# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY ONLY

## I Background Information:

### A 510(k) Number

K193489

### B Applicant

Siemens Healthcare Diagnostics Inc.

### C Proprietary and Established Names

ADVIA Centaur BR

### 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 previously cleared device: addition of plasma (K2EDTA) sample matrix

### B Measurand:

CA 27.29

### 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:**

The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum and plasma (EDTA) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage III breast cancer. Serial testing for CA 27.29 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment.

**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 systems

## IV Device/System Characteristics:

**A Device Description:**

ADVIA Centaur BR contains the following materials:

- ReadyPack primary reagent pack for 50 or 250 tests

The ReadyPack for ADVIA Centaur BR consists of the following:

- Lite Reagent: 2.5 mL containing monoclonal mouse anti-human CA 27.29 antibody labeled with acridinium ester in buffered saline with preservatives.
- Solid Phase Reagent: 12.5 mL human CA 27.29 covalently coupled to paramagnetic particles in buffer with preservatives.

**B Principle of Operation:**

The ADVIA Centaur BR assay is a fully automated, competitive immunoassay using direct, chemiluminescent technology. The Lite Reagent is composed of a monoclonal mouse antibody specific for CA 27.29, labeled with acridinium ester. The antibody binds to a peptide epitope in the tandem repeat region of the MUC-1 gene product. The Solid Phase is composed of purified CA 27.29, which is covalently coupled to paramagnetic particles. After onboard pretreatment, the sample is incubated with both Lite Reagent and Solid Phase simultaneously for 7.5 minutes. After incubation, the immuno-complex is washed and the Acid Reagent and Base Reagent to initiate the chemiluminescent reaction. An inverse relationship exists between the amount of CA 27.29 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):

Chiron Diagnostics Corporation ACS: Centaur BR Immunoassay

### B Predicate 510(k) Number(s):

K982680

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | New Device<br>K193489 | Predicate<br>K982680 |
|---|---|---|
| Device Trade Name | ADVIA Centaur BR | ADVIA Centaur BR |
| **General Device Characteristic Similarities** | | |
| Intended Use/ Indications For Use | The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum and plasma (EDTA) using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems. The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage III breast cancer. Serial testing for CA 27.29 in the serum and plasma of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. | The ADVIA Centaur® BR assay is an in vitro diagnostic test for the quantitative serial determination of cancer antigen CA 27.29 in human serum using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. The test is intended for use as an aid in monitoring patients previously treated for Stage II or Stage Ill breast cancer. Serial testing for CA 27 .29 in the serum of patients who are clinically free of disease should be used in conjunction with other clinical methods used for the early detection of cancer recurrence. The test is also intended for use as an aid in the management of breast cancer patients with metastatic disease by monitoring the progression or regression of disease in response to treatment. |

| | | |
|---|---|---|
| Assay Technology | Direct chemiluminescent | Same |
| Capture Phase | Human CA 27.29 (~0.72 U/mL) covalently coupled to paramagnetic particles | Same |
| Detection Antibody | Monoclonal mouse anti-CA 27.29 antibody (~1.2 µg/mL) labeled with acridinium ester | Same |
| Calibration | 2-point (Low and High) | Same |
| Controls | 2 levels | Same |
| Traceability | Traceable to an internal standard | Same |
| **General Device Characteristic Differences** | | |
| Sample Type | Serum and K2-EDTA plasma | Serum |
| Measuring range | 9.0–450 U/mL | 3.5–450 U/mL |

## VI Standards/Guidance Documents Referenced:

CLSI EP07, Interference Testing in Clinical Chemistry; Approved Guideline—Third Edition

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition

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 K982680.

2. Linearity:

   The linearity of the assay was demonstrated in K982680.

3. Analytical Specificity/Interference:

   The analytical specificity of the assay was demonstrated in K982680.

