July 13, 2021

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

Re: K200210
Trade/Device Name: ADVIA Centaur® Total hCG assay
Regulation Number: 21 CFR 862.1155
Regulation Name: Human Chorionic Gonadotropin (HCG) Test System
Regulatory Class: Class II
Product Code: DHA
Dated: October 16, 2020
Received: October 20, 2020

Dear Mey Vasquez:

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.
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)*
K200210

Device Name
ADVIA Centaur® Total hCG assay

Indications for Use *(Describe)*
For in vitro diagnostic use in the quantitative determination of human chorionic gonadotropin (hCG) in serum or plasma (EDTA or lithium heparin) using the ADVIA Centaur® XP system.

Human chorionic gonadotropin measurements are intended for use as an aid in the early detection of pregnancy.

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 of Safety and Effectiveness

Introduction: According to the requirements of SMDA 1990 and 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: _____K200210_____

1. APPLICANT

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue,
Tarrytown, NY 10591 USA

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Regulatory Clinical Affairs Specialist
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Date Prepared: October 16, 2020

2. Regulatory Information

Assay

Trade Name	ADVIA Centaur® Total hCG assay
Device	system, test, human chorionic gonadotropin
Regulation Description	Human chorionic gonadotropin (HCG) test system
FDA Classification	Class II
Review Panel	Clinical Chemistry
Product Code	DHA
Regulation Number	21 CFR 862.1155

3. PREDICATE DEVICE

Assay

Name of Device: Atellica IM Total hCG (ThCG)

510 (k): K172322

4. DEVICE DESCRIPTION

The ADVIA Centaur® Total hCG assay reagents come in the following configurations:

Contents	Number of Tests
5 ReadyPack primary reagent packs containing ADVIA Centaur Total hCG Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP Total hCG Master Curve card	250
1 ReadyPack primary reagent pack containing ADVIA Centaur Total hCG Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP Total hCG Master Curve card	50

The ReadyPack consists of the following:

ADVIA Centaur ThCG ReadyPack® primary reagent pack; Lite Reagent
5.0 mL/reagent pack polyclonal goat anti-hCG antibody (~0.1 µg/mL) labeled with acridinium ester in buffered saline with sodium azide (0.1%) and preservatives

ADVIA Centaur ThCG ReadyPack primary reagent pack; Solid Phase Reagent
22.5 mL/reagent pack monoclonal mouse anti-hCG antibody (~0.02 mg/mL) covalently coupled to paramagnetic particles in buffered saline with sodium azide (0.1%) and preservatives

ADVIA Centaur ThCG ReadyPack ancillary reagent pack; ThCG Diluent
25.0 mL/reagent pack buffered heat-treated equine serum with EDTA, sodium azide (< 0.1%), and preservatives

ADVIA Centaur ThCG Diluent
50.0 mL/vial buffered heat-treated equine serum with EDTA, sodium azide (< 0.1%), and preservatives

5. INDICATIONS FOR USE

For *in vitro* diagnostic use in the quantitative determination of human chorionic gonadotropin (hCG) in serum or plasma (EDTA or lithium heparin) using the ADVIA Centaur® XP system.

Human chorionic gonadotropin measurements are intended for use as an aid in the early detection of pregnancy.

6. INTENDED USE

Same as Indications for Use

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® Total hCG assay.

8. COMPARISION OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The following table demonstrates substantial equivalence between the ADVIA Centaur® Total hCG 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 Atellica IM® Total hCG (ThCG) (Predicate Device) that was cleared under 510(k) K172322.

