November 22, 2019

Siemens Healthcare Diagnostics, Inc.
Anoop Joy
Regulatory Affairs Specialist
511 Benedict Avenue
Tarrytown, New York 10591

Re: K192777
Trade/Device Name: ADVIA Centaur CA 15-3 assay
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-Associated Antigen Immunological Test System
Regulatory Class: Class II
Product Code: MOI
Dated: September 27, 2019
Received: September 30, 2019

Dear Anoop Joy:

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,

Takeesha Taylor-Bell
Acting Deputy Division Director
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K192777

Device Name
ADVIA Centaur CA 15-3 assay

Indications for Use *(Describe)*

The ADVIA Centaur CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.

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 of Safety and Effectiveness

ADVIA Centaur CA 15-3 assay

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

The assigned 510(k) Number: K192777

I. APPLICANT

Siemens Healthcare Diagnostics Inc.
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Tarrytown, NY 10591 USA

Contact: Anoop Joy
Regulatory Clinical Affairs Specialist
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Date Prepared: November 21, 2019

II. Regulatory Information

Name of Device: ADVIA Centaur CA 15-3
Classification: Class II
Regulation Section: 21 CFR § 866.6010
Product Code: MOI
Panel: Immunology

III. PREDICATE DEVICE

Name of Device: ADVIA Centaur CA 15-3 assay
510 (k): K012357

IV. DEVICE DESCRIPTION

The ADVIA Centaur CA 15-3 assay reagents come in the following configurations:

Contents	Number of Tests
5 ReadyPack primary reagent packs containing ADVIA Centaur CA 15-3 Lite Reagent, Solid Phase, and Conjugate Reagent ADVIA Centaur CA 15-3 Master Curve card	500
1 ReadyPack primary reagent pack containing ADVIA Centaur CA 15-3 Lite Reagent, Solid Phase, and Conjugate Reagent ADVIA Centaur CA 15-3 Master Curve card	100

The ReadyPack consists of the following:

ADVIA Centaur CA 15-3 ReadyPack® primary reagent pack; Lite Reagent
5.0 mL/reagent pack monoclonal mouse anti-DF3 antibody (~ 2.0 µg/mL) labeled with acridinium ester in buffered saline with bovine serum albumin, sodium azide (< 0.1%), and preservatives.
ADVIA Centaur CA 15-3 ReadyPack primary reagent pack; Solid Phase Reagent
25.0 mL/reagent pack monoclonal mouse capture antibody (~30 µg/mL) covalently coupled to paramagnetic particles in buffer with bovine serum albumin, sodium azide (< 0.1%), and preservatives.
ADVIA Centaur CA 15-3 ReadyPack primary reagent pack; Conjugate Reagent
5.0 mL/reagent pack monoclonal mouse anti-115D8 antibody (~12.5 µg/mL) labeled with a thiocarbamate of fluorescein in buffered saline with bovine serum albumin and preservatives

V. INTENDED USE

The ADVIA Centaur® CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.

VI. INDICATIONS FOR USE

Same as Intended use

VII. COMPARISION OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The following table provides a comparison between the predicate and candidate device.

Table 1: *Substantial Equivalence Comparison*

Item	**Predicate Device**	**Candidate Device (Modified Device)**
	ADVIA Centaur CA 15-3	ADVIA Centaur CA 15-3
Intended Use	The ADVIA Centaur® CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.	The ADVIA Centaur® CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.
Measurement	Quantitative	Same
Assay Range	0.5–200 U/mL	3.0–200 U/mL
Assay Principle	Sandwich immunoassay	Same
Technology	Direct chemiluminescent	Same
Sample Type	Serum	Serum and plasma (EDTA and lithium heparin)
Sample Volume	20 µL	same
Reagent Volume	50 µL of Conjugate Reagent and 250 µL of Solid Phase	same
Incubation Time	20 minutes at 37°C.	same
Standardization	traceable to an internal standard manufactured using highly purified material.	Same
Calibration	2-point	Same

Calibrators	ADVIA Centaur CA 15-3 Calibrator	Same
Number of Calibrator Levels	Two levels	Same
Controls	Commercial Controls	Same
Number of Control Levels	2	Same
Detection Antibody	monoclonal mouse anti-DF3 antibody labeled with acridinium ester	Same
Capture Antibody	monoclonal mouse capture antibody covalently coupled to paramagnetic particles	Same

VIII. PERFORMANCE CHARACTERISTICS DATA

Addition of plasma sample type claim was demonstrated by performing specimen equivalency studies, precision studies and interference studies using EDTA and Heparin. Since the assay principle, design or formulation not changed from original device, the analytical performance data previously reviewed for the ADVIA Centaur CA 15-3 assay continues to apply to this assay.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.

Limit of Blank (LoB)	1.0 U/mL
Limit of Detection (LoD)	2.0 U/mL
Limit of Quantitation (LoQ)	3.0 U/mL

The LoB corresponds to the highest measurement likely to be observed for a blank sample with a probability of 95%.

The LoD corresponds to the lowest concentration of cancer antigen CA 15-3 that can be detected with a probability of 95%.

The LoQ corresponds to the lowest amount of cancer antigen CA 15-3 in a sample at which the within laboratory CV is $\leq$ 20%.

Precision

Precision was determined in accordance with CLSI Document EP05-A3. Samples were assayed in duplicate in 2 runs per day for 20 days. The following results were obtained:

Specimen Type	N [a]	Mean (U/mL)	Repeatability SD [b] (U/mL)	Repeatability CV [c] (%)	Within-Laboratory Precision SD (U/mL)	Within-Laboratory Precision CV (%)
Serum A	80	7.80	0.24	N/A [d]	0.39	N/A
Serum B	80	175.54	2.32	1.3	5.62	3.2
Plasma, EDTA	80	107.13	2.21	2.1	3.84	3.6
Plasma, Heparin	80	34.79	0.79	2.3	1.32	3.8
Control 1	80	25.53	0.48	1.9	1.23	4.8
Control 2	80	59.28	1.70	2.9	2.64	4.4
Control 3	80	115.82	2.06	1.8	5.54	4.8

a Number of results.
b Standard deviation.
c Coefficient of variation.
d Not applicable.

Specimen Equivalency

Specimen equivalency was determined with the Deming linear regression model in accordance with CLSI Document EP09-A3. The following results were obtained:

Tube (y) vs. Serum (x)	N [a]	Sample Interval	Slope	Intercept	r [b]
Dipotassium EDTA plasma	129	3.43–199.49 U/mL	0.96	0.46 U/mL	1.00
Lithium heparin plasma	108	3.13–196.11 U/mL	1.02	-0.72 U/mL	1.00

a Number of samples tested.
b Correlation coefficient.

Interferences

Interference testing was performed in accordance with CLSI Document EP07-ed3. The following results were obtained**:**

Substance	Substance Test Concentration	Analyte Concentration (U/mL)	Bias (%)
Dipotassium EDTA	5.4 mg/mL	15.85	3.3
		107.66	4.9
Heparin	75 U/mL	9.71	0.8
		106.18	1.2

X. CONCLUSION

Comparative testing of the modified ADVIA Centaur CA 15-3 assay is substantially equivalent in principle and performance to the Predicate Device - *ADVIA Centaur CA 15-3 assay* cleared under 510(k) K012357.