

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

K063356

B. Purpose for Submission:

To seek clearance for modifications to:

- Stratus[®] CS Acute Care[™] D-dimer (DDMR) TestPak (Assay)
- Stratus[®] CS Acute Care[™] D-dimer (DDMR) CalPak (Calibrator)
- Stratus[®] CS Acute Care[™] D-dimer (DDMR) DilPak (Diluent)

C. Measurand:

D-Dimer

D. Type of Test:

Solid phase Radial Partition Immunoassay (RPIA)

E. Applicant:

Dade Behring Inc.

F. Proprietary and Established Names:

- Stratus[®] CS Acute Care[™] D-dimer (DDMR) TestPak
- Stratus[®] CS Acute Care[™] D-dimer (DDMR) CalPak
- Stratus[®] CS Acute Care[™] D-dimer (DDMR) DilPak

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7320

2. Classification:

Class II

3. Product code:

DAP

4. Panel:

Hematology

H. Intended Use:

1. Intended use(s):

Method:

The Stratus® CS Acute Care™ D-dimer (DDMR) assay is an *in vitro* diagnostic test for the quantitative measurement of cross-linked fibrin degradation products (D-dimer) in human citrated or heparinized plasma.

Calibrator:

The Stratus® CS Acute Care™ D-dimer (DDMR) Calibrator is an *in vitro* diagnostic product intended to be used for calibration of the Stratus® CS Acute Care™ D-dimer (DDMR) method.

Diluent:

The Stratus® CS Acute Care™ D-dimer (DDMR) Diluent is an *in vitro* diagnostic product intended to be used in conjunction with the Acute Care™ D-dimer TestPak, for the measurement of samples with elevated levels of D-Dimer.

2. Indication(s) for use:

Method:

The Stratus® CS Acute Care™ D-dimer (DDMR) assay is intended for use as an aid in the diagnosis of venous thromboembolism (VTE) [deep vein thrombosis (DVT) or pulmonary embolism (PE)]. This method is for use by trained healthcare professionals in the clinical laboratory and point of care (POC) settings.

Calibrator:

The Stratus® CS Acute Care™ D-dimer (DDMR) Calibrator is an *in vitro* diagnostic product intended to be used for calibration of the Stratus® CS Acute Care™ D-dimer (DDMR) method.

Diluent:

The Stratus® CS Acute Care™ D-dimer (DDMR) Diluent is an *in vitro* diagnostic product intended to be used in conjunction with the Acute Care™ D-dimer assay for the measurement of samples with elevated levels of D-Dimer.

3. Special conditions for use statement(s):

4. Special instrument requirements:

Stratus[®] CS STAT Fluorometric Analyzer

I. Device Description:

The Stratus[®] CS Acute Care™ D-Dimer (DDMR) TestPak is an *in vitro* diagnostic test for the quantitative determination of D-Dimer in human plasma. The principle of assay is based on solid phase Radial Partition Immunoassay (RPIA) technology. Elevated concentrations of D-Dimer are indicative of the presence of a clot and have been reported in DVT, PE, DIC, during pregnancy, use of contraceptives, increased age, and trauma.

The D-dimer TestPak is used in conjunction with Stratus[®] CS Acute Care™ D-dimer (DDMR) CalPak and Stratus[®] CS Acute Care™ D-dimer (DDMR) DilPak to perform the D-dimer assay, calibration, and quality control on the Stratus[®] CS STAT Fluorometric Analyzer.

The Stratus[®] CS Acute Care™ D-dimer method uses whole blood collected in lithium heparin or sodium citrate. Samples are automatically processed by the analyzer via centrifugation. The plasma obtained after centrifugation is used in the analysis. Heparinized or citrated plasma dispensed in a sample cups can also be used by this method. The instrument automatically calculates and prints the concentration of D-dimer in ng/mL [$\mu\text{g/L}$] FEU. The D-dimer assay range is 6-5000 ng/ml [$\mu\text{g/L}$] FEU, samples between 5000 and 17,500 ng/mL [$\mu\text{g/L}$] FEU may be run using a D-dimer DilPak along with a D-dimer TestPak. The instrument will automatically perform a dilution of the sample.

Samples with D-dimer concentration in excess of 17,500 ng/mL [$\mu\text{g/L}$] FEU can be tested after manually diluting the sample with normal saline. Manual dilution is not recommended for healthcare professionals in the Point of Care (POC) setting and the results should be reported as >17,500 ng/ml [$\mu\text{g/L}$] FEU.

