510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K193493

B Applicant

Siemens Healthcare Diagnostics Inc.

C Proprietary and Established Names

ADVIA Centaur Total IgE (tIgE)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DGC	Class II	866.5510	IM

II Submission/Device Overview:

A Purpose for Submission:

Modification of a previously cleared device: addition of Li-Heparin and K2-EDTA plasma matrices.

B Measurand:

Total IgE

C Type of Test:

Quantitative, Chemiluminescent

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT

IV Device/System Characteristics:

A Device Description:

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

ADVIA Centaur Total IgE Ready Pack primary reagent pack consist of the ADVIA Centaur tIgE Lite Reagent and Solid Phase Reagents:

- Lite Reagent: 5.0 mL/pack of goat anti-human IgE antibody (~2.4 μg/mL) labeled with acridinium ester in buffer with sodium azide (0.12%), protein stabilizers, and preservatives.
- Solid Phase Reagent: 22.5 mL/pack of mouse anti-human IgE antibody (~0.02 mg/mL) covalently coupled to paramagnetic particles in buffer with protein stabilizers, sodium azide (0.11%), and preservatives.

Materials Required but not provided

- ADVIA Centaur Calibrator 80 consists of low and high levels of human IgE in equine serum and preservatives.

Optional Reagents

- ADVIA Centaur IgE Master Curve Material (MCM) 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.
- ADVIA Centaur IgE Diluent consist of IgE-free human plasma with sodium azide (0.1%).

B Principle of Operation:

The ADVIA Centaur Total IgE (tIgE) assay is a fully automated, two-site sandwich immunoassay using direct chemiluminescent technology. The sample is incubated with both the Lite and Solid Phase Reagents simultaneously for 7.5 minutes at 37°C. After incubation, the immuno-complex is washed, and the Acid Reagent and Base Reagent are added to initiate the chemiluminescent reaction. A direct relationship exists between the amount of total IgE present in the patient sample and the amount of relative light units (RLUs) detected by the system.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Acs Total Ige Immunoassay

B Predicate 510(k) Number(s):

K920372

C Comparison with Predicate(s):

Device & Predicate Device(s):	K193493	K920372
Device Trade Name	ADVIA Centaur Total IgE (tIgE)	Acs Total Ige Immunoassay
General Device Characteristic Similarities		
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.
Operating Principle	Two-site sandwich immunoassay	Same
Assay Technology	Direct chemiluminescent	Same
Measurement	Quantitative	Same
Sample Volume	30 µL	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
Traceability/ Standardization	World Health Organization (WHO) 75/502	Same
Calibration	Two-point	Same
Calibrator/ Levels	ADVIA Centaur Calibrator 80/ two levels	Same

Controls/Levels	Commercial Controls/ two levels	Same
Master Curve Materials (MCM)	Seven levels (MCM1–7)	Same
General Device Characteristic Differences		
Sample Type	Serum, plasma (EDTA and lithium heparin)	Serum
Detection Capability	LoB: 1.5 IU/mL LoD: 2.0 IU/mL LoQ: 2.5 IU/mL	Analytical Sensitivity: 1.5 IU/mL
Assay Range	2.5–3000 IU/mL	1.5–3000 IU/mL

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition

CLSI EP06-A, Evaluation of Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP07, 3rd Edition, Interference Testing in Clinical Chemistry

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   The precision and reproducibility of the assay were demonstrated in K920372.

2. Linearity:

   The linearity of the assay was demonstrated in K920372.

3. Analytical Specificity/Interference:

   The analytical specificity was demonstrated in in K920372.

   Interference was evaluated with hemoglobin, triglycerides and bilirubin in K920372. To evaluate the performance of the ADVIA Centaur Total IgE (tIgE) assay in the presence of K2-EDTA and lithium heparin, one sample at low and one at high level of tIgE for each matrix were used to titrate the EDTA and heparin anticoagulants in order to simulate the effect of partially filled blood collection plasma tube. The nominal K2-EDTA and lithium

heparin concentrations are 1.8 mg/mL and 15.0 U/mL in blood collection tubes, respectively. Both K2-EDTA and lithium heparin were spiked at three times and five times the additive concentration for testing. Testing was performed in six replicates per sample on one ADVIA Centaur XP instrument using one lot of reagent. The recovery was calculated as the difference between the means of the test samples spiked with the interferent and control samples spiked with the same volume of the interferent vehicle. Results summarized in the table below show no significant assay interference was demonstrated with K2-EDTA and lithium heparin at the indicated test concentrations.

