8%	59.3%	52.9%
95% CI Bootstrap	28.6 – 75.7%	56.6 – 88.9%	7.8 – 30.2%	39.6 – 75.0%	28.6 – 78.9%

Sensitivity and Specificity and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 1)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	52.9% (9/17)	28.6 – 78.9%
Specificity	96.6% (198/205)	95.2 – 99.5%

Concordance of N Latex FLC versus Clinical Status (Evaluation Mode 2)

Response Criteria based on N Latex FLC results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	18	8	10	6	1	**43**
VGPR	16	40	11	8	1	**76**
Partial Response	0	4	15	6	0	**25**
Stable Disease	0	4	17	34	3	**58**
Progressive Disease	0	0	3	5	12	**20**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 2)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	52.9%	71.4%	26.8%	57.6%	70.6%
95% CI Bootstrap	25.0 – 74.3%	56.6 – 88.9%	8.0 – 30.3%	38.2 – 72.9%	47.1 – 88.2%

Sensitivity and Specificity and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 2)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	70.6% (12/17)	47.1 – 88.2%
Specificity	96.1% (197/205)	94.8 – 99.0%

Concordance of N Latex FLC versus Clinical Status (Evaluation Mode 3)

Response Criteria based on N Latex FLC results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	18	8	10	6	1	**43**
VGPR	16	40	10	7	1	**74**
Partial Response	0	4	15	6	0	**25**
Stable Disease	0	4	18	34	2	**58**
Progressive Disease	0	0	3	6	13	**22**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 3)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	52.9%	71.4%	26.8%	57.6%	76.5%
95% CI Bootstrap	24.0 – 74.2%	56.4 – 89.1%	7.9 – 30.3%	37.5 – 72.3%	52.9 – 93.8%

Sensitivity and Specificity and 95% Confidence Intervals of N Latex FLC versus Clinical Status (Evaluation Mode 3)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	76.5% (13/17)	52.9 – 93.8%
Specificity	95.6% (196/205)	93.3 – 99.0%

immunoglobulin light-chain amyloidosis (AL): Agreement Rate Freelite Kappa and Lambda versus Clinical Status

Concordance of Freelite versus Clinical Status (Evaluation Mode 1)

Response Criteria based on Freelite results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	21	14	12	13	1	**61**
VGPR	11	37	5	3	1	**57**
Partial Response	2	2	15	7	0	**26**
Stable Disease	0	3	23	32	4	**62**
Progressive Disease	0	0	1	4	11	**16**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 1)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	61.8%	66.1%	26.8%	54.2%	64.7%
95% CI Bootstrap	40.7 – 87.0%	54.9 – 85.4%	6.2 – 29.2%	34.2 – 70.7%	38.9 – 82.4%

Sensitivity and Specificity and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 1)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	64.7% (11/17)	38.9 – 82.4%
Specificity	97.6% (200/205)	94.8 – 99.5%

Concordance of Freelite versus Clinical Status (Evaluation Mode 2)

Response Criteria based on Freelite results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	20	14	12	13	1	**60**
VGPR	12	34	5	3	0	**54**
Partial Response	2	5	16	7	2	**32**
Stable Disease	0	3	21	31	4	**59**
Progressive Disease	0	0	2	5	10	**17**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 2)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	58.8%	60.7%	28.6%	52.5%	58.8%
95% CI Bootstrap	33.3 – 84.0%	49.1 – 82.6%	6.9 – 30.4%	32.7 – 68.8%	28.6 – 80.0%

Sensitivity and Specificity and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 2)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	58.8% (10/17)	28.6 – 80.0%
Specificity	96.6% (198/205)	94.2 – 99.5%

Concordance of Freelite versus Clinical Status (Evaluation Mode 3)

Response Criteria based on Freelite results	Response Criteria based on Clinical Status					
	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease	Total
Complete Response	22	14	12	13	1	**62**
VGPR	11	36	5	3	1	**56**
Partial Response	1	2	15	7	0	**25**
Stable Disease	0	3	22	30	4	**59**
Progressive Disease	0	1	2	6	11	**20**
Total	**34**	**56**	**56**	**59**	**17**	**222**

Concordance Rate and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 3)

Response Criteria	Complete Response	VGPR	Partial Response	Stable Disease	Progressive Disease
Concordance Rate	64.7%	64.3%	26.8%	50.8%	64.7%
95% CI Bootstrap	44.4 – 91.3%	52.6 – 84.6%	6.4 – 29.3%	31.7 – 66.7%	38.9 – 83.3%

Sensitivity and Specificity and 95% Confidence Intervals of Freelite versus Clinical Status (Evaluation Mode 3)

	Result (n / Total)	95% CI Bootstrap
Sensitivity	64.7% (11/17)	38.9 – 83.3%
Specificity	95.6% (196/205)	93.4 – 99.0%

Comparison to Predicate Devices 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 ≥ one week with a total of at least three collections. Two graphs each were established for the 72 patients included in the study, one using involved free light chain (iFLC) and one using the difference between the two free light chain concentrations (dFLC).

While N Latex FLC kappa and lambda 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 free light assays cannot be used interchangeably (as stated in the sponsor's package insert). They do, for the most part, follow a parallel path.

References

1) National Comprehensive Cancer Network. "NCCN clinical practice guidelines in oncology (NCCN guidelines)." *Systemic Light Chain Amyloidosis Version* 1 (2022): 1-27.
2) Peter Mollee, Jill Tate and Carel J. Pretorius, "Evaluation of the N Latex light chain assay in the diagnosis and monitoring of AL amyloidosis", in Clin Chem Lab Med 2013.
3) Paolo Milani, Giampaolo Merlini and Giovanni Palladini, "Novel Therapies in Light Chain Amyloidosis", in Kidney International Reports (2018) 3, 530–541.
4) Giovanni Palladini and Giampaolo Merlini, "When should treatment of AL amyloidosis start at relapse? Early, to prevent organ progression", in Blood Advances, Point Counterpoint, Jan 2019, Vol 3, No. 2.

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 reagents with the expanded intended use to include monitoring of immunoglobulin light-chain amyloidosis (AL) patients are substantially equivalent to the legally marketed predicate devices FDA cleared under K031016.

END OF SUMMARY