J. Substantial Equivalence Information:

1. Predicate device name(s):

- Stratus[®] CS D-dimer TestPak
- Stratus[®] CS D-dimer DilPak
- Stratus[®] CS D-dimer CalPak

2. Predicate 510(k) number(s):

- K051597
- K022976
- K022977

3. Comparison with predicate:

A. Method: Stratus[®] CS Acute Care™ D-dimer TestPak

Predicate: Stratus[®] CS D-dimer TestPak, K022976/K051597

Similarities		
Item	Device	Predicate
Principle	Same	Solid Phase Radial Partition Immunoassay, quantitative measurement of D-Dimer.
Formulation	Same	Dendrimer monoclonal antibody
Sample	Same	Citrated or Heparinized Plasma
Instrumentation	Same	Stratus [®] CS STAT Fluorometric Analyzer
Measuring Range	Same	6-5000 ng/mL [μ g/L] FEU
Cutoff	Same	450 ng/mL [μ g/L] FEU

Differences		
Item	Device	Predicate
New Name	Stratus [®] CS Acute Care™ D-dimer TestPak	Stratus [®] CS D-dimer TestPak
Indications for Use	Add: This method is for use by trained health care professionals in the clinical laboratory and point of care (POC) settings	Quantitative measurement of crossed-linked fibrin degradation product in citrated or heparinized plasma and as an aid in the diagnosis of VTE
Summary	Add: increased D-dimer levels have also been reported in many clinical conditions (e.g., during pregnancy, use of contraceptives, increased age and trauma)	
Test Result	- Automated dilution & manual dilution results for health care professional in the clinical laboratory - Automated dilution for POC only	Automated & manual dilution results for health care professional in the clinical laboratory.

B. Calibrator: Stratus[®] CS Acute Care[™] D-dimer CalPak

Predicate: Stratus[®] CS D-dimer CalPak, K022977

Similarities		
Item	Device	Predicate
Intended Use	Same	For calibration of the D-dimer method
Formulation	Same	Calibrator level at an approximate concentration of 3500 ng/mL [$\mu\text{g/L}$] FEU in each of three well

Differences		
Item	Device	Predicate
New Name	Stratus [®] CS Acute Care [™] D-dimer CalPak	Stratus [®] CS D-dimer CalPak

C. Diluent: Stratus[®] CS Acute Care[™] D-Dimer DilPak

Predicate: Stratus[®] CS D-dimer DilPak, K022976

Similarities		
Item	Device	Predicate
Intended Use	Same	To be used in conjunction with the D-dimer TestPak
Formulation	Same	Liquid buffered bovine protein matrix

Differences		
Item	Device	Predicate
New name	Stratus [®] CS Acute Care [™] D-dimer DilPak	Stratus [®] CS D-dimer DilPak

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

NCCLS guideline EP15-A: User Demonstration of Performance for Precision and Accuracy: Approved Guidelines

L. Test Principle:

Method: It is a two-site sandwich assay based upon solid phase Radial Partition Immunoassay (RPIA) technology. Dendrimer linked monoclonal antibody is then added to the center portion of a square piece of glass fiber paper in the TestPak. This antibody recognizes a distinct antigenic site on the D-Dimer molecule. Sample is then added onto the paper where it reacts with the immobilized antibody. A conjugate, consisting of enzyme-labeled monoclonal antibody directed against a second distinct antigenic site on the D-dimer molecule, is added onto the reaction zone of the paper. The enzyme-labeled antibody reacts with the bound D-Dimer, forming an antibody-antigen-labeled antibody sandwich. Then the unbound labeled antibody is eluted from the reaction zone. The initiation of the enzyme activity occurs simultaneously with the wash since substrate for the enzyme was included in the wash solution. The enzymatic rate of the bound fraction increases directly with the concentration of the D-Dimer in the sample. The reaction rate is then be measured by an optical system that monitors the reaction rate via front surface fluorescence. The microprocessor within the analyzer performs all data analysis.

Calibrator: The D-dimer CalPak contains D-dimer in a liquid buffered bovine protein matrix which contains one calibrator level at an approximate concentration of 3500 ng/mL in each of three wells. The kit consists of five CalPaks at a single calibrator level and is used for calibration of the Stratus[®] CS Acute Care[™] method.