   *Endogenous Substance Interference*: Interference was evaluated with conjugated bilirubin, unconjugated bilirubin, triglycerides, hemoglobin and total protein in K982680. To evaluate the performance of the ADVIA Centaur BR assay in the presence of K2-EDTA, testing was

performed in accordance with CLSI EP07 using one at low and one at high BR level to titrate the EDTA anticoagulant. The nominal EDTA concentrations is 1.8 mg/mL in blood collection tubes. EDTA was spiked three times the additive concentration (5.4 mg/mL) for testing in this study. The sample matrix had an aliquot as a 'control sample' (spiked with interferent vehicle) and a 'test sample' (an aliquot spiked with interferent). Testing was performed in six replicates per sample using one ADVIA Centaur BR assay reagent lot on one ADVIA Centaur XP instrument. Doses were calculated using 2-point calibration. The recovery was calculated as the difference between the means of the 'test sample' and 'control sample'. 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 (U/mL) | Recovery (%) | Mean (U/mL) | Recovery (%) |
| K2-EDTA | 1.8 mg/mL | 20.46 | 100.0 | 318.39 | 100.0 |
| | 5.4 mg/mL | 20.83 | 101.8 | 330.19 | 103.7 |

4. Assay Reportable Range:

   The claimed measuring range is from 9.0 to 450 U/mL.

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

   The traceability and stability were demonstrated in K982680.

6. Detection Limit:

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

   LoB was determined by testing four blank samples (various diluent pools with no detectable level of CA 27.29) in five replicates per sample, two runs per day, and five days using two ADVIA Centaur BR reagent lots on one ADVIA Centaur XP instrument. Doses were calculated using two-point calibration stored from first day of testing. The LoB was estimated as the 95th percentile of 200 measurements for each of the lots tested and determined to be 2.14 U/mL and 2.24 U/mL for the two lots. The claimed LoB is 3.5 U/mL.

   LoD was determined using 10 samples (various pools of human serum and diluents) that were tested in five replicates per sample per run, two runs per day for five days using two ADVIA Centaur BR reagent lots on one ADVIA Centaur XP instrument. For reagent lot, LoD was determined as 4.14 U/mL—the dose at which 95% of the measurements would be greater than the LoB. The claimed LoD is 7.0 U/mL.

   LoQ was determined using 10 sample pools (various pools of human serum and diluents) in five replicates per sample, two runs per day, for five days using two ADVIA Centaur BR reagent lots on one ADVIA Centaur XP instrument. The LoQ determined for the two lots was 5.66 U/mL and 5.73 U/mL—which corresponds to the lowest amount of BR in a sample

at which the within-laboratory CV is ≤ 20%. The results support the claimed LoQ of 9.0 U/mL which is the lower limit of the measuring range claimed for the assay.

7. Assay Cut-Off:

   See K982680

## B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable

2. Matrix Comparison:

   To demonstrate that K2-EDTA plasma samples yield results comparable with serum samples by the ADVIA Centaur BR assay, a study was performed by using 101 Dipotassium EDTA plasma/Serum paired samples. The paired samples were tested using four ADVIA Centaur BR assay reagent lots on one ADVIA Centaur XP instrument. Deming regression analysis was performed, and the results are summarized in the following table:

| Comparison | N | Range (U/mL) | Slope (95% CI) | Intercept (95% CI) | Correlation coefficient. |
|---|---|---|---|---|---|
| K2 EDTA Plasma vs Serum | 101 | 10.80–444.42 | 0.97 U/mL (0.955 – 0.993) | 2.21 U/mL (1.376 – 3.040) | 1.00 |

   The data support the addition of K2-EDTA plasma sample types to the ADVIA Centaur BR assay.

## C Clinical Studies:

1. Clinical Sensitivity:

   The clinical sensitivity and specificity of the assay was demonstrated in K982680.

2. Clinical Specificity:

   Not applicable

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

   Not applicable

## D Clinical Cut-Off:

See K982680

**E Expected Values/Reference Range:**

See K982680

**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.