JUL 29 2008

# 510(k) Summary


**Submitter information**
**Contact person:** Philip Liu
Manager, Regulatory Affairs & Compliance

**Address:** Siemens Healthcare Diagnostics Inc.
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**Date summary prepared:** May 1, 2008

**Device Trade or Proprietary Names:** ADVIA® Chemistry CardioPhase High Sensitivity C-Reactive Protein (hsCRP) Assay
ADVIA® Chemistry CardioPhase High Sensitivity C-Reactive Protein (hsCRP) Calibrators

**Device Common/Usual Name or Classification Name:** Cardiac C-Reactive Protein, Antigen, Antiserum, and Control
Calibrators

**Classification Number/Class:** NQD / Class II
JIX / Class II

This 510(k) summary of safety and effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92.

The assigned 510(k) number is: K081294

**Assay Predicate Devices:**

| | **Predicate Device** |
|---|---|
| Device Name | CardioPhase™ High Sensitivity C-Reactive Protein (hsCRP) on the BNII Systems |
| Common name | High Sensitivity C-Reactive Protein (hsCRP) |
| 510(k) Number | K033908 |
| Manufacturer | Siemens Healthcare Diagnostics (formerly Dade Behring, Inc.) |

**Calibrator Predicate Device:**

| | **Predicate Device** |
|---|---|
| Device Name | ADVIA Chemistry wrCRP |
| Common name | C-Reactive Protein Calibrators |
| 510(k) Number | K022682 (Randox Labs, Ltd) |
| Manufacturer | Siemens Healthcare Diagnostics<br>(formerly Siemens Medical Solutions Diagnostics) |

**Device Description:**

The ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma on the ADVIA Chemistry systems. The CardioPhaseTM hsCRP latex reagent is a suspension of uniform polystyrene latex particles coated with anti-CRP antibody. When serum or plasma containing CRP is mixed with the latex reagent, agglutination takes place resulting in an increase in turbidity. This turbidity is measured at 571 nm. The CRP concentration in serum or plasma is determined from a calibration curve that is generated with the calibrators.

The ADVIA® Chemistry CardioPhase™ High Sensitivity C-Reactive Protein Calibrators consist of six (6) levels of protein stabilized matrices containing varying concentrations of recombinant human CRP. The Calibrators have targeted expected values (lot specific) of 0, 0.53, 1.05, 1.58, 5.25, and 10.50 mg/L.

The calibrators (1 mL/vial) are liquid and ready to use. Storage is at 2 - 8°C.

**Statement of Intended Use:**

The ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma (lithium heparin and potassium EDTA) on the ADVIA Chemistry systems. In acute phase response, increased levels of a number of plasma proteins, including CRP, are observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. High sensitivity CRP (hsCRP) measurements may be used as an independent risk marker for the identification of individuals at risk for future cardiovascular disease. Measurement of hsCRP, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndromes.

The ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein Calibrators are for *in vitro* diagnostic use in the calibration of ADVIA Chemistry systems for the CardioPhase High Sensitivity C-Reactive Protein method.

## Comparisons to the Predicate Device:

## Assay Similarities

| | ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein (hsCRP) ***(new device)*** | Siemens Healthcare CardioPhase™ High Sensitivity CRP on the BNII Systems (formerly Dade Behring) ***(predicate device)*** |
|---|---|---|
| Intended Use | For in vitro diagnostic use in the quantitative determination of C-Reactive Protein | For in vitro diagnostic use in the quantitative determination of C-Reactive Protein |
| Specimen Type | Human serum or plasma (lithium heparin, potassium EDTA) | Human serum or plasma (lithium heparin, potassium EDTA) |
| Calibration | Multi-point (6) | Reference curves generated by multi-point calibration |
| Standardization | IRMM Reference Material CRM 470 | IRMM Reference Material CRM 470 |
| Expected Values | Healthy individuals ≤ 3 mg/L<br><br>Risk for cardiovascular disease prediction*:<br>Low < 1 mg/L<br>Average 1 - 3 mg/L<br>High > 3 mg/L | Healthy individuals ≤ 3 mg/L<br><br>Relative risk/average hsCRP:<br>Low <1 mg/L<br>Average 1.0-3.0 mg/L<br>High >3.0 mg/L |

*AHA/CDC Scientific Statement

## Assay Differences

| | ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein (hsCRP) ***(new device)*** | Siemens Healthcare CardioPhase™ High Sensitivity CRP on the BNII Systems (formerly Dade Behring) ***(predicate device)*** |
|---|---|---|
| Assay Principle | Latex-enhanced immuno-turbidimetric assay | Particle enhanced immuno-nephelometry on the BN system |
| Calibrator | ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein Calibrators | N Rheumatology Standard SL<br>N Diluent |
| Reagents | Two liquid reagents, ready to use | Ready to use reagent |
| Analytical Range (mg/L) | 0.16 – 10.0 mg/L | 0.10 – 20 mg/L |

## Calibrator Similarities

| | ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein Calibrators *(new device)* | ADVIA Chemistry Wide Range C-Reactive Protein Calibrators *(predicate device)* |
|---|---|---|
| Intended Use | For *in vitro* diagnostic use in the calibration of ADVIA Chemistry systems for the Cardiophase hsCRP method | For *in vitro* diagnostic use in the calibration of ADVIA Chemistry systems for the wrCRP method |
| Matrix | Liquid, ready to use | Liquid, ready to use |
| Calibrator Levels | 6 | 6 |
| Calibrator Ingredients | Recombinant human CRP in a stabilized protein matrix; contains sodium azide | Recombinant human CRP in a stabilized protein matrix; contains sodium azide |
| Shelf Life | 18 months | 18 months |
| Standardization | CRM-470 | CRM-470 |

