April 6, 2020

Siemens Healthcare Diagnostics, Inc.
Fatima Pacheco
Regulatory Clinical Affairs Specialist
511 Benedict Ave.
Tarrytown, New York 10591

Re: K200199
Trade/Device Name: ADVIA Centaur CA 125 II Assay
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-Associated Antigen Immunological Test System
Regulatory Class: Class II
Product Code: LTK
Dated: January 24, 2020
Received: January 27, 2020

Dear Fatima Pacheco:

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
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)*
K200199

Device Name
ADVIA Centaur® CA 125II

Indications for Use *(Describe)*
For in vitro diagnostic use in the quantitative, serial determination of CA 125 in human serum and plasma (EDTA and lithium heparin) and to aid in the management of patients with ovarian carcinoma using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. The test is intended for use as an aid in monitoring patients previously treated for ovarian cancer. Serial testing for CA 125 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 ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the ADVIA Centaur CA 125II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or 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 for

ADVIA Centaur® CA 125II

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.

A. 510(k) Number: K200199

B. Purpose for Submission:
Modified Device – addition of plasma sample type

C. Applicant:

Contact: Fatima Pacheco
Regulatory Clinical Affairs Specialist
Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Ave,
Tarrytown, NY 10591
Phone: (914) 374-3770
Email: fatima.pacheco@siemens-healthineers.com

Date: April 03, 2020

D. Proprietary and Established Names:
ADVIA Centaur® CA 125II

E. Measurand
Cancer Antigen 125 (CA 125)

F. Regulatory Information:

Trade Name	ADVIA Centaur® CA 125II
Common Name	Chemiluminescence Immunoassay, for the determination of CA 125 antigen
Classification Name	Device to test, epithelial ovarian tumor-associated antigen (ca125).
FDA Classification	Class II
Review Panel	Immunology (82)
Product Code	LTK
Regulation Number	21 CFR 866.6010

G. Predicate Devices:
Device Name: Bayer ADVIA Centaur CA 125II
510(k) Number: k020828

H. Intended Use:

Same as Indications for Use

I. Indications for Use:

For *in vitro* diagnostic use in the quantitative, serial determination of CA 125 in human serum and plasma (EDTA and lithium heparin) and to aid in the management of patients with ovarian carcinoma using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. The test is intended for use as an aid in monitoring patients previously treated for ovarian cancer. Serial testing for CA 125 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 ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the ADVIA Centaur CA 125II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or for use on any other system.

J. Special Conditions for use statement(s):

For Prescription Use Only

K. Special Instrument Requirement:

For use on the ADVIA Centaur® XP and ADVIA Centaur XPT

L. Device Description:

The ADVIA Centaur CA 125II assay is comprised of the following reagents:

Component	Volume	Ingredients
CA 125II Lite Reagent	10.0 mL/pack	monoclonal mouse anti-M11 antibody (~0.15 µg/mL) labeled with acridinium ester and monoclonal mouse anti-OC 125 (~1.0 µg/mL) labeled with fluorescein in phosphate buffer with bovine serum albumin and preservatives
CA 125II Solid Phase Reagent	25.0 mL/pack	monoclonal mouse anti-fluorescein antibody (~30 µg/mL) coupled to paramagnetic particles in phosphate buffer with bovine serum albumin and preservatives

M. Substantial Equivalence Information

The following table demonstrates substantial equivalence between the ADVIA Centaur 125II assay (Candidate Device) with modified Package Insert (Instructions for Use) with the addition of plasma sample type (EDTA & Lithium Heparin) and the currently marketed ADVIA Centaur CA 125II (Predicate Device) that was cleared under 510 (k) k020828.

