January 15, 2020

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

Re: K193493
Trade/Device Name: ADVIA Centaur Total IgE (tIgE)
Regulation Number: 21 CFR 866.5510
Regulation Name: Immunoglobulins A, G, M, D, and E immunological test system
Regulatory Class: Class II
Product Code: DGC
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
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)*
K193493

Device Name
ADVIA Centaur® Total IgE (tIgE)

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

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

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: K193493

1. Date Prepared

December 13, 2019

2. Applicant Information

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3. Regulatory Information

Table 1. Regulatory Information for ADVIA Centaur® Total IgE (tIgE)

Trade Name	ADVIA Centaur Total IgE (tIgE)
Device	IgE, Antigen, Antiserum, Control
Regulation Description	Immunoglobulins A, G, M, D, and E immunological test system
FDA Classification	Class II
Review Panel	Immunology
Product Code	DGC
Regulation Number	21 CFR 866.5510

4. Predicate Device Information

Predicate Device Name: ADVIA Centaur® Total IgE (tIgE)

510(k) Number: K920372

The ADVIA Centaur Total IgE (tIgE) assay with the addition of the plasma (EDTA and lithium heparin) sample and new detection capability [Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)] claims in the Instructions for Use (Package Inserts) are substantially equivalent to the ADVIA Centaur Total IgE (tIgE) assay that was cleared under 510(k) K920372, as shown below in the Substantial Equivalence Information section.

5. Intended Use

For in vitro diagnostic use in the quantitative determination of total IgE in serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems.

6. Indications for Use

Same as Intended use.

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

7. Device Description

The ADVIA Centaur Total IgE (tIgE) assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two antibodies to IgE. 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 Total IgE (tIgE) assay is intended for use on the ADVIA Centaur family of analyzers. The ADVIA Centaur Calibrator 80 is a set of 2 level calibrators for the assay. Siemens Healthcare Diagnostics recommends the use of commercially available quality control materials with at least 2 levels (low and high).

The ADVIA Centaur Total IgE (tIgE) reagent kit contains the following:

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

Materials Required but Not provided:

- ADVIA Centaur Calibrator 80: consists of 2 levels (low and high) of human IgE calibrators in equine serum and preservatives; lyophilized.

Optional Reagents:

- ADVIA Centaur IgE Diluent: consists of IgE-free human plasma with sodium azide (0.1%).
- ADVIA Centaur IgE Master Curve Material: consists of MCM 1 that is lyophilized human plasma with sodium azide (0.1% after reconstitution) and preservatives and MCM 2–7 that are various levels of IgE in lyophilized human plasma with sodium azide (0.1% after reconstitution) and preservatives.

8. Purpose of the Submission

The purpose of this submission is for the addition of the plasma (EDTA and lithium heparin) sample claim and updating the detection capability claim for the ADVIA Centaur Total IgE (tIgE) assay.

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

The following table demonstrates substantial equivalence between the ADVIA Centaur Total IgE (tIgE) assay (Candidate Device) that has modified Instructions for Use (Package Inserts) with the addition of plasma (EDTA and lithium heparin) sample and new detection capability (LoB, LoD, and LoQ) claims and the currently marketed ADVIA Centaur Total IgE (tIgE) assay (Predicate Device) that was cleared under 510(k) K920372.

Trade Name	Candidate Device	Predicate Device
	ADVIA Centaur Total IgE (tIgE) (Modified Labeling)	**ADVIA Centaur Total IgE (tIgE) (Unmodified Labeling)**
Intended Use / Indications for Use	For in vitro diagnostic use in the quantitative determination of total IgE in serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems.	For in vitro diagnostic use in the quantitative determination of total IgE in serum using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems.
Measurement	Quantitative	Same
Detection Capability	LoB: 1.5 IU/mL	Analytical Sensitivity: 1.5 IU/mL
	LoD: 2.0 IU/mL	NA*
	LoQ: 2.5 IU/mL	NA
Assay Range	Serum and plasma: 2.5–3000 IU/mL	Serum: 1.5–3000 IU/mL
Operating Principle	two-site sandwich immunoassay	Same
Technology	Direct chemiluminescent	Same
Sample Type	Serum, plasma (EDTA and lithium heparin)	Serum
Sample Volume	30 µL (serum and plasma)	30 µL (serum)
Traceability/ Standardization	World Health Organization (WHO) 75/502	Same
Calibration	2-point	Same
Calibrator/Levels	Calibrator 80/2 levels	Same
Controls/Levels	Commercial Controls/2 levels	Same
Master Curve Materials	Seven levels (MCM1–7)	Same
Detection Antibody	Goat anti-human IgE antibody labeled with acridinium ester	Same
Capture Antibody	Mouse anti-human IgE antibody covalently coupled to paramagnetic particles	Same

* NA = Not applicable.

10. 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:

- 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 (CLSI EP17-A2).

11. Test Principle

The ADVIA Centaur Total IgE (tIgE) assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two antibodies to IgE. The first antibody, in the Lite Reagent, is a goat anti-human IgE antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is a mouse anti-human IgE antibody, which is covalently coupled to paramagnetic particles.

12. Performance Characteristics

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

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

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

12.1 Detection Limit

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

Limit of Blank (LoB) 1.5 IU/mL

Limit of Detection (LoD) 2.0 IU/mL

Limit of Quantitation (LoQ) 2.5 IU/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 total IgE that can be detected with a probability of 95%.

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

12.2 Specimen Equivalence by Method Comparison

Specimen equivalency was determined with the weighted 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	73	2.80 – 2748.84 IU/mL	0.99 (0.975 – 1.012)	0.28 IU/mL (0.086 – 0.475)	1.00
Lithium Heparin vs. Serum	73	2.80 – 2748.84 IU/mL	1.00 (0.989 – 1.020)	0.18 IU/mL (-0.102 – 0.458)	1.00

* N = Number of samples tested.

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

12.3 Interferences: EDTA and Heparin

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

Interferent	Interferent Concentration	Analyte Concentration (IU/mL)	Bias (%)
Dipotassium EDTA	9.0 mg/mL	121.51	-1.7
		1624.13	1.4
Heparin	75 U/mL	167.48	-1.7
		1450.12	-1.1

12.4 Clinical Studies

Not applicable.

12.5 Clinical Cut-off

Not applicable.

13. Conclusion

The ADVIA Centaur Total IgE (tIgE) assay with the addition of the plasma (EDTA and lithium heparin) sample and new detection capability (LoB, LoD, and LoQ) claims in the Instructions for Use (package insert) is substantially equivalent to the currently marketed ADVIA Centaur Total IgE (tIgE) assay (K920372).