## Calibrator Differences

| | ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein Calibrators *(new device)* | ADVIA Chemistry Wide Range C-Reactive Protein Calibrators *(predicate device)* |
|---|---|---|
| Expected Values | Lot specific: **0, 0.53, 1.05, 1.58, 5.25, and 10.50 mg/L** | Lot specific: **0, 2.5, 10, 20, 80, and 160 mg/L** |
| Open Vial (capped) Stability | 60 days stored @2-8°C | 28 days stored @2-8°C |

## Performance:

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, method comparison, interfering substances, serum/plasma equivalency, and analytical range. The following tables summarize the precision (within run), interfering substances, analytical range, and method comparison results.

All of the evaluation studies gave acceptable results compared to the predicate device (this predicate device was used in clinical studies supporting an indication for cardiovascular use). These studies support that the ADVIA Chemistry CardioPhase™ High Sensitivity C-Reactive Protein assay is substantially equivalent to the Siemens Healthcare CardioPhase™ High Sensitivity CRP on the BNII Systems that is currently marketed.

## Imprecision

| ADVIA Chemistry CardioPhase hsCRP | | | Siemens Healthcare (former Dade Behring) CardioPhase hsCRP | |
|---|---|---|---|---|
| ADVIA 1650 | | | BNII | |
| Level (mg/L) | Within run CV (%) | Total CV (%) | Level (mg/L) | Within run CV (%) |
| 0.21 | 3.2% | 4.2% | 0.5 | 2.5% |
| 1.04 | 1.1% | 1.2% | 1.3 | 3.8% |
| 3.12 | 0.8% | 1.3% | 2.1 | 2.1% |
| 10.27 | 1.4% | 1.6% | 14 | 2.6% |
| | | | 24 | 3.9% |

## Correlation

**(y = ADVIA Chemistry CardioPhase hsCRP, x = comparison method/system)**

| Specimen type, System (y) | Comparison System (x) | N | Regression Equation | Sy.x (mg/L) | r | Sample Range (mg/L) |
|---|---|---|---|---|---|---|
| Serum, ADVIA 1650 | former Dade Behring CardioPhase hsCRP on BNII | 167 | Passing Bablok: Y = 1.00x + 0.01 | N/A | N/A | 0.17 – 9.05 |
| Serum, ADVIA 1650 | former Dade Behring CardioPhase hsCRP on BNII | 167 | Least Squares: Y = 1.01x - 0.01 | 0.13 | 0.998 | 0.17 – 9.05 |

## Interfering Substances
**(ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein on ADVIA 1650)**

| Interfering Substance | Interferent Conc. (mg/dL) | CRP conc. (mg/L) | Effect (% change) |
|---|---|---|---|
| Hemoglobin | 500 mg/dL | 0.43 | - 9% |
| Lipids (Intralipid) | 1000 mg/dL | 0.52 | - 7% |
| Bilirubin, free | 30 mg/dL | 0.53 | 4% |
| Bilirubin, conjugated | 30 mg/dL | 0.51 | 0 |
| Rheumatoid Factor | 1040 IU/mL | 3.15 | 8% |

## Analytical Range (Serum/Plasma)

| Platform | ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein |
|---|---|
| ADVIA 1650 | 0.16 to 10 mg/L |

**Conclusions:**

The ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein assay is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Siemens Healthcare Diagnostics (formerly Dade Behring) CardioPhase High Sensitivity CRP on the BNII Systems (this predicate device was used in clinical studies supporting an indication for cardiovascular use).

The ADVIA® Chemistry CardioPhase High Sensitivity C-Reactive Protein Calibrators are substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed ADVIA Chemistry Wide Range C-Reactive Protein Calibrators (k022682).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 29 2008

Siemens Healthcare Diagnostics Inc.
c/o Philip Liu
Manager, Regulatory Affairs & Compliance
511 Benedict Avenue
Tarrytown, NY 10591

Re: k081294
Trade/Device Name: ADVIA® Chemistry CardioPhase High Sensitivity C-Reactive Protein (hsCRP) Assay, ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein Calibrators
Regulation Number: 21CFR Sec.- 866.5270
Regulation Name: C-Reactive Protein Immunological Test System.
Regulatory Class: Class II
Product Code: NQD, JIX
Dated: May 5, 2008
Received: May 7, 2008

Dear Dr. Liu:

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. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); and good manufacturing practice

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

# Indications for Use

510(k) Number (if known):

Device Name(s):

ADVIA CHEMISTRY CardioPhase™ High Sensitivity C-Reactive Protein Assay
ADVIA CHEMISTRY CardioPhase™ High Sensitivity C-Reactive Protein Calibrators

Indications For Use:

The ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma (lithium heparin or potassium EDTA) on the ADVIA Chemistry systems. In acute phase response, increased levels of a number of plasma proteins, including CRP, are observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. High sensitivity CRP (hsCRP) measurements may be used as an independent risk marker for the identification of individuals at risk for future cardiovascular disease. Measurement of hsCRP, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndromes.

The ADVIA Chemistry CardioPhase High Sensitivity C-Reactive Protein Calibrators are for *in vitro* diagnostic use in the calibration of ADVIA Chemistry systems for the CardioPhase High Sensitivity C-Reactive Protein method.

Prescription Use ____X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Carol C Benson

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

K081294