February 13, 2020

Siemens Healthcare Diagnostics Inc.
Ian Thompson
Regulatory Clinical Affairs Specialist
511 Benedict Avenue
Tarrytown, New York 10591

Re: K193489
Trade/Device Name: ADVIA Centaur BR
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-Associated Antigen Immunological Test System
Regulatory Class: Class II
Product Code: MOI
Dated: December 16, 2019
Received: December 17, 2019

Dear Ian Thompson:

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,

Carolina Kagan
Acting Chief
Immunology and Flow Cytometry Branch
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)*
K193489

Device Name
ADVIA Centaur® BR

Indications for Use *(Describe)*
The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum and plasma (EDTA) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage III breast cancer. Serial testing for CA 27.29 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.

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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This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: K193489

1. Date Prepared

December 13, 2019

2. Applicant Information

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3. Regulatory Information

Table 1. Regulatory Information for ADVIA Centaur® BR

Trade Name	ADVIA Centaur® BR
Device	System, Test, Immunological, Antigen, Tumor
Regulation Description	Tumor-associated antigen immunological test system
FDA Classification	Class II
Review Panel	Immunology
Product Code	MOI
Regulation Number	21 CFR 866.6010

4. Predicate Device Information

Predicate Device Name: ADVIA Centaur® BR

510(k) Number: K982680

The ADVIA Centaur BR assay with the addition of the plasma (EDTA) sample and detection capability [Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)] claims in the Instructions for Use (Package Inserts) is substantially equivalent to the ADVIA Centaur BR assay that was cleared under 510(k) K982680, as shown below in the Substantial Equivalence Information section.

5. Intended Use / Indications for Use

The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum and plasma (EDTA) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage III breast

cancer. Serial testing for CA 27.29 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.

Special Conditions for Use Statement(s): For prescription use only

6. Device Description

The ADVIA Centaur BR assay is a fully automated, competitive immunoassay using direct, chemiluminescent technology. Results are determined using a calibration curve that is generated specifically on each instrument by a 2-point calibration and a master curve with the reagent bar code. The ADVIA Centaur BR assay is intended for use on the ADVIA Centaur family of analyzers. The ADVIA Centaur Calibrator G is a set of 2 level calibrators for the assay. Siemens recommends the use of commercially available quality control materials with at least two levels (low and high).

The ADVIA Centaur BR reagent kit contains the following:

- ADVIA Centaur BR ReadyPack primary reagent pack contains Lite Reagent and Solid Phase Reagent.

Materials Required but Not provided:

- ADVIA Centaur Calibrator G: consists of 2 levels (low and high) of CA 27.29 calibrators in equine serum with sodium azide (0.1%) and preservatives; lyophilized.
- ADVIA Centaur BR Pretreatment Reagent: consists of sodium hydroxide (0.24 N)

Optional Reagents:

- ADVIA Centaur Multi-Diluent 1: consists of equine serum with sodium azide (0.1%) and preservatives.
- ADVIA Centaur BR Master Curve Material: consists of a set of 7 levels of CA 27.29 (MCM1-7) spiked in lyophilized equine serum with sodium azide (0.1% after reconstitution) and preservatives.

7. Purpose of the Submission

The purpose of this submission is for the addition of plasma (EDTA) sample claim and updating the detection capability claim for the ADVIA Centaur BR assay.

8. Substantial Equivalence Information – Comparison of Candidate Device and Predicate Device

The following table demonstrates substantial equivalence between the ADVIA Centaur BR assay (Candidate Device) that has modified Instructions for Use (Package Inserts) with the addition of plasma (EDTA) sample and detection capability (LoB, LoD, and LoQ) claims and the currently marketed ADVIA Centaur BR assay (Predicate Device) that was cleared under 510(k) K982680.

