

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

K041438

**B. Purpose for Submission:**

To seek clearance for a modification to their Advanced D-Dimer Assay

**C. Analyte:**

D-Dimer

**D. Type of Test:**

Quantitative turbidimetric immunoassay

**E. Applicant:**

Dade Behring

**F. Proprietary and Established Names:**

Advanced D-Dimer Assay

**G. Regulatory Information:**

1. Regulation section:  
21 CFR 864.7320, Fibrinogen/Fibrin degradation products assay
2. Classification:  
Class II
3. Product Code:  
DAP, Fibrinogen and fibrin split products, antigen, antiserum, control
4. Panel:  
81 Hematology

**H. Intended Use:**

1. Intended use(s):  
Advanced D-Dimer is a latex-enhanced turbidimetric test for the quantitative determination of cross-linked fibrin degradation products containing D-Dimer in human plasma.
2. Indication(s) for use:  
The Advanced D-Dimer is intended for use as an aid in the diagnosis of venous thromboembolism (VTE), deep vein thrombosis (DVT), or pulmonary embolism (PE).
3. Special condition for use statement(s):  
None specified

4. Special instrument Requirements:

The Advanced D-Dimer is intended for use with the Dade Behring coagulation Analyzers, and Sysmex Coagulation Systems.

**I. Device Description:**

Advanced D-Dimer is a latex-enhanced turbidimetric test for the quantitative determination of cross-linked fibrin degradation products containing D-Dimer in human plasma. Elevated concentrations of d-dimer are indicative of the presence of a clot and have been reported in deep vein thrombosis, pulmonary embolism and disseminated intravascular coagulation.

The assay kit consists of Advanced D-Dimer reagent, Advanced D-Dimer accelerator, and Advanced D-Dimer reconstitution medium. Calibration and quality control material must be provided by the user. All steps necessary for preparing the run and performing the measurements are processed automatically by the instrument.

The device is a modification of the Sponsor's currently cleared Advanced D-Dimer (K992957). The Sponsor modified the intended use statement to include use as an aid in the diagnosis of venous thromboembolism and revised the performance section to include a cutoff value

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Dade Behring Advanced D-Dimer
2. Predicate K number(s):  
K992957
3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Principle	<u>Latex-enhanced turbidimetric test</u>	Same
Antibody	Mouse monoclonal	Same
Measuring Range	0.4 to 55 mg/L	Same
Sample Requirement	Citrate plasma	Same
Instrumentation	Dade Behring coagulation Analyzers and Sysmex Coagulation Systems	Same
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended Use	Quantitative determination of cross-linked fibrin degradation products	Quantitative determination of cross-linked fibrin degradation products

	containing D-Dimer in human plasma and as an aid in the diagnosis of VTE.	containing D-Dimer in human plasma.
Instrument specific cut-off	BCS System: 1.6 mg/L Sysmex CA-1500: 1.0 mg/L	none

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

**L. Test Principle:**

Polystyrene particles covalently linked to a monoclonal antibody (DD5) to the cross-linkage region of D-Dimer agglutinate when mixed with samples containing D-Dimer. The stereosymmetrical structure is detected turbidimetrically via the increase in turbidity.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

2 levels of controls and two levels of human plasma were tested following guidelines outlined in NCCLS Guideline EP5-A. Intra-assay precision <3.0%, inter assay precision <4.0%

b. *Linearity/assay reportable range:*

c. *Traceability (controls, calibrators, or method):*

d. *Detection limit:*

e. *Analytical specificity:*

No interference with the Advanced D-dimer assay on the BCS System by:

	<u>Up to</u>
Bilirubin	24 mg/dL
Hemoglobin	100 mg/dL
Lipids	120 mg/dL
Heparin	2.5 IU/mL
Rheumatoid Factor	98 IU/mL

Users should refer to the respective application sheet for additional interference information. Testing for interference from higher levels of lipids or turbid samples can lead to falsely elevated or decreased values. Human Anti-mouse Antibodies (HAMA) testing has not been performed with the Advanced D-Dimer assay. However plasma samples from patients containing heterophilic antibodies and from patients who have received preparation of mouse monoclonal antibodies for diagnosis or therapy may show either falsely elevated or falsely decreased values when tested with assays kits that use

mouse monoclonal antibodies. Dilution of samples may lead to discordant results in certain cases resulting in non-specific reactions (non-specific binding) independent of the concentration of D-Dimer fragment.

*f. Assay cut-off:*

2. Comparison studies:

*a. Method comparison with predicate device:*

*b. Matrix comparison:*

3. Clinical studies:

Frozen samples were collected from out-patients at three sites, and retrospectively evaluated with the Advanced D-Dimer assay on both the BCS System and CA-1500 Analyzer. 322 patients were tested on the BCS system (198 female, 122 male), and 297 on the Sysmex CA-1500 (184 female, 111 male). Patients presenting to the emergency room with clinically suspected VTE were evaluated using the Wells Pre-Test probability models to estimate the probability (high, moderate, or low) of DVT or PE. Patients were diagnosed as DVT or PE positive by standard objective tests as appropriate and patients initially diagnosed as negative were followed for three months.

*a. Clinical sensitivity:*

BCS System	98%
Sysmex CA-1500	100%

*c. Clinical specificity:*

BCS System	38%
Sysmex CA-1500	37%

*c. Other clinical supportive data (when a and b are not applicable):*

4. Clinical cut-off:

The Advanced D-Dimer was tested at one site, on 110 patients using both the BCS System and Sysmex CA-1500 Analyzers (78 females, 32 males, between the ages of 17-89). PE was ruled out for confirmed by ventilation-perfusion (V/Q) lung scan, pulmonary angiography scintigraphy and/or spiral CT. DVT was ruled out or confirmed by compression ultrasonography. Results:

BCS System	1.6
Sysmex CA-1500	1.0

5. Expected values/Reference range:

In a study of 136 health subjects using the BCS system the following data were obtained: Mean 1.20 mg/L, median 1.07 mg/L, 90% interval 0.54-2.09 mg/L.

**N. Conclusion:**

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