November 7, 2017

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

Re: k171072
Trade/Device Name: N Latex Cystatin C; N Protein Standard UY
Regulation Number: 21 CFR 862.1225
Regulation Name: Creatinine test system
Regulatory Class: Class II
Product Code: NDY, JIX
Dated: April 6, 2017
Received: April 10, 2017

Dear Christine Perkins:

This letter corrects our substantially equivalent letter of May 12, 2017.

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and Part 809), please contact the Division of Industry and Consumer Education (DICE) at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education (DICE) at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K171072

Device Name

N Latex Cystatin C; N Protein Standard UY

Indications for Use *(Describe)*

N Latex Cystatin C:

N Latex Cystatin C is an in vitro diagnostics kit containing reagents for the quantitative determination of cystatin C in human serum and lithium-heparinized plasma by means of particle-enhanced immunonephelometry using the BN Systems. Cystatin C measurements are used in the diagnosis and treatment of renal diseases.

N Protein Standard UY:

N Protein Standard UY is used for preparing reference curves for the immunonephelometric determination of α1-microglobulin and Cystatin C using the BN Systems.

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 summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR 807.92 and follows the FDA guidance “The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]”, issued July 28, 2014.

The assigned 510(k) number is: K171072

5.1 Submitter

Siemens Healthcare Diagnostics Products GmbH
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35041 Marburg, Germany

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Date of Preparation:	May 11, 2017

5.2 Device Information

Trade Name:	N Latex Cystatin C
Common or Usual Name:	Test, Cystatin C Creatinine test system
Classification Name:	Creatinine test system (21CFR 862.1225)
Regulatory Class:	Class II
Product Code:	NDY
510(k) Review Panel:	Clinical Chemistry

Trade Name:	N Protein Standard UY
Common or Usual Name:	Calibrator, Multi-Analyte Calibrator
Classification Name:	Calibrator (21 CFR 862.1150)
Regulatory Class:	Class II
Product Code:	JIX
510(k) Review Panel:	Clinical Chemistry

5.3 Predicate Device:

The predicate device is the Tina-quant Cystatin C Gen.2 Test System, for use on Roche/Hitachi cobas c systems cleared by the FDA under K141143.

Assay:	Tina-quant Cystatin C Gen.2
Calibrator:	C.f.a.s. (Calibrator for automated systems) Cystatin C

5.4 Device Description / Test Principle

The N Latex Cystatin C is an in vitro diagnostics kit containing reagents for the quantitative determination of cystatin C in human serum and lithium heparinized plasma by means of particle-enhanced immunonephelometry using the BN II and BN ProSpec® Systems. Used in conjunction with other clinical and laboratory findings, N Latex Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases.

Used in conjunction with the assay reagents, N Protein Standard UY is for use in the establishment of reference curves for the determination of cystatin C on the BN II and BN ProSpec Systems. N Cystatin C Control 1 and 2 are included with N Latex Cystatin C kit and are for use as assayed accuracy controls and precision controls in the determination of cystatin C by immunonephelometry with the BN II and BN ProSpec Systems.

The N Latex Cystatin C test system is based upon the principles of particle-enhanced immunonephelometry. Polystyrene particles coated with specific antibodies to human cystatin C are aggregated when mixed with samples containing human cystatin C. 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 N Latex Cystatin C subject of this 510(k) is materially the same as the assay cleared in K041878. The reason for the submission is for a new standardization to ERM-DA471/IFCC. This is being accomplished solely by changing the calibrator value assignment process.

5.5 Intended Use / Indications for Use

N Latex Cystatin C assay

N Latex Cystatin C is an *in vitro* diagnostics kit containing reagents for the quantitative determination of cystatin C in human serum and lithium-heparinized plasma by means of particle-enhanced immunonephelometry using the BN Systems. Cystatin C measurements are used in the diagnosis and treatment of renal diseases.

N Protein Standard UY

N Protein Standard UY is used for preparing reference curves for the immunonephelometric determination of α1-microglobulin and Cystatin C using the BN Systems.