Trade Name	Candidate Device	Predicate Device
	ADVIA Centaur BR (Modified Labeling)	**ADVIA Centaur BR (Unmodified Labeling)**
Intended Use	The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum and plasma (EDTA) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems.	The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems.
Indications for Use	The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage III breast cancer. Serial testing for CA 27.29 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.	The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage lll breast cancer. Serial testing for CA 27.2G in the serum of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.
Measurement	Quantitative	Same
Detection Capability	LoB: 3.5 U/mL	Analytical Sensitivity: 3.5 U/mL
	LoD: 7.0 U/mL	NA
	LoQ: 9.0 U/mL	NA
Assay Range	Serum and Plasma: 9.0–450 U/mL	Serum: 3.5–450 U/mL
Operating Principle	Competitive immunoassay	Same
Technology	Direct chemiluminescent	Same
Sample Type	Serum, Plasma (EDTA)	Serum
Sample Volume	20 µL (serum and plasma)	20 µL (serum)
Traceability/ Standardization	Traceable to an internal standard manufactured using highly purified CA 27.29	Same
Calibration	2-point	Same
Calibrator/Levels	Calibrator G/2 levels	Same
Controls/Levels	Commercial Controls/2 levels	Same
Master Curve Materials	Seven levels (MCM1–7)	Same
Detection Antibody	Monoclonal mouse anti-CA 27.29 antibody (~1.2 µg/mL) labeled with acridinium ester	Same
Capture Antibody	Human CA 27.29 (~0.72 U/mL) covalently coupled to paramagnetic particles	Same

9. Standard/Guidance Document References

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) were used as a basis of the study procedures described in this submission:

- Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline–Third Edition (CLSI EP09-A3).

- Interference Testing in Clinical Chemistry; Approved Guideline–Third Edition (CLSI EP07-ed3).
- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline–Second Edition (EP17-A2).

10. Test Principle

The ADVIA Centaur BR assay is a fully automated, competitive immunoassay using direct, chemiluminescent technology. The Lite Reagent is composed of a monoclonal mouse antibody specific for CA 27.29, labeled with acridinium ester. The antibody used in the assay, MAb B27.29, binds to a peptide epitope in the tandem repeat region of the MUC-1 gene product. The Solid Phase is composed of purified CA 27.29, which is covalently coupled to paramagnetic particles. After onboard pretreatment, the sample is incubated with both Lite Reagent and Solid Phase simultaneously for 7.5 minutes.

11. Performance Characteristics

The addition of the plasma (EDTA) sample and detection capability (LoB, LoD, LoQ) claims in the Instructions for Use (Package Inserts) for the ADVIA Centaur BR assay was demonstrated by testing the performance characteristics with the following studies:

- Detection Capability (LoB, LoD, LoQ)
- Specimen Equivalence by Method Comparison
- Interferences: EDTA

The plasma (EDTA) sample and detection capability (LoB, LoD, LoQ) claims for the ADVIA Centaur BR assay do not require the collection of additional analytical performance data. Therefore, all analytical performance data previously reviewed for the ADVIA Centaur BR assay continues to apply to this assay, because the assay was not modified.

11.1 Detection Capability

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

Limit of Blank (LoB)	3.5 U/mL
Limit of Detection (LoD)	7.0 U/mL
Limit of Quantitation (LoQ)	9.0 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 27.29 that can be detected with a probability of 95%.

The LoQ corresponds to the lowest amount of cancer antigen CA 27.29 in a sample at which the within laboratory CV is ≤ 20%. CV is ≤ 20%.

11.2 Specimen Equivalence by Method Comparison

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

Comparison	N*	Sample Interval	Slope (95%CI)	Intercept (95%CI)	Correlation Coefficient (r)
Dipotassium EDTA Plasma vs. Serum	101	10.80-444.42 U/mL	0.97 (0.955 – 0.993)	2.21 U/mL (1.376 – 3.040)	1.00

* N = Number of samples tested.

11.3 Interferences: EDTA

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

Interferent	Interferent Concentration	Analyte Concentration (U/mL)	Bias (%)
Dipotassium EDTA	5.4 mg/mL	20.46	1.8
		318.39	3.7

11.4 Clinical Studies

Not applicable.

11.5 Clinical Cut-off

Not applicable.

12. Conclusion

The ADVIA Centaur BR assay with the addition of the plasma (EDTA) sample and detection capability (LoB, LoD, LoQ) claims in the Instructions for Use (package insert) is substantially equivalent to the currently marketed ADVIA Centaur BR assay (K982680).