510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K232624

B Applicant

Siemens Healthcare Diagnostic Products GmbH

C Proprietary and Established Names

CardioPhase hsCRP

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DCN, NQD	Class II	21 CFR 866.5270 - C-Reactive Protein Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Extension of the upper limit of the measuring range of the conventional CRP assay range (CRP1) defined in K212559.

B Measurand:

C-reactive protein

C Type of Test:

Quantitative immunonephelometric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

CardioPhase hsCRP is an in-vitro diagnostic reagent for the quantitative determination of C-reactive protein (CRP) in human serum, and heparin and EDTA plasma by means of particle enhanced immunonephelometry using the BN II and BN ProSpec System. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, is 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. Measurements 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only
For in vitro diagnostic use.

D Special Instrument Requirements:

BN II System and BN ProSpec

IV Device/System Characteristics:

A Device Description:

CardioPhase hsCRP reagent is ready-to-use and consists of a suspension of polystyrene particles coated with mouse monoclonal antibodies (< 0.016 g/L) specific to human CRP and preservatives.

Kit Contents:

- 5 x 5 mL CardioPhase hsCRP Reagent
  -or-
- 3 x 2 mL CardioPhase hsCRP Reagent

Materials required but not provided:

- N Rheumatology Standard SL
- N/T Rheumatology Controls SL/1 and SL/2 and/or Apolipoprotein Control Serum CHD
- N Supplementary Reagent/Precipitation
- N Diluent
- BN II Evaporation Stoppers (optional)
- Additional materials and supplies as described in the BN System Instruction Manual

B Principle of Operation:

Polystyrene particles coated with monoclonal antibodies specific to human CRP are aggregated when mixed with samples containing CRP. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the relevant protein in the sample. The result is evaluated by comparison with a standard of known concentration. Two measuring range settings are available: the conventional CRP1 workflow (3.1 – 200 mg/L) and the high sensitivity CRP2 workflow (0.16 – 10 mg/L).

V Substantial Equivalence Information:

A Predicate Device Name(s):

RCRP Flex reagent cartridge

B Predicate 510(k) Number(s):

K221119

C Comparison with Predicate(s):

Device & Predicate Device(s):	K232624 (Candidate Device)	K221119 (Predicate)
Device Trade Name	CardioPhase hsCRP	RCRP Flex reagent cartridge
General Device Characteristic Similarities		
Intended Use/ Indications For Use	CardioPhase hsCRP is an in-vitro diagnostic reagent for the quantitative determination of C-reactive protein (CRP) in human serum, and heparin and EDTA plasma by means of particle enhanced immunonephelometry using the BN II and BN ProSpec System. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, is 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	The C-Reactive Protein Extended Range (RCRP) method used on the Dimension clinical chemistry system is an in vitro diagnostic test intended for the quantitative determination of CRP in human serum and plasma (lithium heparin). Measurement of C-Reactive Protein is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases.

Device & Predicate Device(s):	K232624 (Candidate Device)	K221119 (Predicate)
	risk for future cardiovascular disease. Measurements 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.	
Traceability	ERM-DA474/IFCC	Same
General Device Characteristic Differences		
Test Principle	Particle-enhanced Immunonephelometry read at 840 nm	Particle-enhanced Immunoturbidometry read at 340 nm
Analytical Measuring Range	3.1 – 200 mg/L (workflow CRP1) 0.16 – 10 mg/L (workflow CRP2)	5.0 – 250.0 mg/L
Calibrators	One level diluted to seven levels	Five individual levels
Sample Matrices	Serum, lithium heparin plasma, and EDTA heparin plasma	Serum, lithium heparin plasma

VI Standards/Guidance Documents Referenced:

CLSI EP09c 3rd Edition: Measurement Procedure Comparison and Bias Estimation Using Patient Samples

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Previously established.

2. Linearity:

   Previously determined under K212559. The linear range was found to be 1.48 – 224 mg/L for CRP1, supporting the linearity of the measuring range up to 200 mg/L.

3. Analytical Specificity/Interference:

   Previously established.

4. Assay Reportable Range:

   Previously established.

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

   The assay is traceable to ERM DA474/IFCC.

   Stability was previously established.

6. Detection Limit:

   The detection limits were established in K212559.

7. Assay Cut-Off:

   Not applicable for CRP1

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was performed to evaluate the comparability between the performance of the CRP1 method of the CardioPhase hsCRP on the BN II System and the RCRP Flex assay on the Dimension clinical chemistry system following CLSI EP09c. A cohort of 129 native serum samples was tested on one lot of the predicate and on three lots of the CardioPhase using the CRP1 method. Samples falling outside the measuring range of either assay were removed from the analysis and the results were determined by Passing-Bablok regression analysis. For each lot, the predicted bias at CRP concentrations of 10 mg/L, 100 mg/L, 150, mg/L and 200 mg/L was ≤ ± 6%. The results of each lot are shown below:

	Lot 1	Lot 2	Lot 3
Number of Samples (n)	119	116	113
Sample Range (mg/L)	5.52 – 197.75	5.38 – 199.15	5.50 – 199.50
Slope (95% Confidence Interval)	0.959 (0.941 – 0.982)	0.995 (0.981 – 1.008)	1.032 (1.015 – 1.044)
Intercept (95% Confidence Interval)	0.932 (0.490 – 1.323)	0.584 (0.228 – 0.942)	-0.070 (-0.324 – 0.340)
Pearson Correlation (r)	0.994	0.996	0.994
Coefficient of Determination (r^2)	0.989	0.991	0.989

2. Matrix Comparison:

   Previously established.

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

   Not applicable for the CRP1 method.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Previously established.

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.