Table 1: *Substantial Equivalence Comparison*

Assay		
Item	**Predicate Device**	**Candidate Device**
	Atellica IM® Total hCG (ThCG)	ADVIA Centaur® Total hCG assay
Intended Use	The Atellica® IM Total hCG (ThCG) assay is for *in vitro* diagnostic use in the quantitative determination of human chorionic gonadotropin (hCG) in human serum or plasma (EDTA or lithium heparin) using the Atellica® IM Analyzer. The Atellica IM ThCG assay is intended for use as an aid in the early detection of pregnancy.	For in vitro diagnostic use in the quantitative determination of human chorionic gonadotropin (hCG) in serum or plasma (EDTA or lithium heparin) using the ADVIA Centaur® XP systems. Human chorionic gonadotropin measurements are intended for use as an aid in the early detection of pregnancy.
Measurement	Quantitative	Same
Assay Range	2.6–1000 mIU/mL (IU/L)	4.0-1000 mIU/mL (IU/L)
Assay Principle	2-site Sandwich immunoassay	Same
Technology	Direct chemiluminescent	Same
Sample Type	Serum, EDTA Plasma, lithium heparin plasma	Serum or plasma (EDTA or lithium heparin)
Sample Volume	25 µL	50 µL
Reagent Volume	50 µL of Lite Reagent and 255 µL of Solid Phase	100 µL of Lite Reagent and 450 µL of Solid Phase
Incubation Time	8 minutes at 37°C.	7.5 minutes at 37°C.
Standardization	The Atellica IM ThCG assay standardization is traceable to the World Health Organization (WHO) 4th IS 75/589 reference material. Assigned values for calibrators are traceable to this standardization.	The ADVIA Centaur Total hCG assay is traceable to the World Health Organization (WHO) 5th IS 7/364 reference material.
Calibration	2-point	2-point

9. PERFORMANCE CHARACTERISTICS DATA

Detection Capability

Detection Capabilities	Package Insert Claims (mIU/mL)
LOQ	4.0
LOD	3.0
LOB	2.0

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 are representative of the performance of the assay:

			Repeatability		Between-Run		Between-Day		Within-Lab	
Sample Type	N	Mean mIU/mL (IU/L)	SD mIU/mL (IU/L)	CV (%)	SD mIU/mL (IU/L)	CV (%)	SD mIU/mL (IU/L)	CV (%)	SD mIU/mL (IU/L)	CV (%)
Serum A	320	6.63	0.29	4.4%	0.09	1.3%	0.24	3.6%	0.39	5.8%
Serum B	320	15.85	0.53	3.3%	0.45	2.8%	0.31	2.0%	0.76	4.8%
Serum C	320	819.28	20.25	2.5%	22.47	2.7%	12.09	1.5%	32.58	4.0%
Control 1	320	7.43	0.30	4.1%	0.15	2.0%	0.32	4.3%	0.46	6.2%
Control 2	320	24.64	0.61	2.5%	0.14	0.6%	0.58	2.3%	0.85	3.5%
Control 3	320	164.66	2.96	1.8%	0.79	0.5%	2.71	1.6%	4.09	2.5%

Method Comparison

Method comparison studies were conducted according to CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition. The following results were obtained:

For 117 samples in the range of 7.6 to 977.6 mIU/mL (IU/L), the relationship between the ADVIA Centaur Total hCG assay and the Atellica IM ThCG assay is described by the equation:

ADVIA Centaur Total hCG = 0.96 (Atellica IM ThCG assay) - 3.0 mIU/mL

Correlation coefficient (r) = 0.997

Specimen Equivalence

Serum/plasma (K2 EDTA and lithium heparin) sample equivalence was evaluated by method comparison studies of matched-sample sets. The studies were conducted in accordance to CLSI EP09-A3: *Method Comparison and Bias Estimation using Patient Samples*. The following results were obtained:

Tube (y) vs. Serum (x)	N[a]	Sample Interval	Slope	Intercept	r[b]
Dipotassium EDTA plasma	53	4.7 – 948.9 mIU/mL (IU/L)	0.99	0.3	1.00
Lithium heparin plasma	51	4.7 – 975.7 mIU/mL (IU/L)	1.01	- 0.3	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

The assay is designed to have a slope of 0.90–1.10 for alternate tube types versus serum.

Agreement of the specimen types may vary depending on the study design and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Linearity

Linearity of the ADVIA Centaur Total hCG assay was performed in accordance to *CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. The following results were obtained:*

The linearity study included samples spanning the entire assay range. Results met acceptance criteria. Therefore, the results from the linearity study support an analytical measuring range from 4.0 mIU/mL to 1000 mIU/mL.

Dilution Recovery

The dilution recovery study was carried out following the dilution ratios: 1:2, 1:4, 1:8 and 1:16. The following results were obtained:

Dilution	Observed mIU/mL (IU/L)	Expected mIU/mL (IU/L)	% Recovery
1:2	609.5	672.4	91%
	794.8	877.1	91%
	893.3	966.9	92%
Mean			91%
1:4	315.5	336.2	94%
	430.9	438.6	98%
	487.5	483.5	101%
	520.3	533.5	98%
	581.1	611.5	95%
	961.8	932.2	103%
Mean			98%
1:8	156.8	168.1	93%
	213.4	219.3	97%
	235.2	241.7	97%
	259.7	266.8	97%
	295.7	305.8	97%
	486.5	466.1	104%
	836.6	1010.8	83%
Mean			95%
1:16	87.9	84.1	105%
	109.8	109.6	100%

