November 25, 2019

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

Re: K192788
Trade/Device Name: ADVIA Centaur Cortisol (COR)
Regulation Number: 21 CFR 862.1205
Regulation Name: Cortisol (Hydrocortisone and Hydroxycorticosterone) Test System
Regulatory Class: Class II
Product Code: JFT
Dated: September 26, 2019
Received: September 30, 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,

Marianela Perez-Torres, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology 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)*
K192788

Device Name
ADVIA Centaur Cortisol (COR)

Indications for Use *(Describe)*
For in vitro diagnostic use in the quantitative determination of cortisol in serum, plasma (EDTA and lithium heparin), and urine using the ADVIA Centaur® XP system.

Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.

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: K192788

1. Date Prepared

September 26, 2019

2. Applicant Information

Contact: Ian Thompson
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3. Regulatory Information

Table 1. Regulatory Information for ADVIA Centaur® Cortisol (COR)

Trade Name	ADVIA Centaur® Cortisol (COR)
Device	Fluorometric, Cortisol
Regulation Description	Cortisol (hydrocortisone and hydroxycorticosterone) test system
FDA Classification	Class II
Review Panel	Clinical Chemistry (75)
Product Code	JFT
Regulation Number	21 CFR 862.1205

4. Predicate Device Information

Predicate Device Name: ADVIA Centaur® Cortisol (COR)

510(k) Number: K142723

The ADVIA Centaur Cortisol (COR) assay with the plasma (EDTA and lithium heparin) sample claim is substantially equivalent to the ADVIA Centaur Cortisol (COR) assay that was cleared under 510(k) K142723, as shown below in the Substantial Equivalence Information section.

5. Intended Use / Indications for Use

For in vitro diagnostic use in the quantitative determination of cortisol in serum, plasma (EDTA and lithium heparin), and urine using the ADVIA Centaur® XP system.

Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.

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

6. Device Description

The ADVIA Centaur Cortisol (COR) assay is a 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 Cortisol (COR) assay is intended for use on the ADVIA Centaur family of analyzers. The ADVIA Centaur Calibrator E 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 COR reagent kit contains the following:

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

Materials Required but Not provided

- ADVIA Centaur Calibrator E: consists of 2 levels (low and high) of multi-analyte calibrators; lyophilized human plasma spiked with analytes (cortisol, progesterone, and testosterone), sodium azide (0.1%) and preservatives.

Optional Reagents

- ADVIA Centaur Multi-Diluent 3 is a human plasma solution with sodium azide (0.1%)
- ADVIA Centaur COR Master Curve Material is a set of 7 levels of cortisol (MCM1-7) spiked in lyophilized human plasma and sodium azide (0.1%).
- Cortisol Urine Reconstitution Buffer is a protein buffer solution with sodium azide (0.1%).

7. Purpose of the Submission

The purpose of this submission is for the addition of plasma (EDTA and lithium heparin) sample claim for the ADVIA Centaur Cortisol (COR) assay.

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

The following table demonstrates substantial equivalence between the ADVIA Centaur Cortisol (COR) assay (Candidate Device) that has modified Instructions for Use (Package Inserts) with the addition of the plasma (EDTA and lithium) sample claim and the currently marketed ADVIA Centaur Cortisol (COR) assay (Predicate Device) that was cleared under 510(k) K142723.

Trade Name	**Candidate Device**	**Predicate Device**
	ADVIA Centaur Cortisol (COR) (Addition of Plasma Claim)	**ADVIA Centaur Cortisol (COR) (Unmodified Labeling)**
Intended Use	For in vitro diagnostic use in the quantitative determination of cortisol in serum, plasma (EDTA and lithium heparin), and urine using the ADVIA Centaur® XP system.	For in vitro diagnostic use in the quantitative determination of cortisol in serum or urine using the ADVIA Centaur® XP system.
Indications for Use	Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.	Same
Measurement	Quantitative	Same
Assay Range	Serum and Plasma: 0.50–75 µg/dL Urine: 0.50–53 µg/dL	Serum: 0.50–75 µg/dL Urine: 0.50–53 µg/dL
Operating Principle	Competitive immunoassay	Same
Technology	Direct chemiluminescent	Same