Comparison of Technological Characteristics

Attributes	**Proposed Device:** N Latex Cystatin C assay	**Predicate Device:** Roche Tina-quant Cystatin C Gen.2 (K141143)
Intended Use / Indications for Use	N Latex Cystatin C is an *in vitro* diagnostics kit containing reagents for the quantitative determination of cystatin C in human serum and lithium-heparinized plasma by means of particle-enhanced immunonephelometry using the BN Systems. Cystatin C measurements are used in the diagnosis and treatment of renal diseases.	Tina-quant Cystatin C Gen. 2 is an in vitro test for the quantitative determination of cystatin C in human serum and plasma on Roche/Hitachi cobas c systems. Cystatin C measurements are used as an aid in the diagnosis and treatment of renal diseases.
Analyte	cystatin C	Same
Assay type/ Technology	Immunonephelometry	Turbidimetry
Sample Type	Human serum and plasma	Human serum and plasma
Permissible anticoagulants	Li-Heparin	Li-Heparin, K_2-EDTA, K_3-EDTA
Composition	N Latex Cystatin C consists of a suspension of polystyrene particles coated with approximately 0.016 g/L anti-human cystatin C from rabbits	Reagent 2 is latex particles in glycine buffer coated with anti-Cystatin C antibodies (rabbit); preservatives and stabilizers.
Ancillary Reagents	N Cystatin C Supplementary Reagent A contains rabbit immunoglobulin (14 g/L) in buffered solution. N Cystatin C Supplementary Reagent B consists of an aqueous solution of polyethylene glycol sorbitan monolaureate (85 g/L) and polyethylene glycol ether (27 g/L).	R1 contains solution of polymers in MOPS-buffered saline; preservative, stabilizers.
Units	mg/L	Same
Analytical measuring range (Calibrator lot dependent)	0.27 – 9.4 mg/L	0.40 – 6.80 mg/L 0.40 – 13.6 mg/L (1:2 dilution)
Reference Interval	Age 21-72 0.49 – 1.19 mg/L	Age 21 – 77 0.61 – 0.95 mg/L

	Proposed Device: N Protein Standard UY	**Predicate Device:** C.f.a.s. Cystatin C (K141143)
Intended Use	N Protein Standard UY is used for preparing reference curves for the immunonephelometric determination of α1-microglobulin and Cystatin C using the BN Systems.	Calibrator for automated systems Cystatin C is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers.
Matrix	N Protein Standard UY consists of lyophilized polygeline with urinary proteins of human origin. Contains sodium azide (<1 g/L) as a preservative.	C.f.a.s. Cystatin C is based on pooled delipidated human serum enriched with recombinant human Cystatin C produced in E. Coli.
How supplied	Lyophilized	Liquid
Analyte Detected	cystatin C, α1-microglobulin*	cystatin C
Traceability	ERM-DA417/IFCC	Same

*N Protein Standard UY α1-microglobulin analyte was initially cleared in K991075 and has not been modified (in terms of composition, value assignment and stability) for the α1-microglobulin analyte since.

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

5.7 Performance Data

Analytical performance studies of N Latex Cystatin C were performed at Siemens Healthcare Diagnostics Products, Marburg Germany on a BN II and a BN ProSpec analyzer.

Matrix comparison, interference, specificity and stability claims were not impacted by the new standardization. The claims are unchanged since clearance (K041878).

The following performance data are provided in support of a substantial equivalence determination.

5.7.1 Analytical Performance

5.7.1.1 Precision

Confirmation of precision studies was performed internally on one BN II and one BN ProSpec instrument for twenty days following the scheme of two runs per day, with two

replicates per run according to CLSI EP05-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition*. The order of the analysis of parameter samples and quality control samples, between morning and afternoon runs, was varied so as not to add an inherent bias to the study.

Precision samples included serum and plasma pools and N Cystatin C Control 1 and 2, spanning the measuring range with sample pools close to the medical decision point (MDP) of 1.1 mg/L.

BN ProSpec Anova					
ID	Unit	n	Mean value	Repeatability CV [%]	Within-device/lab CV [%]
CysC Control 1	mg/L	80	1.155	1.78	1.78
CysC Control 2	mg/L	80	2.176	1.00	1.01
Serum Pool 1	mg/L	80	0.465	3.85	3.85
Serum Pool 2	mg/L	80	1.142	1.39	1.41
Serum Pool 3	mg/L	80	8.425	1.62	1.62
Plasma Pool 1	mg/L	80	0.481	2.38	2.65
Plasma Pool 2	mg/L	80	1.129	2.09	2.09
Plasma Pool 3	mg/L	80	8.863	1.07	1.26