Dilution	Observed mIU/mL (IU/L)	Expected mIU/mL (IU/L)	% Recovery
	120.1	120.9	99%
	129.1	133.4	97%
	149.6	152.9	98%
	258.3	233.0	111%
	454.1	505.4	90%
	985.3	896.4	110%
Mean			101%

Interferences

Interference testing was conducted in accordance with *CLSI EP07:Ed3: Interference Testing in Clinical Chemistry; Approved Guideline —Third Edition*. This study was carried out used the paired-difference approach.

Substance	Substance Test Concentration	Analyte Concentration mIU/mL (IU/L)	% Bias
Human Serum Albumin	6 g/dL	7.0	-0.3%
		494.4	-0.2%
Acetaminophen	20 mg/dL	7.3	2.7%
		498.5	-0.5%
Acetylsalicylic acid	65 mg/dL	7.5	2.7%
		500.4	0.4%
Heparin	7200 IU/dL	7.3	-8.2%
		502.7	1.6%
Ibuprofen	50 mg/dL	7.3	-1.4%
		502.8	0.3%
EDTA	3.4 µmol/L	7.4	4.1%
		473.4	1.8%
Ethanol	600 mg /dL	7.3	2.7%
		500.0	-1.1%
Atropine	20 mg/dL	6.6	0.0%

Substance	Substance Test Concentration	Analyte Concentration mIU/mL (IU/L)	% Bias
		499.0	-1.5%
Caffeine	556 um/L	6.6	6.1%
		485.2	1.1%
Gentisic acid	117 µmol/L	7.0	4.3%
		500.3	-1.1%

Hemolysis, Icterus, and Lipemia (HIL)

Substance	Substance Test Concentration	Analyte Concentration mIU/mL (IU/L)	% Bias
Bilirubin (Conjugated)	40 mg/dL	5.9	3.3%
		508.3	-1.0%
Bilirubin (Unconjugated)	40 mg/dL	6.4	-0.8%
		489.5	1.7%
Hemoglobin	1000 mg/dL	6.4	1.3%
		478.4	-0.5%
Intralipid	3000 mg/dL	6.5	-3.7%
		442.9	-3.3%

Expected Values

The reference range study was performed in accordance CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, 3rd Edition. The following results were obtained:

Sample Category	N[a]	Median (mIU/mL) (IU/L)	Reference Interval mIU/mL) (IU/L) 2.5-97.5 Percentile
Non-Pregnant Females (Age: ≤40)	130	0.03	0.03 – 0.6
Postmenopausal Females (Age: ≥41)	150	0.02	0.02 – 2.9

[a] Number of samples.

Standardization:

The ADVIA Centaur Total hCG assay is traceable to the World Health Organization WHO 5th IS 7/364 reference material.

Cross-Reactivity

Cross-reactant	hCG Value without Cross-reactant (mIU/mL) (IU/L)	hCG Value with Cross-reactant (mIU/mL) (IU/L)
FSH 500mIU/mL	0.5	1.6
	7.7	8.0
	54.9	54.4
	493.1	475.4
TSH 1000uIU/mL	1.3	1.4
	7.6	7.4
	54.2	51.6
	499.9	462.9
LH 500mIU/mL	0.9	1.1
	7.8	7.0
	56.2	47.7
	487.9	428.5
hGH 500 ng/mL	0.8	0.9
	7.3	7.2
	53.0	52.9
	482.3	487.7
PRL 1000 ng/mL	0.8	0.6
	7.9	7.5

Cross-reactant	hCG Value without Cross-reactant (mIU/mL) (IU/L)	hCG Value with Cross-reactant (mIU/mL) (IU/L)
	54.6	54.6
	490.5	494.2

Sample Handling Studies:

The sample handling and stability study show acceptable data to support the labeling claims for serum and plasma samples outlined below.

- Samples can be stored refrigerated (2-8°C) for up to 48 hours.
- Samples can be stored at room temperature (25°C) for up to 8 hours.
- Samples can be kept on-board (30°C) for up to 8 hours.
- Samples can be frozen and thawed up to 1 time.

X. CONCLUSION

Comparative testing of the ADVIA Centaur® Total hCG assay is substantially equivalent in principle and performance to the Predicate Device – Atellica IM ThCG assay cleared under 510(k) K172322.