510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k093626

B. Purpose for Submission:
Expanded indications for the addition of DVT to previously cleared assays (k040882, k081732, k091916)

C. Measurand:
D-dimer

D. Type of Test:
Quantitative Turbidometry

E. Applicant:
Siemens Healthcare Diagnostics, Inc.

F. Proprietary and Established Names:
INNOVANCE® D-Dimer

G. Regulatory Information:
1. Regulation section:
   21 CFR 864.7320; Fibrinogen/Fibrin Degradation Products Assay
2. Classification:
   II
3. Product code:
   DAP; Fibrinogen/Fibrin Split Products, Antigen, Antiserum and Control
4. Panel:
   Hematology (81)

H. Intended Use:
1. Intended Use(s):
   For the quantitative determination of cross-linked fibrin degradation products (D-dimers) in human plasma on Siemens Healthcare Diagnostics and Sysmex® Coagulation Systems. The INNOVANCE® D-Dimer Assay is intended for use in conjunction with a non-high clinical pretest probability (PTP) assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE).
2. Indication(s) for Use:
   Same as Intended Use
3. Special conditions for use statement(s):
   For prescription use only
4. Special instrument requirements:
   BCS®/BCS® XP Systems

I. Device Description:
INNOVANCE® D-Dimer Reagent- lyophilized polystyrene particles coated with monoclonal antibodies to D-dimer
INNOVANCE® D-Dimer Buffer- liquid saline buffer
INNOVANCE® D-Dimer Supplement- liquid saline buffer with heterophilic blocking reagent
INNOVANCE® D-Dimer Diluent- liquid saline buffer to dilute samples

INNOVANCE® D-Dimer Calibrator- lyophilized, single analyte, human plasma based product containing D-dimer preparation

J. Substantial Equivalence Information:

1. Predicate device name(s):
   VIDAS® D-Dimer Exclusion Assay
   INNOVANCE® D-Dimer
2. Predicate 510(k) number(s):
   k040882
   k081732
3. Comparison with predicate:

Similarities			
Item	Device	Predicate 1 VIDAS® D-Dimer	Predicate 2 INNOVANCE® D- Dimer
Intended Use	For the quantitative determination of cross-linked fibrin degradation products (D-dimers) in human plasma on Siemens Healthcare Diagnostics and Sysmex® Coagulation Systems. The INNOVANCE® D-Dimer Assay is intended for use in conjunction with a non-high clinical pretest probability (PTP) assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE).	Same	Same
Test Reaction	Immunochemical	Same	Same
Reagents	Liquid; no preparation	Same	Same
Antibody	Monoclonal from mouse	Same	Same

Differences			
Item	Device	Predicate 1 VIDAS® D-Dimer	Predicate 2 INNOVANCE® D-Dimer
Technology	Turbidometry	Fluometry	Turbidometry
Assay Cutoff	Reported as 0.50 mg/L FEU	Reported as 500 ng/mL FEU	Reported as 0.50 mg/L FEU

K. Standard/Guidance Document Referenced (if applicable):

CLSI-EP5A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition
CLSI-EP6A2, Evaluation of the Linearity of Quantitative Measurement Procedure: A Statistical Approach; Approved Guideline
CLSI-EP7A2, Interference Testing Clinical Chemistry; Approved Guideline-Second Edition
CLSI-EP9A2, Method Comparison and Bias Estimation Using Patient Samples;

Approved Guideline-Second Edition
CLSI-EP17A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

Polystyrene particles covalently coated with a monoclonal antibody (8D3) are aggregated when mixed with samples containing D-dimer. The D-dimer cross-linkage region has a stereosymmetrical structure, i.e., the epitope for the monoclonal antibody occurs twice, one antibody suffices in order to trigger an aggregation reaction. The reaction is then detected turbidimetrically via an increase in turbidity.

M. Performance Characteristics :

1. Analytical performance: Refer to original 510(k) submission (k081732) for analytical performance data (precision/reproducibility, linearity/assay reportable range, detection limit, analytical specificity, assay cut-off, traceability, stability, expected values (controls, calibrators, or methods).
2. Comparison studies:
   a. Method comparison with predicate device:
      A total of 265 citrated samples were analyzed with the INNOVANCE® D-Dimer assay and the VIDAS® D-Dimer Exclusion assay. The range of D-dimer values in the correlation studies was 0.17 to 4.17 mg/L FEU.

Comparative Method **n = 265**	**Slope**	**Regression Statistics**	
		Intercept (mg/L FEU)	**Correlation Coeff**
VIDAS® D-Dimer Exclusion	1.11	-0.075	0.96

   b. Matrix comparison:
      Not applicable
3. Clinical studies:
   a. Clinical Sensitivity and Specificity:
      The INNOVANCE® D-Dimer assay was evaluated on the BCS ® / BCS® XP System in a multi-center study to validate the exclusion of DVT using fresh specimens collected from 455 consecutive patients presenting to the emergency department with suspected DVT. Of these 455 patients, 29 were excluded for a total of 426 patients available for final analysis.

      All patients were evaluated using the Wells' rules to estimate a likely or unlikely pre-test probability (PTP) of DVT. Patient specimens were tested with the INNOVANCE® D-Dimer assay and results were compared to a cutoff value of 0.50 mg/L (FEU). A D-dimer result <0.50 mg/L (FEU) was considered negative and a D-dimer result ≥0.50 mg/L (FEU) was considered positive.

      Patients with a positive D-dimer result were evaluated by imaging methods, e.g. compression ultrasound and/or venography. Patients with a negative D-dimer, as well as those with negative imaging results, were followed for three months to evaluate potential development of DVT. All patients were subject to imaging at the physician's discretion. The overall prevalence of DVT in

those patients available for final analysis was 21.8 % (93/426). The following instrument-specific sensitivity, specificity and negative predictive value (NPV) with upper and lower 95 % confidence limits (CL) were obtained with the INNOVANCE ® D-Dimer clinical cutoff of 0.50 mg/L (FEU). All studies demonstrated acceptable performance.

All Patients

Instrument	DVT Patients (n)	Cutoff mg/L FEU	Sensitivity (CL) %	Specificity (CL) %	NPV (CL) %
BCS®/BCS®XP System	426	0.50	100.0 (96.1 – 100.0)	34.5 (29.4 – 39.9)	100.0 (96.8 – 100.0)

Patients with unlikely pre-test probability

Instrument	DVT Patients (n)	Cutoff mg/L FEU	Sensitivity (CL) %	Specificity (CL) %	NPV (CL) %
BCS®/BCS®XP System	267	0.50	100.0 (83.9 – 100.0)	37.0 (31.0 – 43.4)	100.0 (96.0 – 100.0)

CL = lower and upper 95 % confidence limits

b. Other clinical supportive data:
Not applicable

4. Clinical cut-off**:**
0.50 mg/L FEU
5. Expected values:
Less than 0.59 mg/L for normal healthy subjects

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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