BN II Anova					
ID	Unit	n	Mean value	Repeatability CV [%]	Within-device/lab CV [%]
CysC Control 1	mg/L	80	1.070	1.93	2.24
CysC Control 2	mg/L	80	2.110	1.42	1.54
Serum Pool 1	mg/L	80	0.445	2.54	2.62
Serum Pool 2	mg/L	80	1.078	1.34	1.55
Serum Pool 3	mg/L	80	8.636	1.69	1.80
Plasma Pool 1	mg/L	80	0.451	2.59	2.59
Plasma Pool 2	mg/L	80	1.069	1.62	1.75
Plasma Pool 3	mg/L	80	8.798	1.98	2.42

5.7.1.2 Measuring Range (Linearity and LoQ)

A linearity study was performed according to CLSI EP06-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach.* One N Latex Cystatin C reagent lot, one BN II and one BN ProSpec instrument were used.

A concentrated Cystatin C stock solution was used to spike pooled human serum to a Cystatin C concentration between 10 ± 0.5 mg/L which is just above the upper limit of the measuring interval of 9.4 mg/L. This high pool was serially diluted with human serum containing undetectable levels of Cystatin C down to the minimum measuring range. Each dilution was tested in replicates of five using an individual aliquot.
The N Latex Cystatin C assay demonstrates acceptable linearity over the range of 0.27 to 10.3 mg/L.

Limit of Quantitation (LoQ) testing was performed according to CLSI Guideline EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*. LoQ was demonstrated to be 0.08 mg/L at < 8% CV.

The measuring range of the N Latex Cystatin C assay is 0.27 to 9.4 mg/L.

5.7.1.3 High Dose Hook Effect (Antigen Excess)

A serum sample was spiked with purified cystatin C to obtain a sample with a calculated concentration higher than 28 mg/L. A series of dilutions was prepared using cystatin C deficient serum. Each dilution was run five times. The analyte concentration of the high sample was determined using the mean of at least two manual dilutions that recovered within the measuring range of the assay. The results of the dilutions are compared to the upper limit of the calibration curve. Based on the results, Cystatin C concentrations up to 42.91 mg/L did not exhibit any high dose hook or prozone effects.

5.7.2 Clinical Studies

5.7.2.1 Reference Interval Study

A reference interval was performed according to CLSI EP28-A3C, '*Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory*'.

Two hundred three (203) serum samples from a US population of apparently healthy adults or patients with diseases not linked to renal disease or failure, between the ages of 21 and 72 and evenly distributed across gender were measured. The data analysis within the 2.5% and 97.5% percentile resulted in a range of Cystatin C from 0.49 to 1.19 mg/L.

The sponsor recommends that each facility should determine its own reference intervals since values may vary depending on the population studied.

5.7.2.2 Method comparison

A method comparison study designed according to CLSI EP09-A3: *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition* was conducted at one external site in the United States.

Serum samples (186) were measured on both the predicate device, Roche Tina-quant Cystatin C Gen.2 assay as well as on the N Latex Cystatin C assay. Results were compared by Passing-Bablok regression analysis. Results met the pre-established acceptance criteria for slope, intercept and Pearson correlation coefficient (r). The following summary of Passing-Bablok regression analysis proves substantial equivalence between the N Latex Cystatin C assay and the predicate device.

Method Comparison (Devices)	Correlation-coefficient (r)	Slope	Intercept
N Latex Cystatin C on BN ProSpec vs. Tina-quant Cystatin C Gen.2 on Roche cobas	0.988	0.982	-0.078 mg/L
N Latex Cystatin C on BN II vs. Tina-quant Cystatin C Gen.2 on Roche cobas	0.998	0.981	-0.079 mg/L

5.8 Traceability

The calibration of the assay is traceable to the IFCC European Reference Material ERM-DA471/IFCC, certified for cystatin C measurements.

5.8.1 Calibrator Traceability

N Protein Standard UY is traceable to Siemens internal Master Calibrator which is directly traceable to ERM-DA471/IFCC.

5.9 Conclusion

The N Latex Cystatin C assay including reagents and calibrator and the Roche Tina-quant Cystatin C Gen.2 assay and calibrator are substantially equivalent in principle and

performance based on intended use and indications for use and supported by the performance testing described in the 510(k) submission.