510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K192777

B Applicant

Siemens Healthcare Diagnostics, Inc.

C Proprietary and Established Names

ADVIA Centaur CA 15-3 assay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MOI	Class II	21 CFR 866.6010 - Tumor-Associated Antigen Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

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

B Measurand:

CA 15-3

C Type of Test:

Quantitative, Chemiluminescent

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The ADVIA Centaur CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.

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 device contains the following materials:

- 1 or 5 ReadyPack primary reagent packs for 100 or 500 tests
- ADVIA Centaur CA 15-3 Master Curve card

The ReadyPack for ADVIA Centaur CA 15-3 consists of the following:

- Lite Reagent: 5.0 mL monoclonal mouse anti-DF3 antibody labeled with acridinium ester in buffered saline with bovine serum albumin (BSA), sodium azide (< 0.1%), and preservatives.
- Solid Phase Reagent: 25.0 mL monoclonal mouse capture antibody covalently coupled to paramagnetic particles in buffer with BSA, sodium azide (< 0.1%), and preservatives.
- Conjugate Reagent: 5.0 mL monoclonal mouse anti-115D8 antibody labeled with a thiocarbamate of fluorescein in buffered saline with BSA and preservatives.

B Principle of Operation:

The ADVIA Centaur CA 15-3 assay is a fully automated, two-step sandwich immunoassay using direct chemiluminescent technology. The Lite Reagent is composed of the monoclonal mouse antibody, DF3, specific for CA 15-3, labeled with acridinium ester. The Conjugate Reagent is composed of the monoclonal mouse antibody 115D8, specific for CA15-3, labeled with fluorescein. The Solid Phase is composed of purified monoclonal mouse capture antibody, which is covalently coupled to paramagnetic particles. The sample is incubated with both Conjugate Reagent and Solid Phase simultaneously for 20 minutes. After incubation, the immuno-complex is washed and the Lite Reagent is added, incubated for an additional 20 minutes and then washed again.

V Substantial Equivalence Information:

A Predicate Device Name(s):

CA 15-3 Assay For the Advia Centaur System

B Predicate 510(k) Number(s):

K012357

C Comparison with Predicate(s):

Device & Predicate Device(s):	K192777	K012357
Device Trade Name	ADVIA Centaur CA 15-3	ADVIA Centaur CA 15-3
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The ADVIA Centaur® CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for	The ADVIA Centaur® CA 15-3 assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 15-3 in human serum using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. When used in conjunction with other clinical and diagnostic procedures, serial testing with the ADVIA Centaur CA 15-3 assay is useful for monitoring the course of disease and therapy in metastatic breast cancer patients, and for detection of recurrence in

	detection of recurrence in previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.	previously treated Stage II, with greater than two positive lymph nodes, or Stage III breast cancer patients. This assay is not intended for use on any other system.
Assay Technology	Direct chemiluminescent	Same
Capture Antibody	Monoclonal mouse capture antibody covalently coupled to paramagnetic particles	Same
Detection Antibody	Monoclonal mouse anti-DF3 labeled with acridinium ester	Same
Calibration	2-point	Same
Controls	2 level controls	Same
Traceability	Traceable to an internal standard	Same
General Device Characteristic Differences		
Sample Type	Serum and plasma (Li-Heparin and K2-EDTA)	Serum
Measuring range	3.0 – 200 U/mL	0.5 – 200 U/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, 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 K012357.

2. Linearity:

   The linearity of the assay was demonstrated in K012357.

3. Analytical Specificity/Interference:

   Analytical specificity/interference were demonstrated in K012357

4. Assay Reportable Range:

   The claimed measuring range is from 3.0 U/mL to 200 U/mL.

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

   The traceability and stability were established in K012357.

6. Detection Limit:

   The limit of blank (LoB), limit of detection (LoD), and limit of Quantitation (LoQ) of the ADVIA Centaur CA 15-3 were determined according to the CLSI guideline EP17-A2.

   LoB was determined by testing six analyte free samples in replicates of five per run, two run per day, for six days on one ADVIA Centaur XP system using two lots of reagents. The LoB was estimated as the 95^{th} percentile of 360 measurements for each of the lots tested and determined to be 0.62 U/mL and 0.82 U/mL for the two lots. The claimed LoB is 1.0 U/mL

   LoD was determined using 10 serum samples with low CA15-3 concentrations. Each sample was tested in five replicates per run, two runs per day, for six days on one ADVIA Centaur XP system using two lots of reagents. The LoD was calculated as the LoB + 1.645 x SD of the replicates for the low-level samples and determined as 0.96 mg/L and 1.03 U/mL for the two lots. The claimed LoD is 2.0 U/mL.

   LoQ was determined using a set of 10 serum samples. Each sample was tested in five replicates per run, two runs per day, for six days with two reagent lots on one ADVIA Centaur XP system for a total of 60 data points per sample per reagent lot. The LoQ is defined as the mean value of the sample which fulfills the specification for the total within-laboratory imprecision ≤ 20% CV. The results supports that the claimed LoQ is 3.0 U/mL which is the lower limit of the measuring range claimed for the assay.

7. Assay Cut-Off:

   See K012357

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable

2. Matrix Comparison:

To demonstrate that Li-Heparin plasma and K2-EDTA plasma samples yield results comparable with serum samples by the ADVIA Centaur CA 15-3 assay, a study was performed by using 129 serum/K2-EDTA plasma paired samples and 108 serum/Li-heparin plasma paired samples. Paired samples were each tested in singleton with one reagent lot on one ADVIA Centaur XP system. The Demining regression analysis was performed, and the results are summarized in the following table:

	N	Range (U/mL)	Slope (95% CI)	Intercept (95% CI)	Correlation
Serum vs. K2-EDTA	129	3.43–199.49	0.96 (0.93, 0.99)	0.46 (0.01, 0.91)	1.00
Serum vs. Li-heparin	108	3.13–196.11	1.02 (1.00, 1.05)	-0.72 (-1.44, -0.01)	1.00

The data support the addition of K2-EDTA plasma and Li-heparin plasma sample types to the ADVIA Centaur CA 15-3 assay.

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

   The clinical sensitivity and specificity of the assay was demonstrated in K012357.

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

   Not applicable

D Clinical Cut-Off:

See K012357

E Expected Values/Reference Range:

See K012357

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.