Trade Name	Candidate Device – Modified Labeling	Predicate Device – Current Labeling
	ADVIA Centaur® CA 125II	ADVIA Centaur® CA 125II
Intended Use	For *in vitro* diagnostic use in the quantitative, serial determination of CA 125 in human serum and plasma (EDTA and lithium heparin) and to aid in the management of patients with ovarian carcinoma using the ADVIA Centaur® XP, and ADVIA Centaur® XPT systems. The test is intended for use as an aid in monitoring patients previously treated for ovarian cancer. Serial testing for CA 125 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 ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the ADVIA Centaur CA 125II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or for use on any other system.	For *in vitro* diagnostic use in the quantitative, serial determination of CA 125 in human serum and to aid in the management of patients with ovarian carcinoma 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 ovarian cancer. Serial testing for CA 125 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 ovarian cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. It is recommended that the ADVIA Centaur CA 125II assay be used under the order of a physician trained and experienced in the management of gynecological cancers. This assay is not intended for screening or diagnosis of ovarian cancer or for use on any other system.
Analyte	Cancer Antigen 125 (CA 125)	Same
Automated	Automated assay	Same
Measurement	Quantitative	Same
Sample Type	Human Serum and Plasma (EDTA and Lithium Heparin)	Human Serum
Detection Limit	LoB: 2.0 U/mL	Analytical Sensitivity: 2 U/mL
	LoD: 3.0 U/mL	Not Applicable
	LoQ: 3.0 U/mL	Not Applicable
Assay Measuring Interval	3.0 – 600 U/mL	2 – 600 U/mL

Trade Name	Candidate Device – Modified Labeling	Predicate Device – Current Labeling
	ADVIA Centaur® CA 125II	ADVIA Centaur® CA 125II
Operating Principle	Sandwich	Sandwich
Technology	Direct Chemiluminescent	Same
Instrument	ADVIA Centaur Systems	Same
Sample Volume	50 µL	50 µL
Calibrators	ADVIA Centaur CA 125II Calibrator	Same
Controls	Commercial Controls	Same
Detection Antibody	monoclonal mouse anti-M11 antibody (~0.15 µg/mL) labeled with acridinium ester and monoclonal mouse anti-OC 125 (~1.0 µg/mL) labeled with fluorescein	Same
Capture Antibody	monoclonal mouse anti-fluorescein antibody (~30 µg/mL) coupled to paramagnetic particles	Same

N. Test Principle

The ADVIA Centaur CA 125II assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses two monoclonal mouse antibodies specific for CA 125. The first antibody is directed toward the M11 antigenic domain, and is labeled with acridinium ester. The second antibody is directed toward the OC 125 antigenic domain and is labeled with fluorescein. The immunocomplex formed with CA 125 is captured with monoclonal mouse anti-fluorescein antibody coupled to paramagnetic particles in the Solid Phase.

A direct relationship exists between the amount of CA 125 present in the patient sample and the amount of relative light units (RLUs) detected by the system.

O. Performance Characteristics

The assay principle, design and reagent formulation has not changed from the original device, therefore, the analytical performance studies and data previously reviewed under 510(K) k020828 continues to apply to this assay.

I. Detection Limit

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

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

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

The LoD corresponds to the lowest concentration of CA 125 that can be detected with a probability of 95%.

The LoQ corresponds to the lowest amount of CA 125 in a sample at which the within-laboratory CV is ≤ 20%.

II. Method Comparison

For 224 samples in the range of 3.1 to 466.6 U/mL, the relationship of the ADVIA Centaur CA 125II assay to the Bayer Immuno 1® CA 125II assay is described by the following equation:

ADVIA Centaur CA 125II = 1.025 (Bayer Immuno 1) + 1.15 U/mL

Correlation coefficient (r) = 0.992

III. Specimen Equivalence

The study was performed in accordance with CLSI Document EP09-A3 to demonstrate that EDTA and Li-heparin plasma matrices yield comparable results as serum with the ADVIA Centaur CA 125 II assay. A Deming linear regression analysis was performed, and the corresponding slopes of regression and coefficient determination are summarized in the following table:

Sample Type	N	Sample Interval	Slope (95% CI)	Intercept (95% CI)	Correlation coefficient
Dipotassium EDTA plasma (y) vs. Serum (x)	162	3.0 – 572.7 U/mL	0.95 (0.92 – 0.98)	- 0.4 U/mL (-1.5 – 0.7 U/mL)	1.00
Lithium Heparin plasma (y) vs. Serum (x)	119	3.1 – 572.7 U/mL	1.03 (0.97 – 1.08)	- 0.2 U/mL (-1.8 – 1.4 U/mL)	1.00

IV. Interferences: EDTA and Heparin

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	9.0 mg/mL	39.6	3.7
		526.5	1.3
Heparin	75 U/mL	42.4	3.2
		471.4	-0.9

P. Proposed Labeling

The labeling supports the finding of substantial equivalence for this device.

Q. Conclusion

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.