May 25, 2018

Siemens Healthcare Diagnostics, Inc.
Kathleen Dray-Lyons
Regulatory and Clinical Affairs Specialist
500 GBC Drive
Newark, NJ 19714

Re: K181082
Trade/Device Name: ADVIA Chemistry Cystatin C_2 Assay (CYSC_2)
Regulation Number: 21 CFR 862.1225
Regulation Name: Creatinine test system
Regulatory Class: Class II
Product Code: NDY
Dated: April 23, 2018
Received: April 24, 2018

Dear Kathleen Dray-Lyons:

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.

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.

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,

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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K181082

Device Name
ADVIA® Chemistry Cystatin C_2 (CYSC_2) assay

Indications for Use *(Describe)*

The ADVIA® Chemistry Cystatin C_2 (CYSC_2) assay is for the in vitro diagnostic use in the quantitative determination of cystatin C in human serum and plasma (lithium heparin, potassium EDTA) on ADVIA Chemistry systems. Measurement of cystatin C aids in the diagnosis and treatment of renal disease.

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

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

The assigned 510(k) number is: K181082

1. Submitter

Company	Siemens Healthcare Diagnostics Inc.
Address	500 GBC Drive Newark, DE 19702
Contact	Kathleen Dray-Lyons
Telephone	617-688-6117
Date of Preparation	May 24, 2018

2. Trade Name:

ADVIA® Chemistry Cystatin C_2 Assay (CYSC_2)

Common Name:

Test, Cystatin C

Classification:

21 CFR § 862.1225; Class II

Product Code:

NDY

Panel:

Clinical Chemistry

3. Identification of the Predicate Devices:

N Latex Cystatin C (K171072)

The ADVIA Cystatin C_2 (CYSC_2) assay is substantially equivalent to the N Latex Cystatin C assay cleared under K171072.

4. Device Description:

The ADVIA Cystatin C_2 assay (CYSC_2) is an *in vitro* diagnostics kit containing reagents for the quantitative determination of cystatin C in human serum and plasma by means of particle-enhanced turbidimetry using the ADVIA Chemistry Systems. Used in

conjunction with other clinical and laboratory findings, ADVIA Chemistry Cystatin C_2 measurements are used as an aid in the diagnosis and treatment of renal diseases.

The ADVIA Chemistry Cystatin C_2 latex reagent is a suspension of uniform latex particles coated with anti-cystatin-C antibody. When serum or plasma containing cystatin C is mixed with the latex reagent, agglutination takes place resulting in an increase in turbidity. This turbidity is measured at 571 and 805 nm. The cystatin C concentration in serum or plasma is determined from a calibration curve that is generated with the calibrators.

5. Device Intended Use:

The ADVIA Chemistry Cystatin C_2 (CYSC_2) assay is for the *in vitro* diagnostic use in the quantitative determination of cystatin C in human serum and plasma (lithium heparin, potassium EDTA) on ADVIA Chemistry systems. Measurement of cystatin C aids in the diagnosis and treatment of renal disease.

6. Technical Characteristics:

Similarities and Differences to the predicate:

A comparison of the similarities and differences between the proposed ADVIA Chemistry Cystatin C_2 assay versus the N Latex Cystatin C assay (predicate) is provided in the table below.

ADVIA Cystatin C_2 Assay versus N Latex Cystatin C

Attributes	Proposed ADVIA Cystatin C_2 Assay	Predicate N Latex Cystatin C (K171072)
Intended Use	The ADVIA® Chemistry Cystatin C_2 (CYSC_2) assay is for the *in vitro* diagnostic use in the quantitative determination of cystatin C in human serum and plasma (lithium heparin, potassium EDTA) on ADVIA Chemistry systems. Measurement of cystatin C aids in the diagnosis and treatment of renal disease.	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.
Assay format	Turbidimetry	Immunonephelometry
Antibody	Rabbit	Same
Traceability	The assay calibrator is traceable to the IFCC European Reference Material ERM-DA471/IFCC,	Same

	certified for cystatin C measurements	
Analyzers	ADVIA Chemistry Systems	BN Systems
Sample type	Serum and Plasma (lithium heparin, potassium EDTA)	Serum and Plasma (lithium heparin)
Units	mg/L	Same
Measuring Range	0.25 to 8.93 mg/L 0.25 to 26.79 mg/L (1:3 dilution)	0.27 – 9.4 mg/L
Calibrators	5 levels	One level

7. Non-Clinical Performance Evaluation:

Method Comparison versus the Predicate:

The ADVIA Chemistry Cystatin C_2 assay on the ADVIA 1800 system was compared to the predicate N Latex Cystatin C assay (K171072) on the BN ProSpec system in accordance with CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline Third Edition. One hundred and fifty-eight (158) frozen human serum samples were assayed in singlicate across the assay range of 0.25 - 8.93 mg/L. Analysis of the results using weighted linear regression, standard Passing-Bablok regression and Least Squares was calculated. The correlation coefficient (r) was obtained by linear regression.