Diluent: The D-dimer DilPak contains a liquid buffered bovine protein matrix which is used in conjunction with the D-dimer TestPak for the measurement of samples with elevated levels of D-Dimer.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision analysis was performed to support the addition of Point of Care (POC) to the indication for use. The testing was completed at three different locations: Clinical Laboratory (LAB), Emergency Department (ED), and Cardiac Care Unit (CCU) at three external sites.

Two levels of plasma pools were performed in replicates of four over a period of five days (N=20) by LAB, ED, and CCU personnel on the Status instruments located in their respective areas. ED and CCU personnel had no formal laboratory training. Within-Run (WR) and total coefficients of variation (%CV) were calculated according to the NCCLS EP-15A.

Results are summarized below:

Point of Care Site 1

Locations / Level	Mean (ng/mL) [µg/L] FEU	WR SD (%CV)	Total SD (%CV)
Lab – Plasma Pool L1	481.6	12.48 (2.6)	16.12 (3.3)
ED – Plasma Pool L1	526.4	22.06 (4.2)	22.85 (4.3)
CCU – Plasma Pool L1	512.9	36.96 (7.2)	36.96 (7.2)
Lab – Plasma Pool L2	2375.8	122.79 (5.2)	228.13 (9.6)
ED – Plasma Pool L2	2539.9	96.45 (3.8)	114.29 (4.5)
CCU – Plasma Pool L2	2541.0	187.67 (7.4)	187.67 (7.4)

Point of Care Site 2

Locations / Level	Mean (ng/mL) [µg/L] FEU	WR SD (%CV)	Total SD (%CV)
Lab – Plasma Pool L1	502.7	15.86 (3.2)	32.11 (6.4)
ED – Plasma Pool L1	468.0	19.29 (4.1)	23.55 (5.0)
CCU – Plasma Pool L1	482.6	8.40 (1.7)	10.70 (2.2)
Lab – Plasma Pool L2	2433.5	78.51 (3.2)	120.14 (4.9)
ED – Plasma Pool L2	2350.0	105.89 (4.5)	142.73 (6.1)
CCU – Plasma Pool L2	2356.3	140.46 (6.0)	140.46 (6.0)

Point of Care Site 3

Locations / Level	Mean (ng/mL) [µg/L] FEU	WR SD (%CV)	Total SD (%CV)
Lab – Plasma Pool L1	446.4	10.63 (2.4)	15.94 (3.6)
ED – Plasma Pool L1	484.4	14.80 (3.1)	14.80 (3.1)
CCU – Plasma Pool L1	458.4	16.90 (3.7)	19.72 (4.3)
Lab – Plasma Pool L2	2254.6	86.50 (3.8)	108.48 (4.8)
ED – Plasma Pool L2	2404.4	83.61 (3.5)	94.84 (3.9)
CCU – Plasma Pool L2	2316.7	107.43 (4.6)	107.43 (4.6)

- b. *Linearity/assay reportable range:*
 - c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
 - d. *Detection limit:*
 - e. *Analytical specificity:*
 - f. *Assay cut-off:*
2. Comparison studies:
- a. *Method comparison with predicate device:*

Method comparison studies were performed to compare the performance obtained with the Stratus[®] CS Acute Care[™] D-dimer TestPak with non-

laboratory personnel (ED, CCU) versus laboratory personnel (LAB) at 3 evaluation sites.

The results are summarized below:

POC Site 1	Slope	Intercept ng/mL [μ g/L] FEU	Correlation Coefficient	Standard Error of the Regression	n
Lab v ED ¹	1.12 \pm 0.01	-8.4 \pm 14.3	0.998	78	64
Lab v CCU ¹	1.09 \pm 0.02	-32.2 \pm 25.6	0.992	139	62
POC Site 2					
Lab v ED ²	0.93 \pm 0.01	-2.01 \pm 16.2	0.996	92	67
Lab v CCU ²	0.91 \pm 0.02	-28.9 \pm 25.2	0.991	140	65
POC Site 3					
Lab v ED ³	0.99 \pm 0.02	-4.62 \pm 28.2	0.989	176	74
Lab v CCU ³	1.00 \pm 0.01	-3.75 \pm 22.7	0.994	143	75

¹ range of results = 36– 4220 ng/mL

² range of results = 133 – 3974 ng/mL

³ range of results = 56 – 4778 ng/mL

- b. *Matrix comparison:*
- 3. Clinical studies:
 - a. *Clinical Sensitivity:*
 - b. *Clinical specificity:*
 - c. Other clinical supportive data (when a. and b. are not applicable):
- 4. Clinical cut-off:
- 5. Expected values/Reference range:

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.