Sample Type	Serum, Plasma (EDTA and lithium heparin), Urine	Serum, Urine
Sample Volume	20 µL (serum and plasma)	20 µL (serum)
Traceability/ Standardization	Internal Standards traceable to GCMS	Same
Calibration	2-point	Same
Calibrator/Levels	Calibrator E/2 levels	Same
Controls/Levels	Commercial Controls/3 levels	Same
Master Curve Materials	Seven levels (MCM1–7)	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:

- Method 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).

10. Test Principle

The ADVIA Centaur Cortisol (COR) assay is a competitive immunoassay using direct chemiluminescent technology. Cortisol in the patient sample competes with acridinium ester labeled cortisol in the Lite Reagent for binding to polyclonal rabbit anti-cortisol antibody in the Solid Phase. The polyclonal rabbit anti-cortisol antibody is bound to monoclonal mouse anti-rabbit antibody, which is covalently coupled to paramagnetic particles in the Solid Phase.

11. Performance Characteristics

The inclusion of the plasma (EDTA plasma and lithium heparin) sample claim in the Instructions for Use (Package Inserts) for the ADVIA Centaur Cortisol (COR) assay was demonstrated by testing the performance characteristics with the following studies:

- Specimen Equivalence by Method Comparison
- Interferences: EDTA and Heparin

The plasma (EDTA plasma and lithium heparin) sample claim for the ADVIA Centaur Cortisol (COR) assay does not require the collection of additional analytical performance data. Therefore, all analytical performance data previously reviewed for the ADVIA Centaur Cortisol (COR) assay continues to apply to this assay, because the assay was not modified. These performance data are cross-referenced to the 510(k) submission for the plasma claim for the ADVIA Centaur Cortisol assay (K142723).

Specifically, the following studies are not needed for the purpose of this submission:

- Detection Capability (LoB, LoD, LoQ)
- Linearity/Assay Range
- Precision
- Dilution Recovery
- Method Comparison with Predicate Device
- Expected Values (Reference Intervals)
- Calibrator/Assay Traceability

- Reagent On-Board Stability and Calibration Interval
- Cross reactivity
- Interfering substances
- Shelf Life Stability

11.1 Specimen Equivalence by Method Comparison

Specimen equivalency was determined with the Deming linear regression model in accordance with CLSI Document EP09-A3 for testing completed using the ADVIA Centaur Cortisol (COR) assay.

Comparison	N*	Sample Interval	Slope	Intercept	Correlation Coefficient (r)
Dipotassium EDTA Plasma vs. Serum	83	0.29-67.06 µg/dL	0.95	0.24 µg/dL	1.00
Lithium-Heparin Plasma vs. Serum	99	0.29-67.06 µg/dL	0.96	0.56 µg/dL	1.00

* N = Number of samples tested.

11.2 Interferences: EDTA and Heparin

Interference testing for EDTA and heparin was performed in accordance with CLSI guideline EP07-ed3 using the ADVIA Centaur Cortisol (COR) assay. The following results were obtained:

Interferent	Interferent Concentration	Analyte Concentration (µg/dL)	Bias (%)
Dipotassium EDTA	9.0 mg/mL	12.94	0.5
		50.39	-1.1
Heparin	75 U/mL	7.85	2.9
		46.50	-0.1

11.3 Clinical Studies

Not applicable.

11.4 Clinical Cut-off

Not applicable.

12. Conclusions

The ADVIA Centaur Cortisol (COR) assay with the addition of the plasma (EDTA plasma and lithium heparin) sample claim in the Instructions for Use (package insert) is substantially equivalent to the currently marketed ADVIA Centaur Cortisol (COR) assay (K142723).