Passing-Bablok regression analysis yielded the following:

Methods	n	N Latex Sample Range Analyzed (mg/L)	Slope (95% CI)	Intercept mg/L (95% CI)	r-Value*
ADVIA CYCS_2 versus N Latex Cystatin C	158	0.44 to 8.07	1.008 (0.998 to 1.022)	0.101 (0.086 to 0.113)	1.000

Weighted Least Square Linear regression yielded the following:

Methods	n	N Latex Sample Range Analyzed (mg/L)	Slope (95% CI)	Intercept mg/L (95% CI)	r-Value*
ADVIA CYCS_2	158		1.021	0.079	1.000

versus N Latex Cystatin C		0.44 to 8.07	(1.006 to 1.037)	(0.063 to 0.96)	

***** Correlation coefficient (r) was obtained from ordinary least squares regression.

Repeatability and Within Lab Precision:

Testing was performed over twenty (20) days, two (2) runs per day, two (2) times per run for a total 80 replicates/sample. Analysis of variance (ANOVA) was used to calculate the Repeatability and Within-Lab imprecision. Typical precision observed on the ADVIA Cystatin C_2 assay is summarized below.

Repeatability and Within-Lab Results

Material	N	Mean	Repeatability		Within-Lab Precision	
		mg/L	SD	%CV	SD	%CV
Multiqual 1 Control	80	0.52	0.01	2.0	0.02	3.7
Randox 2 Control	80	0.85	0.01	1.1	0.01	1.5
Randox 3 Control	80	3.91	0.04	1.1	0.07	1.9
Serum Pool 1	80	1.09	0.01	0.9	0.01	1.2
Serum Pool 2	80	8.92	0.12	1.4	0.21	2.4

Linearity

Linearity across the assay range (0.25 to 8.93 mg/L) was confirmed in accordance with CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach, by testing a high concentration of cystatin C on the ADVIA Chemistry 1800 system using one lot of reagent and calibrators. This high concentration sample was serially diluted with a low concentration sample (serum) with equally spaced dilution levels ranging from 0.19 to 9.06 mg/L. Linearity was demonstrated by linear fit deviation of <10% for samples > 2.50 mg/L and linear fit deviation of ≤ 0.25 mg/L for samples ≤ 2.50 mg/L. Samples above 2.5 mg/L were found to deviate no more than 10%, while samples below or equal to 2.5 mg/L did not demonstrate a bias greater than 0.03.

ADVIA Cystatin C_2 Assay

ADVIA System	Linear Regression			Percent Deviation	Absolute Deviation	n	Sample Range mg/L
	Slope	y-intercept	r				
1800	1.087	-0.014	0.999	10%	0.25 mg/L	11	0.19 - 9.06

Detection Capability

LoB: Four (4) blank samples were prepared at a concentration of 0 mg/L. All four samples were tested in replicates of twenty (20) on the ADVIA 1800 system over three (3) days using two (2) reagent lots for a total of N=480 replicates. The LoB for the ADVIA Chemistry CYSC_2 assay is 0.10 mg/L.

LoD: Four (4) samples were prepared at a concentration of approximately 0.1 mg/L. All four samples were tested in replicates of twenty (20) on the ADVIA 1800 system over three (3) days using two (2) reagent lots for a total of N=480 replicates. The LoD for the ADVIA Chemistry CYSC_2 assay is 0.25 mg/L.

LoQ: Four (4) serum samples were prepared at a concentration of approximately 0.1 mg/L. All four samples were tested in replicates of twenty (20) on the ADVIA 1800 system over three (3) days using two (2) reagent lots. The LoQ for the ADVIA Chemistry CYSC_2 assay is 0.25 mg/L.

LoB and LoD values were calculated non-parametrically with proportions of false positives (α) less than 5% and false negatives (β) less than 5%, based on 480. LoQ is the lowest amount of cystatin C that can be determined quantitatively at < 10% CV.

Interference Testing

Interference testing was performed according to CLSI EP07-A2: Approved Guideline Interference Testing in Clinical Chemistry to determine the effect of various endogenous and exogenous substances on the ADVIA Cystatin C_2 assay. For all interferents the percent recovery was determined by testing a control sample without the interferent and comparing it to the value obtained from a test sample to which the potential interferent had been added. Interferents were tested at two levels of cystatin c concentrations: 0.4 to 1.2 mg/L and 2.5 to 3.5 mg/L.

ADVIA Chemistry 1800 system

Interferent	Interferent Level	Cystatin C Sample Concentration	Interference
Bilirubin (conjugated)	60 mg/dL	0.69 mg/L	NSI[a]
	60 mg/dL	2.51 mg/L	NSI
Bilirubin (unconjugated)	60 mg/dL	0.78 mg/L	NSI
	60 mg/dL	2.74 mg/L	NSI
Lipemia (triglycerides from Intralipid)	1000 mg/dL	0.79 mg/L	NSI
	1000 mg/dL	2.75 mg/L	NSI
Hemolysis (hemoglobin)	1000 mg/dL	1.13 mg/L	NSI
	1000 mg/dL	2.64 mg/L	NSI
Rheumatoid Factor	1200 IU/mL	0.89 mg/L	NSI
	1200 IU/mL	3.14 mg/L	NSI

[a] NSI = No significant interference. A percentage effect > 10% is considered a significant interference.

Expected Values:
The expected values for healthy individuals are from 0.64–1.23 mg/L. These are the 2.5 and the 97.5 percentile values from the results of a normal range study, following CLSI Procedure EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory with 208 apparently healthy samples, performed by Siemens.

ADVIA Cystatin C_2 Median	
2.5 Percentile	0.64 mg/L
97.5 Percentile	1.23 mg/L

Calibrator Traceability:
The assay is standardized using calibrators, which are traceable to the IFCC European Reference Material ERM-DA471/IFCC, certified for Cystatin C measurements.

8. Conclusion:
The ADVIA Chemistry Cystatin C_2 assay is substantially equivalent to the predicate devices based on intended use, principle and the performance characteristics above.