Interferent	**Test concentration**	**Low level sample**		**High level sample**	
		Mean (IU/mL)	Recovery (%)	Mean (IU/mL)	Recovery (%)
K2-EDTA	1.8 mg/mL	121.5	100	1624.1	100
	5.4 mg/mL	122.8	101.1	1555.7	95.8
	9.0 mg/mL	119.4	98.3	1646.1	101.4
Lithium heparin	15 U/mL	167.5	100	1450.1	100
	45 U/mL	167.6	100	1542.6	106.4
	75 U/mL	164.7	98.3	1433.7	98.9

4. Assay Reportable Range:

   The claimed measuring range is from 2.5 IU/mL to 3000 IU/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The traceability and reagent stability were established in K920372.

6. Detection Limit:

   The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation for the ADVIA Centaur Total IgE (tIgE) assay were determined in accordance with the CLSI guideline EP17-A2.

   The LoB was determined using two lots of reagents and one ADVIA Centaur XP instrument. For lot 1, four analyte-free serum samples were tested in five replicates per sample, two runs per day for five days to obtain a total of 240 replicates. For lot 2, five analyte-free serum samples were tested in five replicates per sample, two runs per day for five days, to obtain a total of 300 replicates. The LoB was estimated as the 95th percentile of the measurements for each of the lots tested and determined to be 0.69 IU/mL and 0.28 IU/mL for the two lots of reagents. The claimed LoB is 1.5 IU/mL.

   The LoD was determined using 10 patient serum pools with low analyte levels. Each sample was tested in five replicates per run, two runs per day, for six days on one ADVIA Centaur XP instrument using two lots of reagents. A total of 605 replicates was obtained for reagent lot 1 and 557 replicates for reagent lot 2. The LoD was calculated as the LoB + 1.645 x SD of the replicates for the low-level samples and determined as 1.20 IU/mL and 1.21 IU/mL for the two lots of reagents. The claimed LoD is 2.0 IU/mL.

The LoQ was determined using 10 serum samples comprised of patient pools with low analyte levels. Each sample was tested in six replicates per run, two runs per day, for five days on one ADVIA Centaur XP instrument using two lots of reagents. A total of 600 replicates was obtained for reagent lot 1 and 420 replicates for reagent lot 2. The LoQ, defined as the mean value of the sample which fulfills the specification for the total within-laboratory imprecision ≤ 20% CV is 1.64 IU/mL and 1.75 IU/mL for the two lots of reagents. The claimed LoQ is 2.5 IU/mL which is the lower limit of the measuring range claimed for the assay.

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

The method comparison with predicate device was presented in K920372.

2. Matrix Comparison:

To demonstrate that Li-Heparin plasma and K2-EDTA plasma samples yield results comparable with serum samples by the ADVIA Centaur Total IgE (tIgE) assay, a study was performed by using 73 serum/K2-EDTA plasma paired samples and 73 serum/Li-heparin plasma paired samples. Paired samples were each tested in singleton with one reagent lot on one ADVIA Centaur XP system. The Deming regression analysis was performed, and the results are summarized in the following table:

Comparison	Sample Range (IU/mL)	N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
K2-EDTA plasma vs. serum	2.80 – 2748.84	73	0.99 (0.98 – 1.01)	0.28 (0.09 – 0.48)	1.00
Lithium Heparin plasma vs. serum			1.00 (0.99 – 1.02)	0.18 (-0.10 – 0.46)	1.00
N = Number of samples tested					

The data support the addition of K2-EDTA plasma and Li-heparin plasma sample types to the ADVIA Centaur Total IgE (tIgE) assay.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

The expected values were established in K920372.

VIII Proposed Labeling:

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

IX Conclusion:

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